

**FRANKLIN PIERCE LAW CENTER EDUCATIONAL REPORT:  
PATENT LANDSCAPE OF ADJUVANT FOR HIV VACCINES**



**FALL 2009**

**PROFESSORS**

**JON R. CAVICCHI, J.D., LL.M. (Intellectual Property)  
STANLEY P. KOWALSKI, Ph.D, J.D.**

**Project Leader**

**YU-HUI (LISA) SUNG**

**Team Leaders**

**PRAVIN CONDA  
YU-HUI (LISA) SUNG**

**Director of Science and Technology**

**CRAIG T. AJMO, JR. Ph.D.**

**Students**

**JAMES BARRETT  
AMRITA CHILUWAL  
NUPUR CHOUDHARY  
BRIAN DOIGAN  
JENNIFER FADDEN**

## **Acknowledgements**

We would like to take the time to thank those who provided invaluable assistance in the completion of this project

We are thankful to the Franklin Pierce Law Center and Deans John Hutson and Susan Richey for Supporting this project.

We would like to express our sincere gratitude and appreciation to Jon R. Cavicchi, J.D., L.L.M. (I.P.) and Stanley P. Kowalski, Ph.D., J.D., for their tireless effort, their expert guidance and suggestion and their encouragement and support in the completion of this project.

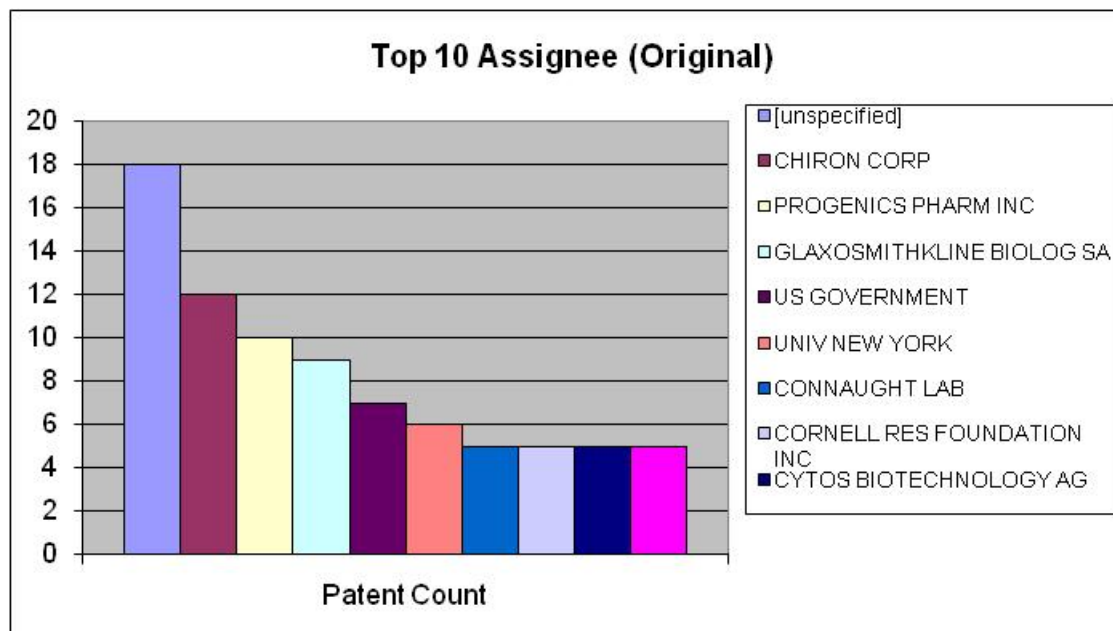
We are thankful to Mr. Mark Bauer and Thomson-Reuters for graciously facilitating access to Thompson-Innovation® and for providing invaluable guidance and training on other aspects of patent database mining and research.

## **Table of Contents**

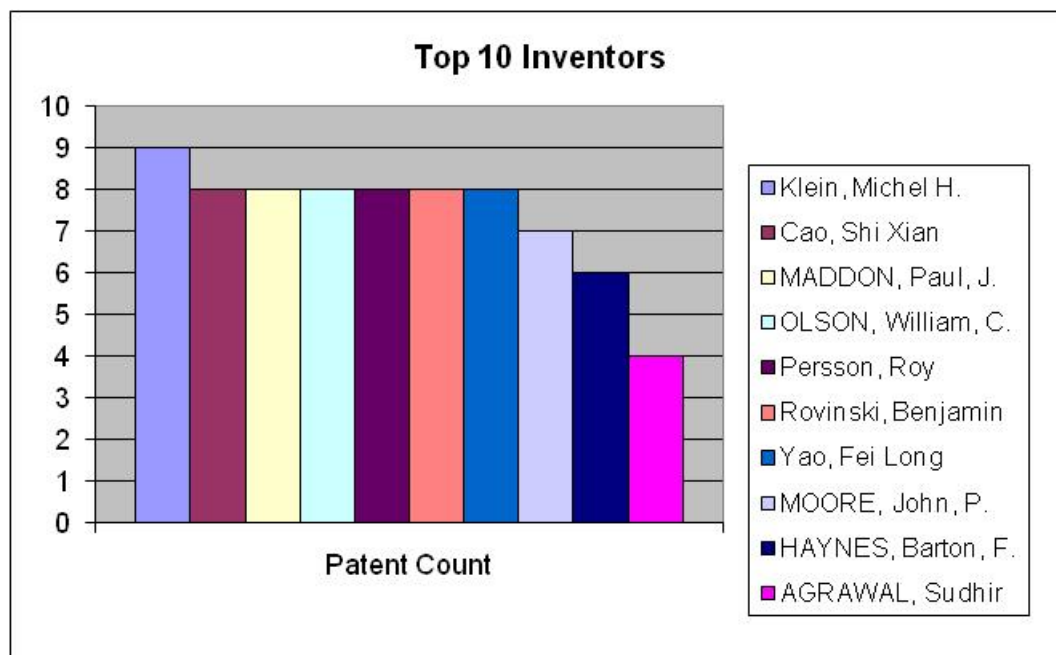
Executive Summary .....	5
Scope of the Technology Analyzed .....	7
Disclaimer .....	8
I. About the Technology .....	9
1. Introduction of HIV vaccine, .....	9
1.A Live Attenuated vaccine and inactivated vaccines .....	9
1.B DNA vaccines, Peptide vaccines and Glycoprotein vaccines .....	10
1.B.1 Glycoprotein vaccines .....	10
1.B.2 DNA vaccines .....	12
1.B.3 Peptide vaccines .....	12
2. Intro to Adjuvants .....	14
2.A HIV adjuvants .....	15
3. Introduction to Chemical Adjuvant .....	16
3.A Inorganic Adjuvants .....	16
3.A.1 Mineral Salts .....	17
3.A.2 Emulsions .....	17
3.A.3 Calcium Phosphate .....	18
3.B Organic Adjuvants .....	19
3.B.1 Muramyl Dipeptide .....	19
3.B.2 Trehalose-6,6'-dimycolate .....	20
3.B.3 Saponins .....	20
3.B.4 Stearyl Tyrosine .....	21
4. Introduction to Immunostimulatory Adjuvants .....	22
4.A Endogenous Immunostimulatory Adjuvants .....	23
4.A.1 Polysaccharides .....	23
4.A.2 Liposomes .....	26
4.A.3 Lipid Polysine Core Peptides .....	27
4.A.4 Cytokine .....	28
4.A.5 Lipid A and Monophosphoryl Lipid A (MPL) .....	30
4.A.6 Lipopeptide .....	31
4.B Exogenous Immunostimulatory Adjuvants .....	32
4.B.1 Proteosomes .....	32
4.B.2 Multiple Antigenic Peptides .....	33
4.B.3 Exogenous Toxins .....	33
5. Conclusion .....	33
II. Patent Search Methodology and Results .....	34
1. Patent Search Methodology .....	34
2. Patent Search Results .....	36
2. A. Patent Search Tables .....	36
3. Patent Search Results Summary .....	67
3. A. Categorization Summary .....	67
3. B. Patent De-duplication Process .....	69
3. C. Patent Coding Results Summary .....	69
3. D. Spreadsheet for Relevant Patents .....	71
3. E. Spreadsheet for Patents with Non-English Claim .....	97

4. Patent document Analytics .....	100
4. A. Patent Count vs. Country .....	100
4. B. Patent Count vs. Publication Date.....	102
4. C. Patent Count vs. Application (Filing) Date.....	104
4. D. Patent Count vs. US Classification .....	106
4. E. Patent Count vs. IPC Classification.....	108
4. F. Patent Count vs. Derwent Class (DWPI Class).....	110
4. G. Patent Count vs. Derwent Manual Code.....	112
4. H. Patent Count vs. Assignees .....	114
4. I. Patent Count vs. Inventors.....	116
4. J. Innovation ThemeScape® Maps Results .....	118
APPENDIX A: Scientific Papers.....	122
APPENDIX B: Description of Patent Databases & Platforms Used in this Report .....	127
APPENDIX C: Definitions of U.S. Classifications .....	129
APPENDIX D: Definitions of IPC Codes .....	131
APPENDIX E: Derwent Classifications.....	132
APPENDIX F: Derwent Chemical Patents Index (CPI) Manual Codes.....	133
APPENDIX G: LANL Adjuvant List.....	135
APPENDIX H: Latent Semantic Searching on Lexis.....	137
APPENDIX I: Author's Curriculum Vitae .....	139
APPENDIX J: List for General Adjuvants that might be applied to HIV Vaccine.....	150
APPENDIX K: MicroPatent® Summary Report for Relevant Patents .....	150

## Executive Summary



This figure illustrates the patent count by assignee for the patent landscaping of adjuvants potentially applicable to HIV vaccines. The top assignees include Chiron Corp., Progenics Pharmaceuticals Inc., and GlaxoSmithKline Biologicals S.A.



This figure illustrates the patent count by inventor for the patent landscaping of adjuvants potentially applicable to HIV vaccines. The top inventors include Klein, Cao, and Maddon.

## **Value Added Features**

First report to utilize the new Thomson Innovation® patent searching platform including:

- Enhanced analytics including Themescape Maps using *Derwent* Data
- Translated Foreign Patents
- Display and Sort Function (For Deduplication)
- Highlighting Feature (Parsing Through Claims)

Integrated Professor Cavicchi's Summer I.P. Institute Patent Mining Class

- HIV vaccine adjuvants technology was assigned to teams of life science students and preliminary searching was completed during the summer session. Four of the students from this class advanced the research into the Fall Clinic Report.

Lexis® Semantic Search

- Semantic search uses the science of meaning in language ("semantics") to produce highly relevant search results. While semantic search engines are not uncommon, most contain limitations - including lack of transparency and user control - which can ultimately undermine the overall value of results. For example, they typically do not show precisely how search results are generated and the user must simply trust that the right relevance between the original query and the semantic application are, in fact, appropriate to the intent of the searcher. <http://www.lexisnexis.com/semantic-search-1/>

LANL HIV/SIV Vaccine Trials Database

- We used the HIV/SIV Vaccine Trials Database was developed as a tool for compilation, search and comparison of published studies on SIV, HIV and SHIV vaccine trials in nonhuman primates for purposes of brainstorming and keyword identification. LANLe used a set of criteria to scan *Pubmed* for relevant studies to enter into the database. In selecting studies for entry, priority was given to recently published studies in journals generally regarded as the primary source of information pertaining to HIV and SIV vaccine research in nonhuman primates. In most cases, they give priority to challenge studies, where the animals received a live virus to measure the 'efficacy' of the immunogen(s) inoculated during the course of the investigation.  
[http://www.hiv.lanl.gov/cgi-bin/vaccine/search/adjuvant\\_search.cgi?search\\_string=&process=Go](http://www.hiv.lanl.gov/cgi-bin/vaccine/search/adjuvant_search.cgi?search_string=&process=Go)

Added Position: Science & Technology Director

- Due to the technical complexity of the subject, we added a Ph.D. level student [CTA] assigned to facilitate the technical capacity of the team.

Utilized the ITTI Clinic Manual

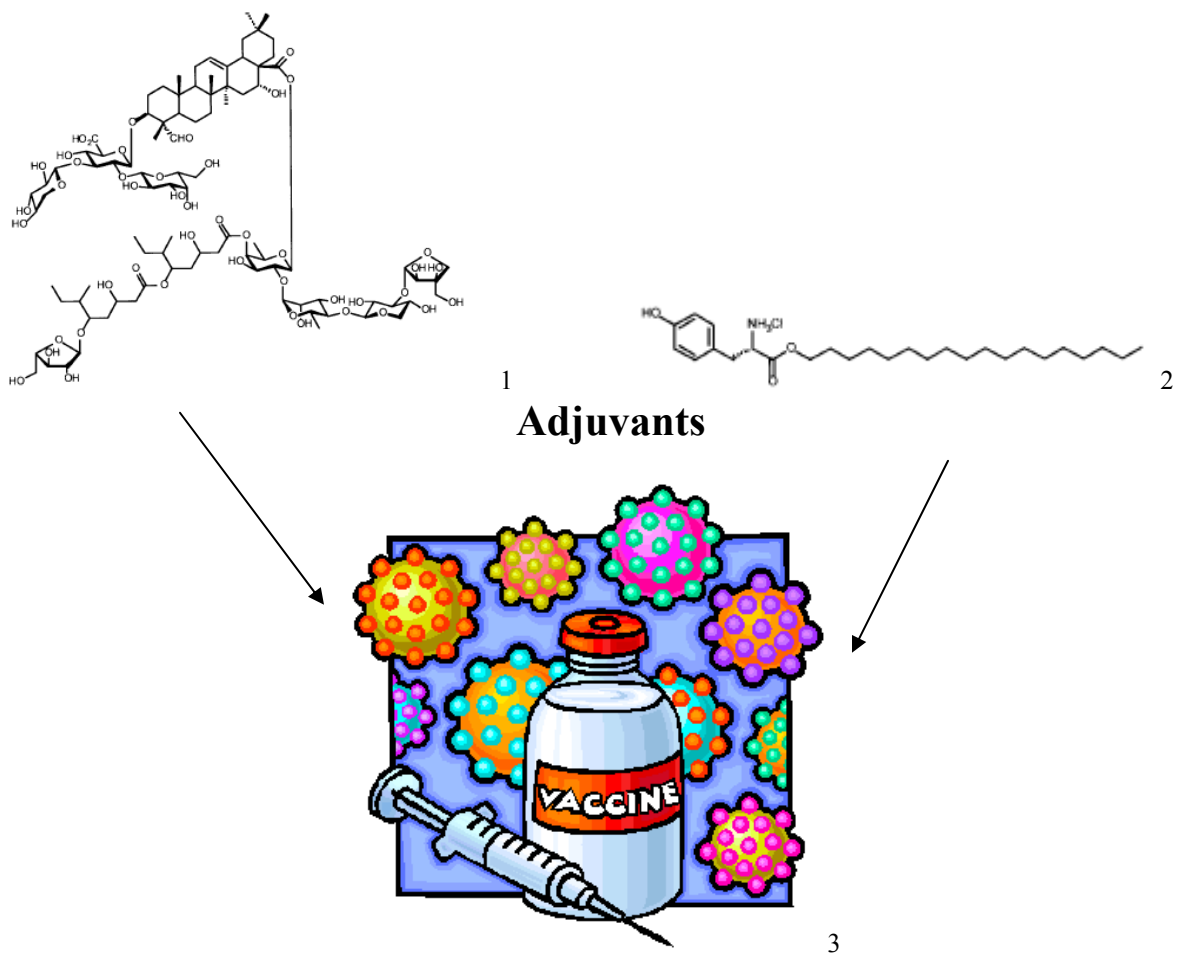
- This Manual was developed as a handbook of best practices based on four years of compiling patent landscape reports.

Consultation with Director of Patent Practice Program Professor Ann McCrackin on biotechnology claims interpretation leading to intensification of claims interpretation.

Increased utilization of project technology

- Web 2.0 Collaborative Tools such as Google Docs, Twitter, Skype, etc.
- New classroom technology including wireless projection and audiovisual tools

## Scope of the Technology Analyzed



Many strategies have been employed to search for a vaccine to combat the rampant spread of HIV worldwide. As research has progressed towards a better understanding of the virology, pathogenesis and immunological properties of HIV, vaccine designs that incorporate adjuvants in the vaccine have emerged as viable candidates for developing effective preventative treatments for HIV. Adjuvant additions to a vaccines enhance both antibody and cell-mediated immune responses to antigens without the required multiple boosts typical of these inoculations. An immunologic adjuvant is any substance that when incorporated into a vaccine formulation acts generally to accelerate, prolong, or enhance the quality of specific immune responses to vaccine antigens. The purpose of this patent landscape study was to search, identify and categorize patent documents that are relevant to the research, development and distribution of adjuvants for HIV vaccines.

1 Ross P. McGeary et al., *Lipid and Carbohydrate Based Adjuvant/Carriers in Immunology*, 9 J. PEPTIDE SCI. 405, 412 (2003).

2 *Id.* at 413

3 Another shot of Rohail, <http://sabahkamal.wordpress.com/2007/03/11/another-shot-for-rohail> (last visited Dec. 1, 2009)

## **Disclaimer**

This is an educational report and is neither inclusive nor comprehensive. Rather, it is an informational resource to facilitate a better understanding of the international patent literature landscape with regard to adjuvants applicable to HIV vaccines.

This report is not a list of all potentially relevant patents. It is not a Freedom to Operate (FTO) opinion, but instead constitutes an educational analysis of potentially relevant material.

While the search engines utilized in this project are extensive, it is likely that the entire spectrum of patents was not obtained utilizing the various search strategies and methods articulated herein. Therefore, it is not the supposition of this team that all relevant patents were discovered during the creation of this report.

As the team members are not experts in the field of adjuvants applicable to HIV vaccines, it is also highly possible that the categorization of the patents found and coded are incomplete. The team cannot guarantee that the patents discovered were evaluated at the level of expert scientific sophistication.

Due to the limited time frame (15 weeks) and press of business imposed upon this project, the number of patents evaluated was established by this constrained scheduled, the overall semester demands, and the general press of business. As such, additional patents may have been available for evaluation but without the necessary time within which to consider them they may not have been considered.

Again, this report is not a Freedom to Operate (FTO) opinion. It is an educational report.

## **I. About the Technology**

### **1. Introduction of HIV vaccine<sup>1, 2</sup>**

Since the discovery of Autoimmune Deficiency Syndrome (AIDS) in 1981, a safe and effective vaccine has been sought for the Human Immunodeficiency Virus (HIV). An ideal HIV vaccine will generate adaptive immune responses sufficient to completely clear the virus during early infection, producing sterilizing immunity. However, HIV is highly mutagenic, and researchers still lack complete knowledge of immune correlates of protection to AIDS. An HIV vaccine that achieves sterilizing immunity by producing a potent neutralizing antibody response is still not available.

Several types of vaccines against HIV have been developed during the past three decades including (1) Live attenuated vaccines, (2) Inactivated vaccines, (3) Virus-like particle (VLP) vaccines, (4) Envelop glycoprotein vaccines, (5) Peptide vaccines, and (6) Naked DNA and live recombinant vaccines.

A combination of different types of vaccines or different viral vectors in a prime-boost regimen, multiple immunizations requiring the vaccine to be successful,<sup>3</sup> would increase the immunogenicity of the vaccine strategy, such as using DNA vaccine for priming and following by an Adenovirus vaccine.

#### **1.A Live Attenuated vaccine and inactivated vaccines**

HIV vaccines have been tested in humans since the late 1980's. A common goal of current HIV vaccines is to induce cytotoxic T-lymphocyte (CTL) responses. A CTL-based vaccine can limit viral replication so as to increase disease free infected individuals and decrease the spread of AIDS.

One of the earliest approaches of HIV vaccines is the attenuated live virus vaccine, such as vaccinia virus or poxvirus vaccine. The vaccinia virus vaccines induced HIV-specific CD4+ T-cell responses. Weak CD8+ CTL responses could also be generated when using a prime-boost combination of vaccinia virus and recombinant gp120 protein vaccines. However, these viruses caused serious diseases in healthy testers. Thereafter, replication-deficient vectors, because of safety concerns, have replaced the replication-competent vaccinia vectors. These replication-deficient vectors have been evaluated in human trials but no positive results have occurred.

Vaccinia virus recombinants were tested in prime-boost combination with recombinant gp120 vaccine in several trials. For example, a research plan for a prime-boost vaccination approach of canarypox vector priming and gp120 boosting was performed by HIV Vaccine Trials Network (HVTN) during 2001 and 2002. The result showed that the antigen productions in human cells increased but the level of CD8+ T cell responses was too low to prove a

---

<sup>1</sup> Paul Spearman, *Current Progress in the Development of HIV Vaccines*, 12 CURRENT PHARM. DESIGN 1149 (2006)

<sup>2</sup> Marc P. Girard et al., *A Review of Vaccine Research and Development: The Human Immunodeficiency Virus (HIV)*, 24 VACCINE 4069 (2006)

<sup>3</sup> Shan Lu, *Heterologous Prime-Boost Vaccination*, 21(3) CURR. OPIN. IMMUNOL. 346 (2009)

correlation of protection for high-risk people of a phase III trial. HVTN later abandoned the phase III trial and further study.<sup>4</sup>

More studies on live vector-based vaccines continue. Scientists have not abandoned this approach because live vectors can generate strong and long-lasting cellular immune responses. However, researchers have to consider the balance between virus safety and the capacity to generate immune response. Wild-type viruses are no longer acceptable due to the level of toxicity. Most of these live vector approaches are highly attenuated or are viral vector systems that are competent for only a single round of infection in the host.

There are several types of live vector-based HIV vaccines used in current human trials including adenovirus vaccine, poxvirus vaccine, alphavirus vector vaccine, adeno-associated virus (AAV), vesicular stomatitis virus (VSV)- based HIV vaccine and poliovirus vector vaccine.<sup>5</sup> Currently, none of these vaccines show viable results.

The adenovirus vaccine is the leading CTL vaccine candidate. It can produce potent cellular immune responses but it will not work for people already immunized from the adenovirus. Almost one-third of North American volunteers have preexisting immunity for adenovirus.<sup>6</sup> The other live vector vaccines have common problems of high production cost, low stability and limited serotypes.

## **1.B DNA vaccines, Peptide vaccines and Glycoprotein vaccines**

Other current HIV vaccine approaches include DNA, peptide and glycoprotein vaccines. Usually these vaccines are not used in isolation; they instead would be arranged in a prime boost regime such as DNA prime and protein boost.<sup>7</sup> The primary goal for these vaccine approaches is to elicit HIV-specific CD8+ CTL responses and to generate a population of supportive HIV-specific CD4+ T cells.

### **1.B.1 Glycoprotein vaccines**

There are two major approaches for HIV vaccines in the early study, the first is the attenuated live viral vaccine, and the other is the monomeric gp120-based vaccine. The monomeric gp120-based vaccine was safe and could generate neutralizing antibodies to gp120 protein. Two gp120 subunit vaccines were valued in a phase II trial in the USA and one of which was tested in a phase III trials in Thailand. The second vaccine is a monomeric gp120 vaccine with alum (VaxGen) as an adjuvant.<sup>8</sup> None of these trials showed a significant reduction of HIV infection after vaccination.

---

<sup>4</sup> Spearman, *supra* note 1, at 1149

<sup>5</sup> *Id.* at 1160

<sup>6</sup> *Id.* at 1157

<sup>7</sup> *Id.* at 1154

<sup>8</sup> Girard et al, *supra* note 2, at 4067

Further research showed this kind of vaccine behaved differently for laboratory-adapted HIV isolates and naturally occurring HIV isolates.<sup>9</sup> Results of two Phase III trials showed that this approach did not produce relevant antibodies in human subjects. Scientists then stopped pursuing this approach.

Later studies show that the monomeric gp-120-based vaccine would fail because the native structure of HIV envelope glycoprotein is in a trimeric conformation, not in a monomeric format. See Figure 1 below for the native conformation of the trimeric glycoprotein. The glycoprotein vaccine is then designed to generate neutralizing antibodies against HIV virus by using the glycoprotein in its native conformation of the trimeric complex.

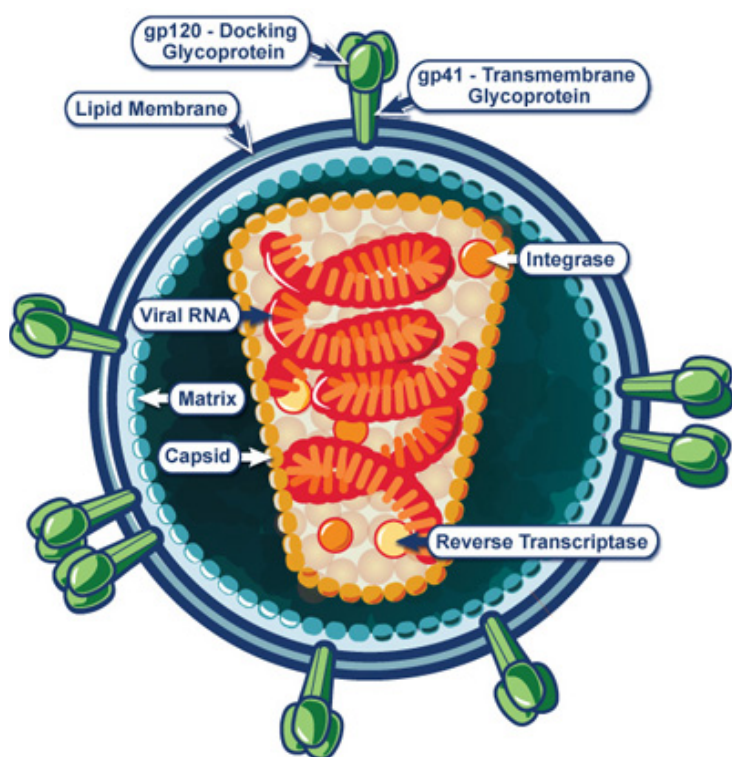


Figure 1: Trimeric Conformation of the HIV gp120 Envelope Glycoprotein<sup>10</sup>

As of yet, no positive results occurred for the trimer glycoprotein approaches; most of them are still under valuation. One approach using an oligomeric gp140 (gp120 with ectodomain of gp41) vaccine is being investigated at Chiron. Studies by Chiron show that a DNA prime and gp140 in MF59 adjuvant boost elicited high ENV-protein-binding antibodies and low heterologous neutralizing antibodies in rabbits and macaques.<sup>11</sup> Glaxo-Smith-Kline (GSK) conducted research on a gp140-GCN4 trimeric immunogens which was emulsified in

<sup>9</sup> Spearman, *supra* note 1, at 1150

<sup>10</sup> National Institute of Allergy and Infectious Diseases, *Structure of HIV*, <http://www3.niaid.nih.gov/topics/HIV/AIDS/Understanding/Biology/structure.htm> (last visited Sept. 21, 2009)

<sup>11</sup> Girard et al., *supra* note 2, at 4067

adjuvants AS01B, AS02A or AS03.<sup>12</sup> Further, Merck and university of Maryland designed another approach for glycoprotein vaccine. They use covalently couple monomeric gp120 or gp140 molecules to induce broadly neutralizing antibody responses.<sup>13</sup>

### **1.B.2 DNA vaccines**

DNA vaccines and peptide vaccines are two common approaches for designing a HIV vaccine. The two approaches share several common characteristics: they all have great potential, they have achieved good results in animal trials and all are safe in human trials. However, studies so far have reported that these approaches only generate weak immune response in humans.

DNA vaccines use a plasmid DNA vector to generate HIV proteins or protein subunits within host cells.<sup>14</sup> The HIV proteins are antigens and induce immunization response against the HIV virus. The plasmid DNA vector is taken up by host cell. This might be procured by simply intramuscular injection. However, there will not be enough antigens if the cellular uptake is inefficient. Ways to improve the cellular uptake include the use of gene guns, formulation into micro-particles and the use of adjuvants that may increase uptake by antigen presenting cells (APCs).<sup>15</sup> Studies show DNA vaccines for HIV can generate cellular and humoral immune responses. Several reports indicated DNA vaccines elicit reasonable levels of HIV-specific immune responses in mice and one report showed that a DNA/MVA vaccination approach provided longstanding protection from SHIV 89.6P.<sup>16</sup> However, there were no convincing conclusions resulting from human trials of DNA vaccines against HIV. Only weak CD8+ CTL responses were reported.

### **1.B.3 Peptide vaccines**

The concept of the peptide vaccine is simple: peptides that present the Major Histocompatibility Complex (MHC) class I or class II molecules as antigens are used to trigger immunization responses against HIV virus. See Figure 2.

---

<sup>12</sup> *Id.*

<sup>13</sup> *Id.* at 4068

<sup>14</sup> Spearman, *supra* note 1, at 1154

<sup>15</sup> *Id.*

<sup>16</sup> *Id.* at 1155

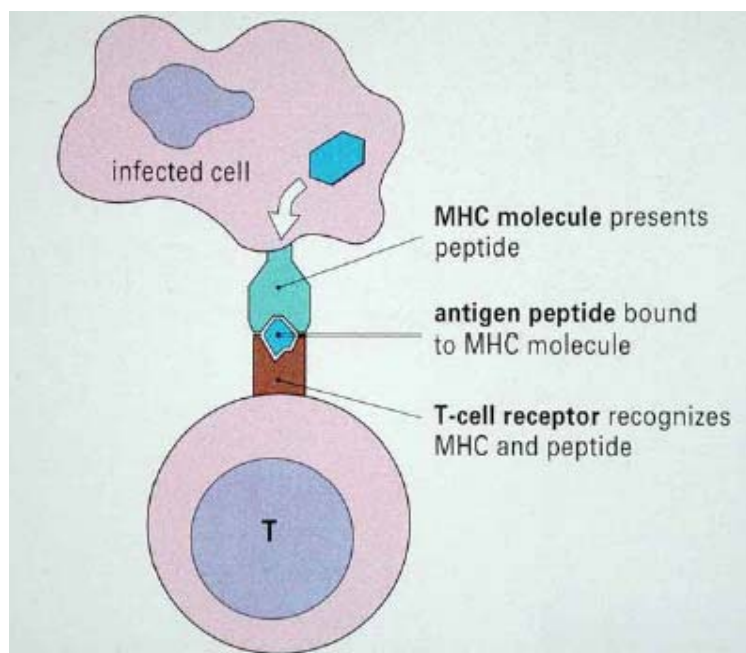


Figure 2: MHC Molecule binds T-cell receptor and antigen<sup>17</sup>

The peptide vaccine can be designed to produce particular immunogens for a special target which may produce combinations of T-helper and CTL epitopes representing specific conserved regions of HIV. Another advantage of peptide vaccines is that it can direct the immune response toward subdominant epitopes that may not elicit responses of viral infection or other broad immune responses. Positive results were reported in small animals. However, a human trial using a live virus prime/peptide boost vaccine showed only weak and transient cellular immune responses were generated inside these healthy volunteers. How the scientists could improve the peptide-based HIV vaccines is still unclear. Several drug makers and research organizations are pursuing peptide vaccines which can induce both CD8+ and CD4+ T cell responses against HIV, including Epimmune, Wyeth Vaccine, Agence Nationale de recherche sur le SIDA (ANRS), US National Institute of Allergy and Infectious Diseases (NIAID), HIV Vaccine Trials Network (HVTN), and Aventis Pasteur.<sup>18</sup> The study sponsored by NIAID and ANRS is to use synthetic lipopeptides containing HMC class I-restricted T-cell epitopes. Animal test result was great—it induces strong CD8+ T-cell responses against HIV in mice and non-human primates. However, a phase II trial was postponed due to a severe neurological side effect on one of volunteers in US.<sup>19</sup>

<sup>17</sup> Mi-Hua Tao, 免疫世界的戰士, available at <http://proj1.sinica.edu.tw/~hispj/program/doc/tao-mi-hua.pdf> (last visited Sept. 22, 2009)

<sup>18</sup> Spearman, *supra* note 1, at 1156

<sup>19</sup> Girard et al., *supra* note 2, at 4071

## 2. Intro to Adjuvants

The purpose of vaccination is to generate a strong and lasting immune response providing long-term protection against infection.<sup>20</sup> However, many licensed vaccines currently induce only suboptimal immunity, requiring multiple boosts to generate a robust protective response.<sup>21</sup> Adjuvant addition to vaccines enhances both antibody and cell-mediated immune responses to antigens without the required multiple boosts typical of these inoculations.<sup>22</sup> An immunologic adjuvant is any substance that when incorporated into a vaccine formulation acts generally to accelerate, prolong, or enhance the quality of specific immune responses to vaccine antigens.<sup>23</sup> Adjuvants can be used for various purposes: (1) to enhance the immunogenicity of highly purified or recombinant antigens; (2) to reduce the amount of antigen or the number of immunizations needed for protective immunity; (3) to improve the efficacy of vaccines in newborns, the elderly or immuno-compromised persons; or (4) as antigen delivery systems for the uptake of antigens by the mucosa.<sup>24</sup>

The concept of adjuvants arose from observations that an abscess at the inoculation site assisted the generation of higher specific antibody titers. Adjuvant activity was first demonstrated in 1926 with aluminum, when diphtheria toxoid absorbed to alum. Despite the discovery of many more potent adjuvants, such as Freund's complete adjuvant or lipopolysaccharide, aluminum-based adjuvants remain the most prominent of the vaccine enhancers. Many of the newly discovered adjuvants have proven to be unsuitable for human use, as they result in local and systemic toxicity and do not meet the rigorous standards of pre-clinical or clinical trials.<sup>25</sup>

Adjuvants have a diverse mechanism of action and must be chosen for use with a particular antigen based on the responses desired.<sup>26</sup> Features associated with adjuvant candidates include: stability, length of shelf life, reduction or knowledge of side effects, inexpensive production and immunological inertness.<sup>27</sup> Administration route is also a major concern.<sup>28</sup> There are marked differences in efficacy depending on the current administration routes, such as mucosal or parenteral routes. While intradermal or subcutaneous immunization is far more effective in stimulating immunity than the intramuscular route, due to local toxicity alum is generally only used intramuscularly.<sup>29</sup>

These features must be considered, as there is a risk of adverse reaction to the incorporation of an adjuvant into a vaccine. Local reactions include pain, local inflammation, swelling, injection site necrosis, lymphadenopathy, granulomas, ulcers and the generation of

---

<sup>20</sup> J. C. Aguilar & E. G. Rodriguez, *Vaccine Adjuvants Revisited*, 25 VACCINE 3752, 3752 (2007)

<sup>21</sup> Andrew G. C. Barnes et al., *Bacillus Subtilis Spores: a Novel Microparticle Adjuvant Which Can Instruct a Balanced Th1 and Th2 Immune Response to Specific Antigen*, 37 EUR. J. OF IMMUNOLOGY 1538, 1538 (2007)

<sup>22</sup> *Id.*

<sup>23</sup> F. R. Vogel, *The Role of Adjuvants in Retroviral Vaccines*, 17 INT'L. J. IMMUNOPHARMACOLOGY 85, 85 (1995)

<sup>24</sup> Aguilar & Rodriguez, *supra* note 39, at 3752

<sup>25</sup> *Id.*

<sup>26</sup> Vogel, *supra* note 42, at 86

<sup>27</sup> Aguilar & Rodriguez, *supra* note 39, at 3752

<sup>28</sup> *Id.*

<sup>29</sup> *Id.*

sterile abscesses. Systemic reactions include nausea, fever, adjuvant arthritis, uveitis, eosinophilia, allergy, anaphylaxis, organ specific toxicity and immunotoxicity, *i.e.* cytokines release, immunosuppression or autoimmune diseases.<sup>30</sup>

With the increase of immunology knowledge there is still a surprising reliance on alum-based adjuvants.<sup>31</sup> However, the introduction of new recombinant subunit and synthetic antigens in HIV, hepatitis C virus, Malaria and other diseases will introduce new adjuvants to the clinical trial pipeline.<sup>32</sup> New adjuvant formulations can be especially relevant for developing new vaccines against infectious agents causing pathological conditions characterized by immunodeficiency, low responders and high-risk groups.<sup>33</sup>

## 2.A HIV Vaccine Adjuvants

The development of an effective Human Immunodeficiency Vaccine (HIV) vaccine remains a critically important yet elusive goal.<sup>34</sup> Despite advances in preventing HIV transmission and treating chronic HIV infection, investigators have not been successful in developing a vaccine, reflecting the challenge of generating effective antibody and T lymphocyte responses to HIV.<sup>35</sup>

Traditional vaccine technologies include live attenuated viruses, whole killed viruses and protein subunits.<sup>36</sup> This vaccine approach has been enormously successful for the development of vaccines against other viruses, but they all have substantial limitations in terms of their utility for HIV. Live attenuated viruses have afforded substantial protective efficacy against Simian Immunodeficiency Virus (SIV) challenges in rhesus monkeys, but they are unlikely to be used in humans owing to significant safety concerns. In contrast, whole killed viruses and protein subunits are limited by their inability to induce broadly reactive neutralizing antibody responses as well as by their inability to elicit CD8<sup>+</sup> T lymphocyte responses.<sup>37</sup>

Novel strategies include vaccines combined with an adjuvant for delivery.<sup>38</sup> New vaccine strategies also include gene-delivery technologies such as plasmid DNA vaccines and live recombinant vectors that are engineered to express HIV-1 antigens. Plasmid DNA vaccines offer considerable promise in terms of simplicity and versatility, but multiple injections of high doses of DNA vaccines are typically required to elicit detectable immune responses in non-human primates and humans.<sup>39</sup> Therefore, there is an urgent need for the development of new

---

<sup>30</sup> *Id.*

<sup>31</sup> *Id.* at 3758-59

<sup>32</sup> *Id.* at 3759

<sup>33</sup> *Id.*

<sup>34</sup> E. G. Rhee & D. H. Barouch, *Translational Mini-Review Series of Vaccines for HIV: Harnessing innate immunity for HIV vaccine development*, 157 CLINICAL & EXPERIMENTAL IMMUNOLOGY 174, 174 (2009)

<sup>35</sup> *Id.*

<sup>36</sup> D. H. Barouch, *Challenges in Developing an HIV-1 Vaccine*, 455 NATURE 613, 615 (2008)

<sup>37</sup> *Id.*

<sup>38</sup> *Id.*

<sup>39</sup> *Id.*

adjuvants and delivery technologies to enable the development of an effective HIV vaccine that does not require multiple boosts or results in adverse effects.<sup>40</sup>

Unfortunately, the most readily available adjuvants are of the alum-based category, which are poor inducers of cell-mediated immunity, and are ineffective for the induction of T lymphocytes.<sup>41</sup> Recent data suggest that Toll-like receptor adjuvants may increase the utility of protein subunit immunogens.<sup>42</sup> Cytokines, interferon and the interleukins, are being investigated as adjuvants for their Immunostimulatory properties.<sup>43</sup> These however are just two of an extensive list of chemicals, proteins, inorganic compounds, and even toxins that are being researched for use as adjuvants in a viable HIV vaccine. A broad list of these adjuvants can be found at the *Nonhuman Primate HIV/SIV Vaccine Trials Database*.<sup>44</sup>

This report takes adjuvants found in literature and breaks them down by chemical and immunological properties to better mine the patent literature. Here, adjuvants have been grouped based on being *Chemical Adjuvants* or *Immunostimulatory Adjuvants*. Adjuvants found under the *Chemical Adjuvant* category are further separated according to organic or inorganic properties. Adjuvants grouped in as *Immunostimulatory Adjuvants* are further separated according to endogenous, of the body, or exogenous, having toxic or non-self properties.

### **3. Introduction to Chemical Adjuvant**

A vaccine might include an adjuvant and a carrier system to induce more effective immunity.<sup>45</sup> Traditional live attenuated vaccines usually contain attenuated pathogens and often are sufficiently potent to generate a strong immune response against infection.<sup>46</sup> Similarly, vaccines based on inactivated virus might be sufficiently immunogenic without adding any adjuvants.

#### **3.A Inorganic Adjuvants**

Inorganic adjuvants are adjuvants that generally are not carbon-based compounds.<sup>47</sup> The inorganic category contains a wide array of adjuvants, such as aluminum-based compounds, oil-in-water emulsions, and calcium phosphate gels. Due to the large array of adjuvants, each adjuvant maintains its own unique strengths and weaknesses for enhancing HIV vaccines.<sup>48</sup>

---

<sup>40</sup> Barouch, *supra* note 36, at 615

<sup>41</sup> Rhee & Barouch, *supra* note 34, at 174

<sup>42</sup> Barouch, *supra* note 36, at 615

<sup>43</sup> Morrow, M. P. and Weiner, D. B., *Cytokines as Adjuvants for Improving anti-HIV Responses*, 22 AIDS 333, 333 (2008)

<sup>44</sup> *Nonhuman Primate HIV/SIV Vaccine Trials Database*, [http://www.hiv.lanl.gov/cgi-bin/vaccine/search/adjuvant\\_search.cgi?search\\_string=&process=Go](http://www.hiv.lanl.gov/cgi-bin/vaccine/search/adjuvant_search.cgi?search_string=&process=Go) (last visited Sept. 23, 2009)

<sup>45</sup> Ross P. McGeary et al., *Lipid and Carbohydrate Based Adjuvant/carriers in Immunology*, 9 J. PEPTIDE SCI., 405, 408 (2003)

<sup>46</sup> Steven G. Reed et al., *New Horizons in Adjuvants for Vaccine Development*, 30 TREND IN IMMUNOLOGY 23, 23 (2008)

<sup>47</sup> L.G. WADE, JR., *Organic Chemistry* (4th ed., 1999)

<sup>48</sup> Aguilar & Rodriguez, *supra* note 39, at 3754

### 3.A.1 Mineral Salts

Salts have been the most widely used adjuvants in humans to date.<sup>49</sup> Aluminum-based compounds, or alums, continue to monopolize human vaccines today.<sup>50</sup> The two most common salts are aluminum phosphate and aluminum hydroxide.<sup>51</sup> Though alums are relatively poor adjuvants in many situations, such as inducing cellular immune responses, they are extremely low in toxicity, making them extremely popular. Alum, despite the popularity, maintains some negative drawbacks.<sup>52</sup>

In addition to a weakness in inducing responses, the mechanism for how alum actually functions is unknown. One hypothesis is the formation of an antigen depot at the inoculation site. Another hypothesized mechanism involves complement activation, or eosinophil or macrophage activation.<sup>53</sup>

Alums also can have negative side effects.<sup>54</sup> Granulomas, inflamed tissue, can form at the injection site when “alum is administered via the subcutaneous or intradermal rather than intramuscular route.”<sup>55 56</sup> Other side effects are increased IgE production, allergenicity, and potential neurotoxicity due to reduced renal function.<sup>57</sup> Alum is typically excreted through the kidneys, however a buildup can occur if kidney function declines.<sup>58</sup> Despite the drawbacks, however, the general lower toxicity than other adjuvant options has led to its popularity over the past 80 years.<sup>59</sup>

### 3.A.2 Emulsions

Emulsions are a suspension of small globules of one liquid within another liquid which will not mix.<sup>60</sup> Most emulsions are typically oil-in-water, water-in-oil, or in some cases water-in-oil-in-water mixtures.<sup>61</sup> Emulsions function by forming depots at the injection sites, which enables the slow release of antigens, and also serve to stimulate antibody producing plasma cells.<sup>62</sup> Emulsions can also be used as delivery systems for certain immunostimulatory adjuvants, like CpG, MPL and QS21.<sup>63</sup>

---

<sup>49</sup> *Id.* at 3753

<sup>50</sup> *Id.* at 3754

<sup>51</sup> C. Clements & E. Griffiths, *The Global Impact of Vaccines Containing Aluminum Adjuvants*, 20 VACCINE S24 – S33 (2002)

<sup>52</sup> Aguilar & Rodriguez, *supra* note 39, at 3754

<sup>53</sup> *Id.*

<sup>54</sup> *Id.*

<sup>55</sup> Granuloma, <http://www.merriam-webster.com/dictionary/Granuloma> (last visited Dec. 5, 2009)

<sup>56</sup> Aguilar & Rodriguez, *supra* note 39, at 3754

<sup>57</sup> *Id.*

<sup>58</sup> *Id.*

<sup>59</sup> *Id.* at 3753

<sup>60</sup> Emulsions, <http://www.merriam-webster.com/dictionary/emulsions>, (last visited Dec. 3, 2009)

<sup>61</sup> Derek T. O’Hagan & Ed Lavelle, *Novel Adjuvants and Delivery Systems for HIV Vaccines*, 16 AIDS S115, S116 (2002)

<sup>62</sup> Aguilar & Rodriguez, *supra* note 39, at 3754

<sup>63</sup> O’Hagan & Lavelle, *supra* note 61, at S118.

Emulsions are generally too toxic for routine human prophylactic vaccine use, although they may be suitable for use in terminal conditions where there is a greater tolerance of side effects. Frequent side effects include inflammatory reactions, granulomas and ulcers at the injection site.<sup>64</sup> However, specific emulsions have shown promise. For example, water in oil in water has been shown to be as potent as Freund's incomplete adjuvant but more stable, less viscous and easier to administer with less resulting granulomas.<sup>65</sup>

The safety and tolerability of MF59 has been well established, since it has been included as a component of a licensed vaccine in Europe beginning in 1997. MF59 is a squalene oil-in-water emulsions that was developed without the presence of additional immunostimulatory adjuvants. Experience has shown MF59 to be safe and well tolerated with a number of vaccines, including recombinant gp120.<sup>66</sup> MF59 has been shown to lead to the recruitment of antigen-presenting cells to the site of injection, and to increase the uptake by these cells of soluble antigen.<sup>67</sup>

Freund's incomplete adjuvant (FIA) is one of the oldest adjuvants used for immunization. FIA is differentiated from Freund's complete adjuvant (FCA), an extremely potent adjuvant that additionally contains heat-killed mycobacteria. FIA produces good stimulation of humoral immunity but is less reactogenic than FCA. The main disadvantages of FIA are its relatively weak adjuvant activity, and the occurrence of possible side effects including abscesses, muscle indurations and granulomas at the site of injection.<sup>68</sup>

There are currently no available therapeutic vaccines against chronic infectious diseases, despite many attempts over the years. Generally, the level of toxicity acceptable for an adjuvant to be used in a therapeutic situation is likely to be higher than for a prophylactic vaccine for use in healthy individuals. The most widely investigated immunotherapeutic strategy against HIV is a combination of whole killed HIV virus depleted of gp120 and combined with Freund's incomplete adjuvant (Remune<sup>TM</sup>).<sup>69</sup> The Montanide family has also been used in trial vaccines against HIV, as has the water-in-mineral oil (Drakeol) adjuvant, being evaluated as an immunotherapeutic vaccine.<sup>70 71</sup>

### 3.A.3 Calcium Phosphate

Calcium phosphate is the name given to a family of minerals containing calcium ions together with orthophosphates, metaphosphates or pyrophosphates and occasionally hydrogen or hydroxide ions.<sup>72</sup> These compounds have been useful in animal vaccinations in HIV trials.

---

<sup>64</sup> Aguilar & Rodriguez, *supra* note 39, at 3754

<sup>65</sup> *Id.* at 3755

<sup>66</sup> O'Hagan & Lavelle, *supra* note 61, at S118

<sup>67</sup> McGeary et al., *supra* note 45, at 410

<sup>68</sup> *Id.*

<sup>69</sup> *Id.*

<sup>70</sup> Aguilar & Rodriguez, *supra* note 39, at 3755

<sup>71</sup> O'Hagan & Lavelle, *supra* note 61, at S118

<sup>72</sup> Calcium Phosphate, <http://www.merriam-webster.com/dictionary/calcium%20phosphate> (last visited Dec. 5, 2009)

Specifically, calcium phosphate has been found to elicit antibodies recognizing the gp160 HIV-1, p55, p25 and p18 proteins. Calcium phosphates permit induction of high levels of circulating antibodies, most of the time without the occurrence of untoward reactions as are observed with aluminum adjuvants of water in oil emulsions. Calcium phosphate adjuvanted preparations have been commercially available in France for many years for the immunization of babies and adults and for hyposensitization treatments of allergic patients. Based on animal trials, calcium phosphate adjuvant show extreme promise for human anti-HIV vaccines.<sup>73</sup>

### 3.B Organic Adjuvants

Organic adjuvants, specifically, are adjuvants that are derived from living organisms or chemically contain carbon.<sup>74</sup>

#### 3.B.1 Muramyl Dipeptide

Muramyl dipeptide (Figure 3 below, *N*-Acetyl muramyl-L-alanine-D-isoglutamine, MDP) is a component of the mycobacterial cell wall related to the adjuvant aspect of peptidoglycan.<sup>75</sup> MDP, and its synthetic analogs such as muramyl tripeptide phosphatidylethanolamine (MTP-PTdEtn), exhibit a wide range of potency as adjuvants.<sup>76</sup> The physiological effects that have been observed from the administration of MDP include adjuvanticity, pyrogenicity and leucocytopoietic activity.<sup>77</sup> There have been over 300 synthetic derivative of MDP in order to try to maintain the adjuvant activity with a reduction in side-effects.<sup>78</sup>

When MDP is administered as water-in-oil emulsions, MDP overcomes its reputation as having poor adjuvant quality in aqueous solution, and has potent *in vivo* adjuvant activity.<sup>79</sup> Thus, numerous lipophilic derivatives of MDP have been created and have been “shown to be potent inducers of the cytokines interleukin-1, interleukin-6, interferon- $\gamma$  and colony stimulation factors in mice.”<sup>80</sup> Murabutide, a derivative of MDP, “has been found to target cells of the reticulo-endothelial system and regulate the release of cytokines *in vivo* without significant induction of proinflammatory mediators.”<sup>81</sup> This derivative triggers “the maturation and activation of monocyte-derived immature dendritic cells, and thus could be an effective adjuvant for DC-based immunotherapy of ... viral infections.”<sup>82</sup> No peer reviewed articles found regarding the use of MDP as an adjuvant in HIV vaccines.

---

<sup>73</sup> E. Relyveld and J. C. Chermann, *Humoral Response in Rabbits Immunized with Calcium Phosphate Adjuvanted HIV-1 gp160 Antigen*, 48 BIOMED. & PHARMACOTHERAPY 79, 82 (1994)

<sup>74</sup> Wade, *supra* note 68

<sup>75</sup> McGeary et al., *supra* note 45, at 411; Reed et al., *supra* note 65, at 28

<sup>76</sup> Reed et al., *supra* note 46, at 28

<sup>77</sup> McGeary et al., *supra* note 45, at 411; Reed et al., *supra* note 65, at 28

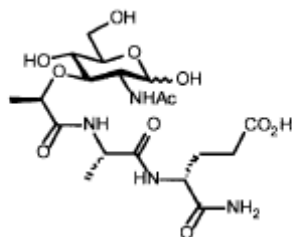
<sup>78</sup> Vogel, *supra* note 42, at 86

<sup>79</sup> McGeary et al., *supra* note 45, at 411

<sup>80</sup> *Id.*

<sup>81</sup> Zi-Hua Jiang & R. Rao Koganty, *Synthetic Vaccines: The Role of Adjuvants in Immune Targeting*, 10 CURRENT MEDICINAL CHEMISTRY 1423, 1432 (2003)

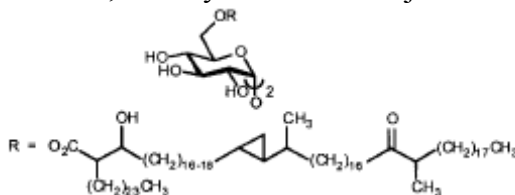
<sup>82</sup> *Id.*



**Figure 3. Muramyl Dipeptide**<sup>83</sup>

### 3.B.2 Trehalose-6,6'-dimycolate

The 6,6'-dimycolate ester of trehalose (Figure 4) is the cord factor from *Mycobacterium tuberculosis*.<sup>84</sup> Trehalose-6,6'-dimycolate has high toxicity, antitumor activity and stimulation of host resistance against infections along with other biological activities.<sup>85</sup> Mycotic acid from *Mycobacterium tuberculosis* has been used to synthesize analogues of trehalose-6,6'-dimycolate in order to conduct structure-activity studies where there was some decrease in the toxicity of the adjuvant while the adjuvant activity was retained.<sup>86</sup> There were no peer reviewed articles found discussing the use of trehalose-6,6'-dimycolate as an adjuvant in vaccines for HIV.



**Figure 4. Trehalose-6,6'-dimycolate**<sup>87</sup>

### 3.B.3 Saponins

Saponins (Triterpenoid glycosides) and have been used as vaccine adjuvants for a number of years.<sup>88</sup> The water soluble QS-21 (Figure 5) have been extensively studied because of its low toxicity and its potent adjuvant activity.<sup>89</sup> The major problems that seem to be associated with saponins are their ability to cause haemolysis of red blood cell and short term pain at the injection site.<sup>90</sup> Saponins insert themselves into the cell membrane, forming pores; this mechanism is thought to allow access for antigens of the cytoplasm promoting the endogenous pathway for cytotoxic T cell induction.<sup>91</sup> Quil-A, made from the bark of the *Quillaja saponaria* (South American soap tree,) and its derivatives are the most widely used adjuvants in research.<sup>92</sup> QS-21, a purified component of Quil-A, has been successful in animal vaccination experiments,

<sup>83</sup> McGeary et al., *supra* note 45, at 411

<sup>84</sup> *Id.*

<sup>85</sup> *Id.*

<sup>86</sup> *Id.*

<sup>87</sup> *Id.* at 412

<sup>88</sup> *Id.* at 411-412

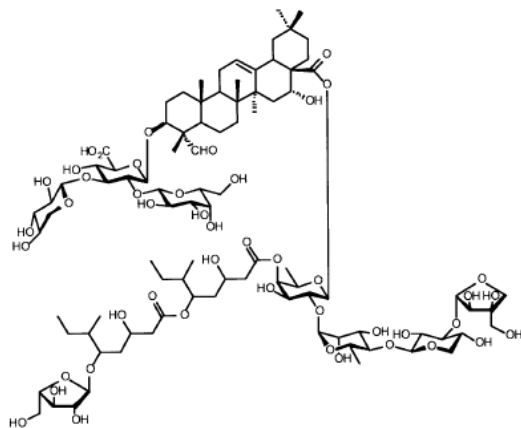
<sup>89</sup> *Id.* at 412

<sup>90</sup> *Id.*

<sup>91</sup> *Id.* at 412-413

<sup>92</sup> Reed et al., *supra* note 46, at 27; U.S. Patent No. 5,057,540 col.1 l.65-66 (filed Aug. 27, 1990)

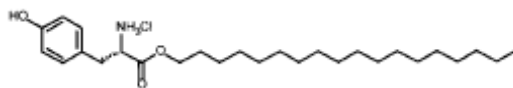
showing a higher antibody response than aluminum hydroxide.<sup>93</sup> Recently QS-21 has been used in Phase I and Phase II testing as an adjuvant for vaccines “including cancer, HIV, influenza, herpes, hepatitis B and malarial antigens.”<sup>94</sup> The phase I and II trials are trying to overcome the main problems with saponins which is short term pain at the injection site and haemolysis of red blood cells.<sup>95</sup> The success rate of these trials of QS-21 as an adjuvant in a HIV vaccine was not described in detail in the article.



**Figure 5. QS-21 Saponin<sup>96</sup>**

### 3.B.4 Stearyl Tyrosine

The synthetic, low molecular weight adjuvant octadecyl ester hydrochloride salt of tyrosine (Stearyl tyrosine, Figure 6) was designed to mimic surface-active adjuvants.<sup>97</sup> The goal of this adjuvant was to reduce the toxicity while still maintaining or improving the adjuvant activity.<sup>98</sup> A slow-release system of stearyl tyrosine comes from its poor water solubility allowing “it to adsorb soluble antigens and form insoluble complexes.”<sup>99</sup> Stearyl is both biocompatible and biodegradable with “very low acute or chronic toxicity.”<sup>100</sup> Stearyl tyrosine “has been studied in a number of animal models, without any observable toxicity” but there were no peer reviewed articles found using stearyl tyrosine as an adjuvant in a HIV vaccine.<sup>101</sup>



**Figure 6. Stearyl Tyrosine<sup>102</sup>**

<sup>93</sup> McGeary et al., *supra* note 45, at 412; Reed et al., *supra* note 46, at 27

<sup>94</sup> McGeary et al., *supra* note 45, at 412

<sup>95</sup> *Id.*

<sup>96</sup> *Id.*

<sup>97</sup> *Id.* at 413

<sup>98</sup> *Id.*

<sup>99</sup> *Id.*

<sup>100</sup> *Id.*

<sup>101</sup> *Id.*

<sup>102</sup> *Id.*

#### 4. Introduction to Immunostimulatory Adjuvants

The Immunostimulants or Immunostimulatory class includes adjuvants that directly act upon the immune system. The Vehicles class describes adjuvants that are used as antigen that present itself to the immune system in an optimal manner.<sup>103</sup>

Typically, Immunostimulatory adjuvants are classified according to their component sources, physiochemical properties or mechanism of action that enhance the efficiency and duration of specific immune response to antigen. Immunostimulants are can also Table 1 depicts a list of immunostimulants adjuvants.<sup>104</sup>

**Table 1. Immune responses triggered by immunostimulants 6**

Immunostimulant	Cellular interaction	Type of immune response
<b>TLR ligands</b>		
Bacterial lipopeptide, lipoprotein and lipoteichoic acid; mycobacterial lipoglycan; yeast zymosan, porin	TLR-2, 1/2, 2/6	Th1, antibody (Ab), NK cell
Viral double stranded RNA	TLR-3	NK cell
Lipopolysaccharide, Lipid A, monophosphoryl lipid A (MPL®), AGPs	TLR-4	Strong Th1, Ab
Flagellin	TLR-5	Th1, CTL, Ab
Viral single stranded RNA, imidazoquinolines	TLR-7/8	Strong Th1, CTL
Bacterial DNA, CpG DNA, hemozoin	TLR-9	Strong Th1, CTL and Ab; NK cell
Uropathogenic bacteria, protozoan profilin	TLR-11	Th1
<b>Other</b>		
Saponins (Quil-A, QS-21, Tomatine, ISCOM, ISCOMATRIX™)	Antigen processing	Strong Th1, CTL and Ab; long term memory
Cytokines: GM-CSF, IL-2, IFN-γ, Flt-3.	Cytokine receptors	Th1, Ab
Bacterial toxins (CT, LT)	ADP ribosylating factors	Ab

In addition, the vehicle class consists of vaccine antigens that present themselves to the immune system in an optimal manner. For instance, the vehicle or chemical class of adjuvants includes the use of delivery system or a controlled release. Furthermore, the vehicle class can also serve to increase the delivery mechanism of the immunostimulants class mentioned above. Examples of the chemical or vehicle class of adjuvants are seen in Table 2.<sup>106</sup>

**Table 2. Immune responses triggered by vehicles or delivery systems 8**

Vehicle or delivery systems	Type of immune response					
	Th1 responses	Th2 responses	Cross priming	B-cell responses	Mucosal responses	Persistent T- and B-cell responses
Mineral Salts (aluminium salts, calcium phosphate, AS04 [Alum+MPL®])	+	++	—	+++	—	+
Emulsions [MF59™ (squalene/water), QS21, AS02 (squalene+MPL®+QS21), IFA, Montanide®, ISA51, Montanide®, ISA720]	++	—	—	+++	—	—
Liposomes (DMPC/Chol, AS01)	+++	—	+	+	—	+
Virosomes (IRIV), ISCOMs	++	++	++	+++	—	—
DC Chol, mineral oil, IFA, Montanide®, squalene	—	++	—	+++	—	—
Mucosal delivery systems: Chitosan	—	—	—	—	—	++
Microspheres	+	—	++	—	—	—

Immunostimulatory adjuvants can also be classified as endogenous and exogenous. Endogenous adjuvants are adjuvants that are originated from within the body.<sup>108</sup> Examples of

<sup>103</sup> Reed et al., *supra* note 46, at 23

<sup>104</sup> *Id.*

<sup>105</sup> *Id.* at 24

<sup>106</sup> *Id.*

<sup>107</sup> *Id.*

<sup>108</sup> Reed, et.al., *supra* note 46, at 23

these adjuvants include Lipopeptides, Lipid A, Monophosphoryl Lipid A (MPL), Liposomes, Polysaccharides, Lipid Polylysine Core Peptides, Cytokines / Interleukins, and Proteosomes.<sup>109</sup> These adjuvants are formed with either molecules or compounds originating within the body or through a normal cell metabolism.<sup>110</sup> Interestingly, certain molecules released by necrotic cell death and stressed or damage tissues can act as very powerful adjuvants.<sup>111</sup>

The second class of Immunostimulatory adjuvants is exogenous adjuvants, which are defined as adjuvants that are made up of either molecules or compounds that are external to the body.<sup>112</sup> Few examples of these adjuvants are Multiple Antigenic Peptide, and exogenous toxins. Exogenous adjuvants typically need to be co-injected with an antigen.<sup>113</sup> Certain adjuvants can also be ingested or inhaled.

#### **4.A Endogenous Immunostimulatory Adjuvants**

Immunostimulatory adjuvants can be classified as endogenous depending on whether the compound, or protein used within the adjuvant is found within the body. Typically, endogenous immunostimulatory adjuvants help stimulate the immune system and are not considered foreign bodies. This usually means that side effects and drug resistance will be avoided because the endogenous immunostimulatory adjuvant is already found within the body.<sup>114</sup>

##### **4.A.1 Polysaccharides**

Polysaccharides are a form of carbohydrates. Polysaccharides are carbohydrates which have high molecular weight. They break down to monosaccharides when hydrolysis happens. This is a complex form. Mono-saccharides join together and create the polysaccharide. Glycosidic bonds are the binding force between the mono-saccharides. A general formula that denotes Polysaccharide is  $C_n (H_2O)_n$  where the carbon chain may be 200 to 2500 carbons in length.<sup>115</sup> Generally 10 or more monosaccharides make a polysaccharide.

##### **4.A.1.a Polysaccharides as Adjuvants for use in HIV Vaccines**

Current carbohydrate-based vaccines, while effective, do not protect against the carrier protein and, therefore, an immunogenic response is heterogeneous in nature.<sup>116</sup> Using polysaccharides, this objective can be achieved by preparing well-known carbohydrate antigens,

---

<sup>109</sup> *Id.* at 25

<sup>110</sup> *Id.*

<sup>111</sup> Albert Bendelac & Ruslan Medzhitov, *Adjuvants of Immunity: Harnessing Innate Immunity to Promote Adaptive Immunity*, 195(5) J EXPERIMENTAL MED. F19, F23 (2002)

<sup>112</sup> Reed et al., *supra* note 46, at 23

<sup>113</sup> *Natural Endogenous Adjuvants*,

<http://www.heatshock.net/showabstract.php?pmid=15609001&redirect=yes&terms=endogenous+or+exogenous+adjuvants> (last visited Sept. 23, 2009)

<sup>114</sup> Lim Yeok Loo et al., *Identification of Novel Endogenous Proteins For the Control of Angiogenesis-Based on Bioinformatics Support*, 10 BMC GENOMICS 392 (2009)

<sup>115</sup> *What are polysaccharides?*, <http://www.articlesbase.com/health-articles/what-are-polysaccharides-185384.html> (last visited on Jan. 10, 2009)

<sup>116</sup> Carbohydrate-Based Vaccines, [http://chem.wayne.edu/andreanagroup/research\\_page.htm#proj3](http://chem.wayne.edu/andreanagroup/research_page.htm#proj3) (last visited 01-10-09)

such as the well-defined polysaccharide (Man<sub>9</sub>GlcNAc<sub>2</sub>-HIV gp120), in which the oligosaccharides are linked to a T-cell inducing ZPS.<sup>117</sup>

A synthetic carbohydrate vaccine without proteins as carriers and adjuvants as elicitors of immune responses are capable of producing an antibody with 'Fab' portions specific for carbohydrates exclusively. This will ensure specificity in binding as well as a strong binding affinity, vital for immunity against the HIV virus.<sup>118</sup>

Polysaccharides based on glucose and mannose that have adjuvant action include *glucans*, *dextrans*, *glucomannans* and *galactomannans*. These have been shown to up-regulate T-helper 1 responses. *Levans* and *xyalns* also have immune-enhancing activity. Macrophages have glucan and manna receptors, activation of which stimulates phagocytosis and cytokine secretion okys release of leukotrienes and prostaglandins<sup>119</sup>. High-molecular weight *sulfated and diethylaminoethyl-dextrans* have been used as veterinary adjuvants<sup>120</sup>. *In vitro*, mannan activates monocytes and macrophages to secrete IFN, TNF, GM-CSF, IL-1 and IL-6.

*Chitosan*: A polymer of D-glucosamine and Nacetyl- D-glucosamine, obtained by partial deacetylation of chitin, exhibits a range of effects on the immune system. It has been shown to activate macrophages, induce cytokines, and increase antibody production. Nevertheless chitosan has very low toxicity, is non-allergenic, and is biodegradable.<sup>121</sup>

*Inulin*: The extensive data on inulin-based adjuvants indicate that these are excellent candidates to replace alum as the adjuvant of choice for many vaccines. Particular advantages offered by inulin-based adjuvants is that they induce cellular in addition to humoral immunity and offer excellent safety, tolerability, ease of manufacture and formulation.<sup>122</sup> Inulin is the term used to describe a family of low molecular weight unbranched polymers of fructose and glucose. It is found in *Compositae* where it serves as the storage carbohydrate, replacing the normal starch as a reserve food. Gamma inulin is a potent alternate complement humoral and cellular immune adjuvant, by increasing production of activated C3 and thereby activating macrophages.<sup>123</sup>

*Beta – Glucans*: These fungal polysaccharides stimulate innate immunity via TLRs and other PRRs (endocytic - Pattern Recognition Receptors). B-Glucans are Beta (1 to 3) D-glucose polymers with or without Beta (1 to 6) linked Beta (1 to 3) glucan side-chains forming single or triple helix conformers. B-Glucans' immune-modulating properties are dependent on size, branching and conformation, with single helix conformers being the more effective ones. High molecular weight B-Glucans cross link membrane complement receptor type three from

---

<sup>117</sup> *Id.*

<sup>118</sup> *Id.*

<sup>119</sup> Nikolai Petrovsky, *Novel human polysaccharide adjuvants with dual Th1 and Th2 potentiating activity*, 24 VACCINE S26 (Supp. 2 2006)

<sup>120</sup> McGreary et al., *supra* note 46, 405-418

<sup>121</sup> *Id.*

<sup>122</sup> Petrovsky, *supra* note 119, at S26

<sup>123</sup> *Id.*

neutrophils and monocytes, triggering degranulation and cytokine release in the absence of target T-cells.<sup>124</sup>

*Lipo-Polysaccharides or endotoxin*: A lipopolysaccharide of Gram-Negative Bacteria or Cell Wall Peptidoglycan enhances the immune response against co-administered antigens despite themselves not being very immunogenic.<sup>125</sup> *Endotoxin* has a hydrophilic polysaccharide and a lipophilic phospholipid. The latter stimulates the excessive production of pro-inflammatory cytokines, leading to septic shock. Also the lipopolysaccharides derived from the cell wall of Gram Negative Bacteria, are potent B-cell mitogens, and activate T-cells to produce IFN-gamma and TNF and thereby enhance cellular immune responses<sup>126</sup>. The main structural element responsible for their adjuvant effect is Lipid A, which can be hydrolysed to obtain monophosphoryl lipid A.

*MGN-3*: An arabinoxylane from rice bran that has been enzymatically modified with extract from *Hyphomycetes* mycelia, was tested for anti-HIV activity in vitro. MGN-3 activity against HIV-1 (SF strain) was examined in primary cultures of peripheral blood mononuclear cells. MGN-3 inhibited HIV-1 replication by: (1) inhibition of HIV-1 p24 antigen production in a dose dependent manner; and (2) inhibition of syncytia formation maximized. Based on these results, it has been concluded that MGN-3 possesses potent anti-HIV activity and in the absence of any notable side effects, MGN-3 shows promise as an agent for treating patients with AIDS.<sup>127</sup>

*Actinidia eriantha (AEPS)*: The plant polysaccharides are recognized as an effective biological response modifier with low toxicity. The water-soluble polysaccharide from the roots of AEPS has been evaluated as a safe and efficacious adjuvant candidate suitable for a wide spectrum of prophylactic and therapeutic vaccines.<sup>128</sup>

*Eldexomer*: Inclusion of eldexomer (a bio-adhesive polysaccharide) in intranasal HIV vaccine preparations may enhance induction of systemic antibody responses, and allow for the use of lower, more cost effective doses of antigen.<sup>129</sup>

*CpG ODN*: Adjuvant effect of CpG ODN for polysaccharide antigens has been observed to be prominent in neonates. Although CpG ODN may not be an effective adjuvant for many pure polysaccharide antigens, however they are quite effective if a protein carrier is conjugated to the polysaccharide.<sup>130</sup>

---

<sup>124</sup> Dante J. Marciani, *Vaccine Adjuvants: Role and Mechanisms of Action in Vaccine Immunogenicity*, 8 DRUG DELIVERY TODAY 934, 934 (2003)

<sup>125</sup> Nikolai Petrovsky et al., *Vaccine Adjuvants: Current State and Future Trends*, 82 IMMUNOLOGY & CELL BIOLOGY 488, 488 (2004)

<sup>126</sup> *Id.*

<sup>127</sup> *Anti-HIV activity in vitro of MGN-3, an Activated Arabinoxylane From Rice Bran*, <http://www.ncbi.nlm.nih.gov/pubmed/9473473> (last visited Sept. 22, 2009)

<sup>128</sup> Hong-Xiang Sun & Wang Hui, *Novel Polysaccharide Adjuvant from the Roots of Actinidia Eriantha with Dual Th1 and Th2 Potentiating Activity*, 27 VACCINE 3984 (2009)

<sup>129</sup> *Enhancement of Nasally Administered HIV Peptide Immunogenicity Using a Polysaccharide Bioadhesive*, <http://gateway.nlm.nih.gov/MeetingAbstracts/ma?f=102256254.html> (last visited Sept. 22, 2009)

<sup>130</sup> *Vaccine Adjuvants: Immunological and Clinical Principles*, at 93 (Charles J. Hackett & Donald A. Ham eds., 2006)

## 4.A.2 Liposomes

Phospholipids liposomes are the basic building block of every cell membrane in the human body. Each phospholipid molecule has three major parts, one head and two tails. The head is made from three molecular components: choline, phosphate, and glycerol.<sup>131</sup> The head is hydrophilic, that is, it is attracted to water. Each tail is a long, essential fatty acid chain. These fatty acids are hydrophobic, that is, they are repelled by water. Liposomes are single or multilamellar bilayer membrane vesicles that can vary in size from 20 nm to 3  $\mu$  m.<sup>132</sup>

### 4.A.2.a Liposomes as Adjuvants for HIV Vaccines

Liposomes are another class of oil-in-water emulsion that can transport antigens to lymphoid tissues following local injection. When given orally, they are also able to be endocytosed by M cells, allowing the antigen to be transported to the lymph cells in the Peyer's patches.

The lipid components are usually phospholipids or other amphiphiles, often supplemented with cholesterol and other charged lipids. Liposomes can entrap both hydrophobic and water-soluble antigens, either within, or between the lipid bilayers. The first description of the use of liposomes as immunological adjuvants showed that diphtheria toxoid encapsulated in liposomes elicited a stronger humoral immune response after injection into mice, than the free toxoid. Liposomes are poorly immunogenic themselves, but are useful for presenting antigens to the immune system, either encapsulated within the liposome, or adsorbed on the surface. It has been shown that the attachment of simple sugars to liposomes led to an increase in the humoral immune response to these antigens.<sup>133</sup>

*Dehydration-rehydration liposome vesicles (DRVs)* : These containing various cytokines were evaluated for their ability to induce delayed-type hypersensitivity (DTH) and humoral immunity to the recombinant envelope protein gp120 of the MN strain of human immunodeficiency virus type 1 (HIV-1). Induction of DTH by vaccines may increase protection from viral pathogens such as HIV. Cytokine-containing liposomes may be an effective adjuvant for the induction of a DTH response to envelope-antigen subunit vaccines.<sup>134</sup>

*Cytotoxic T lymphocyte (CTL)* : Liposomes that contain an immunodominant peptide (15 amino acids) of the envelope glycoprotein gp120 of HIV-1 and that are coated with mannopentaose-dipalmitoylphosphatidylethanolamine conjugate induce a major histocompatibility complex class I-restricted CD8<sup>+</sup> CTL response in mice with a single

---

<sup>131</sup> *Liposomes: What They Are, What They Do, How Are They Made?*, <http://www.lyposphere.com/liposomes.html> (last visited Oct. 1, 2009)

<sup>132</sup> *Id.*

<sup>133</sup> *Liposomes as Adjuvants for Vaccines*, <http://www.stormingmedia.us/89/8911/A891133.html> (last visited Sept. 22, 2009)

<sup>134</sup> *Cytokine-Containing Liposomes as Adjuvants for HIV Subunit Vaccines*, <http://www.ncbi.nlm.nih.gov/pubmed/7492439> (last visited Sept. 22, 2009)

subcutaneous immunization, whereas non-coated liposomes do not.<sup>135</sup> Since no damage to the skin at the injection site was caused by the liposomes, and since the oligomannose-coated liposomes consist of innocuous materials ubiquitously distributed throughout the human body, they may be highly suitable for use as a safe adjuvant in vaccines inducing a CTL response against HIV.<sup>136</sup>

CAF01: This liposome induced cellular immune responses against HIV-1 minimal CTL epitopes in HLA-A\*0201 transgenic mice to levels comparable with that of incomplete Freund's adjuvant.<sup>137</sup>

Liposomes containing lipid A (LA): This is a potent adjuvant and antigen. Incorporation of lipid A into liposomes renders the liposomes themselves immunogenic, resulting in generation of specific antibodies that recognize either the individual liposomal lipids, or the unique pattern presented by the combination of lipids.<sup>138</sup> Stable liposomal oil-in-water emulsions provide an effective means of obtaining both antibody and CTL responses against an HIV envelope antigen.<sup>139</sup>

#### 4.A.3 Lipid Polysine Core Peptides

Synthetic lipopeptide vaccines are being increasingly investigated mainly because of the advantages they offer over traditional vaccines, including safety of use in humans, high specificity in eliciting immune responses, greater purity and large scale/cost-effective production capacity.<sup>140</sup>

The lipid polylysine core peptide (LCP) system essentially combines the MAP and tripalmitoyl-Sglyceryl cysteine (Pam3Cys) systems. The LCP system incorporates lipoamino acids coupled to a polylysine core containing up to two different antigenic peptides, and is uniquely designed to incorporate antigen, carrier and adjuvant in a single molecular entity. There has also been a description about a variation of his MAP system ('lipidatedMAP') that incorporates lipids in order to boost mucosal immunization<sup>141</sup>.

LCP-based vaccine candidates incorporating variable domains of *Chlamydia trachomatis* outer membrane protein have been shown to significantly enhance peptide immunogenicity when compared with peptide monomers given alone in adjuvant, and an LCP compound incorporating

---

<sup>135</sup> Masashi Fukawasa, *Liposome Oligomannose-Coated with Neoglycolipid, a New Candidate for a Safe Adjuvant for Induction of CD8<sup>+</sup> Cytotoxic T Lymphocytes*, 441 FEBS LETTERS, 353, 353 (1998)

<sup>136</sup> *Id.*

<sup>137</sup> A Novel Liposome-Based Adjuvant CAF01 for Induction of CD8<sup>+</sup> Cytotoxic T-Lymphocytes (CTL) to HIV-1 Minimal CTL Peptides in HLA-A\*0201 Transgenic Mice, <http://www.plosone.org/article/info:doi%2F10.1371%2Fjournal.pone.0006950> (last visited Sept. 22, 2009)

<sup>138</sup> Lipid A and Liposomes Containing Lipid A as Antigens and Adjuvants, <http://cat.inist.fr/?aModele=afficheN&cpsidt=20508789> (last visited Sept. 22, 2009)

<sup>139</sup> Richards Roberta et al., *Liposome-stabilized oil-in-water emulsions as adjuvants: increased emulsion stability promotes induction of cytotoxic T lymphocytes against an HIV envelope antigen*, 82 IMMUNOLOGY & CELL BIOLOGY 531, 531-38 (2004)

<sup>140</sup> Istvan Toth et al., *Recent advances in Design and Synthesis of Self-Adjuvanting Lipopeptide Vaccines*, 14 Int'l J. of Peptide Research & Therapeutics 333, 333 (2008)

<sup>141</sup> McCreary et al., *supra* note 45, 405-418

a foot-and-mouth disease viral peptide was immunogenic, resulting in the induction of anti-peptide antibodies in the absence of additional adjuvant.<sup>142</sup>

Recently the LCP system was investigated as a vaccine delivery strategy for group A streptococci (GAS) — the causative agents of rheumatic fever (RF) and subsequent rheumatic heart disease (RHD) — diseases for which currently no available vaccine exists. The bacterial surface anti-phagocytic M protein and major GAS vaccine candidate, was the targeted antigen. Mice immunized parenterally, in the absence of conventional adjuvant, with an LCP formulation containing a protective C-region determinant of the GAS M protein elicited high titre, heterologous opsonic antibodies that did not cross-react with human heart tissue proteins, indicating the potential of such a vaccine in inducing broadly protective immune responses.<sup>143</sup>

#### 4.A.4 Cytokine

Cytokines are a broad range of small proteins, best known for their roles in immunostimulatory function.<sup>144</sup> They are released by different cell types in response to immunological stimuli and function to regulate immune system.<sup>145</sup> Cytokines act on their target cells by binding to the cell's specific membrane receptors, mediating their immunostimulatory effects in a more controlled and specific manner.<sup>146</sup> The receptors and their corresponding cytokines have been divided into several families based on their structure and immunostimulatory activities: interferons (IFN), interleukin (IL), chemokines etc.<sup>147</sup> Cytokines are involved in virtually all aspects of both cellular and humoral immune responses. Thus, vaccines with limited immunogenicity, such as HIV vaccine comprising inactivated virus or HIV-DNA vaccine, that require more robust immunogenicity, can benefit from the usage of cytokine as adjuvants. Additionally, cytokines are extremely suitable as adjuvants for HIV vaccine because both cellular and humoral immune responses will be required for optimal and sustained protection against HIV infection.<sup>148</sup>

Cytokines that enhance antigen-specific cellular immune response include interferon (INF)- $\gamma$ , interleukin (IL)-2, IL-12 and IL-15.<sup>149</sup> Whereas, cytokines that augment antigen-specific humoral immune response include IL-4, IL-10 and granulocyte-macrophage cell stimulating factor (GM-CSF).<sup>150</sup> Similarly, chemokines enhance the immune system by increasing Antigen Presenting Cell (APC) availability and antigen presentation.<sup>151</sup> Cytokines that have been commonly examined as immunological adjuvants are discussed below:

---

<sup>142</sup> *Id.*

<sup>143</sup> *Id.*

<sup>144</sup> Dan H. Barouch et al., *The Role of Cytokine DNAs as Vaccine Adjuvants for Optimizing Cellular Immune Responses*, 202 IMMUNOLOGICAL REVIEWS 266, 266 (2004)

<sup>145</sup> Vaccine Adjuvants and Delivery Systems 328 (Manmohan Singh ed., 2007)

<sup>146</sup> *Id.*

<sup>147</sup> Barouch et al., *supra* note 144, at 268-270

<sup>148</sup> *Id.*

<sup>149</sup> Matthew P. Morrow & David B. Weiner, *Cytokines as Adjuvants for Improving Anti-HIV Responses*, 22 AIDS 333, 333 (2008)

<sup>150</sup> *Id.*

<sup>151</sup> Barouch et al., *supra* note 144, at 270

**GM-CSF-** This class of cytokine is known to induce antigen-specific humoral immune response.<sup>152</sup> Its immunological role includes activation of granulocytes and macrophages, and promotes the generation and recruitment of dendritic cell in response to immunological stimuli.<sup>153</sup> Furthermore, it enhances co-stimulatory molecule expression on APCs, and also enhances the up-regulation of MHC classes I and II.<sup>154</sup> GM-CSF administered with HIV peptide immunogen has shown to augment the induction of anti-HIV antibody responses.<sup>155</sup>

**IL-2-** This class of cytokine activates CD4+ and CD8+ T lymphocytes and also activates natural killer cells.<sup>156</sup> IL-2 is an optimal choice as an adjuvant for HIV vaccine because HIV infection results in CD4+ deficiency.<sup>157</sup>

**IL-12-** This class of cytokine induces the production of INF- $\gamma$  and promotes the development of T helper 1 (Th1) cells, and stimulates effector T lymphocytes.<sup>158</sup> IL-12 administration has shown to enhance the induction of HIV-specific CTL after intrarectal immunization with HIV peptide immunogen.<sup>159</sup>

**IL-15-** This class of cytokine plays a critical role in establishing and maintaining memory CH8+ T lymphocytes.<sup>160</sup> It is also a key regulator of NK and NKT-cell development.<sup>161</sup> Studies have demonstrated that IL-15 enhances HIV-1 specific central memory T-cells induced by HIV antigen.<sup>162</sup>

#### **4.A.4.a Delivery Mechanisms of cytokine adjuvants-**

1. Mucosal administration of purified cytokine protein as adjuvants- Because HIV infection predominantly occurs at mucosal surfaces, inactivated HIV vaccine, in combination with cytokine adjuvant, is administered to mucosal surfaces to induce protection.<sup>163</sup> In particular, cytokines IL-1, IL-12, IL-18, and GM-CSF, when used in formulation with C4-V3<sub>MN</sub> HIV antigen exhibits mucosal adjuvant activity inducing immune response against the specific HIV antigen.<sup>164</sup>

---

<sup>152</sup> Morrow & Weiner, *supra* note 149, at 333

<sup>153</sup> Singh, *supra* note 145, at 328

<sup>154</sup> *Id.*

<sup>155</sup> Curtis P. Bradney et al., *Cytokines as Adjuvants for the Induction of Anti-Human Immunodeficiency Virus Peptide Immunoglobulin G (IgG) and IgA Antibodies in Serum and Mucosal Secretions after Nasal Immunization*, 76(2) J. OF VIROLOGY 517, 522 (2002)

<sup>156</sup> Barouch et al., *supra* note 144, at 269

<sup>157</sup> Yves Levy et al, *Enhanced T Cell Recovery in HIV-1-Infected Adults Through IL-7 Treatment*, 119 (4) J. CLIN. INVEST. 997, 997 (2009)

<sup>158</sup> Singh, *supra* note 145, at 328-29

<sup>159</sup> Bradney et al., *supra* note 155, at 522

<sup>160</sup> Barouch et al., *supra* note 144, at 270

<sup>161</sup> Singh, *supra* note 145, at 330

<sup>162</sup> Sandra A. Calarota et al., *IL-15 as Memory T-cell Adjuvant for Topical HIV-1 DermaVir Vaccine* 26 VACCINE 5188, 5189 (2008)

<sup>163</sup> Bradney et al, *supra* note 155, at 520

<sup>164</sup> *Id.* at 521

2. Incorporation of cytokine expressing gene into DNA vaccine encoding HIV antigen- Studies that have used HIV-DNA constructs augmented with plasmid expressing cytokines have shown an enhanced cellular and humoral responses elicited by DNA encoding HIV antigen.<sup>165</sup>

The table 3 below includes commonly incorporated plasmid cytokines into HIV-DNA vaccine.

Adjuvant	Animal model	
	Mouse	Primate
Interferon Gamma	Increased antibody and CTLs	Little activity
GM-CSF	Increased antibody titers	Little to no activity
CD40 Ligand	Increased CD4 T-Cell activity	Little to no activity
B7.2	Increased CTL activity	Little to no activity
IL-2	Increased antibody titers	Increased antibody titers
IL-4	Increased antibody titers	Increased antibody titers
IL-12	Increased CTL activity	Increased CD4 T cell and CTL activity
IL-15	Increased CTL activity	Increased CTL activity and antibody titers

CTL, Cytotoxic T lymphocyte; IL, interleukin.

AIDS

Table 3: List of plasmid adjuvants and their effect in immune responses.<sup>166</sup>

#### 4.A.5 Lipid A and Monophosphoryl Lipid A (MPL)

Lipid A is a lipid component of the gram-negative bacterial lipopolysaccharide (LPS, see Figure 7 below). It is a potent adjuvant for mucosally or intramuscularly delivered antigens, and is involved augmentation of both humoral and cell-mediated immunity.<sup>167</sup> Intramuscular administration of HIV-1 Gag p24 antigen encapsulated in liposomal lipid A has shown a significant increase in immune response in comparison to administering the antigen encapsulated in liposome alone.<sup>168</sup> However, lipid A is known to be highly toxic, thus, precluding its use as an adjuvant in human vaccines. The toxic feature of lipid A is reduced by removing the 1'-phosphate group. This removal of 1'-phosphate from lipid A results in MPL, a detoxified derivative of lipid A, which has lower toxicity but strong immunostimulatory activity.<sup>169</sup>

The adjuvant effects of MPL and lipid A is exerted when they bind to TLR-4 receptor on antigen present cells (APCs), which results in activation of APCs, further enhancing APCs' capacities to process and present antigen to T and B lymphocytes.<sup>170</sup> MPL has successfully been used as adjuvants for both protein vaccines and DNA vaccines. As a protein vaccine adjuvant, it has been used in formulation with HIV-1 envelope gp120 antigen.<sup>171</sup> While, as a DNA vaccine adjuvant, MPL has been injected as a solution that comprises a construct expressing *env* and *rev*

<sup>165</sup> Barouch et al., *supra* note 144, at 269-71

<sup>166</sup> Morrow & Weiner, *supra* note 149, at 335

<sup>167</sup> McGeary et al., *Lipid and carbohydrate based adjuvant/carriers in immunology*, 9 J. PEPTIDE SCI. 405, 410 (2003)

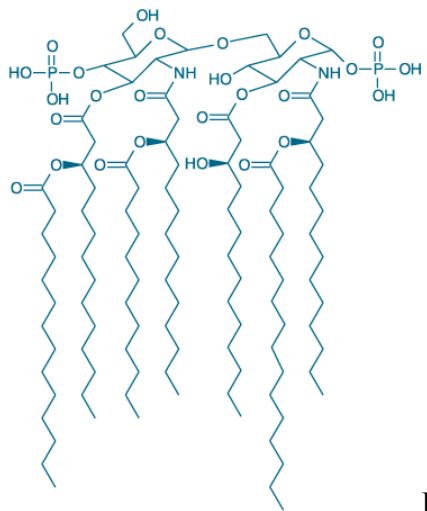
<sup>168</sup> Nicolas J. Steers et al., *Liposome-Encapsulated HIV-1 Gag p24 Containing Lipid A Induces Effector CD4+ T-Cells, Memory CD8+ T-Cells, and Pro-Inflammatory Cytokines*, 27 VAC 6939, 6948-6949 (2009)

<sup>169</sup> McGeary et al., *supra* note 167, at 410-411

<sup>170</sup> *Vaccine Adjuvants: Immunological and Clinical Principles*, 235-238 (Charles J. Hackett & Donald A. Harn eds. 2006)

<sup>171</sup> Anne Moore et al., *The Adjuvant Combination Monophosphoryl Lipid A and QS21 Switches T cell Responses Induced with a Soluble Recombinant HIV Protein from Th2 to Th1*, 17 VACCINE 2517, 2517- 2527 (1999)

genes of HIV-1 (IIIB) strain.<sup>172</sup> In both cases, MPL adjuvanted HIV vaccines have shown to enhance both cellular and humoral immune responses.



**Figure 7:** Structure of the lipid A component of *Salmonella minnesota* lipopolysaccharide (LPS).<sup>173</sup>

#### 4.A.6 Lipopeptide

Lipopeptides are molecules consisting of lipid connected to a peptide. They are derived from the lipoprotein of bacterial cell wall.<sup>174</sup> Lipopeptides function as potent mucosal adjuvants by activating B-lymphocytes, macrophages and monocytes, upon binding to Toll-like receptors (TLR)-2/6 on the target cell surface. Lipopeptides also promote the activation and maturation of dendritic cells, further improving their antigen processing and presenting function.<sup>175</sup> In HIV vaccines, lipopeptides were shown to be potent and antigen-specific mucosal adjuvant when combined with mucosal HIV vaccine. For example, intranasal co-administration of HIV-1 Tat antigen in formulation with macrophage-activating lipoprotein (MALP-2, see Figure 8 below) was shown to elicit strong Tat-specific humoral response at both mucosal and systemic levels.<sup>176</sup> Similarly, intranasal immunization of recombinant HIV-1 p17 protein co-administered with MALP-2 resulted in strong stimulation of humoral and cellular immune response at systemic and mucosal levels.<sup>177</sup>

<sup>172</sup> Shin Sasaki et al., *Monophosphoryl Lipid A Enhances Both Humoral and Cell-Mediated Immune Responses to DNA Vaccination against Human Immunodeficiency Virus Type 1*, 65 INFECTION AND IMMUNITY 3520, 3525-527 (1997)

<sup>173</sup> *Molecular Probes*, <http://www.invitrogen.com/site/us/en/home/References/Molecular-Probes-The-Handbook/Probes-for-Endocytosis-Receptors-and-Ion-Channels/Probes-for-Following-Receptor-Binding-Endocytosis-and-Exocytosis.html> (last visited Oct. 2, 2009)

<sup>174</sup> McGeary et al., *supra* note 167, at 410

<sup>175</sup> Stefan Borsutzky et al., *The Mucosal Adjuvant Macrophage-Activating Lipopeptide-2 Directly Stimulates B Lymphocytes via the TLR2 without the Need of Accessory Cells*, 174 J. OF IMMUNOLOGY 6308, 6311-312 (2005)

<sup>176</sup> Stefan Borsutzky et al., *Efficient Systemic and Mucosal Responses Against the HIV-1 Tat Protein by Prime/Boost Vaccination Using the Lipopeptide MALP-2 as Adjuvant*, 24 VACCINE 2049, 2053-054 (2005)

<sup>177</sup> Pablo D. Becker et al., *The HIV-1 Matrix Protein p17 Can Be Efficiently Delivered by Intranasal Route in Mice Using the TLR 2/6 Agonist MALP-2 as Mucosal Adjuvant*, 24 VACCINE 5269, 5273-274 (2005)

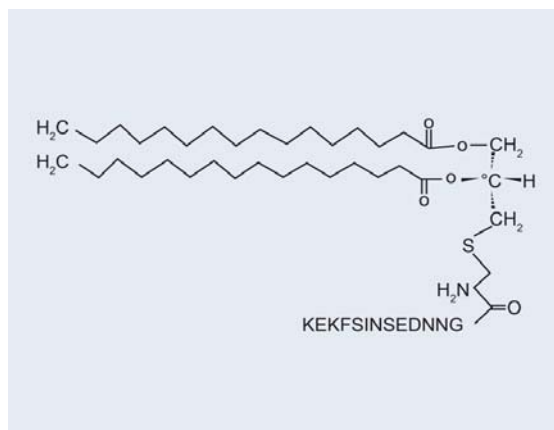


Figure 8: Structure of MALP-2<sup>178</sup>

## 4.B Exogenous Immunostimulatory Adjuvants

Exogenous Immunostimulatory Adjuvants are a classification of adjuvants that are compounds, or proteins that are not found in the human body.<sup>179</sup> Typically to illicit a profound response, the exogenous immunostimulatory adjuvants need to be co-injected with an antigen.<sup>180</sup>

### 4.B.1 Proteosomes

Proteosomes are highly hydrophobic outer membrane proteins from the surfaces of cells usually from various species of bacteria.<sup>181</sup> They can serve as an adjuvant or a carrier protein for a vaccine, and are created when a cell wall is treated with a detergent to isolate the components of a cell wall.<sup>182</sup> Because of their high dislike for water, proteosomes can self assemble into vesicular structures which can then be recognized by the immune system to cause a response.<sup>183</sup> The proteosome can then be combined with the macromolecules that form the basis of the vaccine, such as other proteins, polysaccharides or lipopolysaccharides, in order to cause the immune system to react more strongly then with the vaccine antigen alone.<sup>184</sup> Proteosomes have been especially successful when being used to develop safe mucosal vaccinations.<sup>185</sup> Additionally, the peptides used to create proteosomes are safe for human use, since a number of them have been used in other vaccines such as influenza and meningococcal diseases.<sup>186</sup> In HIV, the proteosomes could be useful in creating a working vaccine that would protect the mucosal

<sup>178</sup> MALP-2S in the context of other TLR agonists: Preclinical studies, <http://www.mbiotec.com/preclinicalstudies.aspx> (last visited Oct. 2, 2009)

<sup>179</sup> Kenneth L. Rock et al., *Natural Endogenous Adjuvants*, <http://www.heatshock.net/showabstract.php?pmid=15609001&redirect=yes&terms=Natural+Endogenous+Adjuvants> (last visited Oct. 2, 2009)

<sup>180</sup> *Id.*

<sup>181</sup> McGeary et al., *Lipid and carbohydrate based adjuvant/carriers in immunology*, 9(7) J. Peptide Sci. 405, 410 (2003)

<sup>182</sup> George H. Lowell et al., *Proteosome Technology for Vaccines and Adjuvants* in *New Generation Vaccines* 271 (Myron Max Levine ed., 3rd ed. 2004)

<sup>183</sup> *Id.*

<sup>184</sup> McGeary et al., *supra* note 181, at 414

<sup>185</sup> *Id.*

<sup>186</sup> Lowell et al, *supra* note 182, at 273

membranes of the mouth, vagina, and anus as well as stimulate a wider immune response against the virus.<sup>187</sup>

#### **4.B.2 Multiple Antigenic Peptides**

Multiple antigenic peptide (MAP) is a system that allows for identical or different peptide sequences to be assembled around a lysine core.<sup>188</sup> The result is a large macromolecule that has a high amount peptide antigen as compared to the core lysine molecule.<sup>189</sup> The synthetic peptides can induce antibodies to react with the proteins on the outer peptides.<sup>190</sup> By coupling the multiple peptides around the lysine core, the adjuvant can cause a more powerful immune response by giving the immune cells a larger target for attack.<sup>191</sup>

#### **4.B.3 Exogenous Toxins**

Exogenous Toxins are a class of peptides that are based on the toxic products of certain bacteria, such as E. Coli, Cholera, and Pertussis.<sup>192</sup> The toxins are heat-treated or are mutated since any inclusion into a vaccine would normally cause ill effects unless the toxins were modified to act as adjuvants and therefore be non-toxic to the patient.<sup>193</sup> Similar to Proteosomes, exogenous toxins are proteins or protein subunits that have found to be effective in protecting mucus membranes and causing a greater immune response to the antigen.<sup>194</sup>

### **5. Conclusion**

HIV adjuvants can be categorized within descriptive groups such as Organic, Inorganic, Endogenous and Exogenous. Looking at the various adjuvants shown in the LANL list (see Appendix G), these adjuvants were categorized within the descriptive groups mentioned above. The technical background for HIV adjuvant proved useful for determining these categories and synonyms for key words such as HIV, Vaccine and adjuvant. Understanding the background of HIV adjuvants also proved helpful in interpreting claim language of the patents and understanding the purpose of an adjuvant in a vaccine.

---

<sup>187</sup> *Id.* at 298

<sup>188</sup> J. P. Tam, *Synthetic Peptide Vaccine Design: Synthesis and Properties of a High-Density Multiple Antigenic Peptide System*, 85 PROCEEDINGS OF THE NAT'L ACAD. OF SCIS. 4945, 5409 (1988)

<sup>189</sup> *Id.* at 5409

<sup>190</sup> McGeary et al., *supra* note 181, at 414

<sup>191</sup> Tam, *supra* note 188, at 5412

<sup>192</sup> Elizabeth J. Ryan et al. *Mutants of Escherichia coli Heat-Labile Toxin Act as Effective Mucosal Adjuvants for Nasal Delivery of an Acellular Pertussis Vaccine: Differential Effects of the Nontoxic AB Complex and Enzyme Activity on Th1 and Th2 Cells*, 67 INFECTION & IMMUNITY 6225, 6270 (1999)

<sup>193</sup> *Id.* at 6271

<sup>194</sup> J. C Bowen et al. *Cholera Toxin Acts as a Potent Adjuvant for the Induction of Cytotoxic T-Lymphocyte Responses with Non-Replicating Antigens*, 81 IMMUNOLOGY 337, 338 (1994)

## **II. Patent Search Methodology and Results**

### **1. Patent Search Methodology**

The search on the project topic began in the Summer 2009 Patent Mining course, taught by Professor Cavicchi with technical supervision of Dr. Stanley Kowalski, wherein the team began by reviewing the recent literature on the technology relating to adjuvants used for HIV vaccines. The summer team commenced their searching with the basic search terms: HIV, vaccine and adjuvant; and reviewed the results.

The International Technology Transfer Institute (ITTI Clinic) continued the search methodology from the summer course and began with a conference call between Professor Cavicchi, Dr. Stanley Kowalski and Dr. Kerri Clark (the clinic contact person at PIPRA) in May 2009. The scope of the project was defined as conducting a patent landscape analysis of technologies pertaining to adjuvant vaccines applicable to HIV. The team, with the Clinic members, began by reviewing past and recent literature relating to HIV vaccines and, in particular, to developing adjuvant compositions used in HIV vaccines.

This semester, Thomson Innovation®, a recently released patent search platform (integrating the best of the suite of Thomson tools, Aureka, Delphion and Micropatent), was utilized. *Thomson Innovation* is a single, integrated solution that combines intellectual property, scientific literature, business data and news with analytic, collaboration and alerting tools in a robust platform.

The six-member team was divided into two groups. Each group was headed by a team leader whom the project leader oversaw. The groups were assigned to research on different aspects of the adjuvant compositions. The topics were separated into two main categories and four sub-categories, each sub-category assigned to a different team member/group. The two categories and four sub-categories were:

- 1) Immuno-stimulatory compositions
  - a) Endogenous
  - b) Exogenous
- 2) Chemical Compositions
  - a) Organic
  - b) Inorganic

Recent literature and a synonym list developed from the Summer Course were utilized to determine keywords. These keywords were then used to do preliminary searches on Thomson Innovation and/or the USPTO. The initial keywords used in the two main categories in the search rounds were:

<b>Adjuvant</b>	<b>HIV</b>	<b>Vaccine</b>
Delivery System	HIV Vaccine	Therapy
Antigen Delivery System	Infection	Immunizing
Vaccine	Immunogenicity	Immunoenhancing
Emulsions	Immuno-compromised	Immune Response
Immune System	Immunodeficiency	Immunotherapy
Particulate	Infection	Recombinant Protein Vaccine

Particulate Antigen Delivery Systems	Immunostimulatory	Immunization
Cytokines	Retro-virus	Efficacy of Vaccine
Mucosal Immunization	Lentivirus	Immunological compound
Nano-beads	Toll-like receptors	Antibody
Microorganism-derived	Immunodeficiency Virus	Counteragent
Liposomes	Human Immunodeficiency Virus	Antigen
Lipid Particles	Gp 120	Vaccinum
Tensoactive Compounds	Retrovirus	Immunogen
Enhancer	Pathogen Associated Molecular Patterns	Immunizing Agent
Depot Formation	Pathogen Recognition Receptors	Additive
T-Cell Response	Cell Mediated Immunity	Lipid Particles
Catalyst	Peptide	SAF
Montanides	Mineral Oil	ISCOMs
MPL	Immunospecific	AS01
QS21	Immunoefector	TLR-9 ISS
CpG	Immunizing	TLR-9 IMO
Costimulatory Molecules	Viral Infection	TLR-7/9
Microparticles	Virus Infection	Chemokines

The teams then commenced an intense three-month journey of patent searching and coding. Thomson Innovation was the primary patent searching database used by the team members.

These searches utilized keywords derived from the literature reviewed and initial searches to generate useful search strings; the searches also used United State Patent Classifications and International Patent Classifications that were identified through subsequent searches and team meetings. The combination of keywords and classifications in search strings was useful for parsing the technology into compartments and allowing each team member to generate a different set of search results that keywords alone could not provide. This approach generated a broad set of patents. From here, keywords and classifications generated from this broad set of patents were used in subsequent rounds of searching. After each round of searching, team meetings would identify the most important keywords, and classifications for use in subsequent search strings that became more defined and effective.

Many of these keywords were searched using the search field of “Title, Abstract and Claims” within Thomson Innovation since searches under the field of “Description” or “Specification” were found to be too broad. It was useful to limit each search using the specific Adjuvant terms under the search field of “Claims”. The keywords above were then combined with U.S. Classifications and subclasses, International patent classifications and subclasses to generate different sets of search results. Some of the most common classifications used were US Classifications 424, 435, 514, 530, 535 and 536, IPC Codes A61K 38, A61K 39, A61K 45, A61K 47, A61N 1, C07, and K61K.

During the brainstorming session, the Clinic also decided to use the Non Human Primate HIV/SIV Vaccine Trial online database (LANL), to generate a list of specific adjuvants known to be used in HIV vaccines.<sup>195</sup> The LANL list is shown in Appendix G.

During the course of our brainstorming, the ITTI team came across a new technology, Lexis Nexus Semantic Searching®. Lexis Nexus Semantic Searching® proposed that utilizing the system would result in more precise and relevant patents. Lexis Nexus Semantic Searching® combines semantic search technology with familiar Boolean search technology, which gives the users greater control over the patent research process via a simple, streamlined user interface that matches their typical daily workflow. The results from our search are depicted in Appendix H.

## 2. Patent Search Results

The search strings gave us an outcome of more than 3,500 patents.

### 2. A. Patent Search Tables

(Note: the following search tables are a part of the whole search tables for this project which is included in the attached DVD disc.)

#### Search Round #4

Database	Thomson Innovation (DWPI)
Classification	Not Applicable
Search String	ALLD=(Hiv or GP ADJ 120 or HIV ADJ vaccine or Human ADJ Immunodeficiency ADJ virus or Immunodeficiency or Immunodeficiency ADJ virus or Immunocompromised or Immuno ADJ compromised or Immunogenicity or Immunostimulatory or Infection or Lentivirus or Retrovirus or Toll ADJ like ADJ receptors or Viral ADJ infection or Virus ADJ infection) AND ALLD=(Adjuvant or Additive or Antigen ADJ delivery ADJ system or AS01 or Catalyst or Chemokines or Costimulatory ADJ molecules or CpG or Cytokines or delivery ADJ system or Depot ADJ formation or Emulsions or Enhancer or Immune ADJ systems or ISCOMs or Lipid ADJ particles or Liposomes or Microorganism ADJ derived or Microparticles or Montanides or Mucosal ADJ immunizations or Particulate ADJ antigen ADJ delivery ADJ systems or T ADJ cell ADJ response) AND ALLD=(Vaccine or Antibody or Antigen or Counteragent or Efficacy ADJ of ADJ vaccines or Immune ADJ response or Immunization or Immunizing or Immunizing ADJ agent or Immunoenhancing or Immunogen or Immunological ADJ compound or Immunotherapy or Recombinant ADJ protein ADJ vaccine or Therapy or Vaccinum) AND ALLD=(RIBI);
Results	Total Results = 32 hits

Database	Thomson Innovation (DWPI)
Classification	Not Applicable
Search String	ALLD=(Hiv or GP ADJ 120 or HIV ADJ vaccine or Human ADJ Immunodeficiency ADJ virus or Immunodeficiency or Immunodeficiency ADJ virus or Immunocompromised or Immuno ADJ compromised or Immunogenicity or Immunostimulatory or Infection or Lentivirus or Retrovirus or Toll ADJ like ADJ receptors or Viral ADJ infection or Virus ADJ infection) AND ALLD=(Adjuvant or Additive or Antigen ADJ delivery ADJ system or AS01 or Catalyst or Chemokines or Costimulatory ADJ molecules or CpG or Cytokines or delivery ADJ system or Depot ADJ formation or Emulsions or Enhancer or Immune ADJ systems or ISCOMs or Lipid ADJ particles or Liposomes or Microorganism ADJ derived or Microparticles or Montanides or Mucosal ADJ immunizations or Particulate ADJ antigen ADJ delivery ADJ systems or T ADJ cell

<sup>195</sup> [http://www.hiv.lanl.gov/cgi-bin/vaccine/search/adjuvant\\_search.cgi?search\\_string=&process=Go](http://www.hiv.lanl.gov/cgi-bin/vaccine/search/adjuvant_search.cgi?search_string=&process=Go)

	ADJ response) AND ALLD=(Vaccine or Antibody or Antigen or Counteragent or Efficacy ADJ of ADJ vaccines or Immune ADJ response or Immunization or Immunizing or Immunizing ADJ agent or Immunoenhancing or Immunogen or Immunological ADJ compound or Immunotherapy or Recombinant ADJ protein ADJ vaccine or Therapy or Vaccinum) AND ALLD=(Quil adj A or quila);
Results	Total Results = 75 hits

Database	Thomson Innovation (DWPI)
Classification	Not Applicable
Search String	ALLD=(Hiv or GP ADJ 120 or HIV ADJ vaccine or Human ADJ Immunodeficiency ADJ virus or Immunodeficiency or Immunodeficiency ADJ virus or Immunocompromised or Immuno ADJ compromised or Immunogenicity or Immunostimulatory or Infection or Lentivirus or Retrovirus or Toll ADJ like ADJ receptors or Viral ADJ infection or Virus ADJ infection) AND ALLD=(Adjuvant or Additive or Antigen ADJ delivery ADJ system or AS01 or Catalyst or Chemokines or Costimulatory ADJ molecules or CpG or Cytokines or delivery ADJ system or Depot ADJ formation or Emulsions or Enhancer or Immune ADJ systems or ISCOMs or Lipid ADJ particles or Liposomes or Microorganism ADJ derived or Microparticles or Montanides or Mucosal ADJ immunizations or Particulate ADJ antigen ADJ delivery ADJ systems or T ADJ cell ADJ response) AND ALLD=(Vaccine or Antibody or Antigen or Counteragent or Efficacy ADJ of ADJ vaccines or Immune ADJ response or Immunization or Immunizing or Immunizing ADJ agent or Immunoenhancing or Immunogen or Immunological ADJ compound or Immunotherapy or Recombinant ADJ protein ADJ vaccine or Therapy or Vaccinum) AND ALLD=(QS adj 21 or QS ADJ 21 or QS21);
Results	Total Results = 172 hits

Database	Thomson Innovation (DWPI)
Classification	Not Applicable
Search String	ALLD=(Hiv or GP ADJ 120 or HIV ADJ vaccine or Human ADJ Immunodeficiency ADJ virus or Immunodeficiency or Immunodeficiency ADJ virus or Immunocompromised or Immuno ADJ compromised or Immunogenicity or Immunostimulatory or Infection or Lentivirus or Retrovirus or Toll ADJ like ADJ receptors or Viral ADJ infection or Virus ADJ infection) AND ALLD=(Adjuvant or Additive or Antigen ADJ delivery ADJ system or AS01 or Catalyst or Chemokines or Costimulatory ADJ molecules or CpG or Cytokines or delivery ADJ system or Depot ADJ formation or Emulsions or Enhancer or Immune ADJ systems or ISCOMs or Lipid ADJ particles or Liposomes or Microorganism ADJ derived or Microparticles or Montanides or Mucosal ADJ immunizations or Particulate ADJ antigen ADJ delivery ADJ systems or T ADJ cell ADJ response) AND ALLD=(Vaccine or Antibody or Antigen or Counteragent or Efficacy ADJ of ADJ vaccines or Immune ADJ response or Immunization or Immunizing or Immunizing ADJ agent or Immunoenhancing or Immunogen or Immunological ADJ compound or Immunotherapy or Recombinant ADJ protein ADJ vaccine or Therapy or Vaccinum) AND ALLD=(protein ADJ cochleate*);
Results	Total Results = 9 hits

Database	Thomson Innovation (DWPI)
Classification	Not Applicable
Search String	ALLD=(Hiv or GP ADJ 120 or HIV ADJ vaccine or Human ADJ Immunodeficiency ADJ virus or Immunodeficiency or Immunodeficiency ADJ virus or Immunocompromised or Immuno ADJ compromised or Immunogenicity or Immunostimulatory or Infection or Lentivirus or Retrovirus or Toll ADJ like ADJ receptors or Viral ADJ infection or Virus ADJ infection) AND ALLD=(Adjuvant or Additive or Antigen ADJ delivery ADJ system or AS01 or Catalyst or Chemokines or Costimulatory ADJ molecules or CpG or Cytokines or delivery ADJ system or Depot ADJ formation or Emulsions or Enhancer or Immune ADJ systems or ISCOMs or Lipid ADJ particles or Liposomes or Microorganism ADJ derived or Microparticles or Montanides or Mucosal ADJ immunizations or Particulate ADJ antigen ADJ delivery ADJ systems or T ADJ cell

	ADJ response) AND ALLD=(Vaccine or Antibody or Antigen or Counteragent or Efficacy ADJ of ADJ vaccines or Immune ADJ response or Immunization or Immunizing or Immunizing ADJ agent or Immunoenhancing or Immunogen or Immunological ADJ compound or Immunotherapy or Recombinant ADJ protein ADJ vaccine or Therapy or Vaccinum) AND ALLD=(polysorbate ADJ 80 or polysorbate);
Results	Total Results = 47 hits

Database	Thomson Innovation (DWPI)
Classification	Not Applicable
Search String	ALLD=(Hiv or GP ADJ 120 or HIV ADJ vaccine or Human ADJ Immunodeficiency ADJ virus or Immunodeficiency or Immunodeficiency ADJ virus or Immunocompromised or Immuno ADJ compromised or Immunogenicity or Immunostimulatory or Infection or Lentivirus or Retrovirus or Toll ADJ like ADJ receptors or Viral ADJ infection or Virus ADJ infection) AND ALLD=(Adjuvant or Additive or Antigen ADJ delivery ADJ system or AS01 or Catalyst or Chemokines or Costimulatory ADJ molecules or CpG or Cytokines or delivery ADJ system or Depot ADJ formation or Emulsions or Enhancer or Immune ADJ systems or ISCOMs or Lipid ADJ particles or Liposomes or Microorganism ADJ derived or Microparticles or Montanides or Mucosal ADJ immunizations or Particulate ADJ antigen ADJ delivery ADJ systems or T ADJ cell ADJ response) AND ALLD=(Vaccine or Antibody or Antigen or Counteragent or Efficacy ADJ of ADJ vaccines or Immune ADJ response or Immunization or Immunizing or Immunizing ADJ agent or Immunoenhancing or Immunogen or Immunological ADJ compound or Immunotherapy or Recombinant ADJ protein ADJ vaccine or Therapy or Vaccinum) AND ALLD=(Poly ADJ C);
Results	Total Results = 16 hits

Database	Thomson Innovation (DWPI)
Classification	Not Applicable
Search String	ALLD=(Hiv or GP ADJ 120 or HIV ADJ vaccine or Human ADJ Immunodeficiency ADJ virus or Immunodeficiency or Immunodeficiency ADJ virus or Immunocompromised or Immuno ADJ compromised or Immunogenicity or Immunostimulatory or Infection or Lentivirus or Retrovirus or Toll ADJ like ADJ receptors or Viral ADJ infection or Virus ADJ infection) AND ALLD=(Adjuvant or Additive or Antigen ADJ delivery ADJ system or AS01 or Catalyst or Chemokines or Costimulatory ADJ molecules or CpG or Cytokines or delivery ADJ system or Depot ADJ formation or Emulsions or Enhancer or Immune ADJ systems or ISCOMs or Lipid ADJ particles or Liposomes or Microorganism ADJ derived or Microparticles or Montanides or Mucosal ADJ immunizations or Particulate ADJ antigen ADJ delivery ADJ systems or T ADJ cell ADJ response) AND ALLD=(Vaccine or Antibody or Antigen or Counteragent or Efficacy ADJ of ADJ vaccines or Immune ADJ response or Immunization or Immunizing or Immunizing ADJ agent or Immunoenhancing or Immunogen or Immunological ADJ compound or Immunotherapy or Recombinant ADJ protein ADJ vaccine or Therapy or Vaccinum) AND ALLD=(Poly ADJ rA or Poly ADJ R ADJ A or PolyRA or Poly ADJ rU or Poly ADJ R ADJ U or PolyRU);
Results	Total Results = 10 hits

Database	Thomson Innovation (DWPI)
Classification	Not Applicable
Search String	ALLD=(Hiv or GP ADJ 120 or HIV ADJ vaccine or Human ADJ Immunodeficiency ADJ virus or Immunodeficiency or Immunodeficiency ADJ virus or Immunocompromised or Immuno ADJ compromised or Immunogenicity or Immunostimulatory or Infection or Lentivirus or Retrovirus or Toll ADJ like ADJ receptors or Viral ADJ infection or Virus ADJ infection) AND ALLD=(Adjuvant or Additive or Antigen ADJ delivery ADJ system or AS01 or Catalyst or Chemokines or Costimulatory ADJ molecules or CpG or Cytokines or delivery ADJ system or Depot ADJ formation or Emulsions or Enhancer or Immune ADJ systems or ISCOMs or Lipid ADJ particles or Liposomes or Microorganism ADJ derived or Microparticles or Montanides or Mucosal ADJ immunizations or Particulate ADJ antigen ADJ delivery ADJ systems or T ADJ cell ADJ response) AND ALLD=(Vaccine or Antibody or Antigen or Counteragent or Efficacy ADJ

	of ADJ vaccines or Immune ADJ response or Immunization or Immunizing or Immunizing ADJ agent or Immunoenhancing or Immunogen or Immunological ADJ compound or Immunotherapy or Recombinant ADJ protein ADJ vaccine or Therapy or Vaccinum) AND ALLD=(PODDS or PODD);
Results	Total Results = 7 hits

Database	Thomson Innovation (DWPI)
Classification	Not Applicable
Search String	ALLD=(Hiv or GP ADJ 120 or HIV ADJ vaccine or Human ADJ Immunodeficiency ADJ virus or Immunodeficiency or Immunodeficiency ADJ virus or Immunocompromised or Immuno ADJ compromised or Immunogenicity or Immunostimulatory or Infection or Lentivirus or Retrovirus or Toll ADJ like ADJ receptors or Viral ADJ infection or Virus ADJ infection) AND ALLD=(Adjuvant or Additive or Antigen ADJ delivery ADJ system or AS01 or Catalyst or Chemokines or Costimulatory ADJ molecules or CpG or Cytokines or delivery ADJ system or Depot ADJ formation or Emulsions or Enhancer or Immune ADJ systems or ISCOMs or Lipid ADJ particles or Liposomes or Microorganism ADJ derived or Microparticles or Montanides or Mucosal ADJ immunizations or Particulate ADJ antigen ADJ delivery ADJ systems or T ADJ cell ADJ response) AND ALLD=(Vaccine or Antibody or Antigen or Counteragent or Efficacy ADJ of ADJ vaccines or Immune ADJ response or Immunization or Immunizing or Immunizing ADJ agent or Immunoenhancing or Immunogen or Immunological ADJ compound or Immunotherapy or Recombinant ADJ protein ADJ vaccine or Therapy or Vaccinum) AND ALLD=(PMMA);
Results	Total Results = 10 hits

Database	Thomson Innovation (DWPI)
Classification	Not Applicable
Search String	ALLD=(Hiv or GP ADJ 120 or HIV ADJ vaccine or Human ADJ Immunodeficiency ADJ virus or Immunodeficiency or Immunodeficiency ADJ virus or Immunocompromised or Immuno ADJ compromised or Immunogenicity or Immunostimulatory or Infection or Lentivirus or Retrovirus or Toll ADJ like ADJ receptors or Viral ADJ infection or Virus ADJ infection) AND ALLD=(Adjuvant or Additive or Antigen ADJ delivery ADJ system or AS01 or Catalyst or Chemokines or Costimulatory ADJ molecules or CpG or Cytokines or delivery ADJ system or Depot ADJ formation or Emulsions or Enhancer or Immune ADJ systems or ISCOMs or Lipid ADJ particles or Liposomes or Microorganism ADJ derived or Microparticles or Montanides or Mucosal ADJ immunizations or Particulate ADJ antigen ADJ delivery ADJ systems or T ADJ cell ADJ response) AND ALLD=(Vaccine or Antibody or Antigen or Counteragent or Efficacy ADJ of ADJ vaccines or Immune ADJ response or Immunization or Immunizing or Immunizing ADJ agent or Immunoenhancing or Immunogen or Immunological ADJ compound or Immunotherapy or Recombinant ADJ protein ADJ vaccine or Therapy or Vaccinum) AND ALLD=(Pluronic ADJ L121 or pluronic or pluronic ADJ L ADJ 121);
Results	Total Results = 37 hits

Database	Thomson Innovation (DWPI)
Classification	Not Applicable
Search String	ALLD=(Hiv or GP ADJ 120 or HIV ADJ vaccine or Human ADJ Immunodeficiency ADJ virus or Immunodeficiency or Immunodeficiency ADJ virus or Immunocompromised or Immuno ADJ compromised or Immunogenicity or Immunostimulatory or Infection or Lentivirus or Retrovirus or Toll ADJ like ADJ receptors or Viral ADJ infection or Virus ADJ infection) AND ALLD=(Adjuvant or Additive or Antigen ADJ delivery ADJ system or AS01 or Catalyst or Chemokines or Costimulatory ADJ molecules or CpG or Cytokines or delivery ADJ system or Depot ADJ formation or Emulsions or Enhancer or Immune ADJ systems or ISCOMs or Lipid ADJ particles or Liposomes or Microorganism ADJ derived or Microparticles or Montanides or Mucosal ADJ immunizations or Particulate ADJ antigen ADJ delivery ADJ systems or T ADJ cell ADJ response) AND ALLD=(Vaccine or Antibody or Antigen or Counteragent or Efficacy ADJ

	of ADJ vaccines or Immune ADJ response or Immunization or Immunizing or Immunizing ADJ agent or Immunoenhancing or Immunogen or Immunological ADJ compound or Immunotherapy or Recombinant ADJ protein ADJ vaccine or Therapy or Vaccinum) AND ALLD=(PLG or PLGA or PGA or PLA);
Results	Total Results = 76 hits

Database	Thomson Innovation (DWPI)
Classification	Not Applicable
Search String	ALLD=(Hiv or GP ADJ 120 or HIV ADJ vaccine or Human ADJ Immunodeficiency ADJ virus or Immunodeficiency or Immunodeficiency ADJ virus or Immunocompromised or Immuno ADJ compromised or Immunogenicity or Immunostimulatory or Infection or Lentivirus or Retrovirus or Toll ADJ like ADJ receptors or Viral ADJ infection or Virus ADJ infection) AND ALLD=(Adjuvant or Additive or Antigen ADJ delivery ADJ system or AS01 or Catalyst or Chemokines or Costimulatory ADJ molecules or CpG or Cytokines or delivery ADJ system or Depot ADJ formation or Emulsions or Enhancer or Immune ADJ systems or ISCOMs or Lipid ADJ particles or Liposomes or Microorganism ADJ derived or Microparticles or Montanides or Mucosal ADJ immunizations or Particulate ADJ antigen ADJ delivery ADJ systems or T ADJ cell ADJ response) AND ALLD=(Vaccine or Antibody or Antigen or Counteragent or Efficacy ADJ of ADJ vaccines or Immune ADJ response or Immunization or Immunizing or Immunizing ADJ agent or Immunoenhancing or Immunogen or Immunological ADJ compound or Immunotherapy or Recombinant ADJ protein ADJ vaccine or Therapy or Vaccinum) AND ALLD=(MPL ADJ SE or MPL adj SE);
Results	Total Results = 1 hits

Database	Thomson Innovation (DWPI)
Classification	Not Applicable
Search String	ALLD=(Hiv or GP ADJ 120 or HIV ADJ vaccine or Human ADJ Immunodeficiency ADJ virus or Immunodeficiency or Immunodeficiency ADJ virus or Immunocompromised or Immuno ADJ compromised or Immunogenicity or Immunostimulatory or Infection or Lentivirus or Retrovirus or Toll ADJ like ADJ receptors or Viral ADJ infection or Virus ADJ infection) AND ALLD=(Adjuvant or Additive or Antigen ADJ delivery ADJ system or AS01 or Catalyst or Chemokines or Costimulatory ADJ molecules or CpG or Cytokines or delivery ADJ system or Depot ADJ formation or Emulsions or Enhancer or Immune ADJ systems or ISCOMs or Lipid ADJ particles or Liposomes or Microorganism ADJ derived or Microparticles or Montanides or Mucosal ADJ immunizations or Particulate ADJ antigen ADJ delivery ADJ systems or T ADJ cell ADJ response) AND ALLD=(Vaccine or Antibody or Antigen or Counteragent or Efficacy ADJ of ADJ vaccines or Immune ADJ response or Immunization or Immunizing or Immunizing ADJ agent or Immunoenhancing or Immunogen or Immunological ADJ compound or Immunotherapy or Recombinant ADJ protein ADJ vaccine or Therapy or Vaccinum) AND ALLD=(nago or n ADJ a ADJ g ADJ o);
Results	Total Results = 9 hits

Database	Thomson Innovation (DWPI)
Classification	Not Applicable
Search String	ALLD=(Hiv or GP ADJ 120 or HIV ADJ vaccine or Human ADJ Immunodeficiency ADJ virus or Immunodeficiency or Immunodeficiency ADJ virus or Immunocompromised or Immuno ADJ compromised or Immunogenicity or Immunostimulatory or Infection or Lentivirus or Retrovirus or Toll ADJ like ADJ receptors or Viral ADJ infection or Virus ADJ infection) AND ALLD=(Adjuvant or Additive or Antigen ADJ delivery ADJ system or AS01 or Catalyst or Chemokines or Costimulatory ADJ molecules or CpG or Cytokines or delivery ADJ system or Depot ADJ formation or Emulsions or Enhancer or Immune ADJ systems or ISCOMs or Lipid ADJ particles or Liposomes or Microorganism ADJ derived or Microparticles or Montanides or Mucosal ADJ immunizations or Particulate ADJ antigen ADJ delivery ADJ systems or T ADJ cell

	ADJ response) AND ALLD=(Vaccine or Antibody or Antigen or Counteragent or Efficacy ADJ of ADJ vaccines or Immune ADJ response or Immunization or Immunizing or Immunizing ADJ agent or Immunoenhancing or Immunogen or Immunological ADJ compound or Immunotherapy or Recombinant ADJ protein ADJ vaccine or Therapy or Vaccinum) AND ALLD=(Murapalmitine);
Results	Total Results = 11 hits

Database	Thomson Innovation (DWPI)
Classification	Not Applicable
Search String	ALLD=(Hiv or GP ADJ 120 or HIV ADJ vaccine or Human ADJ Immunodeficiency ADJ virus or Immunodeficiency or Immunodeficiency ADJ virus or Immunocompromised or Immuno ADJ compromised or Immunogenicity or Immunostimulatory or Infection or Lentivirus or Retrovirus or Toll ADJ like ADJ receptors or Viral ADJ infection or Virus ADJ infection) AND ALLD=(Adjuvant or Additive or Antigen ADJ delivery ADJ system or AS01 or Catalyst or Chemokines or Costimulatory ADJ molecules or CpG or Cytokines or delivery ADJ system or Depot ADJ formation or Emulsions or Enhancer or Immune ADJ systems or ISCOMs or Lipid ADJ particles or Liposomes or Microorganism ADJ derived or Microparticles or Montanides or Mucosal ADJ immunizations or Particulate ADJ antigen ADJ delivery ADJ systems or T ADJ cell ADJ response) AND ALLD=(Vaccine or Antibody or Antigen or Counteragent or Efficacy ADJ of ADJ vaccines or Immune ADJ response or Immunization or Immunizing or Immunizing ADJ agent or Immunoenhancing or Immunogen or Immunological ADJ compound or Immunotherapy or Recombinant ADJ protein ADJ vaccine or Therapy or Vaccinum) AND ALLD=(mtp adj pe ADJ liposome* or mtp ADJ pe ADJ liposome*);
Results	Total Results = 7 hits

Database	Thomson Innovation (Korean Utility, Korean Application, Korean Grant)
Classification	Not Applicable
Search String	ALL=(Vaccine or Antibody or Antigen or Counteragent or Efficacy ADJ of ADJ vaccines or Immune ADJ response or Immunization or Immunizing or Immunizing ADJ agent or Immunoenhancing or Immunogen or Immunological ADJ compound or Immunotherapy or Recombinant ADJ protein ADJ vaccine or Therapy or Vaccinum) AND CTB=(Adjuvant or Additive or Antigen ADJ delivery ADJ system or AS01 or Catalyst or Chemokines or Costimulatory ADJ molecules or CpG or Cytokines or delivery ADJ system or Depot ADJ formation or Emulsions or Enhancer or Immune ADJ systems or ISCOMs or Lipid ADJ particles or Liposomes or Microorganism ADJ derived or Microparticles or Montanides or Mucosal ADJ immunizations or Particulate ADJ antigen ADJ delivery ADJ systems or T ADJ cell ADJ response) AND CTB=(Hiv or GP ADJ 120 or HIV ADJ vaccine or Human ADJ Immunodeficiency ADJ virus or Immunodeficiency or Immunodeficiency ADJ virus or Immunocompromised or Immuno ADJ compromised or Immunogenicity or Immunostimulatory or Infection or Lentivirus or Retrovirus or Toll ADJ like ADJ receptors or Viral ADJ infection or Virus ADJ infection) AND DSC=(Adjuvant or Additive or Antigen ADJ delivery ADJ system or AS01 or Catalyst or Chemokines or Costimulatory ADJ molecules or CpG or Cytokines or delivery ADJ system or Depot ADJ formation or Emulsions or Enhancer or Immune ADJ systems or ISCOMs or Lipid ADJ particles or Liposomes or Microorganism ADJ derived or Microparticles or Montanides or Mucosal ADJ immunizations or Particulate ADJ antigen ADJ delivery ADJ systems or T ADJ cell ADJ response) AND DSC=(Hiv or GP ADJ 120 or HIV ADJ vaccine or Human ADJ Immunodeficiency ADJ virus or Immunodeficiency or Immunodeficiency ADJ virus or Immunocompromised or Immuno ADJ compromised or Immunogenicity or Immunostimulatory or Infection or Lentivirus or Retrovirus or Toll ADJ like ADJ receptors or Viral ADJ infection or Virus ADJ infection) AND ALL=((MTP adj PE or (MTP ADJ PE) or (MTP-PE ADJ Liposome*) or (MTP ADJ PE ADJ Liposome*)));
Results	Total Results = 10 hits

Database	Thomson Innovation (Japanese Utility, Japanese Grant, Japanese Application)
Classification	Not Applicable

Search String	ALL=(Vaccine or Antibody or Antigen or Counteragent or Efficacy ADJ of ADJ vaccines or Immune ADJ response or Immunization or Immunizing or Immunizing ADJ agent or Immunoenhancing or Immunogen or Immunological ADJ compound or Immunotherapy or Recombinant ADJ protein ADJ vaccine or Therapy or Vaccinum) AND CTB=(Adjuvant or Additive or Antigen ADJ delivery ADJ system or AS01 or Catalyst or Chemokines or Costimulatory ADJ molecules or CpG or Cytokines or delivery ADJ system or Depot ADJ formation or Emulsions or Enhancer or Immune ADJ systems or ISCOMs or Lipid ADJ particles or Liposomes or Microorganism ADJ derived or Microparticles or Montanides or Mucosal ADJ immunizations or Particulate ADJ antigen ADJ delivery ADJ systems or T ADJ cell ADJ response) AND CTB=(Hiv or GP ADJ 120 or HIV ADJ vaccine or Human ADJ Immunodeficiency ADJ virus or Immunodeficiency or Immunodeficiency ADJ virus or Immunocompromised or Immuno ADJ compromised or Immunogenicity or Immunostimulatory or Infection or Lentivirus or Retrovirus or Toll ADJ like ADJ receptors or Viral ADJ infection or Virus ADJ infection) AND DSC=(Adjuvant or Additive or Antigen ADJ delivery ADJ system or AS01 or Catalyst or Chemokines or Costimulatory ADJ molecules or CpG or Cytokines or delivery ADJ system or Depot ADJ formation or Emulsions or Enhancer or Immune ADJ systems or ISCOMs or Lipid ADJ particles or Liposomes or Microorganism ADJ derived or Microparticles or Montanides or Mucosal ADJ immunizations or Particulate ADJ antigen ADJ delivery ADJ systems or T ADJ cell ADJ response) AND DSC=(Hiv or GP ADJ 120 or HIV ADJ vaccine or Human ADJ Immunodeficiency ADJ virus or Immunodeficiency or Immunodeficiency ADJ virus or Immunocompromised or Immuno ADJ compromised or Immunogenicity or Immunostimulatory or Infection or Lentivirus or Retrovirus or Toll ADJ like ADJ receptors or Viral ADJ infection or Virus ADJ infection) AND ALL=((MTP adj PE or (MTP ADJ PE) or (MTP-PE ADJ Liposome*) or (MTP ADJ PE ADJ Lipsome*)));
Results	Total Results = 20hits

Database	Thomson Innovation (US Application, US Patent)
Classification	Not Applicable
Search String	ALL=(Vaccine or Antibody or Antigen or Counteragent or Efficacy ADJ of ADJ vaccines or Immune ADJ response or Immunization or Immunizing or Immunizing ADJ agent or Immunoenhancing or Immunogen or Immunological ADJ compound or Immunotherapy or Recombinant ADJ protein ADJ vaccine or Therapy or Vaccinum) AND CTB=(Adjuvant or Additive or Antigen ADJ delivery ADJ system or AS01 or Catalyst or Chemokines or Costimulatory ADJ molecules or CpG or Cytokines or delivery ADJ system or Depot ADJ formation or Emulsions or Enhancer or Immune ADJ systems or ISCOMs or Lipid ADJ particles or Liposomes or Microorganism ADJ derived or Microparticles or Montanides or Mucosal ADJ immunizations or Particulate ADJ antigen ADJ delivery ADJ systems or T ADJ cell ADJ response) AND CTB=(Hiv or GP ADJ 120 or HIV ADJ vaccine or Human ADJ Immunodeficiency ADJ virus or Immunodeficiency or Immunodeficiency ADJ virus or Immunocompromised or Immuno ADJ compromised or Immunogenicity or Immunostimulatory or Infection or Lentivirus or Retrovirus or Toll ADJ like ADJ receptors or Viral ADJ infection or Virus ADJ infection) AND DSC=(Adjuvant or Additive or Antigen ADJ delivery ADJ system or AS01 or Catalyst or Chemokines or Costimulatory ADJ molecules or CpG or Cytokines or delivery ADJ system or Depot ADJ formation or Emulsions or Enhancer or Immune ADJ systems or ISCOMs or Lipid ADJ particles or Liposomes or Microorganism ADJ derived or Microparticles or Montanides or Mucosal ADJ immunizations or Particulate ADJ antigen ADJ delivery ADJ systems or T ADJ cell ADJ response) AND DSC=(Hiv or GP ADJ 120 or HIV ADJ vaccine or Human ADJ Immunodeficiency ADJ virus or Immunodeficiency or Immunodeficiency ADJ virus or Immunocompromised or Immuno ADJ compromised or Immunogenicity or Immunostimulatory or Infection or Lentivirus or Retrovirus or Toll ADJ like ADJ receptors or Viral ADJ infection or Virus ADJ infection) AND ALL=((MTP adj PE or (MTP ADJ PE) or (MTP-PE ADJ Liposome*) or (MTP ADJ PE ADJ Lipsome*)));
Results	Total Results = 280 hits

Database	Thomson Innovation (Korean Grant, Korean Application, Korean Utility)
----------	---

Classification	Not Applicable
Search String	ALL=(Vaccine or Antibody or Antigen or Counteragent or Efficacy ADJ of ADJ vaccines or Immune ADJ response or Immunization or Immunizing or Immunizing ADJ agent or Immunoenhancing or Immunogen or Immunological ADJ compound or Immunotherapy or Recombinant ADJ protein ADJ vaccine or Therapy or Vaccinum) AND CTB=(Adjuvant or Additive or Antigen ADJ delivery ADJ system or AS01 or Catalyst or Chemokines or Costimulatory ADJ molecules or CpG or Cytokines or delivery ADJ system or Depot ADJ formation or Emulsions or Enhancer or Immune ADJ systems or ISCOMs or Lipid ADJ particles or Liposomes or Microorganism ADJ derived or Microparticles or Montanides or Mucosal ADJ immunizations or Particulate ADJ antigen ADJ delivery ADJ systems or T ADJ cell ADJ response) AND CTB=(Hiv or GP ADJ 120 or HIV ADJ vaccine or Human ADJ Immunodeficiency ADJ virus or Immunodeficiency or Immunodeficiency ADJ virus or Immunocompromised or Immuno ADJ compromised or Immunogenicity or Immunostimulatory or Infection or Lentivirus or Retrovirus or Toll ADJ like ADJ receptors or Viral ADJ infection or Virus ADJ infection) AND DSC=(Adjuvant or Additive or Antigen ADJ delivery ADJ system or AS01 or Catalyst or Chemokines or Costimulatory ADJ molecules or CpG or Cytokines or delivery ADJ system or Depot ADJ formation or Emulsions or Enhancer or Immune ADJ systems or ISCOMs or Lipid ADJ particles or Liposomes or Microorganism ADJ derived or Microparticles or Montanides or Mucosal ADJ immunizations or Particulate ADJ antigen ADJ delivery ADJ systems or T ADJ cell ADJ response) AND DSC=(Hiv or GP ADJ 120 or HIV ADJ vaccine or Human ADJ Immunodeficiency ADJ virus or Immunodeficiency or Immunodeficiency ADJ virus or Immunocompromised or Immuno ADJ compromised or Immunogenicity or Immunostimulatory or Infection or Lentivirus or Retrovirus or Toll ADJ like ADJ receptors or Viral ADJ infection or Virus ADJ infection) AND ALL=(MPL adj SE or MPL ADJ SE);
Results	Total Results = 3 hits

Database	Thomson Innovation (WIPO Application)
Classification	Not Applicable
Search String	ALL=(Vaccine or Antibody or Antigen or Counteragent or Efficacy ADJ of ADJ vaccines or Immune ADJ response or Immunization or Immunizing or Immunizing ADJ agent or Immunoenhancing or Immunogen or Immunological ADJ compound or Immunotherapy or Recombinant ADJ protein ADJ vaccine or Therapy or Vaccinum) AND CTB=(Adjuvant or Additive or Antigen ADJ delivery ADJ system or AS01 or Catalyst or Chemokines or Costimulatory ADJ molecules or CpG or Cytokines or delivery ADJ system or Depot ADJ formation or Emulsions or Enhancer or Immune ADJ systems or ISCOMs or Lipid ADJ particles or Liposomes or Microorganism ADJ derived or Microparticles or Montanides or Mucosal ADJ immunizations or Particulate ADJ antigen ADJ delivery ADJ systems or T ADJ cell ADJ response) AND CTB=(Hiv or GP ADJ 120 or HIV ADJ vaccine or Human ADJ Immunodeficiency ADJ virus or Immunodeficiency or Immunodeficiency ADJ virus or Immunocompromised or Immuno ADJ compromised or Immunogenicity or Immunostimulatory or Infection or Lentivirus or Retrovirus or Toll ADJ like ADJ receptors or Viral ADJ infection or Virus ADJ infection) AND DSC=(Adjuvant or Additive or Antigen ADJ delivery ADJ system or AS01 or Catalyst or Chemokines or Costimulatory ADJ molecules or CpG or Cytokines or delivery ADJ system or Depot ADJ formation or Emulsions or Enhancer or Immune ADJ systems or ISCOMs or Lipid ADJ particles or Liposomes or Microorganism ADJ derived or Microparticles or Montanides or Mucosal ADJ immunizations or Particulate ADJ antigen ADJ delivery ADJ systems or T ADJ cell ADJ response) AND DSC=(Hiv or GP ADJ 120 or HIV ADJ vaccine or Human ADJ Immunodeficiency ADJ virus or Immunodeficiency or Immunodeficiency ADJ virus or Immunocompromised or Immuno ADJ compromised or Immunogenicity or Immunostimulatory or Infection or Lentivirus or Retrovirus or Toll ADJ like ADJ receptors or Viral ADJ infection or Virus ADJ infection) AND ALL=(MPL adj SE or MPL ADJ SE);
Results	Total Results = 15 hits

Database	Thomson Innovation (EPO Application, EPO Grant)
Classification	Not Applicable

Search String	ALL=(Vaccine or Antibody or Antigen or Counteragent or Efficacy ADJ of ADJ vaccines or Immune ADJ response or Immunization or Immunizing or Immunizing ADJ agent or Immunoenhancing or Immunogen or Immunological ADJ compound or Immunotherapy or Recombinant ADJ protein ADJ vaccine or Therapy or Vaccinum) AND CTB=(Adjuvant or Additive or Antigen ADJ delivery ADJ system or AS01 or Catalyst or Chemokines or Costimulatory ADJ molecules or CpG or Cytokines or delivery ADJ system or Depot ADJ formation or Emulsions or Enhancer or Immune ADJ systems or ISCOMs or Lipid ADJ particles or Liposomes or Microorganism ADJ derived or Microparticles or Montanides or Mucosal ADJ immunizations or Particulate ADJ antigen ADJ delivery ADJ systems or T ADJ cell ADJ response) AND CTB=(Hiv or GP ADJ 120 or HIV ADJ vaccine or Human ADJ Immunodeficiency ADJ virus or Immunodeficiency or Immunodeficiency ADJ virus or Immunocompromised or Immuno ADJ compromised or Immunogenicity or Immunostimulatory or Infection or Lentivirus or Retrovirus or Toll ADJ like ADJ receptors or Viral ADJ infection or Virus ADJ infection) AND DSC=(Adjuvant or Additive or Antigen ADJ delivery ADJ system or AS01 or Catalyst or Chemokines or Costimulatory ADJ molecules or CpG or Cytokines or delivery ADJ system or Depot ADJ formation or Emulsions or Enhancer or Immune ADJ systems or ISCOMs or Lipid ADJ particles or Liposomes or Microorganism ADJ derived or Microparticles or Montanides or Mucosal ADJ immunizations or Particulate ADJ antigen ADJ delivery ADJ systems or T ADJ cell ADJ response) AND DSC=(Hiv or GP ADJ 120 or HIV ADJ vaccine or Human ADJ Immunodeficiency ADJ virus or Immunodeficiency or Immunodeficiency ADJ virus or Immunocompromised or Immuno ADJ compromised or Immunogenicity or Immunostimulatory or Infection or Lentivirus or Retrovirus or Toll ADJ like ADJ receptors or Viral ADJ infection or Virus ADJ infection) AND ALL=(MPL adj SE or MPL ADJ SE);
Results	Total Results = 4 hits

Database	Thomson Innovation (US Application, US Grant)
Classification	Not Applicable
Search String	ALL=(Vaccine or Antibody or Antigen or Counteragent or Efficacy ADJ of ADJ vaccines or Immune ADJ response or Immunization or Immunizing or Immunizing ADJ agent or Immunoenhancing or Immunogen or Immunological ADJ compound or Immunotherapy or Recombinant ADJ protein ADJ vaccine or Therapy or Vaccinum) AND CTB=(Adjuvant or Additive or Antigen ADJ delivery ADJ system or AS01 or Catalyst or Chemokines or Costimulatory ADJ molecules or CpG or Cytokines or delivery ADJ system or Depot ADJ formation or Emulsions or Enhancer or Immune ADJ systems or ISCOMs or Lipid ADJ particles or Liposomes or Microorganism ADJ derived or Microparticles or Montanides or Mucosal ADJ immunizations or Particulate ADJ antigen ADJ delivery ADJ systems or T ADJ cell ADJ response) AND CTB=(Hiv or GP ADJ 120 or HIV ADJ vaccine or Human ADJ Immunodeficiency ADJ virus or Immunodeficiency or Immunodeficiency ADJ virus or Immunocompromised or Immuno ADJ compromised or Immunogenicity or Immunostimulatory or Infection or Lentivirus or Retrovirus or Toll ADJ like ADJ receptors or Viral ADJ infection or Virus ADJ infection) AND DSC=(Adjuvant or Additive or Antigen ADJ delivery ADJ system or AS01 or Catalyst or Chemokines or Costimulatory ADJ molecules or CpG or Cytokines or delivery ADJ system or Depot ADJ formation or Emulsions or Enhancer or Immune ADJ systems or ISCOMs or Lipid ADJ particles or Liposomes or Microorganism ADJ derived or Microparticles or Montanides or Mucosal ADJ immunizations or Particulate ADJ antigen ADJ delivery ADJ systems or T ADJ cell ADJ response) AND DSC=(Hiv or GP ADJ 120 or HIV ADJ vaccine or Human ADJ Immunodeficiency ADJ virus or Immunodeficiency or Immunodeficiency ADJ virus or Immunocompromised or Immuno ADJ compromised or Immunogenicity or Immunostimulatory or Infection or Lentivirus or Retrovirus or Toll ADJ like ADJ receptors or Viral ADJ infection or Virus ADJ infection) AND ALL=(MPL adj SE or MPL ADJ SE);
Results	Total Results = 17 hits

Database	Thomson Innovation (European Granted / Application)
Classification	Not Applicable

Search String	ALL=((adjuvant* OR Immun* OR Delivery ADJ system* OR Vaccin* OR Additive OR Infect* OR immunostim* OR innocul*) AND (HIV OR Human ADJ Immunodeficiency ADJ Virus)) AND CTB=((adjuvant* or enhancer* AND HIV or AIDS or human ADJ immunodeficiency ADJ virus or autoimmune ADJ deficiency ADJ syndrome));
Results	Total Results = 4077 hits

Database	Thomson Innovation (European Granted / Application)
Classification	Not Applicable
Search String	ALL=((adjuvant* OR Immun* OR Delivery ADJ system* OR Vaccin* OR Additive OR Infect* OR immunostim* OR innocul*) AND (HIV OR Human ADJ Immunodeficiency ADJ Virus))) AND (CL=(adjuvant*)) AND (CL=(adjuvant* and (HIV OR Human ADJ Immunodeficiency ADJ Virus)));
Results	Total Results = 320 hits

Database	Thomson Innovation (German granted / applications / utility)
Classification	Not Applicable
Search String	ALL=((adjuvant* OR Immun* OR Delivery ADJ system* OR Vaccin* OR Additive OR Infect* OR immunostim* OR innocul*) AND (HIV OR Human ADJ Immunodeficiency ADJ Virus)) AND CTB=((adjuvant* or enhancer* AND HIV or AIDS or human ADJ immunodeficiency ADJ virus or autoimmune ADJ deficiency ADJ syndrome));
Results	Total Results = 735 hits

Database	Thomson Innovation (German granted / applications / utility)
Classification	Not Applicable
Search String	ALL=((adjuvant* OR Immun* OR Delivery ADJ system* OR Vaccin* OR Additive OR Infect* OR immunostim* OR innocul*) AND (HIV OR Human ADJ Immunodeficiency ADJ Virus)) AND CL=(adjuvant* and (HIV OR Human ADJ Immunodeficiency ADJ Virus));
Results	Total Results = 12 hits

Database	Thomson Innovation (Japan granted / applications / utility)
Classification	Not Applicable
Search String	ALL=((adjuvant* OR Immun* OR Delivery ADJ system* OR Vaccin* OR Additive OR Infect* OR immunostim* OR innocul*) AND (HIV OR Human ADJ Immunodeficiency ADJ Virus)) AND CTB=((adjuvant* or enhancer* AND HIV or AIDS or human ADJ immunodeficiency ADJ virus or autoimmune ADJ deficiency ADJ syndrome));
Results	Total Results = 807 hits

Database	Thomson Innovation (Japan granted / applications / utility)
Classification	Not Applicable
Search String	ALL=((adjuvant* OR Immun* OR Delivery ADJ system* OR Vaccin* OR Additive OR Infect* OR immunostim* OR innocul*) AND (HIV OR Human ADJ Immunodeficiency ADJ Virus)) AND CL=(adjuvant* and (HIV OR Human ADJ Immunodeficiency ADJ Virus));
Results	Total Results = 56 hits

Database	Thomson Innovation (china utility / application)
Classification	Not Applicable
Search String	ALL=((adjuvant* OR Immun* OR Delivery ADJ system* OR Vaccin* OR Additive OR Infect* OR immunostim* OR innocul*) AND (HIV OR Human ADJ Immunodeficiency ADJ Virus)) AND CTB=((adjuvant* or enhancer* AND HIV or AIDS or human ADJ immunodeficiency ADJ virus or autoimmune ADJ deficiency ADJ syndrome));
Results	Total Results = 626 hits

Database	Thomson Innovation (china utility / application)
Classification	Not Applicable

Search String	ALL=((adjuvant* OR Immun* OR Delivery ADJ system* OR Vaccin* OR Additive OR Infect* OR immunostim* OR innocul*) AND (HIV OR Human ADJ Immunodeficiency ADJ Virus)) AND CL=(adjuvant* and (HIV OR Human ADJ Immunodeficiency ADJ Virus));
Results	Total Results = 102 hits

Database	Thomson Innovation (Korean granted/examed utility)
Classification	Not Applicable
Search String	ALL=((adjuvant* OR Immun* OR Delivery ADJ system* OR Vaccin* OR Additive OR Infect* OR immunostim* OR innocul*) AND (HIV OR Human ADJ Immunodeficiency ADJ Virus)) AND CTB=((adjuvant* or enhancer* AND HIV or AIDS or human ADJ immunodeficiency ADJ virus or autoimmune ADJ deficiency ADJ syndrome));
Results	Total Results = 463 hits

Database	Thomson Innovation (Korean granted/examined utility)
Classification	Not Applicable
Search String	ALL=((adjuvant* OR Immun* OR Delivery ADJ system* OR Vaccin* OR Additive OR Infect* OR immunostim* OR innocul*) AND (HIV OR Human ADJ Immunodeficiency ADJ Virus)) AND CL=(adjuvant* and (HIV OR Human ADJ Immunodeficiency ADJ Virus));
Results	Total Results = 45 hits

Database	Thomson Innovation (Japanese Grant, Japanese Utility, Japanese Application)
Classification	Not Applicable
Search String	ALL=((Adjuvant OR Immun* OR Delivery ADJ system* OR Vaccin* OR Additive OR Infect*) AND (HIV OR Human ADJ Immunodeficiency ADJ Virus) AND (Interleukin*)) AND CTB=(Adjuvant* AND Vaccin* AND (HIV OR HUMAN ADJ IMMUNODEFICIENCY ADJ Virus)) AND DP>=(19040101)
Results	Total Results = 8 hits

Database	Thomson Innovation (Japanese Grant, Japanese Utility, Japanese Application)
Classification	Not Applicable
Search String	ALL=((Adjuvant OR Immun* OR Delivery ADJ system* OR Vaccin* OR Additive OR Infect*) AND (HIV OR Human ADJ Immunodeficiency ADJ Virus) AND (ISCOM*)) AND CTB=(Adjuvant* AND Vaccin* AND (HIV OR HUMAN ADJ IMMUNODEFICIENCY ADJ Virus)) AND DP>=(19040101);
Results	Total Results = 5 hits

Database	Thomson Innovation (Japanese Grant, Japanese Utility, Japanese Application)
Classification	Not Applicable
Search String	ALL=((Adjuvant OR Immun* OR Delivery ADJ system* OR Vaccin* OR Additive OR Infect*) AND (HIV OR Human ADJ Immunodeficiency ADJ Virus) AND (LIPId*)) AND CTB=(Adjuvant* AND Vaccin* AND (HIV OR HUMAN ADJ IMMUNODEFICIENCY ADJ Virus)) AND DP>=(19040101);
Results	Total Results = 15 hits

Database	Thomson Innovation (Japanese Grant, Japanese Utility, Japanese Application)
Classification	Not Applicable
Search String	ALL=((Adjuvant OR Immun* OR Delivery ADJ system* OR Vaccin* OR Additive OR Infect*) AND (HIV OR Human ADJ Immunodeficiency ADJ Virus) AND (MTP*)) AND CTB=(Adjuvant* AND Vaccin* AND (HIV OR HUMAN ADJ IMMUNODEFICIENCY ADJ Virus)) AND DP>=(19040101);
Results	Total Results = 3 hits

Database	Thomson Innovation (Japanese Grant, Japanese Utility, Japanese Application)
Classification	Not Applicable

Search String	ALL=((Adjuvant OR Immun* OR Delivery ADJ system* OR Vaccin* OR Additive OR Infect*) AND (HIV OR Human ADJ Immunodeficiency ADJ Virus) AND (sclavo*)) AND CTB=(Adjuvant* AND Vaccin* AND (HIV OR HUMAN ADJ IMMUNODEFICIENCY ADJ Virus)) AND DP>=(19040101);
Results	Total Results = 1 hits

Database	Thomson Innovation (Japanese Grant, Japanese Utility, Japanese Application)
Classification	Not Applicable
Search String	ALL=((Adjuvant OR Immun* OR Delivery ADJ system* OR Vaccin* OR Additive OR Infect*) AND (HIV OR Human ADJ Immunodeficiency ADJ Virus) AND (sendai*)) AND CTB=(Adjuvant* AND Vaccin* AND (HIV OR HUMAN ADJ IMMUNODEFICIENCY ADJ Virus)) AND DP>=(19040101);
Results	Total Results = 1 hits

Database	Thomson Innovation (Japanese Grant, Japanese Utility, Japanese Application)
Classification	Not Applicable
Search String	ALL=((Adjuvant OR Immun* OR Delivery ADJ system* OR Vaccin* OR Additive OR Infect*) AND (HIV OR Human ADJ Immunodeficiency ADJ Virus)) AND CTB=(Adjuvant* AND Vaccin* AND (HIV OR HUMAN ADJ IMMUNODEFICIENCY ADJ Virus)) AND DP>=(19040101);
Results	Total Results=23

Database	Thomson Innovation (Chinese Utility, Chinese Application)
Classification	Not Applicable
Search String	ALL=((Adjuvant OR Immun* OR Delivery ADJ system* OR Vaccin* OR Additive OR Infect*) AND (HIV OR Human ADJ Immunodeficiency ADJ Virus) AND (Interleukin*)) AND CTB=(Adjuvant* AND Vaccin* AND (HIV OR HUMAN ADJ IMMUNODEFICIENCY ADJ Virus)) AND DP>=(19040101);
Results	Total Results = 6 hits

Database	Thomson Innovation (Chinese Utility, Chinese Application)
Classification	Not Applicable
Search String	ALL=((Adjuvant OR Immun* OR Delivery ADJ system* OR Vaccin* OR Additive OR Infect*) AND (HIV OR Human ADJ Immunodeficiency ADJ Virus) AND (ISCOM*)) AND CTB=(Adjuvant* AND Vaccin* AND (HIV OR HUMAN ADJ IMMUNODEFICIENCY ADJ Virus)) AND DP>=(19040101);
Results	Total Results = 2 hits

Database	Thomson Innovation (Chinese Utility, Chinese Application)
Classification	Not Applicable
Search String	ALL=((Adjuvant OR Immun* OR Delivery ADJ system* OR Vaccin* OR Additive OR Infect*) AND (HIV OR Human ADJ Immunodeficiency ADJ Virus) AND (Lipid*)) AND CTB=(Adjuvant* AND Vaccin* AND (HIV OR HUMAN ADJ IMMUNODEFICIENCY ADJ Virus)) AND DP>=(19040101);
Results	Total Results = 9 hits

Database	Thomson Innovation (Chinese Utility, Chinese Application)
Classification	Not Applicable
Search String	ALL=((Adjuvant OR Immun* OR Delivery ADJ system* OR Vaccin* OR Additive OR Infect*) AND (HIV OR Human ADJ Immunodeficiency ADJ Virus)) AND CTB=(Adjuvant* AND Vaccin* AND (HIV OR HUMAN ADJ IMMUNODEFICIENCY ADJ Virus)) AND

	DP>=(19040101);
Results	Total Results = 58 hits

Database	Thomson Innovation (Chinese Utility, Chinese Application)
Classification	Not Applicable
Search String	ALL=((Adjuvant OR Immun* OR Delivery ADJ system* OR Vaccin* OR Additive OR Infect*) AND (HIV OR Human ADJ Immunodeficiency ADJ Virus) AND (LTK*)) AND CTB=(Adjuvant* AND Vaccin* AND (HIV OR HUMAN ADJ IMMUNODEFICIENCY ADJ Virus)) AND DP>=(19040101);
Results	Total Results = 1 hits

Database	Thomson Innovation (Chinese Utility, Chinese Application)
Classification	Not Applicable
Search String	ALL=((Adjuvant OR Immun* OR Delivery ADJ system* OR Vaccin* OR Additive OR Infect*) AND (HIV OR Human ADJ Immunodeficiency ADJ Virus) AND (Rad5*)) AND CTB=(Adjuvant* AND Vaccin* AND (HIV OR HUMAN ADJ IMMUNODEFICIENCY ADJ Virus)) AND DP>=(19040101);
Results	Total Results = 1 hits

Database	Thomson Innovation (Korean Utility, Korean Application, Korean Granted)
Classification	Not Applicable
Search String	ALL=((Adjuvant OR Immun* OR Delivery ADJ system* OR Vaccin* OR Additive OR Infect*) AND (HIV OR Human ADJ Immunodeficiency ADJ Virus) AND (Interleukin*)) AND CTB=(Adjuvant* AND Vaccin* AND (HIV OR HUMAN ADJ IMMUNODEFICIENCY ADJ Virus)) AND DP>=(19040101);
Results	Total Results = 4 hits

Database	Thomson Innovation (Korean Utility, Korean Application, Korean Granted)
Classification	Not Applicable
Search String	ALL=((Adjuvant OR Immun* OR Delivery ADJ system* OR Vaccin* OR Additive OR Infect*) AND (HIV OR Human ADJ Immunodeficiency ADJ Virus) AND (ISCOM*)) AND CTB=(Adjuvant* AND Vaccin* AND (HIV OR HUMAN ADJ IMMUNODEFICIENCY ADJ Virus)) AND DP>=(19040101);
Results	Total Results = 4 hits

Database	Thomson Innovation (Korean Utility, Korean Application, Korean Granted)
Classification	Not Applicable
Search String	ALL=((Adjuvant OR Immun* OR Delivery ADJ system* OR Vaccin* OR Additive OR Infect*) AND (HIV OR Human ADJ Immunodeficiency ADJ Virus) AND (LTK*)) AND CTB=(Adjuvant* AND Vaccin* AND (HIV OR HUMAN ADJ IMMUNODEFICIENCY ADJ Virus)) AND DP>=(19040101);
Results	Total Results = 1 hits

Database	Thomson Innovation (Korean Utility, Korean Application, Korean Granted)
Classification	Not Applicable
Search String	ALL=((Adjuvant OR Immun* OR Delivery ADJ system* OR Vaccin* OR Additive OR Infect*) AND (HIV OR Human ADJ Immunodeficiency ADJ Virus) AND (Lipid*)) AND CTB=(Adjuvant* AND Vaccin* AND (HIV OR HUMAN ADJ IMMUNODEFICIENCY ADJ Virus)) AND DP>=(19040101);
Results	Total Results = 12 hits

Database	Thomson Innovation (Korean Utility, Korean Application, Korean Granted)
Classification	Not Applicable
Search String	ALL=((Adjuvant OR Immun* OR Delivery ADJ system* OR Vaccin* OR Additive OR Infect*)

	AND (HIV OR Human ADJ Immunodeficiency ADJ Virus)) AND CTB=(Adjuvant* AND Vaccin* AND (HIV OR HUMAN ADJ IMMUNODEFICIENCY ADJ Virus)) AND DP>=(19040101);
Results	Total Results = 20 hits

Database	GB App, FR App, WO App, DE Util, EP Grant, DE Grant, EP App, DE App
Classification	Not Applicable
Search String	ALL=((hiv or hiv adj vaccine or human adj immunodeficiency adj virus or viral adj infection or retrovirus or AIDS or acquired ADJ immuno adj deficiency adj syndrome) and (adjuvant or antigen adj delivery adj system or immune adj system or particulate or particulate adj delivery adj system or mucosal adj immunization or enhance* or cataly* or costimulat* or cell adj mediated adj immunity or immune*) and (vaccine or therapy or therapeutic or immuno* or recombinant adj protein adj vaccine or counteragent)) AND CTB=(HIV and (adjuvant* or immuno* or stimulat* or enhanc*)) AND CL=(Montanide*);
Results	Total Results = 15

Database	GB App, FR App, WO App, DE Util, EP Grant, DE Grant, EP App, DE App
Classification	Not Applicable
Search String	ALL=((hiv or hiv adj vaccine or human adj immunodeficiency adj virus or viral adj infection or retrovirus or AIDS or acquired ADJ immuno adj deficiency adj syndrome) and (adjuvant or antigen adj delivery adj system or immune adj system or particulate or particulate adj delivery adj system or mucosal adj immunization or enhance* or cataly* or costimulat* or cell adj mediated adj immunity or immune*) and (vaccine or therapy or therapeutic or immuno* or recombinant adj protein adj vaccine or counteragent)) AND CTB=(HIV and (adjuvant* or immuno* or stimulat* or enhanc*)) AND CL=(CTB or (cholera adj toxin));
Results	Total Results = 79 hits

Database	GB App, FR App, WO App, DE Util, EP Grant, DE Grant, EP App, DE App
Classification	Not Applicable
Search String	ALL=((hiv or hiv adj vaccine or human adj immunodeficiency adj virus or viral adj infection or retrovirus or AIDS or acquired ADJ immuno adj deficiency adj syndrome) and (adjuvant or antigen adj delivery adj system or immune adj system or particulate or particulate adj delivery adj system or mucosal adj immunization or enhance* or cataly* or costimulat* or cell adj mediated adj immunity or immune*) and (vaccine or therapy or therapeutic or immuno* or recombinant adj protein adj vaccine or counteragent)) AND CTB=(HIV and (adjuvant* or immuno* or stimulat* or enhanc*)) AND CL=(CMV*);
Results	Total Results = 545 hits

Database	GB App, FR App, WO App, DE Util, EP Grant, DE Grant, EP App, DE App, JP Util, JP Grant, JP App, CN Util, CN App, KR Util, KR Grant, KR App
Classification	Not Applicable
Search String	ALL=((hiv or hiv adj vaccine or human adj immunodeficiency adj virus or viral adj infection or retrovirus or AIDS or acquired ADJ immuno adj deficiency adj syndrome) and (adjuvant or antigen adj delivery adj system or immune adj system or particulate or particulate adj delivery adj system or mucosal adj immunization or enhance* or cataly* or costimulat* or cell adj mediated adj immunity or immune*) and (vaccine or therapy or therapeutic or immuno* or recombinant adj protein adj vaccine or counteragent)) AND CTB=(HIV and (adjuvant* or immuno* or stimulat* or enhanc*)) AND CL=(Pluronic adj L121);
Results	Total Results = 7 hits

Database	GB App, FR App, WO App, DE Util, EP Grant, DE Grant, EP App, DE App, JP Util, JP Grant, JP App, CN Util, CN App, KR Util, KR Grant, KR App
Classification	Not Applicable

Search String	ALL=((hiv or hiv adj vaccine or human adj immunodeficiency adj virus or viral adj infection or retrovirus or AIDS or acquired ADJ immuno adj deficiency adj syndrome) and (adjuvant or antigen adj delivery adj system or immune adj system or particulate or particulate adj delivery adj system or mucosal adj immunization or enhance* or cataly* or costimulat* or cell adj mediated adj immunity or immune*) and (vaccine or therapy or therapeutic or immuno* or recombinant adj protein adj vaccine or counteragent)) AND CTB=(HIV and (adjuvant* or immuno* or stimulat* or enhanc*)) AND CL=(PMMA);
Results	Total Results = 6 hits

Database	GB App, FR App, WO App, DE Util, EP Grant, DE Grant, EP App, DE App, JP Util, JP Grant, JP App, CN Util, CN App, KR Util, KR Grant, KR App
Classification	Not Applicable
Search String	ALL=((hiv or hiv adj vaccine or human adj immunodeficiency adj virus or viral adj infection or retrovirus or AIDS or acquired ADJ immuno adj deficiency adj syndrome) and (adjuvant or antigen adj delivery adj system or immune adj system or particulate or particulate adj delivery adj system or mucosal adj immunization or enhance* or cataly* or costimulat* or cell adj mediated adj immunity or immune*) and (vaccine or therapy or therapeutic or immuno* or recombinant adj protein adj vaccine or counteragent)) AND CTB=(HIV and (adjuvant* or immuno* or stimulat* or enhanc*)) AND CL=((Poly adj rA) or (Poly adj rU));
Results	Total Results = 21 hits

Database	GB App, FR App, WO App, DE Util, EP Grant, DE Grant, EP App, DE App, JP Util, JP Grant, JP App, CN Util, CN App, KR Util, KR Grant, KR App
Classification	Not Applicable
Search String	ALL=((hiv or hiv adj vaccine or human adj immunodeficiency adj virus or viral adj infection or retrovirus or AIDS or acquired ADJ immuno adj deficiency adj syndrome) and (adjuvant or antigen adj delivery adj system or immune adj system or particulate or particulate adj delivery adj system or mucosal adj immunization or enhance* or cataly* or costimulat* or cell adj mediated adj immunity or immune*) and (vaccine or therapy or therapeutic or immuno* or recombinant adj protein adj vaccine or counteragent)) AND CTB=(HIV and (adjuvant* or immuno* or stimulat* or enhanc*)) AND CL=((Cochleate*));
Results	Total Results = 7

Database	GB App, FR App, WO App, DE Util, EP Grant, DE Grant, EP App, DE App, JP Util, JP Grant, JP App, CN Util, CN App, KR Util, KR Grant, KR App
Classification	Not Applicable
Search String	ALL=((hiv or hiv adj vaccine or human adj immunodeficiency adj virus or viral adj infection or retrovirus or AIDS or acquired ADJ immuno adj deficiency adj syndrome) and (adjuvant or antigen adj delivery adj system or immune adj system or particulate or particulate adj delivery adj system or mucosal adj immunization or enhance* or cataly* or costimulat* or cell adj mediated adj immunity or immune*) and (vaccine or therapy or therapeutic or immuno* or recombinant adj protein adj vaccine or counteragent)) AND CTB=(HIV and (adjuvant* or immuno* or stimulat* or enhanc*)) AND CL=(QS adj 21);
Results	Total Results = 36 hits

Database	GB App, FR App, WO App, DE Util, EP Grant, DE Grant, EP App, DE App, JP Util, JP Grant, JP App, CN Util, CN App, KR Util, KR Grant, KR App
Classification	Not Applicable
Search String	ALL=((hiv or hiv adj vaccine or human adj immunodeficiency adj virus or viral adj infection or retrovirus or AIDS or acquired ADJ immuno adj deficiency adj syndrome) and (adjuvant or antigen adj delivery adj system or immune adj system or particulate or particulate adj delivery adj system or mucosal adj immunization or enhance* or cataly* or costimulat* or cell adj mediated adj immunity or immune*) and (vaccine or therapy or therapeutic or immuno* or recombinant adj protein adj vaccine or counteragent)) AND CTB=(HIV and (adjuvant* or immuno* or stimulat* or enhanc*)) AND CL=(RIBI);

Results	Total Results = 39 hits
---------	-------------------------

Database	GB App, FR App, WO App, DE Util, EP Grant, DE Grant, EP App, DE App, JP Util, JP Grant, JP App, CN Util, CN App, KR Util, KR Grant, KR App
Classification	Not Applicable
Search String	ALL=((hiv or hiv adj vaccine or human adj immunodeficiency adj virus or viral adj infection or retrovirus or AIDS or acquired ADJ immuno adj deficiency adj syndrome) and (adjuvant or antigen adj delivery adj system or immune adj system or particulate or particulate adj delivery adj system or mucosal adj immunization or enhance* or cataly* or costimulat* or cell adj mediated adj immunity or immune*) and (vaccine or therapy or therapeutic or immuno* or recombinant adj protein adj vaccine or counteragent)) AND CTB=(HIV and (adjuvant* or immuno* or stimulat* or enhanc*)) AND CL=(S adj 28463);
Results	Total Results = 4 hits

Database	GB App, FR App, WO App, DE Util, EP Grant, DE Grant, EP App, DE App, JP Util, JP Grant, JP App, CN Util, CN App, KR Util, KR Grant, KR App
Classification	Not Applicable
Search String	ALL=((hiv or hiv adj vaccine or human adj immunodeficiency adj virus or viral adj infection or retrovirus or AIDS or acquired ADJ immuno adj deficiency adj syndrome) and (adjuvant or antigen adj delivery adj system or immune adj system or particulate or particulate adj delivery adj system or mucosal adj immunization or enhance* or cataly* or costimulat* or cell adj mediated adj immunity or immune*) and (vaccine or therapy or therapeutic or immuno* or recombinant adj protein adj vaccine or counteragent)) AND CTB=(HIV and (adjuvant* or immuno* or stimulat* or enhanc*)) AND CL=((TT) or (Tetanus adj Toxoid));
Results	Total Results = 194 hits

Database	GB App, FR App, WO App, DE Util, EP Grant, DE Grant, EP App, DE App, JP Util, JP Grant, JP App, CN Util, CN App, KR Util, KR Grant, KR App
Classification	Not Applicable
Search String	ALL=((hiv or hiv adj vaccine or human adj immunodeficiency adj virus or viral adj infection or retrovirus or AIDS or acquired ADJ immuno adj deficiency adj syndrome) and (adjuvant or antigen adj delivery adj system or immune adj system or particulate or particulate adj delivery adj system or mucosal adj immunization or enhance* or cataly* or costimulat* or cell adj mediated adj immunity or immune*) and (vaccine or therapy or therapeutic or immuno* or recombinant adj protein adj vaccine or counteragent)) AND CTB=(HIV and (adjuvant* or immuno* or stimulat* or enhanc*)) AND CL=((Ty));
Results	Total Results = 70 hits

Database	DWPI
Classification	Not Applicable
Search String	ALLD=((hiv or hiv adj vaccine or human adj immunodeficiency adj virus or viral adj infection or retrovirus or AIDS or acquired ADJ immuno adj deficiency adj syndrome) and (adjuvant or antigen adj delivery adj system or immune adj system or particulate or particulate adj delivery adj system or mucosal adj immunization or enhance* or cataly* or costimulat* or cell adj mediated adj immunity or immune*) and (vaccine or therapy or therapeutic or immuno* or recombinant adj protein adj vaccine or counteragent)) AND TID=((adjuvant* or immuno* or stimulat* or enhanc*)) AND CL1=(adjuvant or Montanide or CTB or (Cholera adj Toxin) or E112K or CMV* or Pluronic or PMMA or (Poly adj rA) or (Poly adj rU) or Cochleate* or (QS adj 21) or RIBI or (S adj 28463) or TT or (Tetanus adj Toxoid) or Ty);
Results	Total Results = 36 hits

Database	Thomson Innovation (U.S. Application, U.S. Patents)
Classification	435005, 435006, 4352351, 4353201, 435325, 4350691, 4352351, 4350071, 435456, 4241841,

	4241881, 4242081, 4242281, 4242291, 4242311, 4242491, 4242781, 4242831, 424450, 4242041, 4240932, 4241851, 514002, 514025, 514044r, 514292, 514012, 530350, 53602372, 5360235, 5360231
Search String	UC = (435005 or 435006 or 4352351 or 4353201 or 435325 or 4350691 or 4352351 or 4350071 or 435456 or 4241841 or 4241881 or 4242081 or 4242281 or 4242291 or 4242311 or 4242491 or 4242781 or 4242831 or 424450 or 4242041 or 4240932 or 4241851 or 514002 or 514025 or 514044r or 514292 or 514012 or 530350 or 53602372 or 5360235 or 5360231) AND DSC = (hiv* or (human adj immunodeficien* adj virus) or lentivirus* or retrovirus*) AND CTB = ((vaccin* or immunostimulat* or immunoenhanc* or immunogenic*) or (adjuvant* or (antigen* adj deliver*))) AND CTB = (hiv* or (human adj immunodeficien* adj virus) or lentivirus* or retrovirus*) AND DSC = (prim* or boost*)
Results	Total Results = 4,344 hits

Database	Thomson Innovation (U.S. Application, U.S. Patents)
Keywords	HIV*, human immunodeficien* virus, lentivirus*, retrovirus*, vaccin*, immunostimulat*, immunoenhanc*, immunogenic*, adjuvant*, antigen* deliver*,
Classification/Sub-Classification	435005, 435006, 4352351, 4353201, 435325, 4350691, 4352351, 4350071, 435456, 4241841, 4241881, 4242081, 4242281, 4242291, 4242311, 4242491, 4242781, 4242831, 424450, 4242041, 4240932, 4241851, 514002, 514025, 514044r, 514292, 514012, 530350, 53602372, 5360235, 5360231
Search String	UC = (435005 or 435006 or 4352351 or 4353201 or 435325 or 4350691 or 4352351 or 4350071 or 435456 or 4241841 or 4241881 or 4242081 or 4242281 or 4242291 or 4242311 or 4242491 or 4242781 or 4242831 or 424450 or 4242041 or 4240932 or 4241851 or 514002 or 514025 or 514044r or 514292 or 514012 or 530350 or 53602372 or 5360235 or 5360231) AND DSC = (hiv* or (human adj immunodeficien* adj virus) or lentivirus* or retrovirus*) AND CTB=((vaccin* or immunostimulat* or immunoenhanc* or immunogenic*) or (adjuvant* or (antigen* adj deliver*))) AND ABD=(hiv* or (human adj immunodeficien* adj virus)) AND ABD=(adjuvant* or (antigen* adj deliver*));
Results	Total Results = 807 hits

Database	Thomson Innovation (U.S. Application, U.S. Patents)
Keywords	HIV*, human immunodeficien* virus, lentivirus*, retrovirus*, vaccin*, immunostimulat*, immunoenhanc*, immunogenic*, adjuvant*, antigen* deliver*, prim*, boost*
Classification/Sub-Classification	435005, 435006, 4352351, 4353201, 435325, 4350691, 4352351, 4350071, 435456, 4241841, 4241881, 4242081, 4242281, 4242291, 4242311, 4242491, 4242781, 4242831, 424450, 4242041, 4240932, 4241851, 514002, 514025, 514044r, 514292, 514012, 530350, 53602372, 5360235, 5360231
Search String	UC = (435005 or 435006 or 4352351 or 4353201 or 435325 or 4350691 or 4352351 or 4350071 or 435456 or 4241841 or 4241881 or 4242081 or 4242281 or 4242291 or 4242311 or 4242491 or 4242781 or 4242831 or 424450 or 4242041 or 4240932 or 4241851 or 514002 or 514025 or 514044r or 514292 or 514012 or 530350 or 53602372 or 5360235 or 5360231) AND DSC = (hiv* or (human adj immunodeficien* adj virus) or lentivirus* or retrovirus*) AND CTB=((vaccin* or immunostimulat* or immunoenhanc* or immunogenic*) or (adjuvant* or (antigen* adj deliver*))) AND ABD=(hiv* or (human adj immunodeficien* adj virus)) AND ABD=(adjuvant* or (antigen* adj deliver*) or prim* or boost*) AND TID=(hiv* or (human adj immunodeficien* adj virus) or lentivirus* or retrovirus*)
Results	Total Results = 453 hits

Database	Thomson Innovation (U.S. Application, U.S. Patents)
Keywords	HIV*, human immunodeficien* virus, lentivirus*, retrovirus*, vaccin*, immunostimulat*, immunoenhanc*, immunogenic*, adjuvant*, antigen* deliver*, prim*, boost*
Classification/Sub-	435005, 435006, 4352351, 4353201, 435325, 4350691, 4352351, 4350071, 435456, 4241841, 4241881, 4242081, 4242281, 4242291, 4242311, 4242491, 4242781, 4242831, 424450, 4242041,

Classification	4240932, 4241851, 514002, 514025, 514044r, 514292, 514012, 530350, 53602372, 5360235, 5360231
Search String	UC = (435005 or 435006 or 4352351 or 4353201 or 435325 or 4350691 or 4352351 or 4350071 or 435456 or 4241841 or 4241881 or 4242081 or 4242281 or 4242291 or 4242311 or 4242491 or 4242781 or 4242831 or 424450 or 4242041 or 4240932 or 4241851 or 514002 or 514025 or 514044r or 514292 or 514012 or 530350 or 53602372 or 5360235 or 5360231) AND DSC=(hiv* or (human adj immunodeficien* adj virus) or lentivirus* or retrovirus*) AND CTB=((vaccin* or immunostimulat* or immunoenhanc* or immunogenic*) or (adjuvant* or (antigen* adj deliver*))) AND ABD=(adjuvant* or (antigen* adj deliver*) or prim* or boost*) AND ABD=(hiv* or (human adj immunodeficien* adj virus) or lentivirus* or retrovirus*)
Results	Total Results = 1,527 hits

Database	Thomson Innovation (Enhanced DWPI database)
Keywords	HIV*, human immunodeficien* virus, lentivirus*, retrovirus*, vaccin*, immunostimulat*, immunoenhanc*, immunogenic*, adjuvant*, antigen* deliver*, prim*, boost*
Classification	435005, 435006, 4352351, 4353201, 435325, 4350691, 4352351, 4350071, 435456, 4241841, 4241881, 4242081, 4242281, 4242291, 4242311, 4242491, 4242781, 4242831, 424450, 4242041, 4240932, 4241851, 514002, 514025, 514044r, 514292, 514012, 530350, 53602372, 5360235, 5360231
Search String	UCC=(435005 or 435006 or 4352351 or 4353201 or 4353201 or 435325 or 4350691 or 435005 or 435006 or 4352351 or 4350071 or 435456 or 4241841 or 4241881 or 4242081 or 4242281 or 4242291 or 4242311 or 4242491 or 4242781 or 4242831 or 424450 or 4242041 or 4240932 or 4241851 or 514002 or 514025 or 514044r or 514292 or 514012 or 530350 or 53602372 or 5360235 or 5360231) AND ABD=((vaccin* or immunostimulat* or immunoenhanc* or immunogenic*) or (adjuvant* or (antigen* adj deliver*))) AND ABD=(hiv* or (human adj immunodeficien* adj virus) or lentivirus* or retrovirus*) AND ABD=(prim* or boost*)
Results	Total Results = 568 hits

Database	Thomson Innovation (Enhanced DWPI database)
Keywords	HIV*, human immunodeficien* virus, lentivirus*, retrovirus*, vaccin*, immunostimulat*, immunoenhanc*, immunogenic*, adjuvant*, antigen* deliver*, prim*, boost*
Classification	A61K003900 or A61K003800 or A61K004800 or A61K003921 or A61K003939 or A61K003912 or C07K0014005 or C07K001416 or C07K0014435 or C07K001618 or A61P003100 or A61P003700 or A61P003118 or A61P003112 or A61P003500 or C12N001509 or C12N000700 or C07H002100 or C07H002104 or C12Q000168
Search String	IC= (A61K003900 or A61K003800 or A61K004800 or A61K003921 or A61K003939 or A61K003912 or C07K0014005 or C07K001416 or C07K0014435 or C07K001618 or A61P003100 or A61P003700 or A61P003118 or A61P003112 or A61P003500 or C12N001509 or C12N000700 or C07H002100 or C07H002104 or C12Q000168) AND ABD=((vaccin* or immunostimulat* or immunoenhanc* or immunogenic*) or (adjuvant* or (antigen* adj deliver*))) AND ABD=(hiv* or (human adj immunodeficien* adj virus) or lentivirus* or retrovirus*) AND ABD=(prim* or boost*);
Results	Total Results = 1,006 hits

Database	Thomson Innovation (Enhanced DWPI database)
Keywords	HIV*, human immunodeficien* virus, lentivirus*, retrovirus*, vaccin*, immunostimulat*, immunoenhanc*, immunogenic*, adjuvant*, antigen* deliver*, prim*, boost*
Classification	A61K003900 or A61K003800 or A61K004800 or A61K003921 or A61K003939 or A61K003912 or C07K0014005 or C07K001416 or C07K0014435 or C07K001618 or A61P003100 or A61P003700 or A61P003118 or A61P003112 or A61P003500 or C12N001509 or C12N000700 or C07H002100 or C07H002104 or C12Q000168
Search String	IC= (A61K003900 or A61K003800 or A61K004800 or A61K003921 or A61K003939 or A61K003912 or C07K0014005 or C07K001416 or C07K0014435 or C07K001618 or A61P003100 or A61P003700 or A61P003118 or A61P003112 or A61P003500 or C12N001509 or C12N000700 or C07H002100 or C07H002104 or C12Q000168) AND ABD=((vaccin* or immunostimulat* or immunoenhanc* or immunogenic*) or (adjuvant* or (antigen* adj deliver*))) AND ABD=(hiv* or

	(human adj immunodeficien* adj virus) or lentivirus* or retrovirus*) AND ABD=(prim* or boost*)AND TID==(hiv* or (human adj immunodeficien* adj virus));
Results	Total Results = 257 hits

Database	Thomson Innovation (Enhanced DWPI database)
Keywords	HIV*, human immunodeficien* virus, lentivirus*, retrovirus*, vaccin*, immunostimulat*, immunoenhanc*, immunogenic*, adjuvant*, antigen* deliver*, prim*, boost*
Classification	A61K003900 or A61K003800 or A61K004800 or A61K003921or A61K003939 or A61K003912 or C07K0014005 or C07K001416 or C07K0014435 or C07K001618 or A61P003100 or A61P003700 or A61P003118 or A61P003112 or A61P003500 or C12N001509 or C12N000700 or C07H002100 or C07H002104 or C12Q000168
Search String	IC= (A61K003900 or A61K003800 or A61K004800 or A61K003921or A61K003939 or A61K003912 or C07K0014005 or C07K001416 or C07K0014435 or C07K001618 or A61P003100 or A61P003700 or A61P003118 or A61P003112 or A61P003500 or C12N001509 or C12N000700 or C07H002100 or C07H002104 or C12Q000168) AND ABD=((vaccin* or immunostimulat* or immunoenhanc* or immunogenic*) or (adjuvant* or (antigen* adj deliver*))) AND ABD=(hiv* or (human adj immunodeficien* adj virus) or lentivirus* or retrovirus*) AND ABD=(prim* or boost*) AND TID==(adjuvant* or (antigen* adj deliver*));
Results	Total Results = 29 hits

Database	Thomson Innovation (U.S. Application, U.S. Patents containing DWPI data)
Keywords	HIV*, human immunodeficien* virus, lentivirus*, retrovirus*, vaccin*, immunostimulat*, immunoenhanc*, immunogenic*, adjuvant*, antigen* deliver*, prim*, boost*
Classification	A61K003900 or A61K003800 or A61K004800 or A61K003921or A61K003939 or A61K003912 or C07K0014005 or C07K001416 or C07K0014435 or C07K001618 or A61P003100 or A61P003700 or A61P003118 or A61P003112 or A61P003500 or C12N001509 or C12N000700 or C07H002100 or C07H002104 or C12Q000168
Search String	IC= (A61K003900 or A61K003800 or A61K004800 or A61K003921or A61K003939 or A61K003912 or C07K0014005 or C07K001416 or C07K0014435 or C07K001618 or A61P003100 or A61P003700 or A61P003118 or A61P003112 or A61P003500 or C12N001509 or C12N000700 or C07H002100 or C07H002104 or C12Q000168) AND DSC=(hiv* or (human adj immunodeficien* adj virus) or lentivirus* or retrovirus*) AND CTB=((vaccin* or immunostimulat* or immunoenhanc* or immunogenic*) or (adjuvant* or (antigen* adj deliver*))) AND ABD=(adjuvant* or (antigen* adj deliver*) or prim* or boost*) AND ABD=(hiv* or (human adj immunodeficien* adj virus) or lentivirus* or retrovirus*);
Results	Total Results = 2,009 hits

Database	Thomson Innovation (U.S. Application, U.S. Patents containing DWPI data)
Keywords	HIV*, human immunodeficien* virus, lentivirus*, retrovirus*, vaccin*, immunostimulat*, immunoenhanc*, immunogenic*, adjuvant*, antigen* deliver*, prim*, boost*
Classification	A61K003900 or A61K003800 or A61K004800 or A61K003921or A61K003939 or A61K003912 or C07K0014005 or C07K001416 or C07K0014435 or C07K001618 or A61P003100 or A61P003700 or A61P003118 or A61P003112 or A61P003500 or C12N001509 or C12N000700 or C07H002100 or C07H002104 or C12Q000168
Search String	IC= (A61K003900 or A61K003800 or A61K004800 or A61K003921or A61K003939 or A61K003912 or C07K0014005 or C07K001416 or C07K0014435 or C07K001618 or A61P003100 or A61P003700 or A61P003118 or A61P003112 or A61P003500 or C12N001509 or C12N000700 or C07H002100 or C07H002104 or C12Q000168) AND DSC=(hiv* or (human adj immunodeficien* adj virus)) AND CTB=((vaccin* or immunostimulat* or immunoenhanc* or immunogenic*) or (adjuvant* or (antigen* adj deliver*))) AND ABD=(adjuvant* or (antigen* adj deliver*) or prim* or boost*) AND ABD=(hiv* or (human adj immunodeficien* adj virus));
Results	Total Results = 1,778 hits

Database	Thomson Innovation (U.S. Application, U.S. Patents containing DWPI data)
Keywords	HIV*, human immunodeficien* virus, lentivirus*, retrovirus*, vaccin*, immunostimulat*,

	immunoenhanc*, immunogenic*, adjuvant*, antigen* deliver*, prim*, boost*
Classification	A61K003900 or A61K003800 or A61K004800 or A61K003921 or A61K003939 or A61K003912 or C07K0014005 or C07K001416 or C07K0014435 or C07K001618 or A61P003100 or A61P003700 or A61P003118 or A61P003112 or A61P003500 or C12N001509 or C12N000700 or C07H002100 or C07H002104 or C12Q000168
Search String	IC= (A61K003900 or A61K003800 or A61K004800 or A61K003921 or A61K003939 or A61K003912 or C07K0014005 or C07K001416 or C07K0014435 or C07K001618 or A61P003100 or A61P003700 or A61P003118 or A61P003112 or A61P003500 or C12N001509 or C12N000700 or C07H002100 or C07H002104 or C12Q000168) AND DSC=(hiv* or (human adj immunodeficien* adj virus)) AND CTB=((vaccin* or immunostimulat* or immunoenhanc* or immunogenic*) or (adjuvant* or (antigen* adj deliver*))) AND ABD=(adjuvant* or (antigen* adj deliver*)) AND ABD=(prim* or boost*) AND ABD=(hiv* or (human adj immunodeficien* adj virus));
Results	Total Results = 261 hits

Database	Thomson Innovation (WIPO applications)
Keywords	HIV*, human immunodeficien* virus, lentivirus*, retrovirus*, vaccin*, immunostimulat*, immunoenhanc*, immunogenic*, adjuvant*, antigen* deliver*, prim*, boost*
Classification/ Sub- Classification	A61K003900 or A61K003800 or A61K004800 or A61K003921 or A61K003939 or A61K003912 or C07K0014005 or C07K001416 or C07K0014435 or C07K001618 or A61P003100 or A61P003700 or A61P003118 or A61P003112 or A61P003500 or C12N001509 or C12N000700 or C07H002100 or C07H002104 or C12Q000168
Search String	IC= (A61K003900 or A61K003800 or A61K004800 or A61K003921 or A61K003939 or A61K003912 or C07K0014005 or C07K001416 or C07K0014435 or C07K001618 or A61P003100 or A61P003700 or A61P003118 or A61P003112 or A61P003500 or C12N001509 or C12N000700 or C07H002100 or C07H002104 or C12Q000168) AND DSC=(hiv* or (human adj immunodeficien* adj virus)) AND CTB=((vaccin* or immunostimulat* or immunoenhanc* or immunogenic*) or (adjuvant* or (antigen* adj deliver*))) AND ABD=(adjuvant* or (antigen* adj deliver*)) AND ABD=(prim* or boost*) AND ABD=(hiv* or (human adj immunodeficien* adj virus));
Results	Total Results = 205 hits

Database	Thomson Innovation (WIPO applications)
Keywords	HIV*, human immunodeficien* virus, lentivirus*, retrovirus*, vaccin*, immunostimulat*, immunoenhanc*, immunogenic*, adjuvant*, antigen* deliver*, prim*, boost*
Classification	A61K003900 or A61K003800 or A61K004800 or A61K003921 or A61K003939 or A61K003912 or C07K0014005 or C07K001416 or C07K0014435 or C07K001618 or A61P003100 or A61P003700 or A61P003118 or A61P003112 or A61P003500 or C12N001509 or C12N000700 or C07H002100 or C07H002104 or C12Q000168
Search String	IC= (A61K003900 or A61K003800 or A61K004800 or A61K003921 or A61K003939 or A61K003912 or C07K0014005 or C07K001416 or C07K0014435 or C07K001618 or A61P003100 or A61P003700 or A61P003118 or A61P003112 or A61P003500 or C12N001509 or C12N000700 or C07H002100 or C07H002104 or C12Q000168) AND DSC=(hiv* or (human adj immunodeficien* adj virus)) AND CTB=((vaccin* or immunostimulat* or immunoenhanc* or immunogenic*) or (adjuvant* or (antigen* adj deliver*))) AND ABD=(adjuvant* or (antigen* adj deliver*)) or prim* or boost*) AND ABD=(hiv* or (human adj immunodeficien* adj virus));
Results	Total Results = 1,281 hits

Database	Thomson Innovation (EP application and EP patents)
Keywords	HIV*, human immunodeficien* virus, lentivirus*, retrovirus*, vaccin*, immunostimulat*, immunoenhanc*, immunogenic*, adjuvant*, antigen* deliver*, prim*, boost*
Classification	A61K003900 or A61K003800 or A61K004800 or A61K003921 or A61K003939 or A61K003912 or C07K0014005 or C07K001416 or C07K0014435 or C07K001618 or A61P003100 or A61P003700 or A61P003118 or A61P003112 or A61P003500 or C12N001509 or C12N000700 or C07H002100 or C07H002104 or C12Q000168

Search String	IC= (A61K003900 or A61K003800 or A61K004800 or A61K003921 or A61K003939 or A61K003912 or C07K0014005 or C07K001416 or C07K0014435 or C07K001618 or A61P003100 or A61P003700 or A61P003118 or A61P003112 or A61P003500 or C12N001509 or C12N000700 or C07H002100 or C07H002104 or C12Q000168) AND DSC=(hiv* or (human adj immunodeficien* adj virus)) AND CTB=((vaccin* or immunostimulat* or immunoenhanc* or immunogenic*) or (adjuvant* or (antigen* adj deliver*))) AND ABD=(adjuvant* or (antigen* adj deliver*)) AND ABD=(prim* or boost*) AND ABD=(hiv* or (human adj immunodeficien* adj virus))
Results	Total Results = 49 hits

Database	Thomson Innovation (EP application and EP patents)
Keywords	HIV*, human immunodeficien* virus, lentivirus*, retrovirus*, vaccin*, immunostimulat*, immunoenhanc*, immunogenic*, adjuvant*, antigen* deliver*, prim*, boost*
Classification	A61K003900 or A61K003800 or A61K004800 or A61K003921 or A61K003939 or A61K003912 or C07K0014005 or C07K001416 or C07K0014435 or C07K001618 or A61P003100 or A61P003700 or A61P003118 or A61P003112 or A61P003500 or C12N001509 or C12N000700 or C07H002100 or C07H002104 or C12Q000168
Search String	IC=(A61K003900 or A61K003800 or A61K004800 or A61K003921 or ADJ A61K003939 or A61K003912 or C07K0014005 or C07K001416 or C07K0014435 or C07K001618 or A61P003100 or A61P003700 or A61P003118 or A61P003112 or A61P003500 or C12N001509 or C12N000700 or C07H002100 or C07H002104 or C12Q000168) AND DSC=(hiv* or (human adj immunodeficien* adj virus) or lentivirus* or retrovirus*) AND CTB=((vaccin* or immunostimulat* or immunoenhanc* or immunogenic*) or (adjuvant* or (antigen* adj deliver*))) AND ABD=(adjuvant* or (antigen* adj deliver*)) AND ABD=(hiv* or (human adj immunodeficien* adj virus));
Results	Total Results = 274 hits

Database	Thomson Innovation (JP published application and JP patents)
Keywords	HIV*, human immunodeficien* virus, lentivirus*, retrovirus*, vaccin*, immunostimulat*, immunoenhanc*, immunogenic*, adjuvant*, antigen* deliver*, prim*, boost*
Classification	A61K003900 or A61K003800 or A61K004800 or A61K003921 or A61K003939 or A61K003912 or C07K0014005 or C07K001416 or C07K0014435 or C07K001618 or A61P003100 or A61P003700 or A61P003118 or A61P003112 or A61P003500 or C12N001509 or C12N000700 or C07H002100 or C07H002104 or C12Q000168
Search String	IC=(A61K003900 or A61K003800 or A61K004800 or A61K003921 or ADJ A61K003939 or A61K003912 or C07K0014005 or C07K001416 or C07K0014435 or C07K001618 or A61P003100 or A61P003700 or A61P003118 or A61P003112 or A61P003500 or C12N001509 or C12N000700 or C07H002100 or C07H002104 or C12Q000168) AND DSC=(hiv* or (human adj immunodeficien* adj virus) or lentivirus* or retrovirus*) AND CTB=((vaccin* or immunostimulat* or immunoenhanc* or immunogenic*) or (adjuvant* or (antigen* adj deliver*))) AND ABD=(adjuvant* or (antigen* adj deliver*)) AND ABD=(hiv* or (human adj immunodeficien* adj virus));
Results	Total Results = 48 hits

Database	Thomson Innovation (Chinese patents)
Keywords	HIV*, human immunodeficien* virus, lentivirus*, retrovirus*, vaccin*, immunostimulat*, immunoenhanc*, immunogenic*, adjuvant*, antigen* deliver*, prim*, boost*
Classification	A61K003900 or A61K003800 or A61K004800 or A61K003921 or A61K003939 or A61K003912 or C07K0014005 or C07K001416 or C07K0014435 or C07K001618 or A61P003100 or A61P003700 or A61P003118 or A61P003112 or A61P003500 or C12N001509 or C12N000700 or C07H002100 or C07H002104 or C12Q000168
Search String	IC=(A61K003900 or A61K003800 or A61K004800 or A61K003921 or ADJ A61K003939 or A61K003912 or C07K0014005 or C07K001416 or C07K0014435 or C07K001618 or A61P003100 or A61P003700 or A61P003118 or A61P003112 or A61P003500 or C12N001509 or C12N000700 or C07H002100 or C07H002104 or C12Q000168) AND DSC=(hiv* or (human adj immunodeficien* adj virus) or lentivirus* or retrovirus*) AND CTB=((vaccin* or immunostimulat* or immunoenhanc* or immunogenic*) or (adjuvant* or (antigen* adj deliver*))) AND ABD=(adjuvant* or (antigen* adj deliver*)) AND ABD=(hiv* or (human adj immunodeficien* adj virus));

	deliver*)) AND ABD=(hiv* or (human adj immunodeficien* adj virus));
Results	Total Results = 0

Database	Thomson Innovation (DWPI)
Keywords	RIBI
Classification	Derwent class A03, A10, A11, A14, A23, A96, B02, B03, B04, B05, B12, B14, C04, C12, D16, E34, N01
Search String	DC=(A03 or A10 or A11 or A14 or A23 or A96 or B02 or B03 or B04 or B05 or B12 or B14 or C04 or C12 or D16 or E34 or N01) AND DP>=(19000101) AND ALLD=(ribi)
Results	Total Results = 68 hits

Database	Thomson Innovation (DWPI)
Keywords	Squalene
Classification	Derwent Class A03, A10, A11, A14, A23, A96, B02, B03, B04, B05, B12, B14, C04, C12, D16, E34, N01
Search String	DC=(A03 or A10 or A11 or A14 or A23 or A96 or B02 or B03 or B04 or B05 or B12 or B14 or C04 or C12 or D16 or E34 or N01) AND DP>=(19000101) AND ALLD=(squalene)
Results	Total Results = 1592 hits

Database	Thomson Innovation (DWPI)
Keywords	Squalene 2
Classification	Derwent Class A03, A10, A11, A14, A23, A96, B02, B03, B04, B05, B12, B14, C04, C12, D16, E34, N01
Search String	DC=(A03 or A10 or A11 or A14 or A23 or A96 or B02 or B03 or B04 or B05 or B12 or B14 or C04 or C12 or D16 or E34 or N01) AND DP>=(19000101) AND ALLD=(squalene adj 2);
Results	Total Results = 11 hits

Database	Thomson Innovation (DWPI)
Keywords	Steryl tyrosine
Classification	Derwent Class A03, A10, A11, A14, A23, A96, B02, B03, B04, B05, B12, B14, C04, C12, D16, E34, N01
Search String	DC=(A03 or A10 or A11 or A14 or A23 or A96 or B02 or B03 or B04 or B05 or B12 or B14 or C04 or C12 or D16 or E34 or N01) AND DP>=(19000101) AND ALLD=(stearyl adj tyrosine);
Results	Total Results = 11 hits

Database	Thomson Innovation (DWPI)
Keywords	theramide
Classification	Derwent Class A03, A10, A11, A14, A23, A96, B02, B03, B04, B05, B12, B14, C04, C12, D16, E34, N01
Search String	DC=(A03 or A10 or A11 or A14 or A23 or A96 or B02 or B03 or B04 or B05 or B12 or B14 or C04 or C12 or D16 or E34 or N01) AND DP>=(19000101) AND ALLD=(theramide);
Results	Total Results = 9 hits

Database	Thomson Innovation (DWPI)
Keywords	1z
Classification	Derwent Class A03, A10, A11, A14, A23, A96, B02, B03, B04, B05, B12, B14, C04, C12, D16, E34, N01
Search String	DC=(A03 or A10 or A11 or A14 or A23 or A96 or B02 or B03 or B04 or B05 or B12 or B14 or C04 or C12 or D16 or E34 or N01) AND DP>=(19000101) AND ALLD=(1z);
Results	Total Results = 75 hits

Database	Thomson Innovation (DWPI)
----------	---------------------------

Keywords	Adju phos
Classification	Derwent Class A03, A10, A11, A14, A23, A96, B02, B03, B04, B05, B12, B14, C04, C12, D16, E34, N01
Search String	DC=(A03 or A10 or A11 or A14 or A23 or A96 or B02 or B03 or B04 or B05 or B12 or B14 or C04 or C12 or D16 or E34 or N01) AND DP>=(19000101) AND ALLD=(adju adj phos);
Results	Total Results = 9 hits

Database	Thomson Innovation (DWPI)
Keywords	adju mer
Classification	Derwent Class A03, A10, A11, A14, A23, A96, B02, B03, B04, B05, B12, B14, C04, C12, D16, E34, N01
Search String	DC=(A03 or A10 or A11 or A14 or A23 or A96 or B02 or B03 or B04 or B05 or B12 or B14 or C04 or C12 or D16 or E34 or N01) AND DP>=(19000101) AND ALLD=(adju mer);
Results	Total Results = 9 hits

Database	Thomson Innovation (DWPI)
Keywords	alum
Classification	Derwent Class A03, A10, A11, A14, A23, A96, B02, B03, B04, B05, B12, B14, C04, C12, D16, E34, N01
Search String	DC=(A03 or A10 or A11 or A14 or A23 or A96 or B02 or B03 or B04 or B05 or B12 or B14 or C04 or C12 or D16 or E34 or N01) AND DP>=(19000101) AND ALLD=(alum);
Results	Total Results = 2095 hits

Database	Thomson Innovation (DWPI)
Keywords	As2 adjuvant
Classification	Derwent Class A03, A10, A11, A14, A23, A96, B02, B03, B04, B05, B12, B14, C04, C12, D16, E34, N01
Search String	DC=(A03 or A10 or A11 or A14 or A23 or A96 or B02 or B03 or B04 or B05 or B12 or B14 or C04 or C12 or D16 or E34 or N01) AND DP>=(19000101) AND ALLD=(as2 adj adjuvant);
Results	Total Results = 1 hits

Database	Thomson Innovation (DWPI)
Keywords	Calcium phosphate gel
Classification	Derwent Class A03, A10, A11, A14, A23, A96, B02, B03, B04, B05, B12, B14, C04, C12, D16, E34, N01
Search String	DC=(A03 or A10 or A11 or A14 or A23 or A96 or B02 or B03 or B04 or B05 or B12 or B14 or C04 or C12 or D16 or E34 or N01) AND DP>=(19000101) AND ALLD=(calcium adj phosphate adj gel);
Results	Total Results = 33 hits

Database	Thomson Innovation (DWPI)
Keywords	Doc alum complex
Classification	Derwent Class A03, A10, A11, A14, A23, A96, B02, B03, B04, B05, B12, B14, C04, C12, D16, E34, N01
Search String	DC=(A03 or A10 or A11 or A14 or A23 or A96 or B02 or B03 or B04 or B05 or B12 or B14 or C04 or C12 or D16 or E34 or N01) AND DP>=(19000101) AND ALLD=(doc adj alum adj complex);
Results	Total Results = 10 hits

Database	Thomson Innovation (DWPI)
Keywords	Non ionic surfactant vesicles
Classification	Derwent Class A03, A10, A11, A14, A23, A96, B02, B03, B04, B05, B12, B14, C04, C12, D16, E34, N01

Search String	DC=(A03 or A10 or A11 or A14 or A23 or A96 or B02 or B03 or B04 or B05 or B12 or B14 or C04 or C12 or D16 or E34 or N01) AND DP>=(19000101) AND ALLD=(non adj ionic adj surfactant adj vesicles);
Results	Total Results = 10 hits

Database	Thomson Innovation (DWPI)
Keywords	peptomer
Classification	Derwent Class A03, A10, A11, A14, A23, A96, B02, B03, B04, B05, B12, B14, C04, C12, D16, E34, N01
Search String	DC=(A03 or A10 or A11 or A14 or A23 or A96 or B02 or B03 or B04 or B05 or B12 or B14 or C04 or C12 or D16 or E34 or N01) AND DP>=(19000101) AND ALLD=(peptomer);
Results	Total Results = 3 hits

Database	Thomson Innovation (DWPI)
Keywords	rehydrigel
Classification	Derwent Class A03, A10, A11, A14, A23, A96, B02, B03, B04, B05, B12, B14, C04, C12, D16, E34, N01
Search String	DC=(A03 or A10 or A11 or A14 or A23 or A96 or B02 or B03 or B04 or B05 or B12 or B14 or C04 or C12 or D16 or E34 or N01) AND DP>=(19000101) AND ALLD=(rehydrigel);
Results	Total Results = 5 hits

Database	Thomson Innovation (DWPI)
Keywords	Walter reed liposomes*
Classification	Derwent Class A03, A10, A11, A14, A23, A96, B02, B03, B04, B05, B12, B14, C04, C12, D16, E34, N01
Search String	DC=(A03 or A10 or A11 or A14 or A23 or A96 or B02 or B03 or B04 or B05 or B12 or B14 or C04 or C12 or D16 or E34 or N01) AND DP>=(19000101) AND ALLD=(walter adj reed adj liposome*);
Results	Total Results = 7 hits

Database	Thomson Innovation (DWPI)
Keywords	Alum, adjuvant*
Classification	Derwent Class A03, A10, A11, A14, A23, A96, B02, B03, B04, B05, B12, B14, C04, C12, D16, E34, N01
Search String	DC=(A03 or A10 or A11 or A14 or A23 or A96 or B02 or B03 or B04 or B05 or B12 or B14 or C04 or C12 or D16 or E34 or N01) AND ALLD=(adjuvant*)) AND ALLD=(alum);
Results	Total Results = 395 hits

Database	Thomson Innovation (JP Util, JP Grant, JP App, CN Util, CN App, KR Util, KR Grant, KR App)
Classification	Not Applicable
Search String	ALL=(adjuvant or (delivery adj system) or emulsion* or (immune adj system) or particulate or mucosal or (nano adj bead*) or (micro adj organism adj derived) or (lipid adj particle*) or (tensoactive adj compound*) or enhanc* or (depot adj formation?) or (costimulatory adj molecule?) or montanides) AND ALL=(hiv or (human adj immunodeficiency adj virus) or immuno* or retrovirus or (toll adj like adj receptor or receptors) or (gp adj 120) or vir* ADJ infection or aids or (acquired adj immune adj deficiency adj syndrome)) AND ALL=(vaccine or therapy or (efficacy adj of adj vacc!) or antigen or antibody or counteragent or (immune adj response));
Results	Total Results = 21578 hits

Database	Thomson Innovation (JP Util, JP Grant, JP App, CN Util, CN App, KR Util, KR Grant, KR App)
Classification	Not Applicable

Search String	ALL=(adjuvant or (delivery adj system) or emulsion* or (immune adj system) or particulate or mucosal or (nano adj bead*) or (micro adj organism adj derived) or (lipid adj particle*) or (tensoactive adj compound*) or enhanc* or (depot adj formation?) or (costimulatory adj molecule?) or montanides) AND ALL=(hiv or (human adj immunodeficiency adj virus) or immuno* or retrovirus or (toll adj like adj receptor or receptors) or (gp adj 120) or vir* ADJ infection or aids or (acquired adj immune adj deficiency adj syndrome)) AND ALL=(vaccine or therapy or (efficacy adj of adj vacc!) or antigen or antibody or counteragent or (immune adj response)) AND CTB=((adjuvant or (delivery adj system) or emulsion* or (immune adj system) or particulate or mucosal or (nano adj bead*) or (micro adj organism adj derived) or (lipid adj particle*) or (tensoactive adj compound*) or enhanc* or (depot adj formation?) or (costimulatory adj molecule?) or montanides) AND (hiv or (human adj immunodeficiency adj virus) or immuno* or retrovirus or (toll adj like adj receptor or receptors) or (gp adj 120) or vir* ADJ infection or aids or (acquired adj immune adj deficiency adj syndrome)) AND (vaccine or therapy or (efficacy adj of adj vacc!) or antigen or antibody or counteragent or (immune adj response))));
Results	Total Results = 2626 hits

Database	Thomson Innovation (JP Util, JP Grant, JP App, CN Util, CN App, KR Util, KR Grant, KR App)
Classification	Not Applicable
Search String	ALL=(adjuvant or (delivery adj system) or emulsion* or (immune adj system) or particulate or mucosal or (nano adj bead*) or (micro adj organism adj derived) or (lipid adj particle*) or (tensoactive adj compound*) or enhanc* or (depot adj formation?) or (costimulatory adj molecule?) or montanides) AND ALL=(hiv or (human adj immunodeficiency adj virus) or immuno* or retrovirus or (toll adj like adj receptor or receptors) or (gp adj 120) or vir* ADJ infection or aids or (acquired adj immune adj deficiency adj syndrome)) AND ALL=(vaccine or therapy or (efficacy adj of adj vacc!) or antigen or antibody or counteragent or (immune adj response)) AND CTB=((adjuvant or (delivery adj system) or emulsion* or (immune adj system) or particulate or mucosal or (nano adj bead*) or (micro adj organism adj derived) or (lipid adj particle*) or (tensoactive adj compound*) or enhanc* or (depot adj formation?) or (costimulatory adj molecule?) or montanides) AND (hiv or (human adj immunodeficiency adj virus) or immuno* or retrovirus or (toll adj like adj receptor or receptors) or (gp adj 120) or vir* ADJ infection or aids or (acquired adj immune adj deficiency adj syndrome)) AND (vaccine or therapy or (efficacy adj of adj vacc!) or antigen or antibody or counteragent or (immune adj response)))) AND ALL=(RIBI);
Results	Total Results = 138 hits

Database	Thomson Innovation (JP Util, JP Grant, JP App, CN Util, CN App, KR Util, KR Grant, KR App)
Classification	Not Applicable
Search String	ALL=(adjuvant or (delivery adj system) or emulsion* or (immune adj system) or particulate or mucosal or (nano adj bead*) or (micro adj organism adj derived) or (lipid adj particle*) or (tensoactive adj compound*) or enhanc* or (depot adj formation?) or (costimulatory adj molecule?) or montanides) AND ALL=(hiv or (human adj immunodeficiency adj virus) or immuno* or retrovirus or (toll adj like adj receptor or receptors) or (gp adj 120) or vir* ADJ infection or aids or (acquired adj immune adj deficiency adj syndrome)) AND ALL=(vaccine or therapy or (efficacy adj of adj vacc!) or antigen or antibody or counteragent or (immune adj response)) AND CTB=(hiv) AND ALL=(RIBI);
Results	Total Results = 54 hits

Database	Thomson Innovation (JP Util, JP Grant, JP App, CN Util, CN App, KR Util, KR Grant, KR App)
Classification	Not Applicable

Search String	ALL=(adjuvant or (delivery adj system) or emulsion* or (immune adj system) or particulate or mucosal or (nano adj bead*) or (micro adj organism adj derived) or (lipid adj particle*) or (tensoactive adj compound*) or enhanc* or (depot adj formation?) or (costimulatory adj molecule?) or montanides) AND ALL=(hiv or (human adj immunodeficiency adj virus) or immuno* or retrovirus or (toll adj like adj receptor or receptors) or (gp adj 120) or vir* ADJ infection or aids or (acquired adj immune adj deficiency adj syndrome)) AND ALL=(vaccine or therapy or (efficacy adj of adj vacc!) or antigen or antibody or counteragent or (immune adj response)) AND CTB=((adjuvant or (delivery adj system) or emulsion* or (immune adj system) or particulate or mucosal or (nano adj bead*) or (micro adj organism adj derived) or (lipid adj particle*) or (tensoactive adj compound*) or enhanc* or (depot adj formation?) or (costimulatory adj molecule?) or montanides) AND (hiv or (human adj immunodeficiency adj virus) or immuno* or retrovirus or (toll adj like adj receptor or receptors) or (gp adj 120) or vir* ADJ infection or aids or (acquired adj immune adj deficiency adj syndrome)) AND (vaccine or therapy or (efficacy adj of adj vacc!) or antigen or antibody or counteragent or (immune adj response))) AND ALL=(squalene);
Results	Total Results = 182 hits

Database	Thomson Innovation (JP Util, JP Grant, JP App, CN Util, CN App, KR Util, KR Grant, KR App)
Classification	Not Applicable
Search String	ALL=(adjuvant or (delivery adj system) or emulsion* or (immune adj system) or particulate or mucosal or (nano adj bead*) or (micro adj organism adj derived) or (lipid adj particle*) or (tensoactive adj compound*) or enhanc* or (depot adj formation?) or (costimulatory adj molecule?) or montanides) AND ALL=(hiv or (human adj immunodeficiency adj virus) or immuno* or retrovirus or (toll adj like adj receptor or receptors) or (gp adj 120) or vir* ADJ infection or aids or (acquired adj immune adj deficiency adj syndrome)) AND ALL=(vaccine or therapy or (efficacy adj of adj vacc!) or antigen or antibody or counteragent or (immune adj response)) AND CTB=((adjuvant or (delivery adj system) or emulsion* or (immune adj system) or particulate or mucosal or (nano adj bead*) or (micro adj organism adj derived) or (lipid adj particle*) or (tensoactive adj compound*) or enhanc* or (depot adj formation?) or (costimulatory adj molecule?) or montanides) AND (hiv or (human adj immunodeficiency adj virus) or immuno* or retrovirus or (toll adj like adj receptor or receptors) or (gp adj 120) or vir* ADJ infection or aids or (acquired adj immune adj deficiency adj syndrome)) AND (vaccine or therapy or (efficacy adj of adj vacc!) or antigen or antibody or counteragent or (immune adj response))) AND ALL=(squalene near 2);
Results	Total Results = 4 hits

Database	Thomson Innovation (JP Util, JP Grant, JP App, CN Util, CN App, KR Util, KR Grant, KR App)
Classification	Not Applicable
Search String	ALL=(adjuvant or (delivery adj system) or emulsion* or (immune adj system) or particulate or mucosal or (nano adj bead*) or (micro adj organism adj derived) or (lipid adj particle*) or (tensoactive adj compound*) or enhanc* or (depot adj formation?) or (costimulatory adj molecule?) or montanides) AND ALL=(hiv or (human adj immunodeficiency adj virus) or immuno* or retrovirus or (toll adj like adj receptor or receptors) or (gp adj 120) or vir* ADJ infection or aids or (acquired adj immune adj deficiency adj syndrome)) AND ALL=(vaccine or therapy or (efficacy adj of adj vacc!) or antigen or antibody or counteragent or (immune adj response)) AND CTB=((adjuvant or (delivery adj system) or emulsion* or (immune adj system) or particulate or mucosal or (nano adj bead*) or (micro adj organism adj derived) or (lipid adj particle*) or (tensoactive adj compound*) or enhanc* or (depot adj formation?) or (costimulatory adj molecule?) or montanides) AND (hiv or (human adj immunodeficiency adj virus) or immuno* or retrovirus or (toll adj like adj receptor or receptors) or (gp adj 120) or vir* ADJ infection or aids or (acquired adj immune adj deficiency adj syndrome)) AND (vaccine or therapy or (efficacy adj of adj vacc!) or antigen or antibody or counteragent or (immune adj response))) AND ALL=(stearyl near tyrosine);
Results	Total Results = 4 hits

Database	Thomson Innovation (JP Util, JP Grant, JP App, CN Util, CN App, KR Util, KR Grant, KR App)
----------	--

Classification	Not Applicable
Search String	ALL=(adjuvant or (delivery adj system) or emulsion* or (immune adj system) or particulate or mucosal or (nano adj bead*) or (micro adj organism adj derived) or (lipid adj particle*) or (tensoactive adj compound*) or enhanc* or (depot adj formation?) or (costimulatory adj molecule?) or montanides) AND ALL=(hiv or (human adj immunodeficiency adj virus) or immuno* or retrovirus or (toll adj like adj receptor or receptors) or (gp adj 120) or vir* ADJ infection or aids or (acquired adj immune adj deficiency adj syndrome)) AND ALL=(vaccine or therapy or (efficacy adj of adj vacc!) or antigen or antibody or counteragent or (immune adj response)) AND CTB=((adjuvant or (delivery adj system) or emulsion* or (immune adj system) or particulate or mucosal or (nano adj bead*) or (micro adj organism adj derived) or (lipid adj particle*) or (tensoactive adj compound*) or enhanc* or (depot adj formation?) or (costimulatory adj molecule?) or montanides) AND (hiv or (human adj immunodeficiency adj virus) or immuno* or retrovirus or (toll adj like adj receptor or receptors) or (gp adj 120) or vir* ADJ infection or aids or (acquired adj immune adj deficiency adj syndrome)) AND (vaccine or therapy or (efficacy adj of adj vacc!) or antigen or antibody or counteragent or (immune adj response))) AND ALL=(theramide);
Results	Total Results = 5 hits

Database	Thomson Innovation (JP Util, JP Grant, JP App, CN Util, CN App, KR Util, KR Grant, KR App)
Classification	Not Applicable
Search String	ALL=(adjuvant or (delivery adj system) or emulsion* or (immune adj system) or particulate or mucosal or (nano adj bead*) or (micro adj organism adj derived) or (lipid adj particle*) or (tensoactive adj compound*) or enhanc* or (depot adj formation?) or (costimulatory adj molecule?) or montanides) AND ALL=(hiv or (human adj immunodeficiency adj virus) or immuno* or retrovirus or (toll adj like adj receptor or receptors) or (gp adj 120) or vir* ADJ infection or aids or (acquired adj immune adj deficiency adj syndrome)) AND ALL=(vaccine or therapy or (efficacy adj of adj vacc!) or antigen or antibody or counteragent or (immune adj response)) AND CTB=((adjuvant or (delivery adj system) or emulsion* or (immune adj system) or particulate or mucosal or (nano adj bead*) or (micro adj organism adj derived) or (lipid adj particle*) or (tensoactive adj compound*) or enhanc* or (depot adj formation?) or (costimulatory adj molecule?) or montanides) AND (hiv or (human adj immunodeficiency adj virus) or immuno* or retrovirus or (toll adj like adj receptor or receptors) or (gp adj 120) or vir* ADJ infection or aids or (acquired adj immune adj deficiency adj syndrome)) AND (vaccine or therapy or (efficacy adj of adj vacc!) or antigen or antibody or counteragent or (immune adj response))) AND ALL=(1z or (1 adj z));
Results	Total Results = 10 hits

Database	Thomson Innovation (JP Util, JP Grant, JP App, CN Util, CN App, KR Util, KR Grant, KR App)
Classification	Not Applicable
Search String	ALL=(adjuvant or (delivery adj system) or emulsion* or (immune adj system) or particulate or mucosal or (nano adj bead*) or (micro adj organism adj derived) or (lipid adj particle*) or (tensoactive adj compound*) or enhanc* or (depot adj formation?) or (costimulatory adj molecule?) or montanides) AND ALL=(hiv or (human adj immunodeficiency adj virus) or immuno* or retrovirus or (toll adj like adj receptor or receptors) or (gp adj 120) or vir* ADJ infection or aids or (acquired adj immune adj deficiency adj syndrome)) AND ALL=(vaccine or therapy or (efficacy adj of adj vacc!) or antigen or antibody or counteragent or (immune adj response)) AND CTB=((adjuvant or (delivery adj system) or emulsion* or (immune adj system) or particulate or mucosal or (nano adj bead*) or (micro adj organism adj derived) or (lipid adj particle*) or (tensoactive adj compound*) or enhanc* or (depot adj formation?) or (costimulatory adj molecule?) or montanides) AND (hiv or (human adj immunodeficiency adj virus) or immuno* or retrovirus or (toll adj like adj receptor or receptors) or (gp adj 120) or vir* ADJ infection or aids or (acquired adj immune adj deficiency adj syndrome)) AND (vaccine or therapy or (efficacy adj of adj vacc!) or antigen or antibody or counteragent or (immune adj response))) AND ALL=(adju near phos);
Results	Total Results = 2

Database	Thomson Innovation (JP Util, JP Grant, JP App, CN Util, CN App, KR Util, KR Grant, KR App)
Classification	Not Applicable
Search String	ALL=(adjuvant or (delivery adj system) or emulsion* or (immune adj system) or particulate or mucosal or (nano adj bead*) or (micro adj organism adj derived) or (lipid adj particle*) or (tensoactive adj compound*) or enhanc* or (depot adj formation?) or (costimulatory adj molecule?) or montanides) AND ALL=(hiv or (human adj immunodeficiency adj virus) or immuno* or retrovirus or (toll adj like adj receptor or receptors) or (gp adj 120) or vir* ADJ infection or aids or (acquired adj immune adj deficiency adj syndrome)) AND ALL=(vaccine or therapy or (efficacy adj of adj vacc!) or antigen or antibody or counteragent or (immune adj response)) AND CTB=((adjuvant or (delivery adj system) or emulsion* or (immune adj system) or particulate or mucosal or (nano adj bead*) or (micro adj organism adj derived) or (lipid adj particle*) or (tensoactive adj compound*) or enhanc* or (depot adj formation?) or (costimulatory adj molecule?) or montanides) AND (hiv or (human adj immunodeficiency adj virus) or immuno* or retrovirus or (toll adj like adj receptor or receptors) or (gp adj 120) or vir* ADJ infection or aids or (acquired adj immune adj deficiency adj syndrome)) AND (vaccine or therapy or (efficacy adj of adj vacc!) or antigen or antibody or counteragent or (immune adj response))) AND ALL=(adjuvant);
Results	Total Results = 1 hits

Database	Thomson Innovation (JP Util, JP Grant, JP App, CN Util, CN App, KR Util, KR Grant, KR App)
Classification	Not Applicable
Search String	ALL=(adjuvant or (delivery adj system) or emulsion* or (immune adj system) or particulate or mucosal or (nano adj bead*) or (micro adj organism adj derived) or (lipid adj particle*) or (tensoactive adj compound*) or enhanc* or (depot adj formation?) or (costimulatory adj molecule?) or montanides) AND ALL=(hiv or (human adj immunodeficiency adj virus) or immuno* or retrovirus or (toll adj like adj receptor or receptors) or (gp adj 120) or vir* ADJ infection or aids or (acquired adj immune adj deficiency adj syndrome)) AND ALL=(vaccine or therapy or (efficacy adj of adj vacc!) or antigen or antibody or counteragent or (immune adj response)) AND CTB=((adjuvant or (delivery adj system) or emulsion* or (immune adj system) or particulate or mucosal or (nano adj bead*) or (micro adj organism adj derived) or (lipid adj particle*) or (tensoactive adj compound*) or enhanc* or (depot adj formation?) or (costimulatory adj molecule?) or montanides) AND (hiv or (human adj immunodeficiency adj virus) or immuno* or retrovirus or (toll adj like adj receptor or receptors) or (gp adj 120) or vir* ADJ infection or aids or (acquired adj immune adj deficiency adj syndrome)) AND (vaccine or therapy or (efficacy adj of adj vacc!) or antigen or antibody or counteragent or (immune adj response))) AND ALL=(alum);
Results	Total Results = 287 hits

Database	Thomson Innovation (JP Util, JP Grant, JP App, CN Util, CN App, KR Util, KR Grant, KR App)
Classification	Not Applicable

Search String	ALL=(adjuvant or (delivery adj system) or emulsion* or (immune adj system) or particulate or mucosal or (nano adj bead*) or (micro adj organism adj derived) or (lipid adj particle*) or (tensoactive adj compound*) or enhanc* or (depot adj formation?) or (costimulatory adj molecule?) or montanides) AND ALL=(hiv or (human adj immunodeficiency adj virus) or immuno* or retrovirus or (toll adj like adj receptor or receptors) or (gp adj 120) or vir* ADJ infection or aids or (acquired adj immune adj deficiency adj syndrome)) AND ALL=(vaccine or therapy or (efficacy adj of adj vacc!) or antigen or antibody or counteragent or (immune adj response)) AND CTB=((adjuvant or (delivery adj system) or emulsion* or (immune adj system) or particulate or mucosal or (nano adj bead*) or (micro adj organism adj derived) or (lipid adj particle*) or (tensoactive adj compound*) or enhanc* or (depot adj formation?) or (costimulatory adj molecule?) or montanides) AND (hiv or (human adj immunodeficiency adj virus) or immuno* or retrovirus or (toll adj like adj receptor or receptors) or (gp adj 120) or vir* ADJ infection or aids or (acquired adj immune adj deficiency adj syndrome)) AND (vaccine or therapy or (efficacy adj of adj vacc!) or antigen or antibody or counteragent or (immune adj response))) AND ALL=(calcium near phosphate near gel);
Results	Total Results = 1 hits

Database	Thomson Innovation (JP Util, JP Grant, JP App, CN Util, CN App, KR Util, KR Grant, KR App)
Classification	Not Applicable
Search String	ALL=(adjuvant or (delivery adj system) or emulsion* or (immune adj system) or particulate or mucosal or (nano adj bead*) or (micro adj organism adj derived) or (lipid adj particle*) or (tensoactive adj compound*) or enhanc* or (depot adj formation?) or (costimulatory adj molecule?) or montanides) AND ALL=(hiv or (human adj immunodeficiency adj virus) or immuno* or retrovirus or (toll adj like adj receptor or receptors) or (gp adj 120) or vir* ADJ infection or aids or (acquired adj immune adj deficiency adj syndrome)) AND ALL=(vaccine or therapy or (efficacy adj of adj vacc!) or antigen or antibody or counteragent or (immune adj response)) AND CTB=((adjuvant or (delivery adj system) or emulsion* or (immune adj system) or particulate or mucosal or (nano adj bead*) or (micro adj organism adj derived) or (lipid adj particle*) or (tensoactive adj compound*) or enhanc* or (depot adj formation?) or (costimulatory adj molecule?) or montanides) AND (hiv or (human adj immunodeficiency adj virus) or immuno* or retrovirus or (toll adj like adj receptor or receptors) or (gp adj 120) or vir* ADJ infection or aids or (acquired adj immune adj deficiency adj syndrome)) AND (vaccine or therapy or (efficacy adj of adj vacc!) or antigen or antibody or counteragent or (immune adj response))) AND ALL=(rehydragel*);
Results	Total Results = 5 hits

Database	Thomson Innovation (GB App, FR App, WO App, DE Util, EP Grant, DE Grant, EP App, DE App)
Classification	Not Applicable
Search String	ALL=(adjuvant or (delivery adj system) or emulsion* or (immune adj system) or particulate or mucosal or (nano adj bead*) or (micro adj organism adj derived) or (lipid adj particle*) or (tensoactive adj compound*) or enhanc* or (depot adj formation?) or (costimulatory adj molecule?) or montanides) AND ALL=(hiv or (human adj immunodeficiency adj virus) or immuno* or retrovirus or (toll adj like adj receptor or receptors) or (gp adj 120) or vir* ADJ infection or aids or (acquired adj immune adj deficiency adj syndrome)) AND ALL=(vaccine or therapy or (efficacy adj of adj vacc!) or antigen or antibody or counteragent or (immune adj response)) AND CTB=((hiv or (human adj immunodeficiency adj virus))) AND DSC=((adjuvant or (delivery adj system) or emulsion* or (immune adj system) or particulate or mucosal or (nano adj bead*) or (micro adj organism adj derived) or (lipid adj particle*) or (tensoactive adj compound*) or enhanc* or (depot adj formation?) or (costimulatory adj molecule?) or montanides) AND (hiv or (human adj immunodeficiency adj virus) or immuno* or retrovirus or (toll adj like adj receptor or receptors) or (gp adj 120) or vir* ADJ infection or aids or (acquired adj immune adj deficiency adj syndrome)) AND (vaccine or therapy or (efficacy adj of adj vacc!) or antigen or antibody or counteragent or (immune adj response))) AND CTB=(alum or aluminum or aluminium) AND DSC=(alum or aluminum or aluminium);
Results	Total Results = 271 hits

Database	Thomson Innovation (US Grant, US App)
----------	---------------------------------------

Classification	Not Applicable
Search String	ALL=(adjuvant or (delivery adj system) or emulsion* or (immune adj system) or particulate or mucosal or (nano adj bead*) or (micro adj organism adj derived) or (lipid adj particle*) or (tensoactive adj compound*) or enhanc* or (depot adj formation?) or (costimulatory adj molecule?) or montanides) AND ALL=(hiv or (human adj immunodeficiency adj virus) or immuno* or retrovirus or (toll adj like adj receptor or receptors) or (gp adj 120) or vir* ADJ infection or aids or (acquired adj immune adj deficiency adj syndrome)) AND ALL=(vaccine or therapy or (efficacy adj of adj vacc!) or antigen or antibody or counteragent or (immune adj response)) AND CTB=(HIV) AND DSC=((adjuvant or (delivery adj system) or emulsion* or (immune adj system) or particulate or mucosal or (nano adj bead*) or (micro adj organism adj derived) or (lipid adj particle*) or (tensoactive adj compound*) or enhanc* or (depot adj formation?) or (costimulatory adj molecule?) or montanides) AND (hiv or (human adj immunodeficiency adj virus) or immuno* or retrovirus or (toll adj like adj receptor or receptors) or (gp adj 120) or vir* ADJ infection or aids or (acquired adj immune adj deficiency adj syndrome)) AND (vaccine or therapy or (efficacy adj of adj vacc!) or antigen or antibody or counteragent or (immune adj response))) AND ALL=(alum*);
Results	Total Results = 4009 hits

Database	Thomson Innovation (US Grant, US App)
Classification	Not Applicable
Search String	ALL=(adjuvant or (delivery adj system) or emulsion* or (immune adj system) or particulate or mucosal or (nano adj bead*) or (micro adj organism adj derived) or (lipid adj particle*) or (tensoactive adj compound*) or enhanc* or (depot adj formation?) or (costimulatory adj molecule?) or montanides) AND ALL=(hiv or (human adj immunodeficiency adj virus) or immuno* or retrovirus or (toll adj like adj receptor or receptors) or (gp adj 120) or vir* ADJ infection or aids or (acquired adj immune adj deficiency adj syndrome)) AND ALL=(vaccine or therapy or (efficacy adj of adj vacc!) or antigen or antibody or counteragent or (immune adj response)) AND CTB=(HIV and (adjuvant or enhancer)) AND DSC=((adjuvant or (delivery adj system) or emulsion* or (immune adj system) or particulate or mucosal or (nano adj bead*) or (micro adj organism adj derived) or (lipid adj particle*) or (tensoactive adj compound*) or enhanc* or (depot adj formation?) or (costimulatory adj molecule?) or montanides) AND (hiv or (human adj immunodeficiency adj virus) or immuno* or retrovirus or (toll adj like adj receptor or receptors) or (gp adj 120) or vir* ADJ infection or aids or (acquired adj immune adj deficiency adj syndrome)) AND (vaccine or therapy or (efficacy adj of adj vacc!) or antigen or antibody or counteragent or (immune adj response))) AND ALL=(alum*);
Results	Total Results = 546 hits

Database	Thomson Innovation (US Grant, US App)
Classification	Not Applicable
Search String	ALL=(adjuvant or (delivery adj system) or emulsion* or (immune adj system) or particulate or mucosal or (nano adj bead*) or (micro adj organism adj derived) or (lipid adj particle*) or (tensoactive adj compound*) or enhanc* or (depot adj formation?) or (costimulatory adj molecule?) or montanides) AND ALL=(hiv or (human adj immunodeficiency adj virus) or immuno* or retrovirus or (toll adj like adj receptor or receptors) or (gp adj 120) or vir* ADJ infection or aids or (acquired adj immune adj deficiency adj syndrome)) AND ALL=(vaccine or therapy or (efficacy adj of adj vacc!) or antigen or antibody or counteragent or (immune adj response)) AND CTB=(HIV) AND DSC=((adjuvant or (delivery adj system) or emulsion* or (immune adj system) or particulate or mucosal or (nano adj bead*) or (micro adj organism adj derived) or (lipid adj particle*) or (tensoactive adj compound*) or enhanc* or (depot adj formation?) or (costimulatory adj molecule?) or montanides) AND (hiv or (human adj immunodeficiency adj virus) or immuno* or retrovirus or (toll adj like adj receptor or receptors) or (gp adj 120) or vir* ADJ infection or aids or (acquired adj immune adj deficiency adj syndrome)) AND (vaccine or therapy or (efficacy adj of adj vacc!) or antigen or antibody or counteragent or (immune adj response))) AND ALL=(RIBI);
Results	Total Results = 376 hits

Database	Thomson Innovation (US Grant, US App)
Classification	Not Applicable
Search String	ALL=(adjuvant or (delivery adj system) or emulsion* or (immune adj system) or particulate or mucosal or (nano adj bead*) or (micro adj organism adj derived) or (lipid adj particle*) or (tensoactive adj compound*) or enhanc* or (depot adj formation?) or (costimulatory adj molecule?) or montanides) AND ALL=(hiv or (human adj immunodeficiency adj virus) or immuno* or retrovirus or (toll adj like adj receptor or receptors) or (gp adj 120) or vir* ADJ infection or aids or (acquired adj immune adj deficiency adj syndrome)) AND ALL=(vaccine or therapy or (efficacy adj of adj vacc!) or antigen or antibody or counteragent or (immune adj response)) AND CTB=(HIV or (human adj immunodeficiency adj virus)) AND DSC=((adjuvant or (delivery adj system) or emulsion* or (immune adj system) or particulate or mucosal or (nano adj bead*) or (micro adj organism adj derived) or (lipid adj particle*) or (tensoactive adj compound*) or enhanc* or (depot adj formation?) or (costimulatory adj molecule?) or montanides) AND (hiv or (human adj immunodeficiency adj virus) or immuno* or retrovirus or (toll adj like adj receptor or receptors) or (gp adj 120) or vir* ADJ infection or aids or (acquired adj immune adj deficiency adj syndrome)) AND (vaccine or therapy or (efficacy adj of adj vacc!) or antigen or antibody or counteragent or (immune adj response))) AND ALL=(1z);
Results	Total Results = 63 hits

Database	Thomson Innovation (U.S. Application, U.S. Patents)
Classification	Not Applicable
Search String	(ALL = (B7 adj 2 and (Vacci* or Therapy or DNA ADJ vaccine or Immun* or Immunoenhancing or Immune ADJ response or immunotherapy or Recombinant ADJ protein or vaccine) and (HIV or HIV ADJ vaccine or Infect* or Immunogenicity or Immuno-compromised or Immunodeficiency or Immunostimulatory or Retro-virus or retrovirus) and (adjuvant* or costimulatory ADJ receptor or ligand or CTL ADJ response or coadminister or regulate or CTL or response or costimulate or CD28)) AND DP >= (20000101)) AND (DSC = (HIV))
Results	Total Results =1475 hits

Database	Thomson Innovation (WIPO Application)
Classification	Not Applicable
Search String	CTB = (B7 adj 2 and (Vacci* or Therapy or DNA ADJ vaccine or Immun* or Immunoenhancing or Immune ADJ response or immunotherapy or Recombinant ADJ protein or vaccine) and (HIV or HIV ADJ vaccine or Infect* or Immunogenicity or Immuno-compromised or Immunodeficiency or Immunostimulatory or Retro-virus or retrovirus) and (adjuvant* or costimulatory ADJ receptor or ligand or CTL ADJ response or coadminister or regulate or CTL or response or costimulate or CD28))
Results	Total Results = 62 hits

Database	Thomson Innovation (EPO Granted, EPO Application )
Classification	Not Applicable
Search String	CTB = (B7 adj 2 and (Vacci* or Therapy or DNA ADJ vaccine or Immun* or Immunoenhancing or Immune ADJ response or immunotherapy or Recombinant ADJ protein or vaccine) and (HIV or HIV ADJ vaccine or Infect* or Immunogenicity or Immuno-compromised or Immunodeficiency or Immunostimulatory or Retro-virus or retrovirus) and (adjuvant* or costimulatory ADJ receptor or ligand or CTL ADJ response or coadminister or regulate or CTL or response or costimulate or CD28)) ;
Results	Total Results = 22 hits

Database	Thomson Innovation (U.S. Application, U.S. Patents)
Classification	Not Applicable
Search String	(ALL = (bupivacaine and (Vacci* or Therapy or DNA ADJ vaccine or Immun* or Immunoenhancing or Immune ADJ response or immunotherapy or Recombinant ADJ protein or vaccine) and (HIV or HIV ADJ vaccine or Infect* or Immunogenicity or Immuno-compromised or Immunodeficiency or Immunostimulatory or Retro-virus or retrovirus) and (adjuvant* or facilitating

	ADJ agent or facilitate! or (enhance* and (DNA ADJ uptake)) or DNA ADJ uptake)) AND DP >= (20000101)) AND (CTB = (HIV))
Results	Total Results = 131 hits

Database	Thomson Innovation U.S. Application, U.S. Patents
Classification	Not Applicable
Search String	ALL = (bupivacaine adj HCl and (Vacci* or Therapy or DNA ADJ vaccine or Immun* or Immunoenhancing or Immune ADJ response or immunotherapy or Recombinant ADJ protein or vaccine) and (HIV or HIV ADJ vaccine or Infect* or Immunogenicity or Immuno-compromised or Immunodeficiency or Immunostimulatory or Retro-virus or retrovirus) and (adjuvant* or facilitating ADJ agent or facilitate! or (enhance* and (DNA ADJ uptake)) or DNA ADJ uptake))
Results	Total Results = 96 hits

Database	Thomson Innovation (U.S. Application, U.S. Patents)
Classification	Not Applicable
Search String	ALL = (CCR5 ADJ peptide and (Vacci* or Therapy or DNA ADJ vaccine or Immun* or Immunoenhancing or Immune ADJ response or immunotherapy or Recombinant ADJ protein or vaccine) and (HIV or HIV ADJ vaccine or Infect* or Immunogenicity or Immuno-compromised or Immunodeficiency or Immunostimulatory or Retro-virus or retrovirus) and (adjuvant* or (enhance* and CD4))) AND DP >= (20000101)
Results	Total Results = 30 hits

### 3. Patent Search Results Summary

#### 3. A. Categorization Summary

Patent Documents for Adjuvants for HIV Vaccine were coded using three relevancy categories and four descriptive categories. The following categories were defined as follows for the purpose of this report.

Relevancy Categories:

1. “Primary” Relevance – The first requirement to be primary relevant is that the patent must claim subject matter deals with HIV vaccine or vaccines for infectious diseases. In order to be a primary relevant patent category, the patent must claim the adjuvant composition and not the method of enhancing immune response. For instance, the claim language “a method of enhancing immunizing” would be insufficient for this category of the report. However, a claim that is described as “an adjuvant composition comprising” would be sufficient to be primary relevant. Furthermore, a primary relevant patent will also claim the adjuvant using the language, “an adjuvant comprising” and not “an immunological agent”. This distinction was made because a primary relevant patent must claim composition is used as an adjuvant and not a broad category of an immunostimulatory agent. Moreover, a general patent that claims an immunostimulatory agent can be used to describe a vaccine and not an adjuvant composition. A primary relevant patent requires language specifying HIV in the abstract or the claims. If the patent only mentions HIV in the specification it will not be considered as a primary relevant patent. Once a patent contains a primary relevant claim then all claims in reference to this claim will also be categorized as primary relevant.

2. “Secondary” Relevance – Similar to above, the first requirement to be a secondary relevant patent is that the patent must claim that the subject matter deals with HIV vaccine or vaccines for infectious disease. The secondary relevant patent category differs from a primary relevant patent in that the patent could claim a method for use of a specific adjuvant. For example, a patent claim, “a method for enhancing the immune response ...with adjuvant, MPL” would be considered as a secondary relevant patent. Also, a secondary relevant patent could also claim a HIV vaccine with a specific adjuvant. For instance, “an anti-HIV vaccine ... containing the adjuvant, ISCOM” would fall under a secondary relevant category. In order to fall under secondary relevant category the patent must specify the adjuvant being used.
3. “Tertiary” Relevance – The tertiary relevant patent category only contains peripherally relevant claim language in the patent for either a HIV vaccine or a vaccine for infectious disease. For instance, the claim “a HIV vaccine containing an adjuvant” would be considered tertiary relevant because it only specifies that the patent deal with HIV vaccines and contain an unknown adjuvant. Since there is no specification on the adjuvant, a tertiary relevant claim merely claims that an adjuvant is used in an HIV vaccine. Furthermore, a tertiary relevant patent would only further comprise an adjuvant as a dependant claim to an HIV vaccine.

#### Descriptive Categories:

1. Organic Chemical Adjuvants – Patents will fall into this descriptive category if the patent claims an organic chemical adjuvant. Only primary and secondary adjuvants can be properly characterized because they clearly describe the adjuvant. Organic Chemicals Adjuvants are adjuvants which are organic and are typically either vehicles for vaccines or immunostimulatory compounds. The list in Appendix G contains the organic chemical adjuvants from the LANL list.
2. Inorganic Chemical Adjuvants - Patents will fall into this descriptive category if the patent claims an inorganic chemical adjuvant. Only primary and secondary adjuvants can be properly characterized because they clearly describe the adjuvant. Inorganic Chemicals Adjuvants are adjuvants which are Inorganic and are typically either vehicles for vaccines or immunostimulatory compounds. The list in Appendix G contains the inorganic chemical adjuvants from the LANL list.
3. Endogenous Immunostimulatory Adjuvants – Patents will fall into this category describes endogenous stimulatory adjuvant. Only “primary” and “secondary” relevant patents can be properly characterized as endogenous immunostimulatory adjuvants because these patents clearly describe the specific adjuvant. Endogenous immunostimulatory adjuvants

are adjuvants that are from within the human body, which are used to exert a direct immunostimulatory effects on innate immune cells. The list in Appendix G contains the Endogenous Immunostimulatory Adjuvants from the LANL list.

4. Exogenous Immunostimulatory Adjuvants – Patents will fall into this category describes endogenous stimulatory adjuvant. Only “primary” and “secondary” relevant patents can be properly characterized as exogenous immunostimulatory adjuvants because these patents clearly describe the specific adjuvant. Exogenous immunostimulatory adjuvants are adjuvants that are from outside the human body, which are used to exert a direct immunostimulatory effects on innate immune cells. The list in Appendix G contains the Endogenous Immunostimulatory Adjuvants from the LANL list.

### **3. B. Patent De-duplication Process**

The search strings gave the team an outcome of 3,798 patent/applications, which then were de-duplicated according to the INPADOC Family ID. The de-duplication step refers to the removal of patents/applications within the same family so as to reduce redundancy during the patent coding process. There is no option to directly de-duplicate patents into one-per-family in Innovation®, we utilized the Display and Sort option in Innovation® to group together the family members having the same INPADOC family ID, and then manually reduced to 2,040 patents/applications.

The manually de-duplication process includes several steps. First, all issued US patents within one INPADOC family were kept. Second, for a family having no US issued patent, all EP issued patents were be kept for coding. Finally, when no issued patent was available within one INPADOC family, patent applications with earliest priority date was be kept for review, and usually WIPO application or applications are the ones with the earliest priority date within one family. However, some families only contain foreign patents or patent applications such as Japan patents/applications, Korea patents/applications or China patents/applications. For these foreign patents or patent applications, we reviewed the translations made by Innovation and coded them accordingly.

### **3. C. Patent Coding Results Summary**

Final de-duplication brought in a result of 2,040 patent documents. The result was then extracted into PDF files containing title, abstracts and claims for coding by using MicroPatent®. The 2,040 patent documents were divided among the eight team members for coding.

Each team member analyzed the claims in the documents and coded under one or more of the following eight categories.

1. Primary Relevant
2. Secondary Relevant
3. Tertiary Relevant
4. Irrelevant
5. Organic Composition
6. Inorganic Composition

7. Exogenous
8. Endogenous

Of the 2,040 patent documents, 315 patent documents were found to be relevant. The coding results were inserted into the Master Sheet showing relevancy and categories of each patent document. The result is shown in Section 3.D.

On the other hand, 44 out of 2,040 patent documents have no English claims for team members to decide its relevancy to adjuvants applicable for HIV vaccine. A list for these cannot-code patent documents is shown in Section 3.E.

Each patent/application was initially coded by individual team member and emphasis was placed on claim language to decide whether the patent/application was relevant to adjuvant used for HIV vaccine. When the claim scope of a patent/application covered adjuvants but the claim language did not specifically point out the applicability to vaccine against HIV, the patent/application was originally classified as irrelevant. However, after coding more than half of the 2,040 patent documents, team members realized that such patent/application might disclose adjuvants applicable to vaccine against HIV in the description portion, even it did not directly claim such usage.

Due to the limited coding time (about 7 weeks), it is impractical for each team member to review these “irrelevant” patents again by reviewing the whole patent specification to determine whether these patents were relevant to adjuvant applicable to HIV vaccine. Of the 2,040 patents/applications, 1,679 patents/applications were coded as “irrelevant.” However, we reassembled the 1,679 “irrelevant” patents/applications together, and picked out 98 possibly relevant patents/applications among them. The 98 patents were picked out by using the refine search function in Innovation. The refine search criteria included adjuvant in a claim, HIV or human immunodeficiency virus in the description, and adjuvant in the title. A list of the 98 patents/applications is provided in Appendix J. Please note that these 98 patents/applications are not coded by team members to decide the relevancy to vaccines against HIV.

### 3. D. Spreadsheet for Relevant Patents

Publication Number	Title	Primary	Secondary	Tertiary	Organic	Inorganic	Exogenous	Endogenous	Remark	Reviewed by
EP1123711B9	Attenuated toxins as adjuvants	1 -4, 10	5				Y			Nupur
EP1318835B1	USE OF IMIDAZOQUINOLINAMINES AS ADJUVANTS IN DNA VACCINATION	16	1		Y		Y			Nupur
EP1326639B1	ADJUVANT COMPOSITION COMPRISING AN IMMUNOSTIMULATORY OLIGONUCLEOTIDE AND A TOCOL	1 ~ 11	16		Y	Y				Nupur
EP1904099B1	THERMOREVERSIBLE IMMUNO-ADJUVANT EMULSION	1, 14				Y				Ted
US20070280929A1	ADJUVANT IN THE FORM OF A LIPID-MODIFIED NUCLEIC ACID	1	2 - 24		Y			Y		Ted
US20080241139A1	ADJUVANT COMBINATIONS COMPRISING A MICROBIAL TLR AGONIST, A CD40 OR 4-1BB AGONIST, AND OPTIONALLY AN ANTIGEN AND THE USE THEREOF FOR INDUCING A SYNERGISTIC ENHANCEMENT IN CELLULAR IMMUNITY	1 - 27		28	Y	Y	Y	Y		Lisa
US5961970A	Submicron emulsions as vaccine adjuvants	1			Y	Y				James
US6544518B1	Vaccines	1 - 7, 13- 15			Y	Y				Nupur
US6573245B1	Modified polysaccharide adjuvant-protein antigen conjugates, the preparation thereof and the use thereof	1- 18, 21 -27, 31, 31			Y					Nupur
US6846489B1	Vaccines containing a saponin and a sterol	1, 2, 3, 4			Y			Y		James
WO2001012220A1	NON-IMMUNOSUPPRESSANT HIV TAT	9 ~ 11			Y					Nupur

Publication Number	Title	Primary	Secondary	Tertiary	Organic	Inorganic	Exogenous	Endogenous	Remark	Reviewed by
WO2002030458A1	YERSINIA ADHESION PROTEIN AS VACCINE ADJUBANT	1, 2, 4, 5			Y	Y				Nupur
WO2003029289A2	USE OF HEAT SHOCK PROTEINS	30, 31		32,33	Y			Y		Pravin
WO2003035105A2	A NOVEL SYNTHETIC CHIMERIC FUSION TRANSGENE WITH IMMUNO-THERAPEUTIC USES	9 - 18			Y					Brian
WO2003063899A2	VACCINE ADJUVANT	1~18, 19~22			Y					Pravin
WO2005117958A1	VACCINE COMPOSITIONS COMPRISING VIROSOMES AND A SAPONIN ADJUVANT	7, 8	1, 2, 3		Y		Y	Y		Brian
WO2006120439A2	NOVEL COMPOSITIONS AND USES THEREOF	81-115, 168-169	116, 120, 167	122, 123, 154, 171, 199	Y		Y	Y		Ted
WO2007107739A1	ADJUVANT	2- 24	60 8, 18, 19, 25	1, 9, 11, 23, 26						Ted
WO2008056174A2	NOVEL COMPOSITIONS AND USES THEREOF	91-99	32	33	Y			Y		Ted
WO2008056179A1	NOVEL COMPOSITIONS AND USES THEREOF	1-26, 90 , 91	42, 92, 93, 95, 96	44, 45, 76	Y			Y		Ted
WO2008118691A2	METHOD OF PREPARING AN IMMUNOLOGICALLY-ACTIVE ADJUVANT-BOUND DRIED VACCINE COMPOSITION	44, 45	1,2,3,21,22	30		Y				Lisa
WO2009003474A1	THE USE OF MONOMYCOLYL GLYCEROL (MMG) AS AN ADJUVANT	4, 5, 6, 7	1, 10		Y	Y				Lisa
WO2009072767A2	A POWERFUL VACCINE COMPOSITION COMPRISING A LIPOPEPTIDE AND POLY I:C AS AN ADJUVANT	1			Y					Lisa
WO2009104831A1	USE OF MUTANT HIV-1 PROTEASE OR SIV PROTEASE AS AN ADJUVANT	1 - 14		15	Y		Y			Lisa
WO2009118523A1	ADJUVANT	1,2	3	5,13,15	Y		Y	Y		Lisa

Publication Number	Title	Primary	Secondary	Tertiary	Organic	Inorganic	Exogenous	Endogenous	Remark	Reviewed by
CN101057975A	Cocktail vaccine for anti immune tolerance and immunodeficiency virus and its application		4	1, 5, 9, 11, 18, 19, 20, 21	Y			Y		Ted
EP1011720B1	MUCOSAL CYTOTOXIC T LYMPHOCYTE RESPONSES		4	3	Y		Y			Amrita
EP1017283B1	POLYNUCLEOTIDE VACCINE FORMULATIONS		1, 2			Y	Y			Amrita
EP1035865B1	HIV-1 TAT, OR DERIVATIVES THEREOF FOR PROPHYLACTIC AND THERAPEUTIC VACCINATION		22	21	Y	Y				Nupur
EP1156781B1	MICROEMULSIONS WITH ADSORBED MACROMOLECULES AND MICROPARTICLES		31, 41, 44, 45	1, 31, 32, 40	Y	Y				Nupur
EP1198249B1	USE OF CPG AS AN ADJUVANT FOR HIV VACCINE		1, 4			Y				Nupur
EP1227840B1	ADJUVANTED GENETIC VACCINES		8,9	1,7	Y		Y			Nupur
EP1279404A1	Use of HIV-1 tat, fragments or derivatives thereof, to target or to activate antigen-presenting cells, to deliver cargo molecules for vaccination or to treat other diseases		4, 45	41, 50	Y	Y	Y	Y		Brian
EP1550458A1	Synergistic liposomal adjuvants		23, 32	1, 2, 3, 4, 5, 8	Y	Y	Y	Y		JLF
EP1773999B1	VACCINE FOR PREVENTION AND TREATMENT OF HIV-INFECTION		18	17	Y		Y			JLF
EP327180A2	Vaccine containing polypeptides derived from the envelope gene of human immunodeficiency virus type 1.		8, 9	7		Y				James
EP792165B1	IMMUNOGENIC COMPOSITIONS		8		Y		Y	Y		James
GB2452958A	HIV vaccine compositions		1, 17, 18, 19, 20	4	Y			Y		Ted
KR808348B1	VACCINE FOR THE PROPHYLACTIC OR THERAPEUTIC IMMUNIZATION AGAINST HIV   The vaccine for the prevention about H &#65321; V or for treating immunization.		11, 12, 13, 14		Y		Y			JLF

Publication Number	Title	Primary	Secondary	Tertiary	Organic	Inorganic	Exogenous	Endogenous	Remark	Reviewed by
US20020072495A1	LL-37 is an immunostimulant		20		Y					Pravin
US20030180351A1	Pharmaceutically active composition and dispensing device		19, 22, 27							Nupur
US20030191076A1	Prime-boost vaccination strategy		3	2		Y				Nupur
US20040192612A1	Caspase inhibitors and uses thereof		23	22						Brian
US20040223977A1	Fusion peptide HIV vaccines		4, 5		Y		Y			JLF
US20040241192A1	Use of tryptanthrin compounds for immune potentiation		1		Y		Y			Brian
US20050192248A1	Use of synthetic glycolipids as universal adjuvants for vaccines against cancer and infectious diseases		1,27,41		Y					JLF
US20060251684A1	Compositions for inactivating pathogenic microorganisms, methods of making the compositions, and methods of use thereof		75	74	Y		Y			JLF
US20070009926A1	Biomarkers of resistance to infections in humans and biological applications thereof		8		Y			Y		JLF
US20070253969A1	Materials and methods relating to DNA vaccination		7,24		Y		Y			Lisa
US20080102078A1	MUTATED E. COLI HEAT-LABILE ENTEROTOXIN		5			Y				Lisa
US20080131466A1	VACCINE COMPOSITION CONTAINING SYNTHETIC ADJUVANT		1, 3	2	Y					Lisa
US20090104268A1	Nanoparticles Comprising Antigens and Adjuvants, and Immunogenic Structures		5, 7	1, 2, 3, 53, 57, 61, 73				Y	No HiV mentioned in the claims instean only mentions infectious diseases	JLF
US20090136522A1	Multivalent Immunogen		12, 13					Y		Ted
US4965069A	Oxidized viruses or viral antigens and utilization for diagnostic prophylactic and/or therapeutic applications		3	2	Y	Y				James
US5653985A	Purified gp120 composition retaining natural conformation		3,6	4		Y				James
US5837249A	Method for generating an immunogenic T cell response protective against a virus		3		Y	Y				James

Publication Number	Title	Primary	Secondary	Tertiary	Organic	Inorganic	Exogenous	Endogenous	Remark	Reviewed by
US5840313A	Peptides for use in vaccination and induction of neutralizing antibodies against human immunodeficiency virus		3 ,4 ,6, 7		Y	Y				James
US5843454A	HIV immunogenic complexes		1			Y				James
US5866320A	Nucleic acids encoding for non-infectious, replication-defective, self-assembling HIV-1 viral particles containing antigenic markers in the gag coding region		14	15	Y	Y	Y			Amrita
US5876724A	Induction of neutralizing antibody against viral infection by synergy between virus envelope glycoprotein and peptides corresponding to neutralization epitopes of the glycoprotein		12, 30	11,		Y	Y			James
US5879925A	Genetically engineered human immunodeficiency virus-like particles with modified chimeric envelope glycoproteins containing influenza virus transmembrane spanning domains		18	17	Y	Y	Y			Amrita
US5889176A	Nucleic acid molecules encoding non-infectious, non-replicating, HIV retrovirus-like particles containing heterologous antigenic anchor sequences		23	22	Y	Y	Y			Amrita
US5951986A	Tandem synthetic HIV-1 peptides		9	8		Y				James
US5980898A	Adjuvant for transcutaneous immunization		6, 7, 8	1	Y		Y			Amrita
US5981505A	Compositions and methods for delivery of genetic material		18		Y		Y			James
US6080408A	Human immunodeficiency virus type 1 nucleic acids devoid of long terminal repeats capable of encoding for non-infectious, immunogenic, retrovirus-like particles		14	13		Y	Y			Amrita
US6168923B1	Compositions and methods for use of IL-12 as an adjuvant		1		Y			Y		Amrita

Publication Number	Title	Primary	Secondary	Tertiary	Organic	Inorganic	Exogenous	Endogenous	Remark	Reviewed by
US6210663B1	Methods of augmenting mucosal immunity through systemic priming and mucosal boosting		10, 11		Y			Y		Nupur
US6287568B1	Methods relating to immunogenic dextran-protein conjugates		1		Y		Y			Amrita
US6436407B1	Mutant enterotoxin effective as a non-toxic adjuvant		1			Y				Amrita
US6451322B1	Retrovirus like particles made non infectious by a plurality of mutations		16	15	Y	Y	Y			Amrita
US6514503B1	Antigen delivery system		1		Y			Y		Amrita
US6544527B1	Non-infectious, immunogenic, human immunodeficiency virus-like particles devoid of long terminal repeats and a functional pol coding region		16	15	Y	Y	Y			Amrita
US6596278B2	Immunological response potentiation process		1		Y	Y		Y		James
US6723329B2	Use of parapox B2L protein to modify immune responses to administered antigens		1, 13		Y					Brian
US6737066B1	HIV immunogenic compositions and methods		15 ~ 17	1, 24	Y	Y				Nupur
US6752996B2	Use of parapox PP30 protein to modify immune responses to administered antigens		1, 2		Y		Y			Brian
US6759241B1	Adjuvant comprising a lipopolysaccharide antagonist		2, 3, 4	1, 30, 31, 32	Y					Nupur
US6815201B2	HIV-1 gp120 V1/V2 domain epitopes capable of generating neutralizing antibodies		24	23		Y	Y			Amrita
US6818222B1	Detoxified mutants of bacterial ADP-ribosylating toxins as parenteral adjuvants		1		Y		Y			Amrita
US6923970B2	Retrovirus-like particles made non-infectious by a plurality of mutations		21	20	Y	Y	Y			Amrita
US6933377B2	Compositions comprising multiple immunodeficiency virus subunits for inducing an immune response		7		Y			Y		Brian

Publication Number	Title	Primary	Secondary	Tertiary	Organic	Inorganic	Exogenous	Endogenous	Remark	Reviewed by
US7009037B2	Modified HIV-1gag p17 peptide and immunogenic composition		6	3		Y				Nupur
US7056521B2	Detoxified mutants of bacterial ADP-ribosylating toxins as parenteral adjuvants		1		Y		Y			Amrita
US7063849B1	Use of HIV-1 gp120 and gp160 proteins modified in the v3 loop for the preparation of vaccine compositions and formulations containing the same		2	3		Y	Y			Pravin
US7097971B2	HIV-1 peptide, antigen, immunogenic composition, diagnostic method and immunoassay kit		5	3		Y				Nupur
US7223739B1	Adjuvanted genetic vaccines		7, 8, 9, 19, 23, 24, 25, 26	1, 10, 15, 16, 17	Y					Ted
US7229625B2	Retrovirus-like particles made non-infectious by a plurality of mutations		24	23	Y	Y	Y			Amrita
US7311915B2	Method of producing an HIV-1 immune response		12		Y	Y	Y			Amrita
US7357936B1	Adjuvant systems and vaccines		1, 6		Y		Y	Y		Amrita
WO1990008198A1	COMPOSITIONS AND METHODS FOR TREATING OR PREVENTING AIDS, ARC AND HIV INFECTION		20, 31	4, 23, 24, 25	Y	Y	Y			James
WO1991001143A1	STABLE VACCINE COMPOSITIONS CONTAINING INTERLEUKINS		2	1	Y			Y		James
WO1995004147A1	RECOMBINANT CONSTRUCTS USING REPLACEMENT SEQUENCES IN HYPERVARIABLE REGIONS		35	36	Y					James
WO1995008335A1	TREATMENT OF HIV INFECTION WITH HUMIC ACID		3		Y		Y			James
WO1995031999A1	COMPOSITIONS OF TRANSACTIVATING PROTEINS OF HUMAN IMMUNODEFICIENCY VIRUS		14		Y	Y	Y			Amrita

Publication Number	Title	Primary	Secondary	Tertiary	Organic	Inorganic	Exogenous	Endogenous	Remark	Reviewed by
WO1998058956A2	IMPROVED METHODS FOR INDUCING AN IMMUNE RESPONSE		9		Y	Y				Amrita
WO1999002132A2	USE OF SUBMICRON OIL-IN-WATER EMULSIONS WITH DNA VACCINES		17		Y			Y		Amrita
WO1999046392A1	METHODS AND COMPOSITIONS OF CHEMOKINE-TUMOR ANTIGEN FUSION PROTEINS AS CANCER VACCINES		19, 23, 34, 46, 59	18, 22, 33, 45, 58	Y			Y		Nupur
WO2000010600A2	ACTIVATION AND PROTECTION OF T-CELLS (CD4<+> AND CD8<+>) USING AN H2 RECEPTOR AGONIST AND OTHER T-CELL ACTIVATING AGENTS		3	2	Y	Y				Nupur
WO2000018432A1	CARBOHYDRATE VACCINES FOR VIRAL DISEASES		10	9	Y					Nupur
WO2000048630A1	IMMUNOGENIC COMPLEXES AND METHODS RELATING THERETO		9, 10, 12, 13, 15	4, 21			Y			Amrita
WO2000069456A2	ADJUVANT COMBINATION FORMULATIONS		1 ~ 8, 15 ~ 17		Y			Y		Nupur
WO2001006756A2	ACTIVATION AND PROTECTION OF CYTOTOXIC LYMPHOCYTES USING A REACTIVE OXYGEN METABOLITE INHIBITOR		3, 5, 6, 24, 26, 27	2, 23	Y	Y				Nupur
WO2001043693A2	POLYNUCLEOTIDE VACCINES EXPRESSING CODON OPTIMIZED HIV-1 NEF AND MODIFIED HIV-1 NEF		25	24		Y	Y			Pravin
WO2002028371A1	VACCINE COMPOSITION COMPRISING AN IMMUNOLOGICALLY ACTIVE SUBSTANCE EMBEDDED IN MICROPARTICLES CONSISTING OF STARCH WITH REDUCED MOLECULAR WEIGHT		19	18	Y	Y				Nupur

Publication Number	Title	Primary	Secondary	Tertiary	Organic	Inorganic	Exogenous	Endogenous	Remark	Reviewed by
WO2002079417A2	METHODS OF DELIVERY OF EXOGENOUS PROTEINS TO THE CYTOSOL AND USES THEREOF		22	23					HIV Vaccine in description	Pravin
WO2002088328A2	METHOD FOR GENERATING HIGHLY ACTIVE HUMAN DENDRITIC CELLS FROM MONOCYTES		17					Y		Pravin
WO2003022869A2	HUMAN IMMUNODEFICIENCY VIRUS ENVELOPE GLYCOPROTEIN MUTANTS AND USES THEREOF		43, 98	42, 97						Brian
WO2003054006A2	MUTATED HIV TAT		10	8, 9	Y					Brian
WO2003090664A2	MUTATED HPV-16 E7 POLYPEPTIDE, PHARMACEUTICAL COMPOSITION COMPRISING IT AND ITS PREPARATION PROCESS		17	16	Y					Brian
WO2004032860A2	HIV VACCINE FORMULATIONS		12, 13	11, 27	Y					Brian
WO2004035006A2	METHODS AND COMPOSITIONS FOR IMMUNIZATION AGAINST HIV		44	40, 41	Y					Brian
WO2004044155A2	MIP-1alpha AND GM-CSF AS ADJUVANTS OF IMMUNE RESPONSE		2		Y			Y		Brian
WO2004047861A1	VACCINES AGAINST VIRUSES WITH CATIONIC SUBSTANCES AS ADJUVANTS		1, 7, 9, 10, 11, 12, 29, 30, 31		Y	Y				Brian
WO2004053086A2	PLASMODIUM FALCIPARUM ANTIGENS AND METHODS OF USE		7	1	Y		Y			Brian
WO2004065578A2	MICROPARTICLES WITH ADSORBED POLYNUCLEOTIDE-CONTAINING SPECIES		36	35	Y	Y	Y			Brian
WO2004067020A1	DNA VACCINE COMPOSITION WITH ENHANCED IMMUNOGENICITY		7	1	Y		Y			Brian

Publication Number	Title	Primary	Secondary	Tertiary	Organic	Inorganic	Exogenous	Endogenous	Remark	Reviewed by
WO2004069272A2	ADJUVANT COMBINATION FOR USE IN THE IMMUNIZATION OF A MAMAL COMPRISING IL2 AND IL12		6, 8			Y		Y		Brian
WO2005021726A2	IMMUNOGENIC HIV COMPOSITIONS AND RELATED METHODS		9,10,11	1, 20	Y	Y	Y			JLF
WO2005027872A2	COMPOSITIONS FOR INACTIVATING PATHOGENIC MICROORGANISMS, METHODS OF MAKING THE COMPOSITIONS, AND METHODS OF USE THEREOF		69	68	Y		Y			JLF
WO2005039630A2	IMMUNOGENIC COMPOSITIONS		1, 9, 10, 11, 19, 20, 21, 23		Y	Y	Y			Brian
WO2005039634A1	VACCINE COMPOSITIONS COMPRISING AN INTERLEUKIN 18 AND SAPONIN ADJUVANT SYSTEM		1, 9, 10, 16, 18		Y	Y	Y			Brian
WO2005048957A2	NOVEL INSERTION SITES IN POX VECTORS		24		Y		Y		adjuvant is the poxvirus	JLF
WO2005051419A1	RETROVIRUS-LIKE PARTICLES AND RETROVIRAL VACCINES		69, 78	68, 77	Y	Y	Y			JLF
WO2005052119A2	ADJUVANTS OF IMMUNE RESPONSE		16	15	Y			Y		JLF
WO2005076001A2	A POLYPEPTIDE DERIVED FROM GP41, A VACCINE COMPOSITION COMPRISING SAID POLYPEPTIDE, AND USES FOR TREATING AN INFECTION BY AN HIV VIRUS IN AN INDIVIDUAL		11	8	Y	Y	Y	Y		Brian
WO2005122739A2	ADJUVANCY AND IMMUNE POTENTIATING PROPERTIES OF NATURAL PRODUCTS OF ONCHOCERCA VOLVULUS		1		Y				Adjuvant has Ov-ASP	JLF

Publication Number	Title	Primary	Secondary	Tertiary	Organic	Inorganic	Exogenous	Endogenous	Remark	Reviewed by
WO2005123120A1	SUSTAINED RELEASE VACCINE COMPOSITION		10, 11, 12, 20, 25, 26, 31, 33, 34, 44, 45, 55, 59, 60, 71, 72, 77, 78, 80, 81	1, 17, 67, 68	Y	Y	Y			JLF
WO2006002079A2	HIV-1 NEUTRALIZING ANTIBODIES ELICITED BY TRIMERIC HIV-1 ENVELOPE GLYCOPROTEIN COMPLEX		34, 39, 40, 42, 83, 88, 89, 91	33, 38, 41, 82	Y		Y			JLF
WO2006030440A2	USE OF TELLURIUM COMPOUNDS AS ADJUVANTS		1,2,3,			Y				JLF
WO2006031878A2	IMIDAZOQUINOLINE COMPOUNDS		60, 61, 67, 68, 70, 71, 72, 77, 78, 79	59, 66, 70, 77				Y		JLF
WO2006037070A2	STABILIZATION OF ALUM-ADJUVANTED IMMUNOLOGICALLY ACTIVE AGENTS		16	11		Y				JLF
WO2006108241A1	IMMUNOMODULATING COMPOSITIONS AND USES THEREFOR		19	17, 18	Y					Ted
WO2006110344A1	NOVEL METHODS FOR INDUCING AN IMMUNE RESPONSE AGAINST HUMAN IMMUNODEFICIENCY VIRUS		25		Y		Y			Ted
WO2006110831A2	METHOD OF INDUCING NEUTRALIZING ANTIBODIES TO HUMAN IMMUNODEFICIENCY VIRUS		9	8	Y					Ted
WO2006118916A2	METHODS AND COMPOSITIONS FOR POLYTOPIC VACCINATION		54 - 57	50 -53	Y	Y	Y	Y		Ted

Publication Number	Title	Primary	Secondary	Tertiary	Organic	Inorganic	Exogenous	Endogenous	Remark	Reviewed by
WO2006123256A2	HIVCON: ANHIV IMMUNOGEN AND USES THEREOF		118	114-117	Y	Y				Ted
WO2006136460A2	NEW ADJUVANT		1, 2, 3, 4, 5			Y				JLF
WO2007038083A2	HEAT SHOCK PROTEINS FROM MYCOBACTERIUM LEPRAE AND USES THEREOF		9		Y			Y		Ted
WO2007041285A2	COMPLEXES OF INACTIVATED PEPSIN FRACTION AND HEAT SHOCK PROTEIN		13	12, 15, 34	Y	Y		Y		Ted
WO2007047916A2	MULTIVALENT HIV VACCINES		3, 9	2, 8	Y	Y				Ted
WO2007071997A2	METHOD OF ELICITING IMMUNE RESPONSE		8	7	Y			Y		Ted
WO2007079448A2	THREE COMPONENT CARBOHYDRATE VACCINE		29, 34	27, 28	Y		Y			Ted
WO2007099387A1	VIROSOME-LIKE VESICLES COMPRISING GP41-DERIVED ANTIGENS		19, 20	17	Y	Y				Ted
WO2007109812A2	IMMUNOPOTENTIATING COMPOUNDS		94, 95		Y					Ted
WO2007109813A1	IMIDAZOQUINOXALINE COMPOUNDS AS IMMUNOMODULATORS		47,48, 54, 55, 58, 59, 65, 66		Y	Y				Ted
WO2007120860A2	NANOEMULSION VACCINES		96, 97	95	Y			Y		Ted
WO2007127372A2	GENETIC ADJUVANTS FOR VIRAL VACCINES		3	1	Y			Y		Lisa
WO2007133573A1	HIV-1 IMMUNOGENIC COMPOSITIONS		1-9, 12, 13		Y	Y	Y	Y		Lisa
WO2007137591A2	HIV VACCINE		22	21	Y	Y	Y			Lisa
WO2008000261A2	EXPANDING THE T CELL REPERTOIRE TO INCLUDE SUBDOMINANT EPITOPES BY VACCINATION WITH ANTIGENS DELIVERED AS PROTEIN FRAGMENTS OR PEPTIDE COCKTAILS		8, 12	7, 16	Y			Y		Lisa

Publication Number	Title	Primary	Secondary	Tertiary	Organic	Inorganic	Exogenous	Endogenous	Remark	Reviewed by
WO2008011120A2	HUMAN ENDOGENOUS RETROVIRUS POLYPEPTIDE COMPOSITIONS AND METHODS OF USE THEREOF		6	5	Y	Y				Lisa
WO2008025848A2	COMPOSITION FOR ELICITING A SPECIFIC CTL RESPONSE, COMPRISING A LYMPHO-ABLATIVE COMPOUND AND A MOLECULE THAT CONTAINS ANTIGENIC SEQUENCES AND TARGETS PROFESSIONAL ANTIGEN PRESENTING CELLS		8	7	Y		Y			Lisa
WO2008063586A2	MULTICOMPONENT VACCINE		18			Y				Lisa
WO2008107370A1	NOVEL METHOD AND COMPOSITIONS		30-33	1-6, 8	Y	Y	Y	Y		Lisa
WO2008124483A1	PROTEIN CAGE IMMUNOTHERAPEUTICS		33, 34, 55, 57, 58	31, 32, 54, 56	Y		Y	Y		Lisa
WO2008140579A2	INDUCTION OF BROADLY REACTIVE NEUTRALIZING ANTIBODIES BY FOCUSING THE IMMUNE RESPONSE ON V3 EPITOPES OF THE HIV-1 GP120 ENVELOPE		39	37	Y	Y	Y			Lisa
WO2008151633A2	VECTORS FOR HIV-1 VACCINE		71	68	Y	Y	Y	Y		Lisa
WO2009009054A1	METHODS FOR GENERATING IMMUNE RESPONSE USING CATIONIC-LIPOSOME-MEDIATED NUCLEIC ACID DELIVERY		4	1	Y			Y	Interleukin is the adjuvant and not specified	Lisa
WO2009025864A1	METHODS OF TREATING AND PROTECTING AGAINST HUMAN IMMUNODEFICIENCY VIRUS		8	7	Y		Y			Lisa
WO2009026353A1	IMMUNOGEN PRESENTING HIV GP120 V3 LOOP IN A CONFORMATION THAT INDUCES BROADLY NEUTRALIZING ANTIBODIES		31	29	Y	Y	Y	Y		Lisa

Publication Number	Title	Primary	Secondary	Tertiary	Organic	Inorganic	Exogenous	Endogenous	Remark	Reviewed by
WO2009038756A2	LONG INTERSPERSED NUCLEAR ELEMENT POLYPEPTIDE COMPOSITIONS AND METHODS OF USE THEREOF		7	6	Y	Y		Y		Lisa
WO2009046984A1	HIV PREVENTIVE VACCINE BASED ON HIV SPECIFIC ANTIBODIES		16		Y			Y		Lisa
WO2009051837A2	VACCINE NANOTECHNOLOGY		65, 66	58	Y	Y		Y		Lisa
WO2009058989A1	ANTIGEN-ANTIBODY COMPLEXES AS HIV-1 VACCINES		18	17		Y				Lisa
WO2009076158A1	COMPOSITIONS FOR INDUCING IMMUNE RESPONSES		1, 9, 10, 11, 12, 13, 14	35	Y	Y		Y	microparticle as 1st adjuvant; imidazoquinoline 2nd adjuvant;	Lisa
WO2009080719A1	VACCINE		28, 29, 30, 31, 32	27	Y		Y	Y		Lisa
WO2009106085A1	VACCINE COMPOSITIONS COMPRISING SACCHARIDE ANTIGENS		1, 2			Y	Y		Claim 1 direct claims a vaccine comprises saponin & alum adjuvant	Lisa
CN100998874A	IIIV vaccine containing recombination virus and its united immune preparation			1						Ted
CN101475605A	Modification method of yellow humic acid, product obtained therefrom, and use thereof in preparation of immunity improving or HIV preventing medicaments			15					increasing immunity by using humic acid	Lisa
EP1150693B1	IMMUNOGENIC COMPOSITIONS FOR USE AS VACCINES			21						Nupur
EP1169057B1	ANTI-HIV 1 VACCINE COMPRISING THE ENTIRE OR PART OF THE TAT HIV-1 PROTEIN			1						Nupur

Publication Number	Title	Primary	Secondary	Tertiary	Organic	Inorganic	Exogenous	Endogenous	Remark	Reviewed by
EP1368044B1	IMMUNOMODULATOR FOR THE MANAGEMENT OF HUMAN IMMUNODEFICIENCY VIRUS (HIV) DISEASE/INFECTION			12						Pravin
EP1380650A1	Conditionally replicating viral vectors and their use			38						Amrita
EP1782826A1	PQS and c-diGMP and its conjugates as adjuvants and their uses in pharmaceutical compositions			1 ,3 ,17, 23, 27, 34						Ted
EP1787660A1	New adjuvants on the basis of bisacyloxypropylcysteine conjugates and their uses in pharmaceutical compositions			10 , 18, 22, 29						Ted
EP1870420A1	Peptides regulating the surface expression of the T cell receptor			37, 38, 39						Lisa
EP1940464B1	HEXOSYLCERAMIDES AS ADJUVANTS AND THEIR USES IN PHARMACEUTICAL COMPOSITIONS			11, 16, 24						Ted
EP1992358A1	AIDS VACCINE BASED ON REPLICATIVE VACCINIA VIRUS VECTOR			9						Ted
EP330359A2	Composition useful in the diagnosis and treating of HIV-1 infection.			11						James
EP693937B1	HIV-1 VACCINES, ANTIBODY COMPOSITIONS RELATED THERETO, AND THERAPEUTIC AND PROPHYLACTIC USES THEREOF			15, 16						James
EP835309B1	VACCINE FOR INFECTIOUS AGENTS, COMPOSITION FOR TREATING AND PREVENTING HIV INFECTIONS			11						Amrita
EP969873B1	MULTIPLE ANTIGEN GLYCOPEPTIDE CARBOHYDRATE, VACCINE COMPRISING THE SAME AND USE THEREOF			17						Amrita

Publication Number	Title	Primary	Secondary	Tertiary	Organic	Inorganic	Exogenous	Endogenous	Remark	Reviewed by
EP972523A2	Method and compositions for inducing immunity to HIV			14, 15, 19						Nupur
GB2294047A	Synthetic peptides for use as epitopes specific for HIV			4, 6, 10, 11						Amrita
US20010039026A1	Assay method			13						Nupur
US20020182222A1	HIV vaccine candidate peptides			6						Brian
US20030068615A1	Polypeptides that bind HIV gp120 and related nucleic acids, antibodies, compositions, and methods of use			51						Nupur
US20030096737A1	Caspase inhibitors and uses thereof			11						Pravin
US20030099934A1	Chemically modified hiv envelope glycoprotein			12						Pravin
US20030129195A1	Use of heat shock proteins			39, 47, 51						Nupur
US20030232846A1	Caspase inhibitors and uses thereof			20,21						Pravin
US20040109869A1	Transcutaneous immunostimulation			1, 9, 13, 15, 19						Pravin
US20040241181A1	Methods of inducing a cytotoxic immune response and recombinant simian adenovirus compositions useful therein			24						Brian
US20050186147A1	Cosmetic and pharmaceutical foam with solid matter			56						JLF
US20050287167A1	Polycistronic HIV vector constructs			48					Adjuvant not specifically described	JLF
US20060211012A1	MHC CLASS II AS A PREVENTIVE VACCINE AGAINST HIV INFECTION			7, 17						Ted
US20060252813A1	Apparatus for curing a composite laminate			63						Brian
US20060281128A1	Compositions and methods using lentivirus-based vectors for generating immune responses			2					Adjuvant not specifically described	JLF
US20060292167A1	Therapeutic Peptides and Vaccines			1, 6						Ted
US20070116785A1	Nitric oxide as an anti-viral agent, vaccine and vaccine adjuvant			11, 22, 28, 34, 41, 48, 51, 54, 62, 70						Ted

Publication Number	Title	Primary	Secondary	Tertiary	Organic	Inorganic	Exogenous	Endogenous	Remark	Reviewed by
US20070293469A1	Compositions and methods for the treatment and prevention of disease			3, 17						Ted
US20080260766A1	Epitopes, combined epitopes, use of epitopes or their combination, composition, uses of the composition, anti-HIV-1 prophylactic vaccines, therapeutic vaccines, method for the identification of epitopes and methods for treatment and prevention			21, 22, 23, 28, 29, 30						Ted
US20080300287A1	Peptidic Compounds			21						Ted
US20090028886A1	Carrier conjugates of gnrh-peptides			37, 41					Adjuvant not described specifically	JLF
US20090098063A1	IMMUNE REGULATORY OLIGONUCLEOTIDE (IRO) COMPOUNDS TO MODULATE TOLL-LIKE RECEPTOR BASED IMMUNE RESPONSE			5						Ted
US20090105186A1	Beta-L-N4-Hydroxycytosine Deoxynucleosides and their use as Pharmaceutical Agents in the Prophylaxis or Therapy of Viral Diseases			8						Ted
US20090175889A1	HIV VACCINE			8						Lisa
US4900548A	Use of diethylcarbamazine to enhance antigen-antibody and antigen-host immune cell interactions			13						James
US5741492A	Preparation and use of viral vectors for mixed envelope protein vaccines against human immunodeficiency viruses			6, 12, 18						Amrita
US5846546A	Preparation and use of viral vectors for mixed envelope protein immunogenic composition against human immunodeficiency viruses			8, 16, 24, 30						Amrita
US5853725A	Prevention and treatment of retroviral disease			7, 12, 17						James
US5891994A	Methods and compositions for impairing multiplication of HIV-1			21						Amrita

Publication Number	Title	Primary	Secondary	Tertiary	Organic	Inorganic	Exogenous	Endogenous	Remark	Reviewed by
US5935579A	AIDS therapy and vaccine			9						James
US6193981B1	Methods and compositions for impairing multiplication of HIV-1			53						Amrita
US6232120B1	Methods to inhibit replication of infective virus			22, 31						Nupur
US6534312B1	Vaccines comprising synthetic genes			9						Amrita
US6723558B1	Preparation and use of viral vectors for mixed envelope protein vaccines against human immunodeficiency viruses			8, 16, 25, 31						Amrita
US6964762B2	Composition and method for stimulating immune response to pathogen using complex adenoviral vector			1						Pravin
US6964769B2	Molecular antigen array			24						Pravin
US7022324B2	Stabilized viral envelope proteins and uses thereof			20						Brian
US7094408B2	Immunogenicity using a combination of DNA and vaccinia virus vector vaccines			6						Pravin
US7153509B2	Immunogenic peptides comprising a T-helper epitope and a B-cell neutralizing antibody epitope			13, 16						Brian
US7262270B2	Fusion protein construct and method for inducing HIV-specific serum IgG and secretory IgA antibodies in-vivo			11					Vaccine in Description	Pravin
US7364744B2	Synthetic peptide vaccines for HIV: the CBD epitope as an effective immunogen to elicit broadly neutralizing antibodies against HIV			7					Adjuvant not described	JLF
US7479553B2	Nucleic acids encoding mutant disulfide bond-stabilized human immunodeficiency virus type 1 (HIV-1) gp140 envelope glycoproteins			26, 52						Brian
US7488491B2	Use of glycosylceramides as adjuvants for vaccines against infections and cancer			1, 2						Brian
US7531181B2	Gp120 specific antigens and uses thereof			36						Brian

Publication Number	Title	Primary	Secondary	Tertiary	Organic	Inorganic	Exogenous	Endogenous	Remark	Reviewed by
US7547769B2	Immunomodulatory constructs and their uses			12						Brian
WO1991009869A1	HIV-1 CORE PROTEIN FRAGMENTS			13						James
WO1995024924A1	COMPOSITIONS AND METHODS FOR VACCINES COMPRISING alpha -GALACTOSYL EPITOPES			7						Amrita
WO1995032000A1	HIV POLYPROTEIN IMMUNOGENS			30						Amrita
WO2000018433A2	USE OF ANTIGENIC COMPLEXES OF HIV ENVELOPE AND HLA CLASS I ANTIGENS AS HIV VACCINE			12						Nupur
WO2000032227A2	ORDERED MOLECULAR PRESENTATION OF ANTIGENS, METHOD OF PREPARATION AND USE			42						Nupur
WO2000035480A2	PEPTIDES USEFUL IN DIAGNOSING AND TREATING HIV-INDUCED ACQUIRED IMMUNE DEFICIENCY DISEASE			1, 3						Amrita
WO2000048641A1	RAPID CRYOBARIC STERILIZATION AND VACCINE PREPARATION			67						Nupur
WO2001021200A1	ORAL RECOMBINANT LACTOBACILLI VACCINES			17						Nupur
WO2001083535A2	PEPTIDES FOR USE AS A VACCINE AND/OR TREATMENT FOR HIV INFECTION			30, 33						Pravin
WO2002013828A1	A RETROVIRAL IMMUNOTHERAPY			6						Nupur
WO2002030434A1	COMPOSITIONS AND METHODS FOR PREVENTION AND TREATMENT OF PRIMARY AND METASTATIC NEOPLASTIC DISEASES AND INFECTIOUS DISEASES WITH COMPOSITIONS COMPRISING UNFRACTIONATED CELLULAR PROTEINS			44						Pravin

Publication Number	Title	Primary	Secondary	Tertiary	Organic	Inorganic	Exogenous	Endogenous	Remark	Reviewed by
WO2002064154A2	METHODS AND COMPOSITIONS FOR INHIBITING HIV-CORECEPTOR INTERACTIONS			6						Pravin
WO2002098457A2	RECOMBINANT RHABDOVIRUSES AS LIVE-VIRAL VACCINES FOR IMMUNODEFICIENCY VIRUSES			6						Pravin
WO2003010297A1	PROBIOTIC BIFIDOBACTERIUM STRAINS			25						Brian
WO2003034981A2	PREVENTION OF RECURRENT VIRAL DISEASE			50						Pravin
WO2003048371A2	DNA VACCINE			49						Pravin
WO2003092615A2	USE OF ANTI-CD1 ANTIBODIES FOR THE MODULATION OF IMMUNE RESPONSES			19						Brian
WO2003105895A1	VACCINATION WITH IMMUNO-ISOLATED CELLS PRODUCING AN IMMUNOMODULATOR			45						Brian
WO2004009816A1	METHODS OF TREATING CONDITIONS ASSOCIATED WITH AN EDG-1 RECEPTOR			44						Brian
WO2004035825A2	MARKER GENE			41					Relevant but Claim detached (HIV Before)	Pravin
WO2004046168A2	RECOMBINANT HIV-1 SUBCLASS D ENVELOPE GLYCOPROTEINS			12						Brian
WO2004050691A2	A METHOD FOR THE PRODUCTION OF HIV-1 GAG VIRUS-LIKE PARTICLES			27						Brian
WO2004050856A2	POLYVALENT, PRIMARY HIV-1 GLYCOPROTEIN DNA VACCINES AND VACCINATION METHODS			34						Brian
WO2004054974A2	CCR5 ANTAGONISTS AS THERAPEUTIC AGENTS			25						Brian
WO2004056979A2	RECOMBINANT VIRUS PRODUCTION FOR THE MANUFACTURING OF VACCINES			31						Brian

Publication Number	Title	Primary	Secondary	Tertiary	Organic	Inorganic	Exogenous	Endogenous	Remark	Reviewed by
WO2004060396A2	IMMUNOGENIC COMPOSITIONS CONTAINING PHOSPHOLIPID			27						Brian
WO2004069863A2	CONSTRAINED HIV V3 LOOP PEPTIDES AS NOVEL IMMUNOGENS AND RECEPTOR ANTAGONISTS			42						Brian
WO2005040365A1	IMMUNOGENIC COMPOSITION AND METHOD OF DEVELOPING A VACCINE BASED ON PORTIONS OF THE HIV MATRIX PROTEIN			20						JLF
WO2005047483A2	RENTA: AN HIV IMMUNOGEN AND USES THEREOF			99, 100, 101, 102					Adjuvant is not specifically described	JLF
WO2005058968A1	A METHOD TO MAKE A PEPTIDE-CARRIER CONJUGATE WITH A HIGH IMMUNOGENICITY			28					Adjuvant not specifically described in claims	JLF
WO2005066152A1	THIOPHENE DERIVATIVES FOR UP-REGULATING HLA-DM ACTIVITY			16, 38, 63					Adjuvant not specifically described	JLF
WO2005070959A2	COMPOSITIONS COMPRISING IMMUNE RESPONSE ALTERING AGENTS AND METHODS OF USE			47					Adjuvant not specifically described	JLF
WO2005080585A1	HIGHLY ACTIVE GLYCOPROTEINS-PROCESS CONDITIONS AND AN EFFICIENT METHOD FOR THEIR PRODUCTION			21					Adjuvant not specifically described	JLF
WO2005089231A2	ENHANCED ACTIVITY OF HIV VACCINE USING A SECOND GENERATION IMMUNOMODULATORY OLIGONUCLEOTIDE			11						JLF
WO2005100390A2	BOB-1 SPECIFIC T CELLS AND METHODS TO USE			21					Adjuvant not specifically described	JLF
WO2006009746A2	PLASMID HAVING THREE COMPLETE TRANSCRIPTIONAL UNITS AND IMMUNOGENIC COMPOSITIONS FOR INDUCING AN IMMUNE RESPONSE TO HIV			30, 37					Adjuvant not specifically described in claims	JLF

Publication Number	Title	Primary	Secondary	Tertiary	Organic	Inorganic	Exogenous	Endogenous	Remark	Reviewed by
WO2006017180A2	GLYCOPEPTIDE DIMERS AND USES THEREOF			8, 9					Adjuvant not described specifically	JLF
WO2006020071A2	VACCINE CONSTRUCTS AND COMBINATIONS OF VACCINES DESIGNED TO IMPROVE THE BREADTH OF THE IMMUNE RESPONSE TO DIVERSE STRAINS AND CLADES OF HIV			17					Adjuvant not described	JLF
WO2006029029A2	COMPOSITIONS FOR DETECTION OF LATENT HIV REACTIVATION AND METHODS OF USING THE SAME			19,51						JLF
WO2006030200A1	VACCINE			22						JLF
WO2006032674A1	VIRUS-LIKE PARTICLES COMPRISING A FUSION PROTEIN OF THE COAT PROTEIN OF AP205 AND AN ANTIGENIC POLYPEPTIDE			18						JLF
WO2006052820A2	HUMAN IMMUNODEFICIENCY VIRUS VACCINE			14						Ted
WO2006091455A2	MOLECULAR SCAFFOLDS FOR HIV-1 IMMUNOGENS			9, 22						Ted
WO2006112929A2	THE HIV GP-41-MEMBRANE PROXIMAL REGION ARRAYED ON HEPATITIS B SURFACE ANTIGEN PARTICLES AS NOVEL ANTIGENS			23, 27						Ted
WO2006127822A2	SCYTOVIRIN DOMAIN 1 RELATED POLYPEPTIDES			17						Ted
WO2007017686A2	PEPTIDES FOR TREATMENT AND DIAGNOSIS OF AUTOIMMUNE DISEASE			30					Adjuvant not specifically described	JLF
WO2007025276A2	USE OF HIV ENVELOPE/CD4 COMPLEXES FOR THE GENERATION ANTIBODIES AND AS IMMUNOGENIC COMPLEXES			29						Ted
WO2007035930A2	GLYCOSYLATED POLYPEPTIDES PRODUCED IN YEAST MUTANTS AND METHODS OF USE THEREOF			13						Ted

Publication Number	Title	Primary	Secondary	Tertiary	Organic	Inorganic	Exogenous	Endogenous	Remark	Reviewed by
WO2007039458A2	HIV PEPTIDE CONJUGATES AND USES THEREOF			12						Ted
WO2007055682A2	IMMUNOSTIMULATORY PROPERTIES OF OLIGONUCLEOTIDE-BASED COMPOUNDS COMPRISING MODIFIED IMMUNOSTIMULATORY DINUCLEOTIDES			61 ,62, 63 ,64 ,65						Ted
WO2007055704A2	IMMUNOSTIMULATORY PROPERTIES OF OLIGONUCLEOTIDE-BASED COMPOUNDS COMPRISING MODIFIED IMMUNOSTIMULATORY DINUCLEOTIDES			33 , 34, 35 ,36, 37						Ted
WO2007056847A1	STABILIZING FORMULATIONS FOR RECOMBINANT VIRUSES			30, 32						Ted
WO2007067729A2	MICROBIAL VACCINE AND VACCINE VECTOR			4 ,16						Ted
WO2007084021A2	COMPOSITIONS AND METHODS FOR DIAGNOSING HIV-2 INFECTION			62						Ted
WO2007100699A2	MICROPARTICLES CONTAINING BIODEGRADABLE POLYMER AND CATIONIC POLYSACCHARIDE FOR USE IN IMMUNOGENIC COMPOSITIONS			1, 11, 20,38, 39, 47, 57, 59, 60						Ted
WO2007104932A2	PEPTIDE SEQUENCES AND COMPOSITIONS			24, 25, 26, 27						JLF
WO2007122388A2	NANOPARTICLES FOR PROVIDING IMMUNE RESPONSES AGAINST INFECTIOUS AGENTS			29						Lisa
WO2007148048A1	COMPOSITIONS COMPRISING CHITIN MICROPARTICLES AND THEIR MEDICAL USES			1,4						Lisa
WO2007149491A2	SOLUBLE STABILIZED TRIMERIC HIV ENV PROTEINS AND USES THEREOF			19, 54						Lisa

Publication Number	Title	Primary	Secondary	Tertiary	Organic	Inorganic	Exogenous	Endogenous	Remark	Reviewed by
WO2008005929A2	RECOMBINANT HIV-1 GP120 IMMUNOGEN WITH THREE DIFFERENT V3 LOOPS FROM VIRUSES OF DIFFERENT CLADES			55, 70						Lisa
WO2008010930A2	HIV-1 PEPTIDES, NUCLEIC ACIDS, AND COMPOSITIONS, AND USES THEREOF			16, 30, 31						Lisa
WO2008063331A2	MODIFIED GP140 ENVELOPE POLYPEPTIDES OF HIV-1 ISOLATES, COMPOSITIONS, STABILIZED TRIMERIC COMPLEXES, AND USES THEREOF			18,19,20						Lisa
WO2008082719A2	COMBINED HUMAN PAPILLOMAVIRUS VLP/GENE DELIVERY SYSTEM AND USE THEREOF AS A VACCINE FOR PROPHYLAXIS AND IMMUNOTHERAPY OF INFECTIOUS DISEASES AND TUMORS			21						Lisa
WO2008091283A2	VIRAL INHIBITORY NUCLEOTIDE SEQUENCES AND VACCINES			44						Lisa
WO2008103428A2	DEMANNOSYLATED HIV-1 GP120 ENVELOPE GLYCOPROTEINS, COMPOSITIONS THEREOF AND METHODS RELATING THERETO			6,14,25, 35						Lisa
WO2008133983A1	ADJUVANT COMBINATIONS OF NKT ACTIVATOR, CD40 AGONIST, AND OPTIONAL ANTIGEN, THE USE THROUGH INDUCING SYNERGISTIC CELLULAR IMMUNITY			22						Lisa
WO2008140622A2	MODIFIED POLYMERASES AND ATTENUATED VIRUSES AND METHODS OF USE THEREOF			16						Lisa

Publication Number	Title	Primary	Secondary	Tertiary	Organic	Inorganic	Exogenous	Endogenous	Remark	Reviewed by
WO2008142479A2	INTERGENIC SITES BETWEEN CONSERVED GENES IN THE GENOME OF MODIFIED VACCINIA ANKARA (MVA) VACCINIA VIRUS			15						Lisa
WO2008143910A2	A STRATEGY FOR CLONING AND EXPRESSING THE EXTRACELLULAR DOMAINS OF RECEPTORS AS SOLUBLE PROTEINS			100						Lisa
WO2008155534A2	NEUROSTEROID COMPOUNDS			1						Ted
WO2009009215A2	ENHANCEMENT OF GLYCOPROTEIN INCORPORATION INTO VIRUS-LIKE PARTICLES			40						Lisa
WO2009012486A1	VARICELLA ZOSTER VIRUS-VIRUS LIKE PARTICLES (VLPS) AND ANTIGENS			39						Lisa
WO2009014789A2	ENVELOPED VIRUS NEUTRALIZING COMPOUNDS			45, 59, 75						Lisa
WO2009026529A1	COMPOSITIONS AND METHODS USING VARIANT TAT PROTEINS			30						Lisa
WO2009029569A1	HIV ENV PROTEINS WITH MODIFICATIONS IN THE V3 LOOP			19						Lisa
WO2009029716A1	PEPTIDES INDUCING A CD4I CONFORMATION IN HIV GP120 WHILE RETAINING VACANT CD4 BINDING SITE			41						Lisa
WO2009034172A1	ENHANCING THE T-CELLS STIMULATORY CAPACITY OF HUMAN ANTIGEN PRESENTING CELLS AND THEIR USE IN VACCINATION			16						Lisa
WO2009042895A2	REAGENTS FOR INDUCING AN IMMUNE RESPONSE			63						Lisa
WO2009043155A2	DISTINCT HIV-1 GAG AND ENV EPITOPES OF HLA ALLELES ASSOCIATED WITH DIFFERENTIAL SUSCEPTIBILITY TO HIV-1 INFECTION			1						Lisa

Publication Number	Title	Primary	Secondary	Tertiary	Organic	Inorganic	Exogenous	Endogenous	Remark	Reviewed by
WO2009065032A1	ANTIBODY PRODUCTION ELICITED BY A DNA VACCINE DELIVERED BY ELECTROPORATION			26						Lisa
WO2009082664A2	GENETICALLY MODIFIED ATTENUATED VESICULAR STOMATITIS VIRUS, COMPOSITIONS AND METHODS OF USE THEREOF			25						Lisa
WO2009089568A1	IMMUNOMODULATING COMPOSITIONS AND USES THEREFOR			9						Lisa
WO2009099672A2	BREAKING IMMUNOLOGICAL TOLERANCE WITH A GENETICALLY ENCODED UNNATURAL AMINO ACID			72						Lisa
WO2009102357A2	HIV-1 ENVELOPE GLYCOPROTEIN OLIGOMER AND METHODS OF USE			15						Lisa
WO2009114207A2	REPLICATION-DEFECTIVE FLAVIVIRUS VACCINES AND VACCINE VECTORS			34					no specific adjuvant listed in claim; need to check spec for further details	Lisa
WO2009117134A2	AEROSOLIZED GENETIC VACCINES AND METHODS OF USE			54,59					no specific adjuvant listed in claim; need to check spec for further details	Lisa

### 3. E. Spreadsheet for Patents with Non-English Claim

Publication Number	Title (English)	Remark	Reviewed by	can not code
CA2354100A1	POLYNUCLEOTIDE AND POLYPEPTIDE ANTIGENS OF CRYPTOCOCCUS NEOFORMANS AND THEIR VACCINE AND DIAGNOSTIC APPLICATIONS	No English Claims	Brian	Y
CN1464062A	Expression vector pBVTB, its construction method and use in HCV vaccin research	No English Claims	Brian	Y
DE10027968A1	Adjuvant therapy of dementia using alpha-lipoic acid or derivative, is effective in combination with antidementia or neurotransmission improving agents in improving cognitive function in e.g. Alzheimer's disease patients	German	Pravin	Y
DE19512142A1	(N/A)	German	Amrita	Y
DE19954514A1	Manipulating activity of cells ex vivo, useful e.g. in immunotherapy of cancer or viral infection, by treating the cells with antigens, adjuvants and stimulants	German	Pravin	Y
EP1065212A2	Lipopeptide inducing T-cytotoxic lymphocytes and their use as vaccines	In French	James	Y
EP1163909A2	Use of sugar ethers as immunity adjuvant in vaccine compositions, therapeutic compositions containing them and their use as vaccine	In French	Pravin	Y
EP459842A1	Process for the production of retroviral immunogenes and vaccines against retroviral infections, especially HIV, and immunogens and vaccines thereof.	In French	James	Y
FR2824279A1	(N/A)	French	Pravin	Y
FR2827606A1	New peptide derived from diphtheria anatoxin, useful as carrier in vaccines, lacks at least one Cys residue, also related nucleic acids	French	Brian	Y
FR2828106A1	Composition containing peptide from low molecular weight outer membrane protein, useful for preparing vaccines against infections or cancer	French	Brian	Y
JP10218789A	ACTIVATOR FOR AIDS VACCINE CONTAINING UBENIMEX AS ACTIVE INGREDIENT	Japanese	Amrita	Y
JP2002322065A	IMMUNE SYSTEM REGULATION	Japanese	Pravin	Y
JP2002332293A	REGULATION OF IMMUNE SYSTEM	No Claims but Looks Relevant	Pravin	Y
JP2003047489A	PROTEIN FROM ACTINOBACILLUS PLEUROPNEUMONIAE	Japanese	Nupur	Y
JP2004339160A	HIV VACCINE BY ORAL ADMINISTRATION	No claims for this patent	JLF	Y
JP2005314277A	SECRETORY IgA ANTIBODY INDUCER	No claims, the spec discusses an adjuvant according to abstract	JLF	Y
JP2008273846A	ADJUVANT AGAINST VIRUS- OR PATHOGENIC BACTERIUM-DERIVED INACTIVATED ANTIGEN AND SECRETORY IgA ANTIBODY INDUCER	No English claim	Lisa	Y
JP2009108048A	HYDROXYLAMINE DERIVATIVE USEFUL FOR ENHANCING PRODUCTION OF MOLECULAR CHAPERON, AND THE PREPARATION THEREOF	Japanese	Amrita	Y

Publication Number	Title (English)	Remark	Reviewed by	can not code
JP3034935A	ANTITRYPTASE ANTIBODY AND REMEDY FOR ACQUIRED IMMUNE DEFICIENCY SYNDROME USING SAME ANTIBODY	Japanese	James	Y
KR2002073569A	(N/A)		Nupur	Y
KR2003044016A	(N/A)		Nupur	Y
KR2004030599A	(N/A)		Nupur	Y
KR2006032925A	IMMUNOLOGICAL ADJUVANT CONTAINING EXTRACTS FROM ANTHRISCUS SYLVESTRIS	No claims in English	JLF	Y
KR2007019635A	IMMUNOGENIC HIV COMPOSITIONS AND RELATED METHODS		Nupur	Y
KR910297B1	MODIFIED VACCINIA ANKARA VIRUS VARIANT   The transformed vaccinia ankara virus variant.	No English claim	Lisa	Y
WO1993025236 A1	HUMORAL IMMUNITY AND CELL MEDIATION ADJUVANT COMPOSITION INDUCING NO RESPONSE TO AUTO-ANTIGENIC DETERMINANTS	In French	James	Y
WO1994021298 A1	STABILISED PHARMACEUTICAL COMPOSITIONS AND METHODS FOR PREPARING SAME	In French	James	Y
WO1999066046 A1	HIV VIRUS MIMOTOPES	French	Nupur	Y
WO2001030814 A1	DEGLYCOSYLATED ENV/CD4 COMPLEX AND THE USE THEREOF FOR VACCINATION AGAINST HIV	French	Nupur	Y
WO2001068129 A2	ADJUVANT FOR VACCINES	German	Pravin	Y
WO2002019968 A2	GENETICALLY ENGINEERED CO-EXPRESSION DNA VACCINES, CONSTRUCTION METHODS AND USES THEREOF	No English Claims	Pravin	Y
WO2002043756 A2	METHOD FOR OBTAINING ANTIGENIC AGGREGATES AND THE USE THEREOF IN FORMULATIONS	Claims in Spanish	Pravin	Y
WO2002045746 A2	PHARMACEUTICAL COMPOSITIONS ENHANCING THE IMMUNOGENICITY OF POORLY IMMUNOGENIC ANTIGENS	Spanish Patent	Pravin	Y
WO2002051865 A2	PROTEINIC ANTIGENS INDUCING ANTIBODIES NEUTRALISING HIV VIRUS	Claims in French	Pravin	Y
WO2002053149 A2	MEDICAMENT CONTAINING A POLYAMINE AS AN ACTIVE SUBSTANCE	Claims in German	Pravin	Y
WO2002062834 A2	MIXTURE OF PEPTIDES ORIGINATING FROM A NEF PROTEIN AND APPLICATIONS THEREOF	French	Pravin	Y
WO2002074283 A1	ADJUVANT EMULSION AND METHOD OF USING SAID EMULSION	German, Looks relevant	Pravin	Y
WO2002080840 A2	IMMUNITY ADJUVANT CONTAINING A COMPLEXED METAL CATION AND VACCINE CONTAINING SAME	French Patent	Pravin	Y
WO2003022883 A2	USE OF PROTEINS FOR THE PRODUCTION OF A MEDICAMENT FOR STIMULATING THE INNATE NON SPECIFIC IMMUNE SYSTEM	Claims in German	Pravin	Y
WO2003025166 A1	THERAPEUTIC VACCINATION METHOD, MUTATED PEPTIDES OF HIV REVERSE TRANSCRIPTASE AND THEIR USE FOR VACCINATION AND DIAGNOSTIC PURPOSES	French, no adjuvant in translation though	Brian	Y

Publication Number	Title (English)	Remark	Reviewed by	can not code
WO2005097179 A2	STABILISED TAT ANTIGEN AND THE USE THEREOF FOR ANTI-HIV VACCINATION	Claims in French	JLF	Y
WO2006112477 A1	POLYAMINO ACID FOR USE AS ADJUVANT	No English Claims	Ted	Y
WO2009027076 A1	LIQUID FORMULATION OF G-CSF	No English claim	Lisa	Y

## 4. Patent document Analytics

The following results reflect an analysis of the 315 relevant patents. The distribution of relevancy is as follows: Number of Primary Relevant: 25 patents; Number of Secondary Relevant 144; Number of Tertiary: 146. This analysis was mostly performed using Thompson Innovation Analyze Charts but other common office analytical tools such as Microsoft Excel® were used.

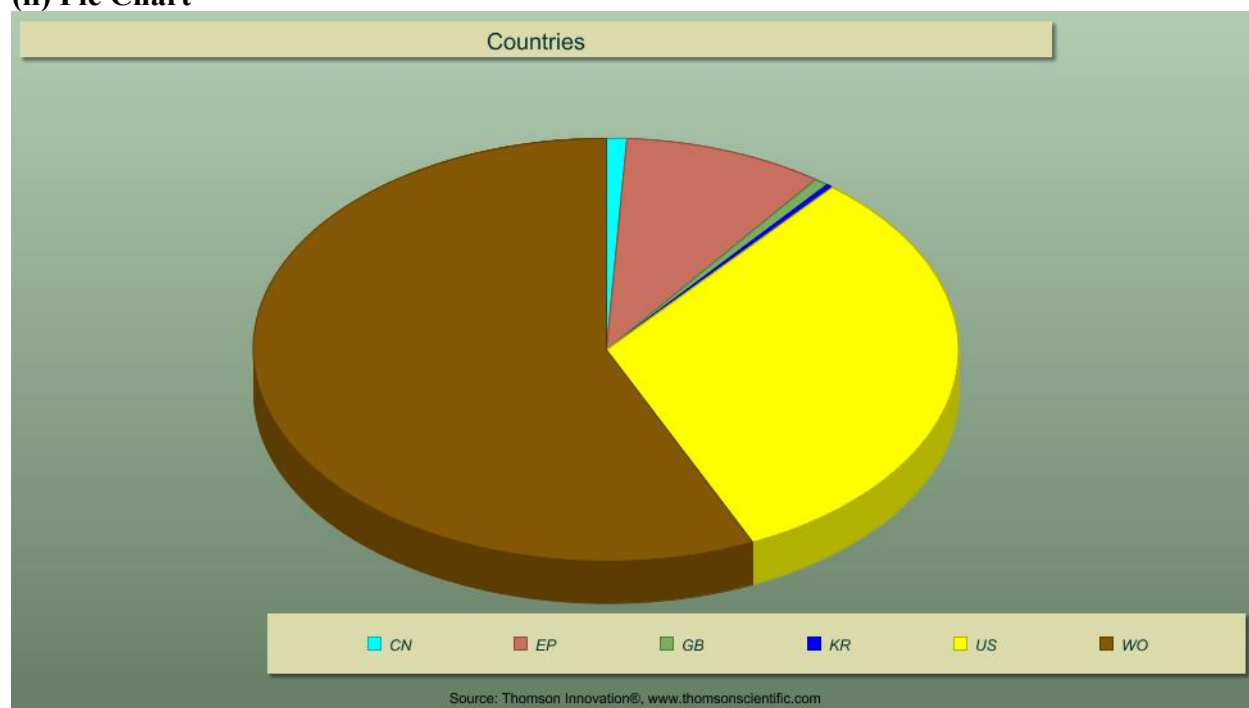
### 4. A. Patent Count vs. Country

(i)

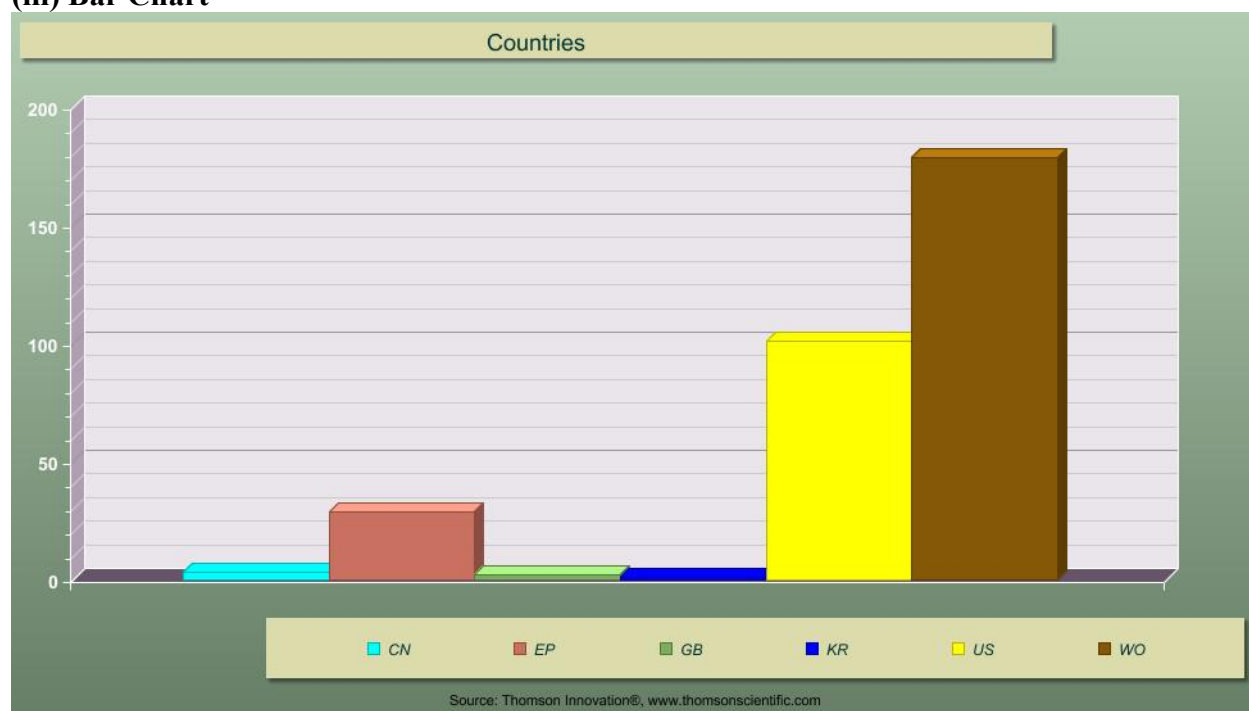
Country	Patent Count	Percentage
CN	3	0.95%
EP	29	9.21%
GB	2	0.63%
KR	1	0.32%
US	101	32.06%
WO	179	56.83%
Total	315	100.00%

CN: China issued patent or patent application; EP: Europe issued patent or patent application; GB: England issued patent or patent application; KR: Korea issued patent or patent application; US: US issued patent or patent application; WO: WIPO PCT patent application.

**(ii) Pie Chart**



**(iii) Bar Chart**



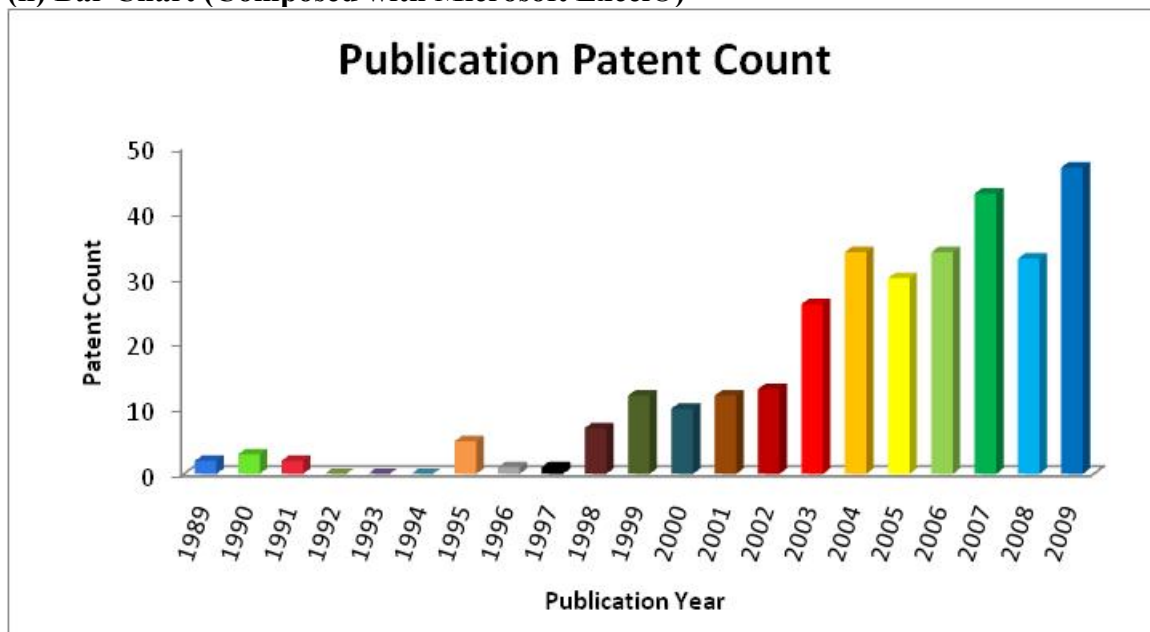
**Fig. 1.** Patent counts according to countries. Shown in a pie chart (ii) and a bar chart (iii).

#### 4. B. Patent Count vs. Publication Date

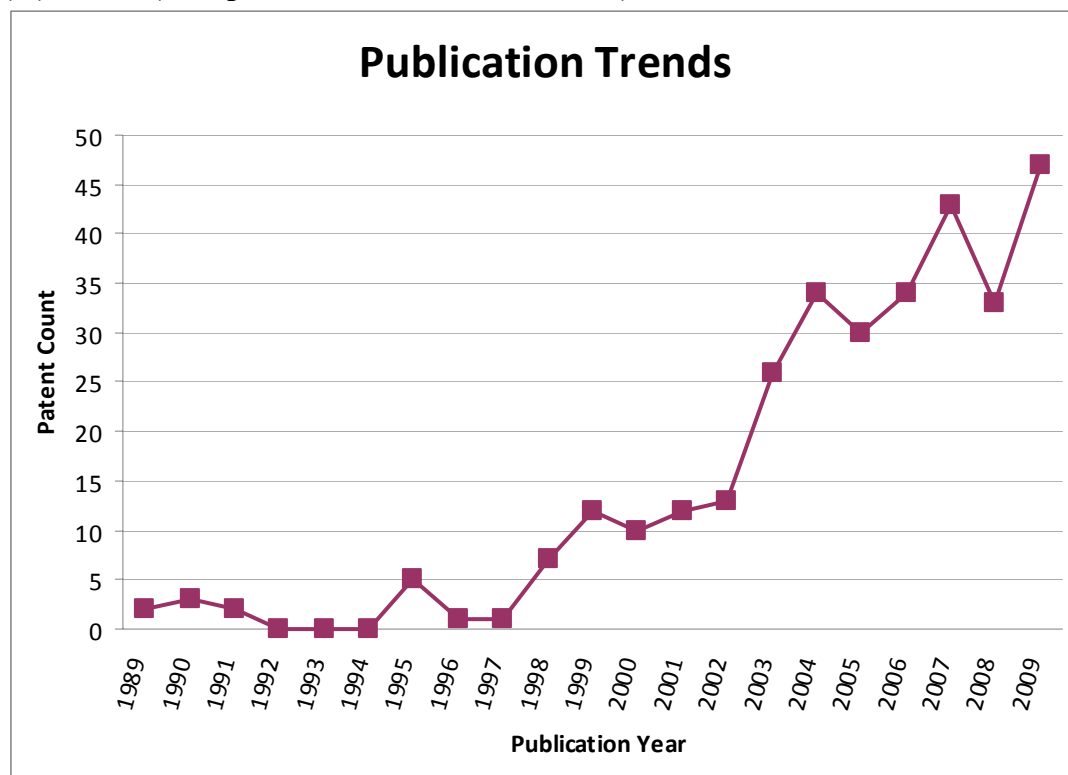
(i)

Publication Year	Patent Count	Percentage
1989	2	0.63%
1990	3	0.95%
1991	2	0.63%
1992	0	0.00%
1993	0	0.00%
1994	0	0.00%
1995	5	1.59%
1996	1	0.32%
1997	1	0.32%
1998	7	2.22%
1999	12	3.81%
2000	10	3.17%
2001	12	3.81%
2002	13	4.13%
2003	26	8.25%
2004	34	10.79%
2005	30	9.52%
2006	34	10.79%
2007	43	13.65%
2008	33	10.48%
2009	47	14.92%
Total	315	100.00%

**(ii) Bar Chart (Composed with Microsoft Excel®)**



**(iii) Trend (Composed with Microsoft Excel®)**



**Fig. 2.** Patent counts according to Publication date years. Shown in a bar chart (ii) and a line chart (iii).

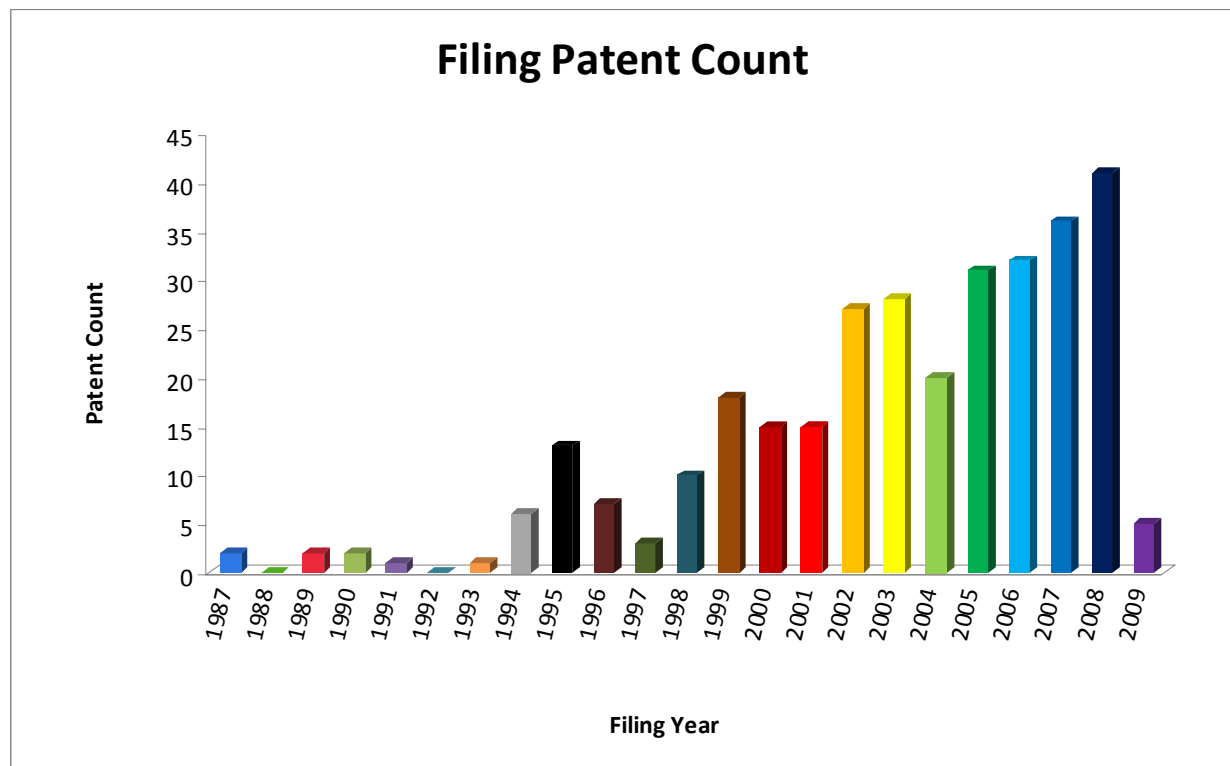
#### 4. C. Patent Count vs. Application (Filing) Date

(i)

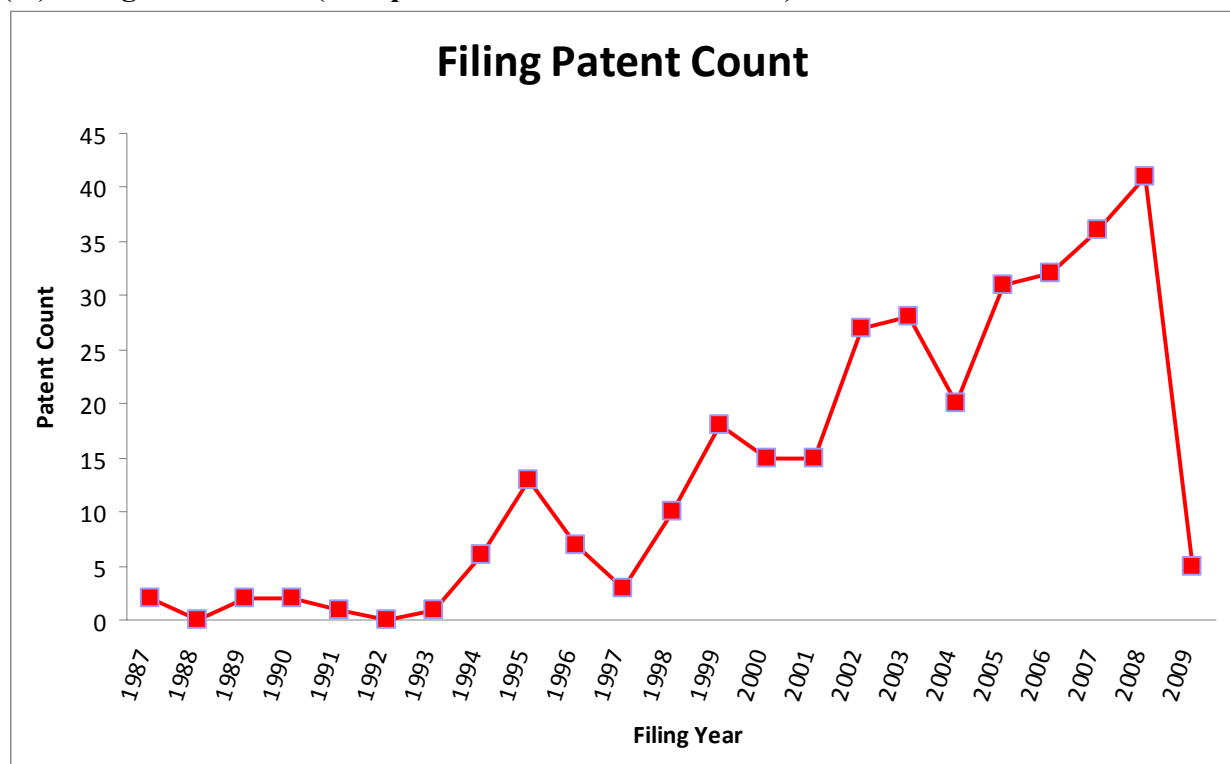
Application Year	Patent Count	Percentage
1987	2	0.63%
1988	0	0.00%
1989	2	0.63%
1990	2	0.63%
1991	1	0.32%
1992	0	0.00%
1993	1	0.32%
1994	6	1.90%
1995	13	4.13%
1996	7	2.22%
1997	3	0.95%
1998	10	3.17%
1999	18	5.71%
2000	15	4.76%
2001	15	4.76%
2002	27	8.57%
2003	28	8.89%
2004	20	6.35%
2005	31	9.84%
2006	32	10.16%
2007	36	11.43%
2008	41	13.02%
2009*	5	1.59%
Total	315	100.00%

\* The data of the application year 2009 is incomplete.

(ii) Filing Bar Chart (Composed with Microsoft Excel®)



(iii) Filing Year Trend (Composed with Microsoft Excel®)



**Fig. 3.** Patent counts according to filing date years. Shown in a bar chart (ii) and a line chart (iii). The data of the application year 2009 is incomplete.

#### 4. D. Patent Count vs. US Classification

US classification information is only available for US issued patents and US patent applications. The following analytics are based on 101 US patents/applications. The 101 patents/applications fall into 13 US class and the Top two US classes are Class 424 and Class 435. When further divided into sub-classification, the top five sub-classifications are all belong to Class 424, including 424/208.1, 424/188.1, 424/184.1, 424/278.1, 424/204.1, 424/208.1. The definition of these US classification and sub-classification are shown in Appendix C.

(i)

US Class (3 digit)	Patent Count
424	82
435	37
514	34
530	30
536	17
546	3
544	2
548	2
977	2
128	1
436	1
560	1
800	1

(ii) Bar Chart for US Class in 3-digits

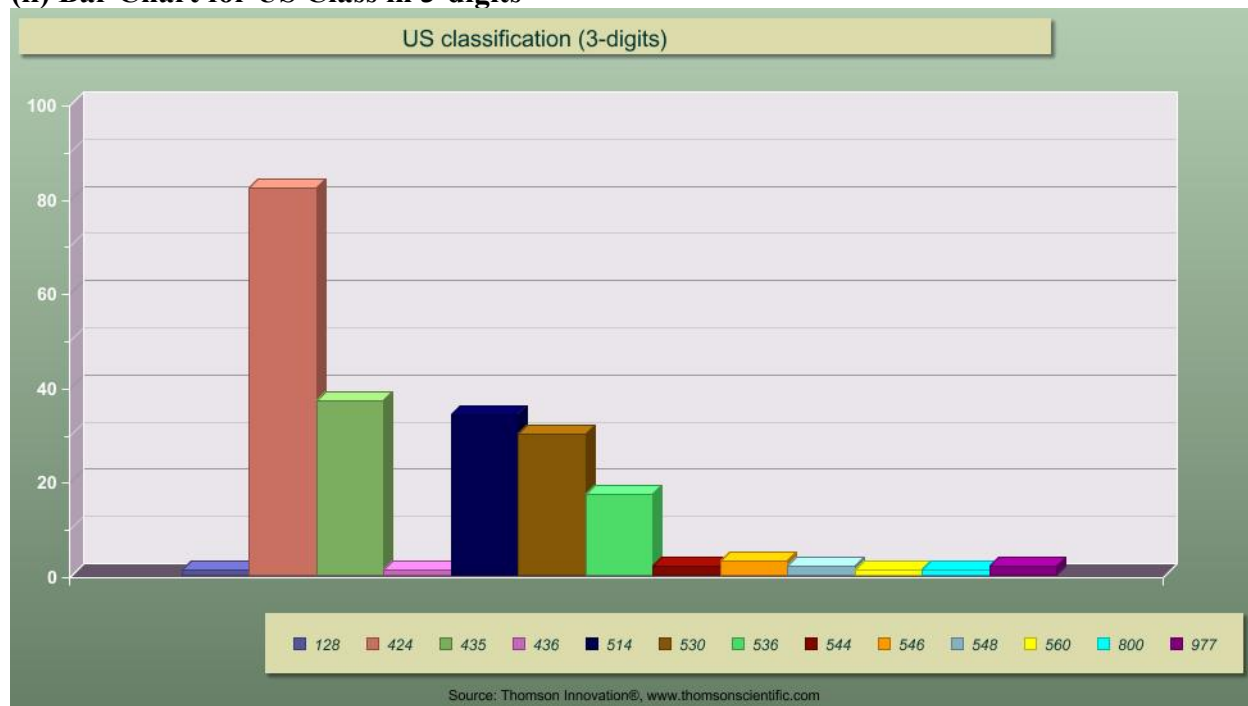
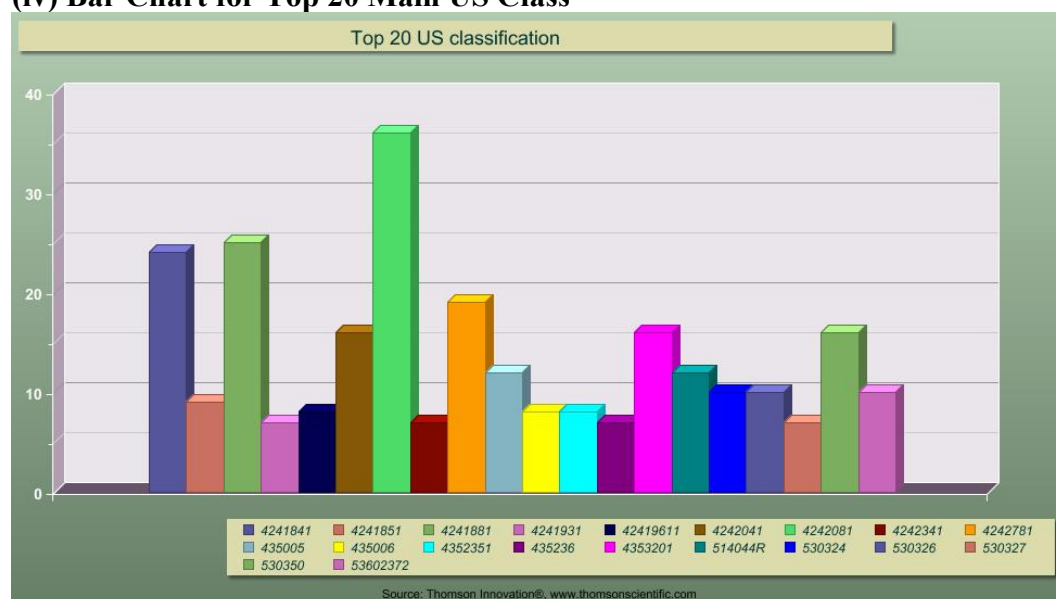


Fig. 4. Patent counts according to US classification in 3 digits. Shown in a bar chart (ii).

**(iii) Top 20 US Classification/Subclassification**

Top 20 US Class Main	Patent Count
424/208.1	36
424/188.1	25
424/184.1	24
424/278.1	19
424/204.1	16
435/320.1	16
530/350	16
435/005	12
514/044R	12
530/324	10
530/326	10
536/023.72	10
424/185.1	9
4241/961.1	8
435/006	8
435/2351	8
424/193.1	7
424/234.1	7
435/236	7
530/327	7

**(iv) Bar Chart for Top 20 Main US Class**



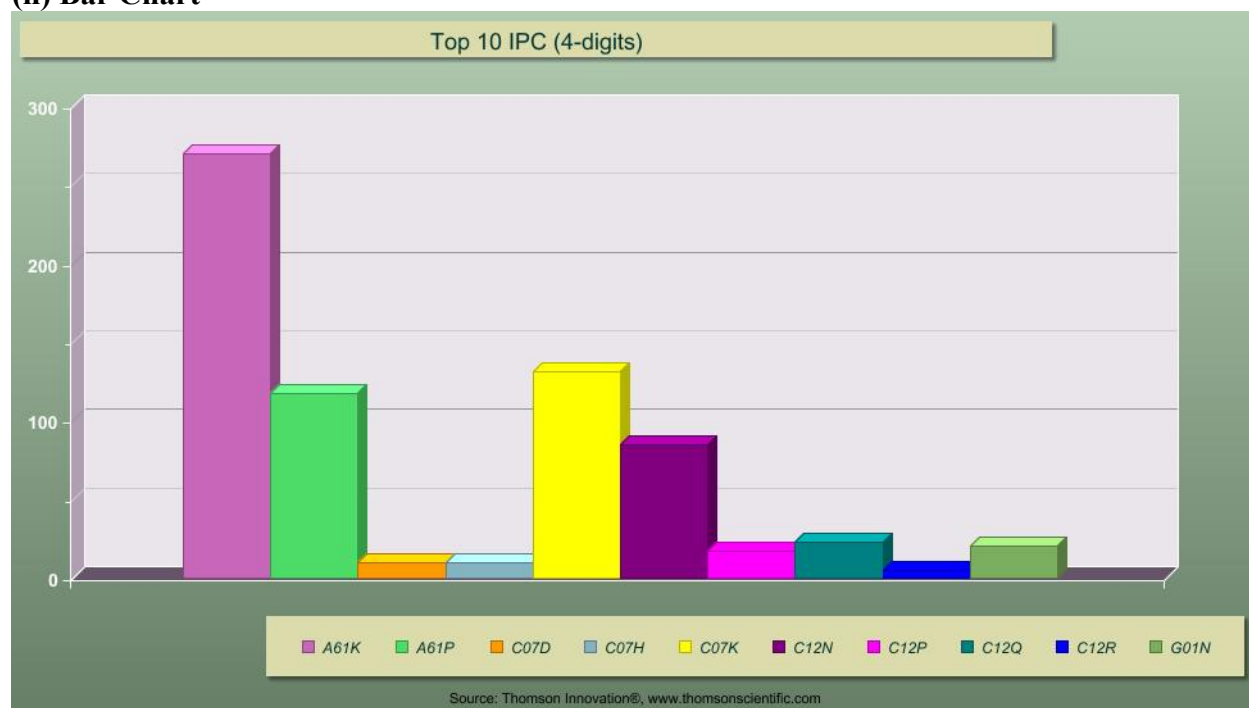
**Fig. 5.** Patent counts according to Top 20 main US classification. Shown in a bar chart (iv).

#### 4. E. Patent Count vs. IPC Classification

##### (i) Top 10 Main IPC

IPC (4-digits)	Patent Count
A61K	270
A61P	117
C07D	10
C07H	10
C07K	131
C12N	85
C12P	17
C12Q	23
C12R	5
G01N	20

##### (ii) Bar Chart



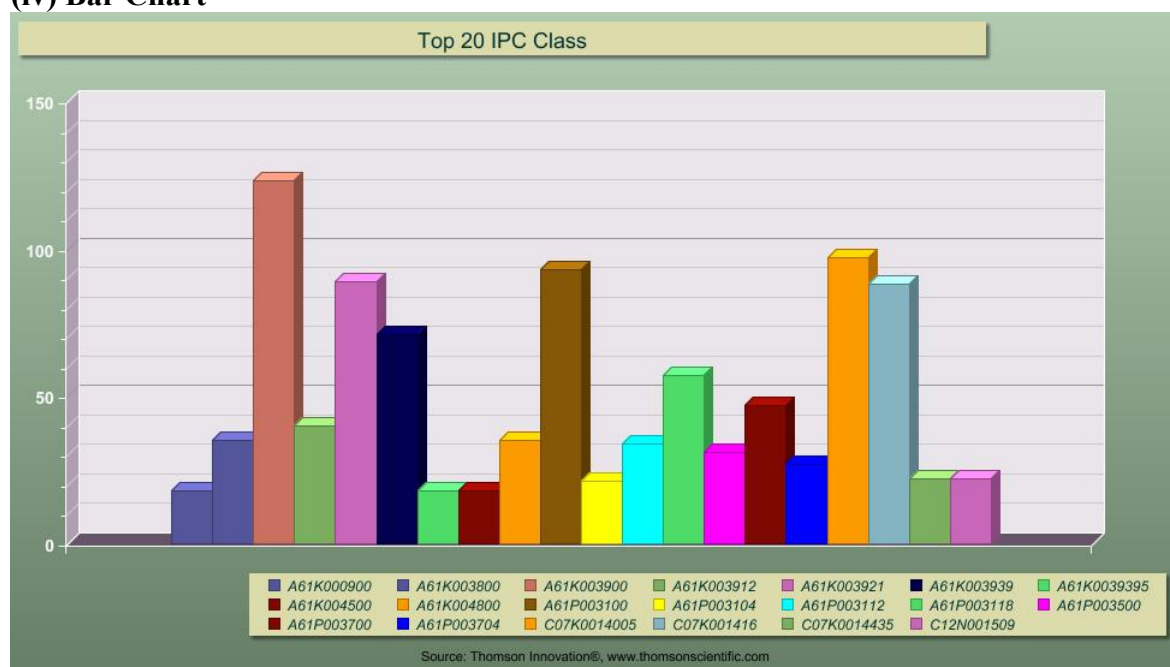
**Fig. 6.** Patent counts according to Top 10 main IPC class in 4 digits. Shown in a bar chart (ii).

The top three IPC classes are A61K, C07K, and A61P. The definitions of these IPC classifications shown in Appendix D.

**(iii) Top 20 Current IPC**

Current IPC	Patent Count
A61K000900	18
A61K003800	35
A61K003900	123
A61K003912	40
A61K003921	89
A61K003939	71
A61K0039395	18
A61K004500	18
A61K004800	35
A61P003100	93
A61P003104	21
A61P003112	34
A61P003118	57
A61P003500	31
A61P003700	47
A61P003704	27
C07K0014005	97
C07K001416	88
C07K0014435	22
C12N001509	22

**(iv) Bar Chart**



**Fig. 7.** Patent counts according to Top 20 current IPC class. Shown in a bar chart (iv).

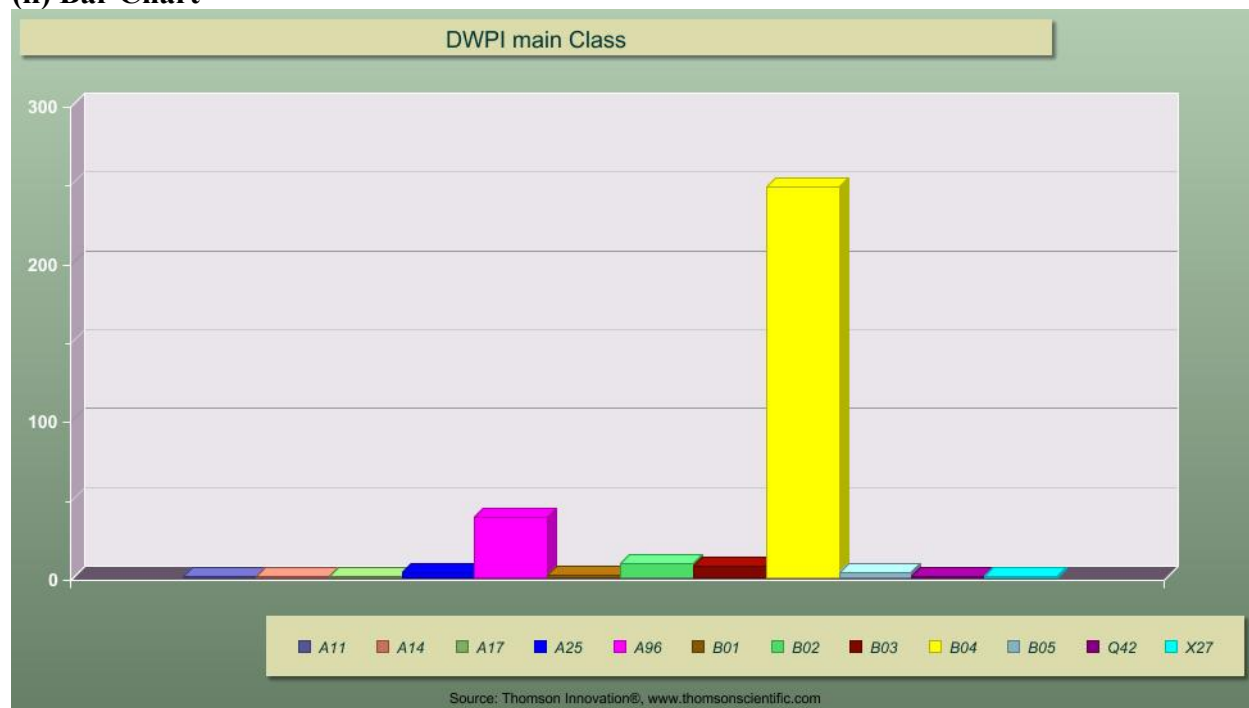
#### 4. F. Patent Count vs. Derwent Class (DWPI Class)

More than three forth of the relevant patents belong to the Derwent B04 class. The definitions of the Derwent class listed below are shown in Appendix E.

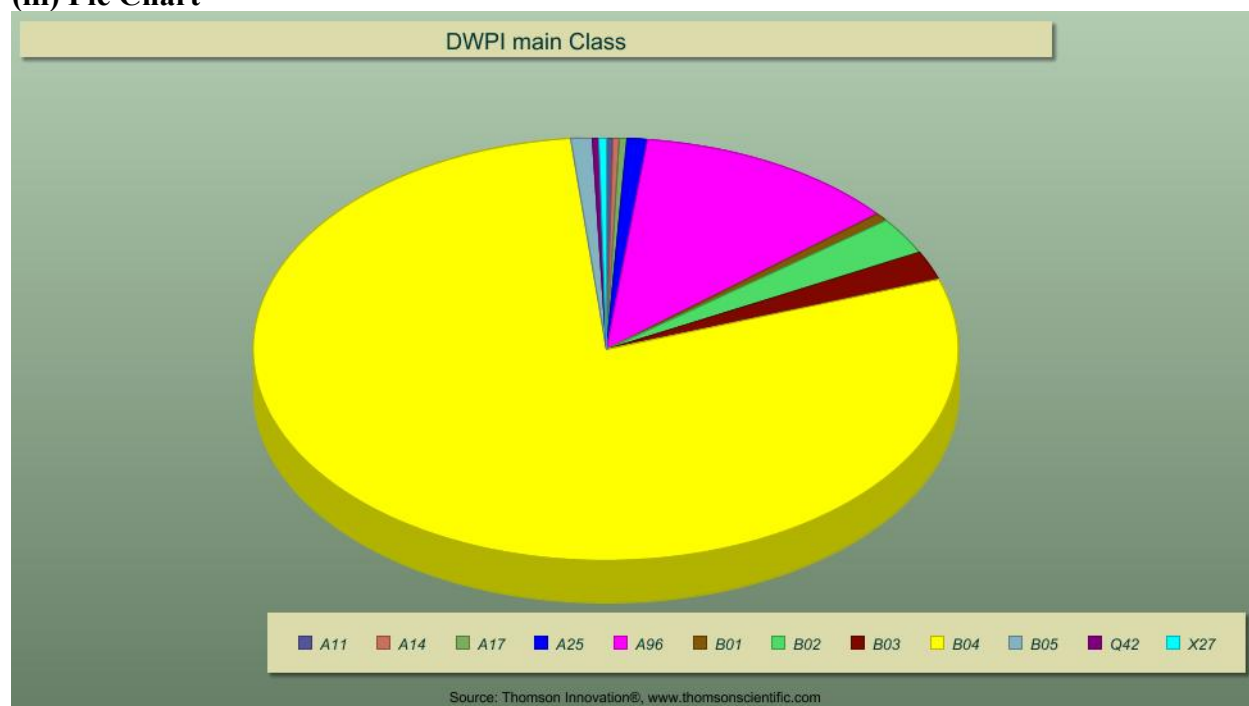
##### (i) All DWPI Class

DWPI Class-Main	Patent Count	Percentage
A11	1	0.32%
A14	1	0.32%
A17	1	0.32%
A25	3	0.95%
A96	38	12.06%
B01	2	0.63%
B02	9	2.86%
B03	7	2.22%
B04	248	78.73%
B05	3	0.95%
Q42	1	0.32%
X27	1	0.32%
Total	315	100.00%

##### (ii) Bar Chart



**(iii) Pie Chart**



**Fig. 8.** Patent counts according to Derwent class. Shown in a bar chart (ii) and a pie chart (iii).

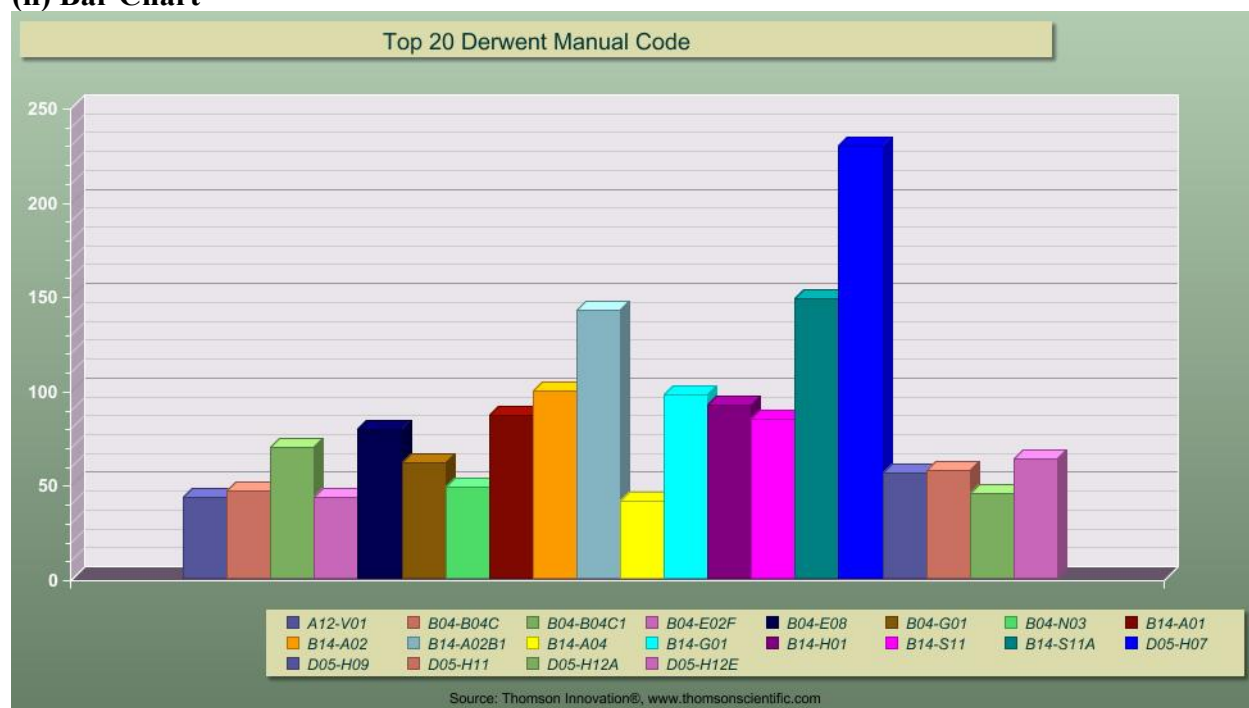
#### 4. G. Patent Count vs. Derwent Manual Code

The top three Derwent manual codes include D05-H07, B14-S11A, and B14-A02B1. The definitions of the Derwent manual codes are shown in Appendix F.

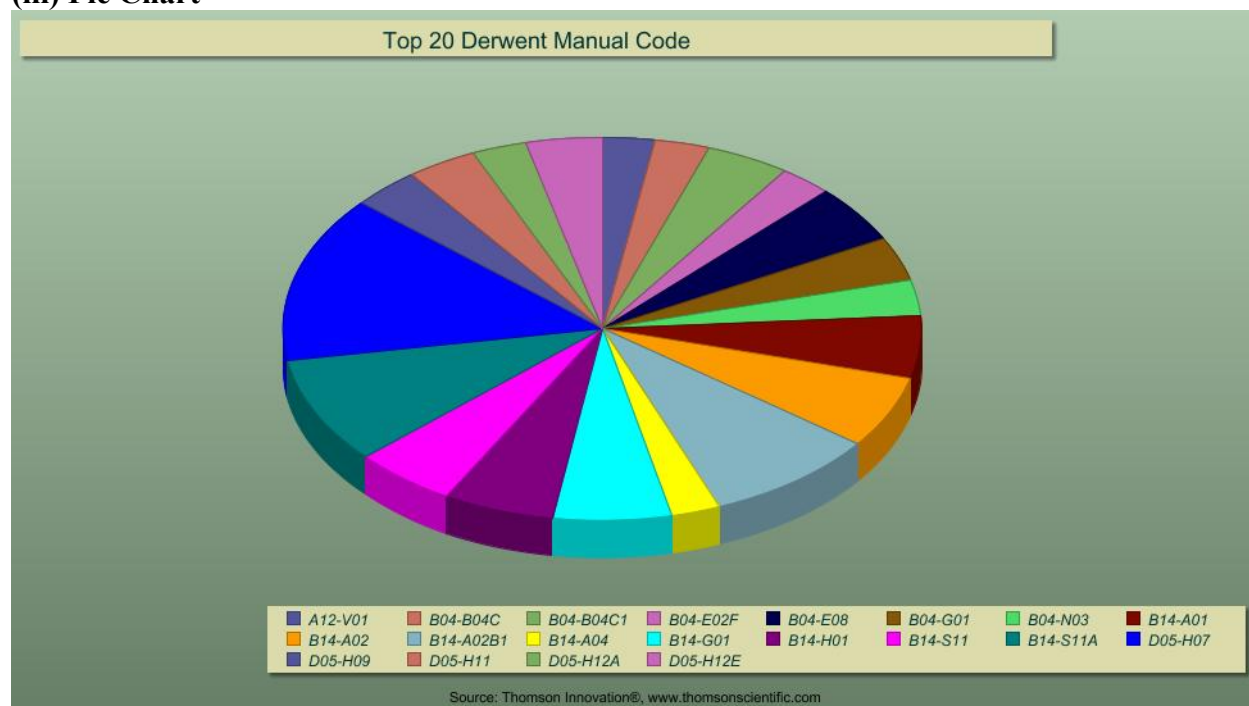
##### (i) Top 20 DWPI Manual Code

Top 20 DWPI Manual Codes	Patent Count
A12-V01	43
B04-B04C	46
B04-B04C1	69
B04-E02F	43
B04-E08	79
B04-G01	61
B04-N03	48
B14-A01	86
B14-A02	99
B14-A02B1	142
B14-A04	41
B14-G01	97
B14-H01	92
B14-S11	84
B14-S11A	148
D05-H07	229
D05-H09	56
D05-H11	57
D05-H12A	45
D05-H12E	63

## (ii) Bar Chart



## (iii) Pie Chart



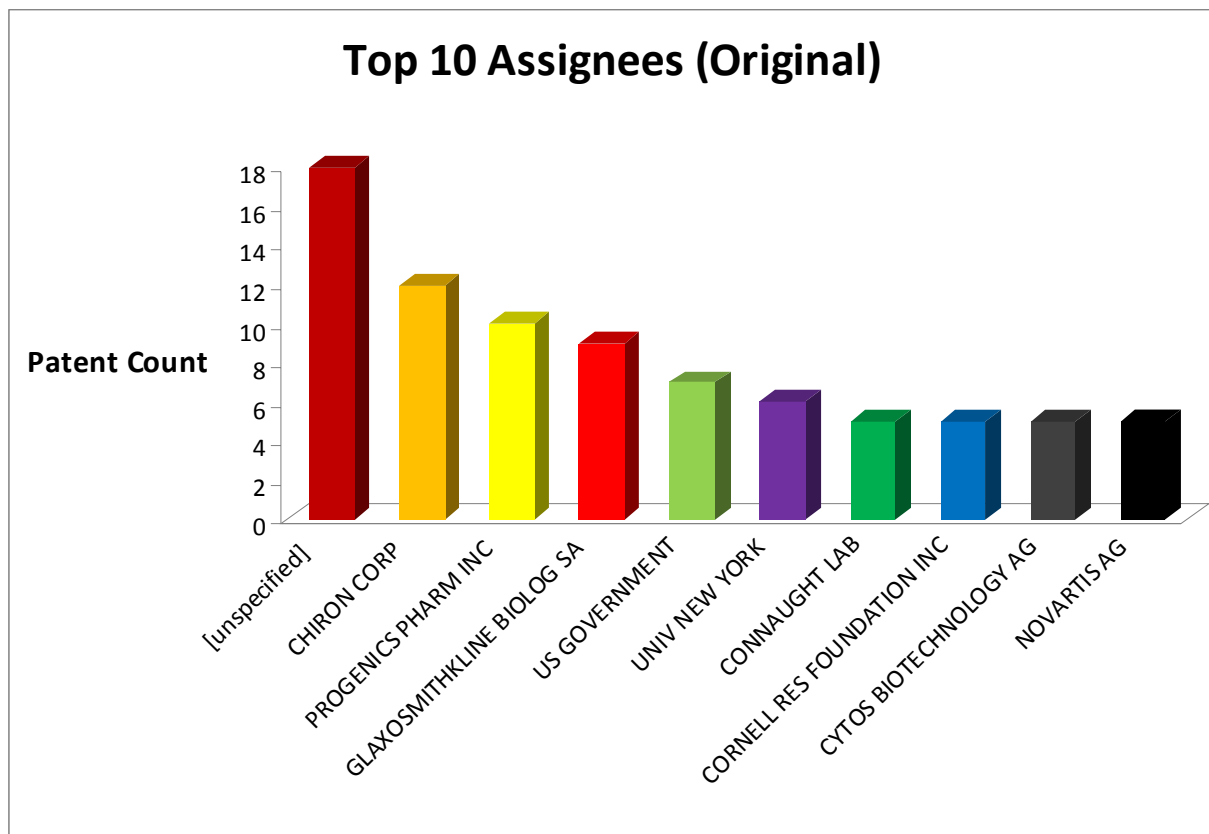
**Fig. 9.** Patent counts according to Derwent manual code. Shown in a bar chart (ii) and a pie chart (iii).

#### 4. H. Patent Count vs. Assignees

##### (i) Top 10 Assignee based on original assignee data

Assignee (Original)	Patent Count
[unspecified]	18
CHIRON CORP	12
PROGENICS PHARM INC	10
GLAXOSMITHKLINE BIOLOG SA	9
US GOVERNMENT	7
UNIV NEW YORK	6
CONNAUGHT LAB	5
CORNELL RES FOUNDATION INC	5
CYTOS BIOTECHNOLOGY AG	5
NOVARTIS AG	5

##### (ii) Bar Chart for Patent count v. Top 10 assignee (original data) (Composed with Microsoft Excel®)



**Fig. 10.** Patent counts according to Top 10 assignee (original data). Shown in a table (i) and a bar chart (ii).

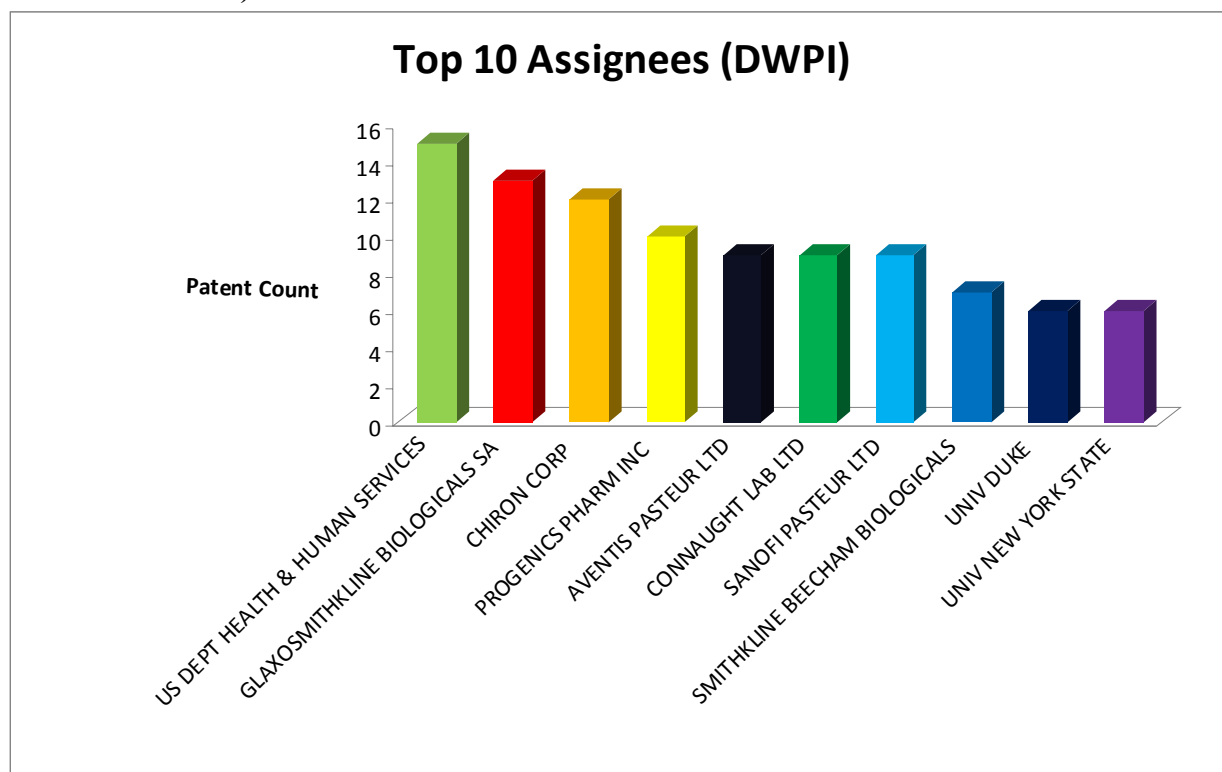
Based on original assignee data, there are eighteen patent documents with the “unspecified” assignee shown in the table (i). This is because US patent applications do not require assignees for publication. After double checking on Innovation Analyze Charts data, the eighteen patent records with “unspecified” assignee are all US patent applications. According to the original assignee information, the Top three assignees are Chiron Corp., Progenics Pharm. Inc., and Glaxosmithkline Biolog. SA.

On the other hand, the table (iii) below shows the top ten assignee according to Derwent assignee. For the 315 relevant we analyzed, the Derwent assignees are all available. We don’t know how Derwent system takes reference to the assignee for these US patent applications with no original assignee. According to Derwent assignee data, the top three assignee are Department Health & Human Service of US Government, Glaxosmithkline Biologicals SA., and Chiron Corp.

**(iii) Top 10 assignee based on DWPI data**

Assignee (DWPI data)	Patent Count
US DEPT HEALTH & HUMAN SERVICES	15
GLAXOSMITHKLINE BIOLOGICALS SA	13
CHIRON CORP	12
PROGENICS PHARM INC	10
AVENTIS PASTEUR LTD	9
CONNAUGHT LAB LTD	9
SANOFI PASTEUR LTD	9
SMITHKLINE BEECHAM BIOLOGICALS	7
UNIV DUKE	6
UNIV NEW YORK STATE	6

**(iv) Bar Chart for Patent count v. Top 10 Assignee (by DWPI data) (Composed with Microsoft Excel®)**



**Fig. 11.** Patent counts according to Top 10 assignee (DWPI data). Shown in a table (iii) and a bar chart (iv).

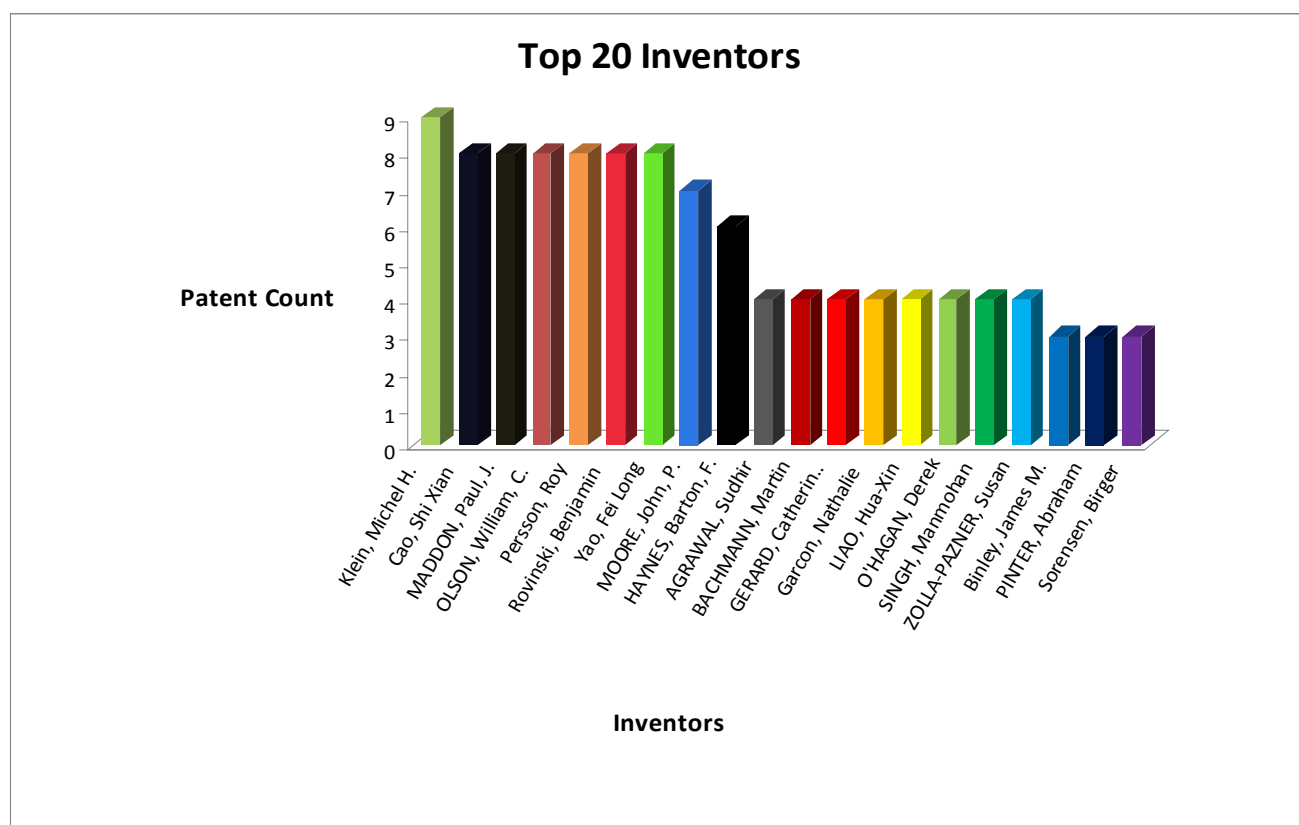
**4. I. Patent Count vs. Inventors (Composed with Microsoft Excel®)**

**(i)**

Inventor	Patent Count
Klein, Michel H.	9
Cao, Shi Xian	8
MADDON, Paul, J.	8
OLSON, William, C.	8
Persson, Roy	8
Rovinski, Benjamin	8
Yao, Fei Long	8
MOORE, John, P.	7

HAYNES, Barton, F.	6
AGRAWAL, Sudhir	4
BACHMANN, Martin	4
GERARD, Catherine, Marie, Ghislaine	4
Garcon, Nathalie	4
LIAO, Hua-Xin	4
O'HAGAN, Derek	4
SINGH, Manmohan	4
ZOLLA-PAZNER, Susan	4
Binley, James M.	3
PINTER, Abraham	3
Sorensen, Birger	3

(ii) Bar Chart of Top 20 Inventors (Composed with Microsoft Excel®)



**Fig. 11.** Patent counts according to Top 20 inventors. Shown in a table (i) and a bar chart (ii).

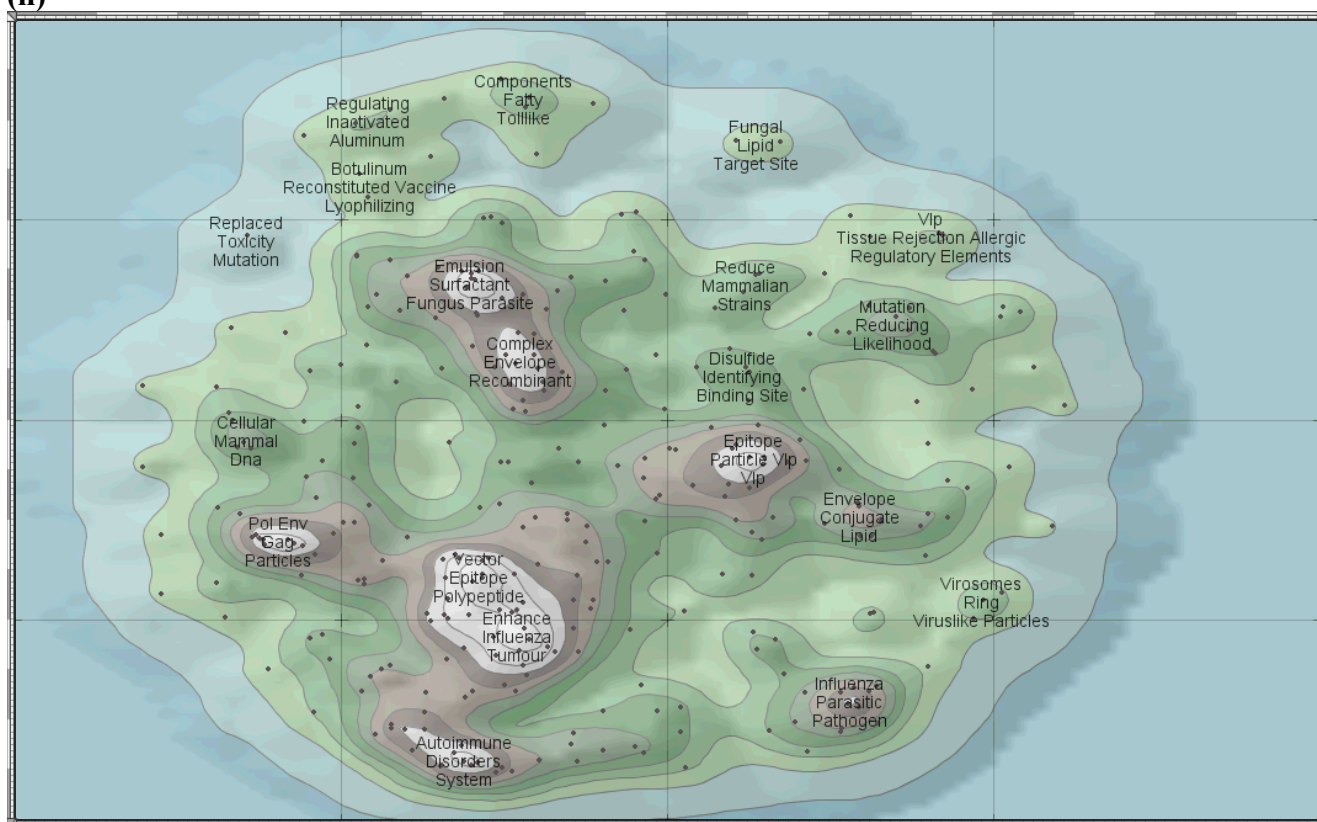
#### 4. J. Innovation ThemeScape® Maps Results

Peaks indicate the concentration of technologies based on the analyzed language.  
Proximity represents the relatedness between the analyzed language.



**Fig. 12 Innovation ThemeScape® Map 1: based on the language from the title and abstract in the 315 relevant patents.**

(ii)



**Fig. 13 Innovation ThemeScape® Map 2: based on the language from the title and abstract of Derwent data in the 315 relevant patents.**

(iii)



**Fig. 14 Innovation ThemeScape® Map 3: based on the language from the claims in the 315 relevant patents.**

(iiv)



**Fig. 15 Innovation ThemeScape® Map 4: based on the language from the title, claim and abstract in the 315 relevant patents.**

## APPENDIX A: Scientific Papers

(<http://www.ncbi.nlm.nih.gov/sites/entrez>)

### 1. Vaccine. 2007 May 10;25(19):3752-62. Epub 2007 Feb 16.

Vaccine adjuvants revisited.

[Aguilar JC](#), [Rodríguez EG](#).

Division of Vaccines, Center for Genetic Engineering and Biotechnology, P.O. Box 6162, La Habana 10600, Cuba. [julio.aguilar@cigb.edu.cu](mailto:julio.aguilar@cigb.edu.cu)

The development of new adjuvants for human vaccines has become an expanding field of research in the last thirty years, for generating stronger vaccines capable of inducing protective and long-lasting immunity in humans. Instead of such efforts, with several adjuvant strategies approaching to requirements for their Clinical application, limitations like adjuvant toxicity remain to be fully surpassed. Here we summarize the current status of adjuvant development, including regulatory recommendations, adjuvant requirements, and adjuvant categories like mineral salts, tensoactive compounds, microorganism-derived adjuvants, emulsions, cytokines, polysaccharides, nucleic acid-based adjuvants, and a section dedicated to particulate antigen delivery systems. The mechanisms of adjuvanticity are also discussed in the light of recent findings on Toll-like receptors' biology and their involvement on immune activation

### 2. Nature. 2008 Oct 2;455(7213):613-9.

Challenges in the development of an HIV-1 vaccine.

[Barouch DH](#).

Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts 02215, USA. [dbarouch@bidmc.harvard.edu](mailto:dbarouch@bidmc.harvard.edu)

The development of a safe and effective human immunodeficiency virus (HIV)-1 vaccine is a critically important global health priority. Despite recent advances in our understanding of HIV-1 pathogenesis and immunology, however, major scientific obstacles remain. Prototype HIV-1 vaccine candidates aimed at eliciting humoral and cellular immune responses have so far failed to protect against HIV-1 infection or to reduce viral loads after infection in Clinical efficacy studies. A renewed and coordinated commitment to basic discovery research, preClinical studies and Clinical trials will therefore be required to overcome the hurdles currently facing the field. Here I review key challenges and future prospects in the quest to develop a prophylactic HIV-1 vaccine.

**3. AIDS. 2008 Jan 30;22(3):333-8.**

Cytokines as adjuvants for improving anti-HIV responses.

[Morrow MP](#), [Weiner DB](#).

Department of Pathology and Laboratory Medicine, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania 19104, USA.

Since AIDS was first identified over 25 years ago, scientific advances have significantly expanded our understanding of the immune system, providing new tools for immune modulation and immunization strategies. The employment of DNA, protein subunits, and recombinant viral vectors in vaccination against HIV have been reviewed elsewhere . The current article focuses on the use of new adjuvants as additions to HIV vaccination and immunotherapy regimens. By adjuvant, we refer to an immune potentiator in a vehicle . A wide variety of adjuvants has been tested for their abilities to elicit cellular and humoral responses to HIV antigens *in vivo*. The goal of studies employing new adjuvants is that their inclusion will promote a stronger and more directed immune response than those generated by current approaches

**4. AIDS. 2002;16 Suppl 4:S115-24.**

Novel adjuvants and delivery systems for HIV vaccines.

[O'Hagan DT](#), [Lavelle E](#).

Immunology and Infectious Diseases, Chiron Corporation, 4560 Horton Street, Emeryville, CA 94608 USA.

Vaccines have traditionally consisted of live attenuated pathogens, whole inactivated organisms or inactivated bacterial toxins. More recently, recombinant protein vaccines have been introduced in combination with traditional adjuvants, based on insoluble aluminum salts (generically called 'alum'), for example Hepatitis B surface antigen adsorbed to alum is an effective vaccine against infection with Hepatitis B virus (HBV). These various approaches have induced protective immunity against a number of pathogens, mainly through the induction of antibody, responses. However, these approaches have proven unsuitable or unsuccessful for the development of an effective HIV vaccine. In contrast to some viruses, which can be easily controlled by neutralizing antibodies, cell mediated immunity (CMI) and particularly cytotoxic T lymphocytes (CTL) appear to be important for the control of HIV CTL specifically recognize and kill virally infected cells displaying foreign antigen in the context of MHC class I molecules. CTL have been shown to play a particularly important role in the early control of HIV infection and an inverse correlation has been established between the magnitude of CTL responses in infected individuals and viral load [1]. Unfortunately, the alum based adjuvants are poor inducers of CMI and are ineffective for the induction of CTL. Therefore, there is an urgent need for the development of new adjuvants and delivery technologies to enable the development of an effective HIV vaccine.

**5. Vaccine. 2005 Mar 31;23(19):2522-9.**

Antibody-dependent cell-mediated cytotoxic responses in participants enrolled in a phase I/II ALVAC-HIV/AIDS VAX B/E prime-boost HIV-1 vaccine trial in Thailand.

[Karnasuta C](#), [Paris RM](#), [Cox JH](#), [Nitayaphan S](#), [Pitisuttithum P](#), [Thongcharoen P](#), [Brown AE](#), [Gurunathan S](#), [Tartaglia J](#), [Heyward WL](#), [McNeil JG](#), [Birx DL](#), [de Souza MS](#); [Thai AIDS Vaccine Evaluation Group, Thailand](#).

Armed Forces Research Institute of Medical Sciences, Bangkok, Thailand.

[chitrapornk@afirms.org](mailto:chitrapornk@afirms.org)

Antibody-dependent cell-mediated cytotoxicity (ADCC) was assessed in volunteers participating in an ALVAC-HIV (vCP1521)/AIDS VAX B/E gp120 prime-boost vaccine trial in Thailand. ADCC activity was measured using chromium release from gp120 subtype B- and CRF01\_AE-coated targets in 95 vaccinees and 28 placebo recipients. There was a significant difference in the magnitude of the ADCC response to both targets between vaccinees and placebo recipients. The frequency of responders to subtype B and to CRF01\_AE was 96% and 84% in the vaccine group versus 11% and 7% in the placebo group. The results demonstrate that this HIV vaccine is a potent inducer of ADCC activity and may be an additional protection of this prime-boost vaccine in preventing HIV disease.

**6. Trends Immunol. 2009 Jan;30(1):23-32. Epub 2008 Dec 6.**

New horizons in adjuvants for vaccine development.

[Reed SG](#), [Bertholet S](#), [Coler RN](#), [Friede M](#).

Infectious Disease Research Institute, 1124 Columbia St. Suite 400, Seattle, WA 98104, USA.

Over the last decade, there has been a flurry of research on adjuvants for vaccines, and several novel adjuvants are now in licensed products or in late stage Clinical development. The success of adjuvants in enhancing the immune response to recombinant antigens has led many researchers to re-focus their vaccine development programs. Successful vaccine development requires knowing which adjuvants to use and knowing how to formulate adjuvants and antigens to achieve stable, safe and immunogenic vaccines. For the majority of vaccine researchers this information is not readily available, nor is access to well-characterized adjuvants. In this review, we outline the current state of adjuvant research and development and how formulation parameters can influence the effectiveness of adjuvants.

**7. Vaccine. 2005 Apr 8;23(20):2665-75.**

The immunogenicity-enhancing effect of emulsion vaccine adjuvants is independent of the dispersion type and antigen release rate--a revisit of the role of the hydrophile-lipophile balance (HLB) value.

[Yang YW](#), [Wei AC](#), [Shen SS](#).

School of Pharmacy, College of Medicine, National Taiwan University, 1, Jen-Ai Road, Section , Taipei 100, Taiwan, ROC. ywyang@ha.mc.ntu.edu.tw

Effective antigen delivery is one of the most important issues in vaccine development. It has been suggested that adjuvant action results from a depot effect by prolonging the duration of the interaction between antigen and cells, and thus is related to the antigen-releasing properties of emulsion adjuvants. The objective of this study was to investigate the effect of the dispersion properties of emulsion-type vaccine adjuvants on the immune response with the aim of optimizing vaccine adjuvant formulation. Emulsion-type adjuvants with various dispersion properties of either the oil-in-water or water-in-oil type were prepared using emulsifiers with various hydrophilic-hydrophobic balance (HLB) values. The physicochemical properties of the emulsions, including the conductivity and viscosity, and antigen release rates were then determined. Cell death induced by the vaccine adjuvants was examined in EL4 cells by Annexin V/propidium iodide (PI) staining and flow cytometric analysis. Mice were immunized with or without the adjuvants and the immunogenicity-enhancing effect of the adjuvants determined by measuring antibody production using an enzyme linked immunosorbent assay. The conductivity, viscosity, and antigen release rates varied widely among emulsions containing emulsifiers with different HLB values. However, the magnitude of the antigen-specific antibody response was similar in most emulsions adjuvants containing Spans or Tweens. L121-adjuvant, the control adjuvant inducing the strongest apoptosis in vitro, was shown to stimulate the highest antibody response in vivo. The results obtained in this study indicate that the immunogenicity-enhancing effect of emulsion adjuvants is independent of the dispersion type and the antigen release rate of the vaccine delivery system.

**8. Clin Exp Immunol. 2009 Aug;157(2):174-80.**

Translational Mini-Review Series on Vaccines for HIV: Harnessing innate immunity for HIV vaccine development.

[Rhee EG](#), [Barouch DH](#).

Division of Viral Pathogenesis, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA 02215, USA.

Innate immunity is critical for shaping vaccine-elicited adaptive immune responses. Several classes of immune sensors, including Toll-like receptors, retinoic acid-inducible gene-I-like receptors, nucleotide-binding oligomerization domain-like receptors and cytosolic DNA receptors mediate important innate immune pathways and provide potential targets for novel adjuvant development. Understanding how innate immunity modulates adaptive immune responses will probably be important for optimizing vaccine candidates. Here, we review recent advances in innate immunity, focusing upon their potential applications in developing adjuvants and vectors for HIV vaccines.

**9. J Pept Sci. 2003 Jul;9(7):405-18.**

Lipid and carbohydrate based adjuvant/carriers in immunology.

[McGeary RP](#), [Olive C](#), [Toth I](#).

School of Molecular and Microbial Sciences, The University of Queensland, Brisbane, Queensland, Australia.

This review discusses various issues regarding vaccines; what are they and how they work, safety aspects, the role of adjuvants and carriers in vaccination, synthetic peptides as immunogens, and new technologies for vaccine development and delivery including the identification of novel adjuvants for mucosal vaccine delivery. There has been a recent increase of interest in the use of lipids and carbohydrates as adjuvants, and so a particular emphasis is placed on adjuvants derived from lipids or carbohydrates, or from both.

## APPENDIX B: Description of Patent Databases & Platforms Used in this Report

### Platform Name– Innovation

#### General Information

- a. Innovation is a Thomson Reuters product
- b. Data Coverage:
  - i. US Grants & Applications
  - ii. European Grants & Applications
  - iii. German Grants & Applications
  - iv. German Utility Models
  - v. WIPO/PCT Applications
  - vi. British Applications
  - vii. French Applications
  - viii. Japanese Grants & Applications
  - ix. Chinese Utility Models & Applications
  - x. Korean Grants & Applications
  - xi. INPADOC
  - xii. Derwent World Patents Index
  - xiii. Non-Patent Literature
  - xiv. Business Information and News

#### Searches and Views

- c. Quick/Number searching and Boolean searching are available
- d. Corporate tree shows you how an Assignee name fits into a corporate hierarchy that takes into account mergers and acquisitions — and then lets you search for patents by selecting Assignee names from that corporate hierarchy
- e. Cross Search enables you to search the Patent, Literature, and Business content sets in a single search
- f. Patent images can be viewed in both high and low resolution.
- g. Saved Searches saves queries for frequently used searches. Searches can be saved directly from a result set. Two or more existing Saved Searches can be merged.
- h. Users can create Alerts for later automated searches.
- i. Work Files save, organize, annotate and share personalized lists of patents. Work files can save up to 20,000 patents. Users can share Work Files with coworkers or clients
- j. Data Extract exports key bibliographic fields in common formats

#### Analysis and Mapping

- k. Charts & Graphs
  - i. Thomson Innovation provides a collection of standard templates, each one designed to illustrate a different aspect of your list of records.
- l. Citation Maps
  - i. Using citation mapping, you analyze your own patent and choose to look at forward-only citations to focus just on other patents citing yours
  - ii. To support the patent's validity, you use citation mapping to review the references cited in your client's patent, as well as the references cited by those, to establish the state of the art at the time of the invention
- m. Text Clustering

- i. Clustering organizes results in a hierarchical format for easy drill-down to enable refinement of search strategies and identification of new links between subject matter and assignees.
- n. ThemeScape Maps
  - i. ThemeScape creates content maps from Thomson Innovation full text patent data, enhanced patent data from DWPI, and scientific literature content.
  - ii. Common conceptual terms are displayed in a two-dimensional map, with peaks representing a concentration of documents and showing the relative relationship of one record to another.
  - iii. The thematic topographical map enables “at a glance” assessments and is searchable.

## **Database Name– Derwent World Patent Index**

### General Information

- I. Most comprehensive database of international patent information
- II. DWPI covers inventions from over 40 patent issuing authorities
- III. Documents are read in their native language. Titles and abstracts are then rewritten in English to create a DWPI record
- IV. Included in the record is the drawing from the patent that is most representative of its claims and special indexing to help search for key patent information.
- V. There are 36.2 million patent documents currently in the database and over 2.5 million patents are added each year.
- VI. A Derwent record has the followings:
  - a. Derwent title
  - b. Link to the original patent; users can immediately access to the full text of the basic patent in PDF
  - c. Derwent classes
  - d. Derwent abstract showing novelty, use, and advantage
  - e. Legal status information from INPADOC
  - f. Claims from the basic patent

### Searches

- Keyword searching, accession/patent number searching, and Boolean text searching are available

## APPENDIX C: Definitions of U.S. Classifications

### United States Patent Classification System

- A Patent Classification is a code which provides a method for categorizing the invention.
- There are about 450 Classes of invention and about 150,000 subclasses of invention in the USPC.
- Classifications are typically expressed as "482/1".
  - The first number, 482, represents the class of invention.
  - The number following the slash is the subclass of invention within the class.
- Patents are always classified at the subclass level.
- A Subclass definition is a complete description of the subclass. The Subclass Definition can incorporate an explanation of the class, a glossary, search notes, references to subclasses within the class, and references to other classes and subclasses.
- Classes and subclasses have titles which provide a short description of the class or subclass.
- Classes and subclasses also have definitions which provide a more detailed explanation.
- Many Classes and subclasses have explicitly defined relationships to one another.
- One or more classifications (i.e., class/subclass designations) are assigned to each granted patent and each published application.
- A patent classification also represents a searchable collection of patents grouped together according to similarly claimed subject matter.
- A classification is used both as a tool for finding patents (patentability searches) and for assisting in the assignment of patent applications to examiners for examination purposes.
- Available at: <http://www.uspto.gov/go/classification/>

### Classification Codes applicable for this report

The top three found classes are underlined.

- **Class 128: Surgery**
- **Class 424: Drug, Bio-Affecting and Body Treating Compositions**
  - Class 424/184.1: Antigen, epitope, or other immunospecific immunoeffector (e.g., immunospecific vaccine, immunospecific stimulator of cell-mediated immunity, immunospecific tolerogen, immunospecific immunosuppressor, etc.)
  - Class 424/185.1: Amino acid sequence disclosed in whole or in part; or conjugate, complex, or fusion protein or fusion polypeptide including the same
  - Class 424/188.1: Immunodeficiency virus (e.g., HIV, etc.)
  - Class 424/193.1: Conjugate or complex
  - Class 424/196.11: Conjugate or complex includes virus or component thereof
  - Class 424/204.1: Virus or component thereof
  - Class 424/208.1: Immunodeficiency virus (e.g., HIV, etc.)
  - Class 424/234.1: Bacterium or component thereof or substance produced by said bacterium (e.g., Legionella, Borrelia, Anaplasma, Shigella, etc.)
  - Class 424/278.1: Nonspecific immunoeffector, per se (e.g., adjuvant, nonspecific immunopotentiator, nonspecific immunostimulator, nonspecific immunosuppressor, nonspecific immunomodulator, etc.); or nonspecific immunoeffector, stabilizer, emulsifier, preservative, carrier, or other additive for a

composition containing an immunoglobulin, an antiserum, an antibody, or fragment thereof, an antigen, an epitope, or other immunospecific immunoeffector

- **Class 435: Chemistry: Molecular Biology and Microbiology**
  - Class 435/005: Involving virus or bacteriophage
  - Class 435/006: Involving nucleic acid
  - Class 435/201: Acting on alpha-1, 4-glucosidic bond, (e.g., hyaluronidase, invertase, amylase, etc. (some 3.2.1))
  - Class 435/235.1: Virus or bacteriophage, except for viral vector or bacteriophage vector; composition thereof; preparation or purification thereof; production of viral subunits; media for propagating
  - Class 435/236: Inactivation or attenuation; producing viral subunits
- **Class 436: Chemistry: Analytical and Immunological Testing**
- **Class 514: Drug, Bio-Affecting and Body Treating Compositions**
  - Class 514/044R: Polynucleotide (e.g., RNA, DNA, etc.)
- **Class 530: Chemistry: Natural Resins or Derivatives; Peptides or Proteins; Lignins or Reaction Products Thereof**
  - Class 530/324: 25 or more amino acid residues in defined sequence
  - Class 530/326: 15 to 23 amino acid residues in defined sequence
  - Class 530/327: 11 to 14 amino acid residues in defined sequence
  - Class 530/350: Proteins, i.e., more than 100 amino acid residues
- **Class 536: Organic Compounds – Part of the Class 532-570 Series**
  - Class 536/023.72: Viral protein
- **Class 544: Organic Compounds – Part of the Class 532-570 Series**
- **Class 546: Organic Compounds – Part of the Class 532-570 Series**
- **Class 548: Organic Compounds – Part of the Class 532-570 Series**
- **Class 560: Organic Compounds – Part of the Class 532-570 Series**
- **Class 800: Multicellular Living Organisms and Unmodified Parts Thereof and Related Processes**
- **Class 977: Nanotechnology**

## APPENDIX D: Definitions of IPC Codes

### International Patent Classification System

- An International Patent Classification (IPC) is administered by the World Intellectual Property Organization (WIPO).
- The IPC consists of several hierarchical levels; it divides technology into eight sections (A through G) with approximately 70,000 subdivisions.
- The IPCs are typically expressed as “A63C 11/14.”
  - A represents a Section.
  - The number following a Section, 63, is a Class.
  - C represents a Subclass.
  - 11 is a Main group.
  - The number following the slash, 14, is a Subgroup.
- The authentic version of the IPC is published in English and French languages. Chinese, Croatian, Czech, Dutch German, Hungarian, Japanese, Korean, Polish, Romanian, Russian, Serbian, and Spanish versions are also available.
- The IPC is used in more than 100 countries. Thus, the IPC is used as a tool for finding, for example, both US and JP documents.
- Available at: [http://www.wipo.int/classifications/fulltext/new\\_ipc/ipcen.html](http://www.wipo.int/classifications/fulltext/new_ipc/ipcen.html)

### Classification Codes applicable for this report

The top four found codes are underlined.

- **Section A: Human Necessities**
  - A61K: Preparations for Medical, Dental, or Toilet Purposes
  - A61P: Therapeutic Activity of Chemical Compounds or Medical Preparations
- **Section C: Chemistry; Metallurgy**
  - C07D: Hydrocyclic Compounds
  - C07H: Organic Chemistry
  - C07K: Peptides
  - C12N: Micro-Organisms or Enzymes; Compositions Thereof; Propagating, Preserving, or Maintaining Micro-Organisms; Mutation or Genetic Engineering; Culture Media
  - C12P: Fermentation or Enzyme-Using Process to Synthesize a Desired Chemical Compound or Composition or to Separate Optical Isomers from a Racemic Mixture
  - C12Q: Measuring or Testing Processes Involving Enzymes or Micro-Organisms; Compositions or Test Papers Therefor; Processes of Preparing Such Compositions; Condition-Responsive Control in Microbiological or Enzymological Processes
  - C12R: Indexing Scheme Associated with Subclasses C12C to C12Q or C12S, Relating to Micro-organisms
- **Section G: Physics**
  - G01N: Investigation or Analyzing Materials by Determining Their Chemical or Physical Properties

## APPENDIX E: Derwent Classifications

(Source: <http://science.thomsonreuters.com/m/pdfs/mgr/derwentclass.pdf>)

### **Description of Derwent Patent Classifications**

- Categorizes patent documents using a simple classification system for all technologies; consistently applied to all patents by Thomson Scientific subject experts, enabling effective and precise searching in a particular area of technology.
- International Patent Classification (IPC) is an internationally recognized classification system, which is controlled by the World Intellectual Property Organization (WIPO) and assigned to patent documents by Patent Offices.
- Where possible Thomson indicated next to the Class the equivalent IPC in an abbreviated form (e.g. A47, F23 5). However, this should only be taken as a guide, since there are areas where the DWPI Classes are assigned intellectually by Thomson's subject experts, and no strict correspondence is claimed.

### **Classification Codes (applicable for this report)**

- **Class A11** - Polysaccharides; natural rubber; other natural polymers (*only a restricted range of (modified) natural polymers are included. Thus starch would be excluded, but chemically modified starch included*).
  - This is a subclass of A1 - Addition and Natural Polymers
- **Class A14** - Polymers of other substituted monoolefins; including PVC, PTFE
  - This is a subclass of A1 - Addition and Natural Polymers
- **Class A17** Polymers of unsubstituted aliphatic monoolefins; including polyethylene
  - This is a subclass of A1 - Addition and Natural Polymers
- **Class A25** - Polyurethanes; polyethers
  - This is a subclass of A2 - Condensation Polymers
- **Class A96** - Medical, dental, veterinary, cosmetic
  - This is a subclass of A8/9 Applications
- **Class B01** - Steroids - including systems containing carbocyclic and/or heterocyclic rings fused onto the basic steroidal ring structure
  - This is a subclass of B - Pharmaceuticals
- **Class B02** - Fused ring heterocyclics
  - This is a subclass of B - Pharmaceuticals
- **Class B03** - Other heterocyclics
  - This is a subclass of B - Pharmaceuticals
- **Class B04** - Natural products and polymers. Including testing of body fluids (other than blood typing or cell counting), pharmaceuticals or veterinary compounds of unknown structure, testing of microorganisms for pathogenicity, testing of chemicals for mutagenicity or human toxicity and fermentative production of DNA or RNA. General compositions.
  - This is a subclass of B - Pharmaceuticals
- **Class B05** - Other organics - aromatics, aliphatic, organo-metallics, compounds whose substituents vary such that they would be classified in several of B01 - B05
  - This is a subclass of B - Pharmaceuticals
- **Class Q42** - Hydraulic engineering, sewerage (E02,3)
  - This is a subclass of Q4 Buildings, Construction

## APPENDIX F: Derwent Chemical Patents Index (CPI) Manual Codes

(Source: [http://www.thomsonscientific.jp/support/code/mc/cpi/cpi\\_mc1\\_eng.pdf](http://www.thomsonscientific.jp/support/code/mc/cpi/cpi_mc1_eng.pdf))

### General Information

- Derwent manual codes increase the accuracy of online patent searches by arranging patents into three general categories - Chemical, Engineering, and Electronic/Electrical.
- The codes can be used by incorporating them into online search strategies when they are initially being developed.
- Many of the codes are redundant by covering a single subject under several codes.
- As a result, the searches are extremely narrow and produce only a handful of relevant search results.

### Classification Codes (applicable to this report in bold)

- A12 POLYMER APPLICATIONS
  - A12-V MEDICAL, DENTAL, COSMETICS AND VETERINARY
    - **A12-V01** - Medicines, pharmaceuticals (Prior to 1970 see A12-V)
- B04 NATURAL PRODUCTS (OR GENETICALLY ENGINEERED), POLYMERS
  - B04-B ANIMAL, MICROBIOLOGICAL AND GENERAL EXTRACTS
    - **B04-B04C** - Antigens, general Antibody (pre-1994)
      - **B04-B04C1** - Microbial antigen (When used as a vaccine then B02-V02 is coded (before 1994) or B14-S11+ (from 1994))
  - B04-E NUCLEIC ACIDS
    - B04-E02 Altered DNA coding sequences. These codes include engineered, recombinant constructs, chimeric genes, heterologous genes, fusion genes, allelic variants and mutant alleles. The codes include RNA transcripts of these sequences.
      - **B04-E02F** - Encoding other protein/polypeptide
      - **B04-E08** - Vectors, plasmids, cosmids, transposons (Viral vectors are also coded under virus (B04-F11))
  - B04-G ANTIBODY DEFINED IN TERMS OF ANTIGEN
    - **B04-G01** - General and other
  - B04-N OTHER PROTEIN/POLYPEPTIDE
    - **B04-N03** - Microorganism protein/polypeptide (No sequence)
- B14 PHARMACEUTICAL ACTIVITIES
  - B14-A ANTIMICROBIALS
    - **B14-A01** - Antibacterial general
    - **B14-A02** - Antiviral general
      - **B14-A02B1** - Retrovirus (Including leuco- and oncoviruses, T-cell leukemia virus, HIV, Rous sarcoma. Non-antiviral AIDS treatment is coded B14-G01B)
    - **B14-A04** - Antifungal general and other
  - B14-G DRUGS ACTING ON THE IMMUNE SYSTEM
    - **B14-G01** Immunostimulant general and other
  - B14-H CANCER RELATED DRUGS
    - **B14-H01** - Anticancer general and other

- B14-S MISCELLANEOUS ACTIVITY TERMS
  - **B14-S11** - Vaccine general
  - **B14-S11A** - Antiviral vaccine
- D05 FERMENTATION INDUSTRY
  - D05-H MICROBIOLOGY, LABORATORY PROCEDURES
    - **D05-H07** - Production of vaccines, antigens
    - **D05-H09** - Testing and detection other than D05-H04 (Newly discovered, testing of, isolation of, identification of and detection of Bacteria), D05-H05 (Newly discovered, testing of, isolation of, identification of and detection of Fungi) and D05-H06 (Newly discovered, testing of, isolation of, identification of and detection of Viruses and Other)
    - **D05-H11** – Antibodies
    - D05-H12 DNA, cDNA, transfer vectors, RNA
    - **D05-H12A** - Wild-type coding sequences: Includes new genes and gene fragments. Wild-type (or “native”) coding sequences code for the normal, functional version of a protein. Wildtype coding sequences that are fused to other sequences are searched under D05-H12A if they encode the major expression product, after any posttranslational processing, e.g. After cleavage from a signal peptide.
    - **D05-H12E** - Vectors: Includes viral vectors (e.g. Baculovirus vectors, phagemids), plasmid vectors, cosmids and transposons.

## APPENDIX G: LANL Adjuvant List

[http://www.hiv.lanl.gov/cgi-bin/vaccine/search/adjuvant\\_search.cgi?search\\_string=&process=Go](http://www.hiv.lanl.gov/cgi-bin/vaccine/search/adjuvant_search.cgi?search_string=&process=Go)

Immunostimulatory	
endogenous	exogenous
autologous dendritic cells	B7-2
autologous PBMC	BAY R1005
antigen formulation	Bupivacaine
BAK	Bupivacaine-HCl
cytokine containing liposomes	CCR5 peptides
GM-CSF	complete Freud's adjuvant
hGM-CSF	Cholera holotoxin
hIL-12(N222L)	Cholera toxin B subunit
hTNF-alpha	Cholera toxin A1-subunit-Protein A D-fragment fusion protein
IFN-gamma in pCDNA3	CpG 2006
IL-12 DNA	CpG 1018
IL-12 plamid	CpG C274
IL-12/GMCSF plasmids	CRL 1005
IL-15 plasmid	D-murapalmitine
IL-2 in pCDNA3	DHEA
IL-2/Ig plasmid	Diphtheria toxoid
IL-2/Ig protein	Fowlpox
IL-4	Freud's complete adjuvant
IL-4 in pCDNA3	incomplete freund's adjuvant
immunoliposomes containing antibodies to costimulatory molecules	Montaide ISA 51
interferon-y	Montanide ISA 720
interleukin-18	nCT native Cholera Toxin
interleukin-12	non-toxic mutant E112k of Cholera Toxin mCT-E112K
interleukin-2	pCMVmCAT1
interleukin-7	pCMVN
ISCOM(s)	Pluronic L121
Iscoprep 7.0.3	PMMA
Lipid-based adjuvant	Poly rA: Poly rU
LT(R192G)	protein cochleates
LT-OA or LT Oral Adjuvant	QS-21
LT-R192G	RIBI
LTK63	RIBI like adjuvant system
LTK72	S-28463
MTP-PE Liposomes	Tetanus toxoid(TT)
NAGO	
pCIL-10	
pCIL-12	
Pleuran	
PODDS	
rAd5-hIL-12N222L	
rAd5-IL15	
Sclavo Peptide	
sendai proteoliposomes, sendai-containing lipid matrices	
Trp-Lys-Tyr-Met-Val-Met immunostimulatory peptide	

Chemistry- organic	
Albumin-heparin microparticles	ISCOM(s)
algal Glucan	kiposomes
antigen formulation	loxoriine
Avridine	MF59
B7-2	Montaide ISA 51
BAK	Montanide ISA 720
BAY R1005	MPL
Bupivacaine-HCl	MPL-SE
Calcitriol	MTP-PE Liposomes
CCR5 peptides	Murametid
complete Freud's adjuvant	Murapalmitine
CpG 2006	NAGO
CpG 1018	p-Hydroxybenzoique acid methyl ester
CpG C274	PLG
CRL 1005	PLGA, PGA, PLA
cytokine containing liposomes	Pluronic L121
D-murapalmitine	PMMA
DDA	PODDS
DHEA	Poly rA: Poly rU
Diphtheria toxoid	Poly:C
DL-PGL	polysorbate 80
DMPC	protein cochleates
DMPG	QS-21
Freud's complete adjuvant	Quadri A saponin
Gamma Inulin	Quil-A
Gerbv Adjuvant	RIBI
GMDP	Squalene 2
imuquimod	Stearyl Tyrosine
ImmTher	Theramide
immunoliposomes containing antibodies to costimulatory molecules	

Chemistry- inorganic
1z
3M-12
Adju-Phos
adjumer
Alum
AS-2 adjuvant
BWZL
Calcium phosphate Gel
DOC/Alum Complex
non-ionic surfactant vesicles
peptomer-NP
rehydragel HPA
Rehydragel LV
Walter Reed Liposomes

## APPENDIX H: Latent Semantic Searching on Lexis

Semantic searching facilitates query creation and improves your search results by using semantics, the science of meaning in language. Semantic searches modified by the searcher and enhanced with Boolean logic generate more complete and relevant results than traditional searches. With semantic searching, you use the same data sources you already use, but your search results will contain only the most relevant items. Using simple English terms, sentences, or paragraphs as the search query, the semantic search engine searches across multiple sources stored in multiple locations, even if they have different indexing systems. Semantic analysis is available for STM (Science, Technology, and Medical) sources, such as a patent or Elsevier Science source. The LexisNexis® Total Research System service can perform a semantic analysis of your input before running your search, generating a weighted list of terms that will be used as search terms. You can review and modify the terms and their weights before submitting your search (by clicking the "Analyze Search Input" button), or you can run your search without first viewing the weighted list of terms (by clicking the "Search Now" button). In both cases, you can add field restrictions or additional Boolean logic to fine tune your search.<sup>196</sup>

For our research purposes, LexisNexis Semantic Search is not a resourceful tool. While it does come up with a number of reliable search term suggestions, the recall of those terms are less than ideal. This search could be useful for general case searching, however in our situation where we are looking for very specific terms within an extensive number of patent, the search terms do not increase the overall search diversity. In many instances, search terms that we deem important within found patents are absent in Semantic search suggestions, or the opposite holds true where extraordinarily common terms are given the most weight. In many search examples, names are suggested.

The Semantic interface is simple enough to use, however it is difficult to switch terms prior to searching. The suggested terms are limited to only twenty, though you may delete terms through the value designation window and add your own terms on the list menu. The results themselves are usefully presented, where the terms are distinguished by size, color, and order displayed. The terms are designated a number value, where 4 is required and -1 is excluded. The weight of the term may be altered by clicking the term and selecting a number along a hierarchy slider. However, clicking the search term won't show you examples of use or link you to relevant patents, which we feel would be a very useful addition to the Semantic Search.

In summation, this is could be a useful tool for broad searching, however in our situation it is lacking in precision and recall.

See below for sample searches.

Sample search: HIV and adjuvant and vaccine;

---

<sup>196</sup> LexisNexis Research Help, <http://web.lexis.com/help/research/searchtips.asp> (last visited Sept. 30, 2009)

**Search**

To adjust a concept's weighting, click the concept name.  
To ignore a concept, clear the check box next to the concept.

Add another concept

[Hide Check Boxes](#)[Update Display](#)

☒ **vaccine** ☒ **hiv** ☒ **adjuvant** ☒ remune

☒ immunogen ☒ "hiv-1 immunogen" ☒ preparation ☒ "infected persons"

☒ products ☒ "international aids" ☒ system ☒ preventive ☒ mf59

☒ approved ☒ "human vaccines" ☒ "vaccine adjuvant"

☒ "aluminium hydroxide" ☒ based ☒ prevent ☒ "metabolizable oil"

Your search terms appear below. Note the weightings in brackets following each term: the higher the weighting the more prominent the term will be in the search results.

**Search Terms**  
(vaccine [4], hiv [4], adjuvant [4], remune [2], immunogen [2], "hiv-1 immunogen" [1], preparation [1], "infected persons" [1], products [1], "international aids" [1], system [1], preventive [1], mf59 [1], approved [1], "human vaccines" [1], "vaccine adjuvant" [1], "aluminium hydroxide" [1], based [1], prevent [1], "metabolizable oil" [1])

Sample search: ((Vaccine or Antibody or Antigen or Counteragent or "Efficacy of vaccines" or "Immune response" or Immunization or Immunizing or "Immunizing agent" or Immunoenhancing or Immunogen or "Immunological compound" or Immunotherapy or "Recombinant protein vaccine" or Therapy or Vaccinum) and ((Adjuvant or Additive or "Antigen delivery system" or AS01 or Catalyst or Chemokines or "Costimulatory molecules" or CpG or Cytokines or "delivery system" or "Depot formation" or Emulsions or Enhancer or "Immune systems" or ISCOMs or Lipid ADJ particles or Liposomes or "Microorganism derived" or Microparticles or Montanides or MPL) AND (Hiv or "GP 120" or "HIV vaccine" or "Human Immunodeficiency virus"

[Patent Law](#) / [Find Patents](#) / [Quality, Design and Patent Analysis](#)  / [Analyze Search Input](#)

**Search**

To adjust a concept's weighting, click the concept name.  
To ignore a concept, clear the check box next to the concept.

Add another concept

[Hide Check Boxes](#)[Update Display](#)

☒ **vaccine** ☒ **antibody** ☒ **antigen**

☒ "particulate adjuvants" ☒ "traditional adjuvants" ☒ adjuvant

☒ "require adjuvants" ☒ "adjuvant delivery" ☒ "improved adjuvants"

☒ "delivery systems" ☒ "depot effect" ☒ "adjuvants approved" ☒ o'hagan

☒ "adjuvant system" ☒ "formulations based" ☒ "human vaccines"

☒ adjuvancy ☒ "delivery system" ☒ "adjuvants act" ☒ "adjuvant component"

Your search terms appear below. Note the weightings in brackets following each term: the higher the weighting the more prominent the term will be in the search results.

**Search Terms**  
(vaccine [4], antibody [4], antigen [4], "particulate adjuvants" [1], "traditional adjuvants" [1], adjuvant [1], "require adjuvants" [1], "adjuvant delivery" [1], "improved adjuvants" [1], "delivery systems" [1], "depot effect" [1], "adjuvants approved" [1], o'hagan [1], "adjuvant system" [1], "formulations based" [1], "human vaccines" [1], adjuvancy [1], "delivery system" [1], "adjuvants act" [1], "adjuvant component" [1])

## APPENDIX I: Author's Curriculum Vitae

### NUPUR CHOUDHARY

82 North State Street,  
Concord, NH 03301  
nchoudhary@piercelaw.edu  
USA

(+1) 603-892-6754

nupur.2986@gmail.com

---

#### EDUCATION

**Franklin Pierce Law Center**, Concord, NH, U.S.A.

Expected Dec 2009

*Master of Laws in Intellectual Property (LLM-IP)*

Coursework in Patent Practice & Procedure, Technology Licensing, Patent Mining, IP Management, IP Valuation, Copyright Law.

**National Law University**, Jodhpur, India

May 2008

*Bachelor of Science (B.Sc.) – Major in Biology;*

*Bachelor of Law; with Honors in IP & Technology (LL.B.)*

Activities: Member, Legal Aid Camp; Member, School of Science.

Coursework in Biology, Genetics, Patent Law, Claim Drafting, IP Valuation & Asset Management, E-Commerce & Information Technology Law, IP Dispute Resolution, All Legal Courses.

#### EXPERIENCE

Researcher,

August 2009 – Present

**International Technology Transfer Institute (ITTI), at Franklin Pierce Law Center**

Working on Patent Landscape of Adjuvants for HIV Vaccines. Involved in Patent Searching on Thomson Innovation, as well as Patent Coding.

Teaching Assistant,

August 2009 - Present

Course of **American Legal System**, at **Franklin Pierce Law Center**

Legal Intern, **Krishna & Saurashtri, Mumbai, India**

December 2007

Prepared Claims for Patent Applications. Assisted Senior Associate in drafting legal opinions relating to Patents, Trademarks and PCT matters.

IP Intern Associate, **Crawford Bayley & Co., Mumbai, India**

November 2006

Prepared Responses to Office Actions for Patent Applications. Filed PCT Applications with the Indian PTO at Mumbai. Involved in Prior Art Searches for Patent Filing

Legal Intern, **AZB & Partners, New Delhi, India**

June 2006

Prepared Memorandum for Patent Cases filed in the Delhi High Court. Conducted Due Diligence on Merger among client Companies.

Judicial Clerk, **Justice Madan B. Lokur, Delhi High Court, Delhi, India**

May 2006

Prepared briefs on cases relating to Trademark Law, Property Law, Non-pecuniary Damages

**SKILLS & BAR MEMBERSHIP:**

- **Language Skills:** Fluent in English and Hindi
- **Computer Skills:** Westlaw, Thomson Innovation, Dialog, Derwent.
- **Bar Admission:** Registered with Bar Council of Rajasthan at Jodhpur, India since November 2008.

# Jennifer L. Fadden

20 Country Club Drive, Apt 29  
Manchester, NH 03102  
(203) 233-2167  
JFadden@piercelaw.edu

## Education

**Franklin Pierce Law Center** – Concord NH

Expected May 2011

J.D. and L.L.M. in Intellectual Property

GPA: 3.02

Treasurer, Phi Alpha Delta

*Relevant Course Work:*

Patent Law, Patent Prosecution and Practice 1, Technology Licensing, Law and Biotechnology, Fundamentals of IP, Pharmaceutical Patents, Mining for Patents, International and Comparative Patent Law

*Summer Study Abroad*, University College Cork in Cork, Ireland

July 2009

Comparative IP for the Information Age, Comparative e-Commerce Law, Current Issues in Cyberlaw, European Union Legal and Political Overview

**University of Connecticut** - Storrs CT

May 2008

B.S., Chemical Engineering

Minors: Chemistry and Mathematics

## Experience

**International Technology Transfer Institute Clinic**

August 2009 – Present

Franklin Pierce Law Center, Concord NH

Student Attorney

During the clinic I used Thomson Innovation to create a biotechnological patent landscape relating to HIV vaccines using adjuvants. Then I analyzed hundreds of patents claims to determine if the patents were relevant to HIV vaccines using adjuvants.

*Pending publication through Franklin Pierce Law Center “Patent Landscape of Adjuvants for HIV Vaccine”*

**United States Army Corps of Engineers**

May 2006 - Present

Cold Region Research and Engineering Laboratory, Hanover NH

Engineering Technician

Design and run experiments on the dissolution of explosive and propellant compounds used on military training ranges. Collect and analyze data on the various dissolution experiments for the lead researcher. *Contributed to the following publications: Simulated rainfall-driven dissolution of TNT, Tritonal, Comp B and Octol particles in “Environmental Science and Technology;” Characterization and Fate of Gun and Rocket Propellant Residues on Testing and Training Ranges (ERDC/CRREL TR-08-19); Outdoor Weathering and Dissolution of TNT and Tritonal (Chemosphere 77 (2009) 1338–1345).*

**Blue Mountain Union School**, Wells River VT

2003 - Present

Substitute Teacher

Teach classes in middle school science and in the elementary school.

**Dartmouth Hitchcock Medical Center**

Summer 2004

Center for Psycho-oncology, Lebanon NH

Data Analysis Technician

Entered and analyzed data on patient's well being and managed patient files. Assisted interviewers by creating interview packets and distributed information to interviewers and lead researchers.

## Volunteer Organizations

Daughters of the American Revolution - Junior member

2003- Present

# BRIAN DANIEL DOIGAN

[Bdoigan@piercelaw.edu](mailto:Bdoigan@piercelaw.edu)

(301) 520-7225

School Address:  
7 Lyndon St.  
Concord, NH 03301

Permanent Address:  
30420 Stonegate Dr.  
Franklin, MI 48025

---

## Education

**Franklin Pierce Law Center**, Concord, NH  
J.D. Candidate 2011  
Summer Intellectual Property Institute, May – June 2009  
*President*, Licensing Executives Society  
*President*, Hillel  
*Member*, Phi Alpha Delta Legal Fraternity  
*Member*, SIPLA

**Connecticut College**, New London, CT  
Bachelor of Arts, Biology, 2006  
GPA 3.3

## Experience

### *Researcher*

**International Technology Transfer Institute**, Pierce Law Center Fall 2009  
Assemble and analyze patent landscapes pertinent to innovations which are relevant to the needs of developing countries. Conduct searches through Lexis, Westlaw, Dialog, and Innovation. Results published in December, 2009.

*Intern* July 2009 - August 2009  
**Carlson, Gaskey, & Olds P.C.**, Birmingham, MI  
Conducted prior art searches and received guidance and feedback on claim drafting of mechanical inventions.

*Temporary Litigation Clerk* March 2007 – April 2008  
**Finnegan, Henderson, Farabow, Garrett & Dunner LLP**, Washington, DC  
Assisted in litigation preparation by reviewing and organizing trial materials such as depositions, transcripts, and exhibits. Organized hard copies of materials and maintained computer databases. Effectively managed multiple projects at once.

*Patent Draftsman* Summer 2002 – Summer 2006  
**123 Studio**, Royal Oak, MI  
Analyzed specs and used AutoCAD to draft patent drawings. Communicated with clients (small companies, large corporations and law firms), in order to effectively interpret, edit and finalize patent applications.

*Academic Research* Spring 2005  
**Connecticut College**, New London, CT  
Studied the structure of developing nectaries in pitcher plants utilizing the electron microscopes to observe plant tissue while correlating results with current studies and papers.

**Personal Interests:** Coaching Youth Soccer, Reading, Sports, Hiking, Rock Climbing, and Playing the Guitar.

**Craig T. Ajmo Jr. Ph.D.**  
88 Falcon Crest Way  
Manchester, NH 03104  
(727) 422-2014 [ctajmo@gmail.com](mailto:ctajmo@gmail.com)

## **EDUCATION**

### **Juris Doctor Candidate, 2011**

Franklin Pierce Law Center, Concord, NH, GPA 3.03, Class Rank: Top 50%

### **Patent Bar, Summer 2010**

### **Intellectual Property Courses, 2009 to Present**

Fundamentals of Intellectual Property, Pharmaceutical Patent Law, Mining for Patents (patent search engine course), International and Comparative Patent Law, Patent Law, Patent Practice & Procedure I, International Technology Transfer Institute, Pierce Law Clinic

### **Doctor of Philosophy, Molecular Pharmacology and Physiology, 2007**

University of South Florida, College of Medicine, Tampa, FL

Member, Society for Neuroscience

Journal Reviewer, Stroke

### **Masters of Science, Pharmacology 2005**

University of South Florida, College of Medicine, Tampa, FL, GPA 3.2

Member, Society for Neuroscience

Journal Reviewer, Stroke

### **Bachelor of Science, Biochemistry 2003**

University of Florida, Gainesville, FL, GPA 3.2

Member, UF sailing team

## **EXPERIENCE**

*Student Attorney, Director of Science and Technology* Fall 2009

**International Technology Transfer Institute, Pierce Law Clinic**, Concord, NH

Development and analysis of patent landscapes focusing on HIV vaccines for developing countries to promote advances in health. **Pending Publication** - Franklin Pierce Law Center Educational Report: Patent Landscape of Adjuvants For HIV.

*Supervisor of Intellectual Property* Summer 2008 to present

**Bach Pharma, Inc.**, North Andover, MA

Over see and prepare patents, manufacturing process forms and trademarks. Compose or edit presentations that are delivered to share holders, investors, and scientific researchers. Directly interact with Bach Pharma's intellectual property attorneys.

*Post Doctoral Fellow* 2007 - 2008

**College of Medicine, University of South Florida**, Tampa, FL

Developed and performed experiments to elucidate delayed treatments of stroke. Published peer reviewed journal articles and gave oral presentations at international symposia regarding scientific research.

## PUBLICATIONS

Christopher C. Leonardo, Aaron A. Hall, Lisa A. Collier, **Craig T. Ajmo, Jr.**, Alison E. Willing, Keith R. Pennypacker: HUCB Cell Therapy Blocks the Morphological Change and Recruitment of CD11b-Expressing, Isolectin-Binding Proinflammatory Cells after MCAO. (*submitted*) J. Neuroscience Research

**Ajmo, C.T. Jr.**, Collier, L.A., Leonardo, C.C., Hall, A.A., Cuevas, J., Pennypacker, K. R.: Blockage of adrenoreceptors inhibits the splenic response to stroke. Exp Neurol. 2009 Apr 14. [Epub ahead of print]

Hall, A., Herrera, Y., **Ajmo, C.T. Jr.**, Cuevas, J., and Pennypacker, K.R.: Sigma Receptors Suppress Multiple Aspects of Microglial Activation. Glia 2008. (in press)

**Ajmo Jr., C.T.**, Vernon, D.O.L., Collier, L.A., Hall, A.A., Willing, A., Pennypacker, K.R.: The Spleen Contributes to Stroke Induced Neurodegeneration. J Neurosci Res 86:2227-2234, 2008. PMID: 18381759

Hall, A., Guyer, A., Leonardo, C., **Ajmo, C. Jr.**, Collier, L., Willing, A., and Pennypacker, K.: Human Umbilical Cord Blood Cells Directly Suppress Ischemic Oligodendrocyte Cell Death. J. Neurosci. Res. 2008. [Epub ahead of print]

**Ajmo Jr., C. T.**; Vernon, Dionne O.L. ; Collier, Lisa A. ; Hall A. A. ; Willing A.; Pennypacker, Keith R. The Spleen Contributes to Stroke Induced Neurodegeneration. Journal of Neuroscience Research (*accepted 12/07*) Journal of Neuroscience Research

**Ajmo Jr., C. T.**; Vernon, Dionne O.L.; Collier, Lisa; Pennypacker, Keith R.; Cuevas, Javier: [Sigma Receptor Activation Reduces Infarct Size at 24 Hours After Permanent Middle Cerebral Artery Occlusion in Rats.](#) Current Neurovascular Research, Vol 3,(2) May 2006, pp. 89-98(10)

Newcomb, J.D., **Ajmo Jr., C.T.**, Sanberg, C.D., Sanberg, P.R., Pennypacker, K.R., and Willing, A.E.: Cord Blood Treatment Leads to Full Recovery in Rats with Experimental Stroke. Cell Transplantation, Vol 15, pp. 213-223, 2006  
**PRESENTATIONS**

**37<sup>TH</sup> Annual Society for Neuroscience 2007**, San Diego California, Splenic Reaction to Stroke is not Dependent on Direct Autonomic Neurotransmission via the Splenic Nerves. **Oral Presentation.**

**36<sup>TH</sup> Annual Society for Neuroscience 2006**, Atlanta Georgia, The Spleen Contributes to Stroke Induced Neurodegeneration. **Oral Presentation.**

**13<sup>th</sup> American Society for Pharmacology and Experimental Therapeutics 2006**, Alternative Treatments of Embolic Stroke in Rats Significantly Reduce Infarction Size. **Oral Presentation.**

**35<sup>TH</sup> Annual Society for Neuroscience 2005**, Washington D.C.; Sigma Receptor Activation Reduces Infarct Size after Permanent Middle Cerebral Artery Occlusion in Rats (pMCAO). **Oral Presentation.**

# Yu Hui (Lisa) Sung

3 Essex Street ♦ Concord NH, 03301 ♦ 626-224-5075 ♦ Lisalssung@gmail.com

## Education

**Franklin Pierce Law Center**, Concord NH

Candidate for JD-LLM in Intellectual Property law, Expected December 2009

**National Chiao Tung University**, HsinChu, Taiwan ROC

M.S. Applied Chemistry (major in Biochemistry and Protein Expression), 1998

**National Chiao Tung University**, HsinChu, Taiwan ROC

B.S. Applied Chemistry, 1995

## Work Experience

Fall 2010	Wilson, Sonsini, Goodrich & Rosati Professional Corporation (Palo Alto office) -- Associate
May 2009 to July 2009	Wilson, Sonsini, Goodrich & Rosati Professional Corporation (Palo Alto office) -- Summer Associate (a) Attend trials in Delaware District Court. (b) Conducted legal searches for post trial briefs. (c) Prepared memo for numerous subjects related to patent issues.
June 2008 to Aug. 2008	Wilson, Sonsini, Goodrich & Rosati Professional Corporation (Palo Alto office) -- Summer Law Clerk (a) Conducted legal searches for claim construction issues (b) Prepared discovery statements and responses. (c) Reviewed prior arts and prepare a summary for relevant prior arts.
June 2007 to Aug. 2007	Paul, Hastings, Janofsky & Walker LLP (Los Angeles office) -- Summer Law Clerk (a) Reviewed patents and file wrappers. (b) Searched prior arts by US/JP classifications and preparing memo for the results. (c) Drafted discovery requests.
April 2004 To Aug. 2006	AU Optonics Corporation -- Assistant Manager, Technology Office Handled all aspects of US litigation support including: (a) Preparing, collecting and responding to discovery for all patent infringement lawsuits in the US, including one International Trade Commission case and two Federal District Court cases. (b) Interviewed witnesses and prepared summaries. (c) Assisted in preparing expert reports, claim construction briefs, summary judgment motions and trial briefs. (d) Serve as company's designated F.R.C.P. 30(b)(6) witness for numerous subjects.
April 2002 To April 2004	BenQ Corporation -- Patent Engineer (i) Negotiation: (a) Attended negotiation meetings with patentees. (b) Responded to warning letters. (c) Assisted in preparing legal opinions. (ii) Patent prosecution: (a) Interviewed RD engineers and assisted in prior art searches. (b) Revised patent applications drafted by law firms.
Sep. 1999 To April 2002	Acer Display Technology Inc. -- Patent Engineer (a) Built up Patent system in the company. (b) Drafted invention disclosures. (c) Revised patent application drafts prepared by outside law firms for filing in 4 different countries (US, Taiwan, China, and Japan).
July 1998 To Sep. 1999	Deep & Far Attorney-at-law-- Patent Engineer (a) Interviewed clients. (b) Drafted US patent applications. (c) Prepared Office Action responses.

## Language Skills:

Chinese - Mandarin (Fluent)	English (Fluent)
-----------------------------	------------------

## Publication and On-going project

### 1. HIV vaccine technology patents landscape projects (Jan. 2008 to Dec. 2008, Aug. 2009 to Dec. 2009):

Two professors and several students in Franklin Pierce Law Center are working with the Public Intellectual Property Resource for Agriculture (PIPRA, <http://www.pipra.org/>) to build an on-line information resource database contains a distilled subset of HIV vaccine technology patents and applications to allow scientists, policy makers and other interested parties to facilitate informed decisions to accelerate research, development, production and deployment of HIV vaccines to developing countries. We also publish a limited access report for the landscaping result each semester.

2. Purification, Characterization and Mechanistic Study of  $\beta$ -Glucosidase from *Flavobacterium meningosepticum* (ATCC 13253) Yaw-Kuen Li, Shi-Her Chu and Yu-Hui Sung, *Journal of the Chinese Chemical Society*, Volume 45, No. 5, October 1998

## **JAMES M. BARRETT**

19 VANDERWATER CT., EAST BRUNSWICK, NJ 08816

Cell: 732-718-7801

james.m.barrett@comcast.net

### **EDUCATION**

#### **Franklin Pierce Law Center, Concord, New Hampshire**

- Juris Doctor Candidate, May 2010
- Patent Bar Eligible

#### **The Advanced Licensing Institute at Franklin Pierce Law Center**

- Attended seminars relating to negotiations, cross licensing, trademark licensing, IP misuse, and antitrust, mining portfolios, IP tax issues, and managing university research assets.

#### **International Technology Transfer Institute Clinic at Franklin Pierce Law Center**

- Worked with the International AIDS Vaccine Initiative (IAVI) to illustrate and clarify patent landscapes pertinent to vaccine technologies related to HIV/AIDS.
- Provided patent landscape analyses to identify patent literature (both patents and patent applications) that might be relevant to adjuvants related to HIV/ AIDS vaccines.
- Assisted creating and editing a report detailing the findings of the patent landscape analysis for IAVI.
- Performed extensive patent searching and examination with Thompson Innovation and Delphion.

#### **Academic Memberships**

- Member, Student Intellectual Property Law Association
- Member, Phi Alpha Delta Law Fraternity
- Participant, Ruby R. Vale Corporate Moot Court Competition

#### **The Pennsylvania State University, State College, Pennsylvania**

- Bachelor of Science, Genetics & Developmental Biology and Applied Anthropology, May 2006
- Chapter Vice President, Chi Psi Fraternity, 2005/2006 Academic Year

#### **Academic Honors**

- Dean's List

### **EXPERIENCE**

#### **Charm Sciences Incorporated, Lawrence, Massachusetts • May 2009 to September 2009 Summer Legal Associate**

- Performed extensive prior art searches for biotechnological applications involving enzymes, bacterial varieties, and animal testing.
- Assisted in-house counsel with writing and filing patent applications for a wide variety of novel antibiotic testing methods and equipment.
- Researched and presented findings on legal issues and ramifications regarding corporate mergers and acquisitions, sales agreements, and trademark use and registration.
- Reviewed and edited technology license agreements.

**Schering-Plough Corporation, Kenilworth, New Jersey • November 2006 to March 2007**

International Fortune 500 Pharmaceutical Company

**Legal Assistant, Contract Legal Department**

- Assisted lawyers in researching and retrieving contracts for large corporate accounts involving the pharmaceutical, financial, and agricultural industries.
- Managed incoming and outgoing new and existing files from different departments including patents, litigation, and international agreements.
- Archived obsolete files into corporate databases.

**Honorable Vincent Le Blon, New Jersey Superior Court, New Brunswick, New Jersey**

**May 2006 to September 2006 and May 2008 to August 2008**

**Judicial Intern**

- Assisted law clerk and judge in researching, analyzing, and drafting decisions on motions for summary judgment concerning medical malpractice, premises liability and motor vehicle liability.
- Observed trials, discovery proceedings, mediation conferences, and assisted in preparation of jury charges.

**Professional Memberships**

- American Bar Association
- New Jersey Bar Association
- American Intellectual Property Law Association
- Licensing Executives Society

**Skills**

- Westlaw, Lexis and traditional research methods
- Hardware upgrades, configuration, and networking in a Windows environment
- IBM WRQ Reflection, iManage, TeamConnect
- Adept reading and comprehension capabilities at over 2000 words per minute enabling rapid turn around of legal briefs, interoffice memoranda, and research tasks

# Amrita K. Chiluwal

77 N. Spring St #2  
Concord, NH 03301  
603-264-5470  
achiluwal@piercelaw.edu

## EDUCATION

---

### Franklin Pierce Law Center, Concord, NH

Juris Doctor, expected, May 2011

Moot Court, Giles Sutherland Rich Moot Court Competition

### Clark University, Worcester, MA

Major: B.S. Biochemistry and Molecular Biology, 2005

Awards: International Merit Scholarship

James and Ada Bickman Summer Science Research Fellowship, June 2004

## WORK EXPERIENCE

---

### Tufts University Medical School, Boston MA

#### Research Technician (Enzymology)

May 2005-August 2008

- Worked towards design of orally active DPPIV inhibitors
- Conducted and analyzed various invitro and invivo experiments for pharmacodynamic and pharmacokinetic studies of potent and functionally selective DPPIV inhibitors
- Screened chemicals to identify potential treatment for Type II diabetes
- Frequently assisted with invivo and invitro experimental designs

### Clark University, Worcester MA

January 2004-May 2005

#### Protein Chemistry Research Lab

- Worked towards identification of the active site in *diamine oxidase*
- Performed kinetic studies to identify biological substrate of *diamine oxidase*
- Wrote a research proposal and devised experimental protocols

### Clark University, Worcester MA

September 2004-May 2005

#### Department of Chemistry, Chemistry Tutor

- Tutored first year undergraduates in Chemistry 101&102
- Assisted students with difficulties in the course and lab work

### Clark University, Worcester MA

Summer 2004

#### Department of Chemistry, Summer Science Resident Advisor

- Supervised a group of twenty high school juniors during a three week summer science program
- Mentored and tutored students, provided resources related to coursework

## ACTIVITIES & LANGUAGE

---

### Tutoring-Plus, High School Tutor Cambridge MA

February 2007-May 2008

- Help academically challenged students with their course work
- Fluent in Nepali & Hindi. Conversant in French.

## PUBLICATION

---

Beth Connolly et al., *Dipeptide Boronic Acid Inhibitors of Dipeptidyl Peptidase IV: Determinants of Potency and in Vivo Efficacy and Safety*, 59 J. MED. CHEM. Sep. 11, 2008, at 6005.

# PRAVIN CONDA

Permanent Address: 27 Allison Drive • East Brunswick, NJ 08816 • 848 391 7375  
[pconda@piercelaw.edu](mailto:pconda@piercelaw.edu)

## EDUCATION:

### FRANKLIN PIERCE LAW SCHOOL

Juris Doctorate May 2010

### RUTGERS UNIVERSITY • School of Engineering

Bachelor of Science Biomedical Engineering May 2005

**Engineering Skills:** Hemocytometer, Nova Bioprofile 100 and 400 series, Sterile Guard Hood, Contrast Phase, Microscope, Sigma 3K12 Centrifuge, Radiometer ABL5, Finn-Aqua Autoclave, Innovartis Cedex, Terumo SCD-IIB

**Computer Skills:** Matlab, Maple, Q Basic, C, Fortran, Visual Basic, Origin Engineering Graphing Software, Delphion, Thomson Innovation

## LEGAL EXPERIENCE:

### FOXMANDAL LITTLE

#### SUMMER LEGAL ASSISTANT

Jul 2009-Aug 2009

Hyderabad, India

- Focus on Section 3(d) in Indian Patent law and tried to defined what “efficiency “ means
- Presented to colleagues about differences between Indian Patent Law and U.S. Patent Law and the Hierarchy of the court system within the U.S.

### ITTI CLINIC

#### CLINIC STUDENT

Jan 2009- May 2009

Concord, NH

- Researched about Peptide Vaccine for Human immunodeficiency Virus (HIV)
- Generated a report on patent documents relating to Peptide Vaccine for HIV

### GRIFFITH HACK

#### SUMMER LEGAL ASSISTANT

Jul 2008-Aug 2008

North Sydney, Australia

- Research about the regulations on Microorganism Deposit in the Budapest Treaty in various countries Ex. Japan, China, South Africa, USA
- Assisted in replying to an infringement action by discovering differences within the claims and specifications of the alleged infringed patent to the client’s patent.
- Researched post-amendment rules on USA patents and how it would assist an Australian patent firm.

## SCIENTIFIC EXPERIENCE:

### GE HEALTHCARE (WAVE BIOTECH DISPOSABLE BIOPROCESS GROUP) RESEARCH SCIENTIST

Feb 2007-Aug 2007

Piscataway, NJ

- Conducted Mass Transfer and kLA studies on carious experimental Wave Cellbags®

## PUBLICATIONS:

*FRANKLIN PIERCE LAW CENTER EDUCATIONAL REPORT: PATENT LANDSCAPE OF PROTEIN/PEPTIDE VACCINES FOR HIV (Jan 09-May 09) – A Patent Landscape project focusing on HIV peptide vaccines conducted by Prof. Stan Kowalski and Prof. Jon Cavvichi and a group pf students from Franklin Pierce Law School.*

**APPENDIX J: List for General Adjuvants that might be applied to HIV Vaccine**

(Please refer to attached DVD disc for the full list)

**APPENDIX K: MicroPatent® Summary Report for Relevant Patents**

(Please refer to attached DVD disc for the full document)