FRANKLIN PIERCE LAW CENTER EDUCATIONAL REPORT: PATENT LANDSCAPE OF PROTEIN/PEPTIDE VACCINES FOR HIV

SPRING 2009

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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.

Our sincere thanks to Dr. Kerri Clark of the Public Intellectual Property Resources for Agriculture (PIPRA) without whom this project would not have been possible.

We are thankful to Mr. Mark Bauer and Thomson-Reuters for graciously facilitating access to Aureka®, Delphion® and for providing invaluable guidance and training on other aspects of patent database mining and research. We also thank Patent iNSIGHT Pro™ for use of their comprehensive patent analysis platform.

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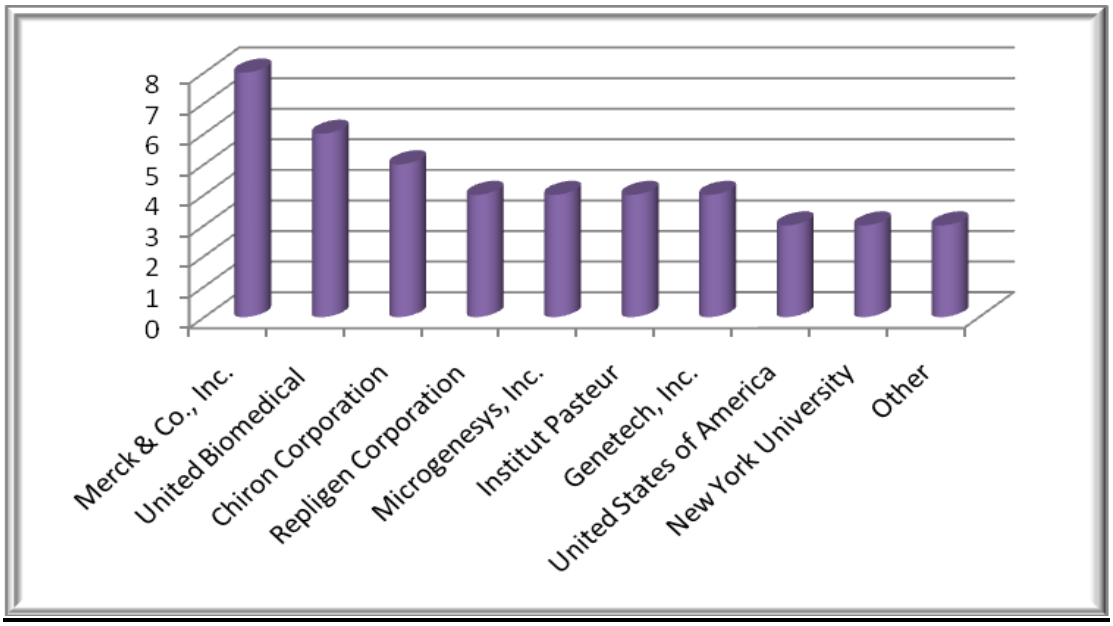
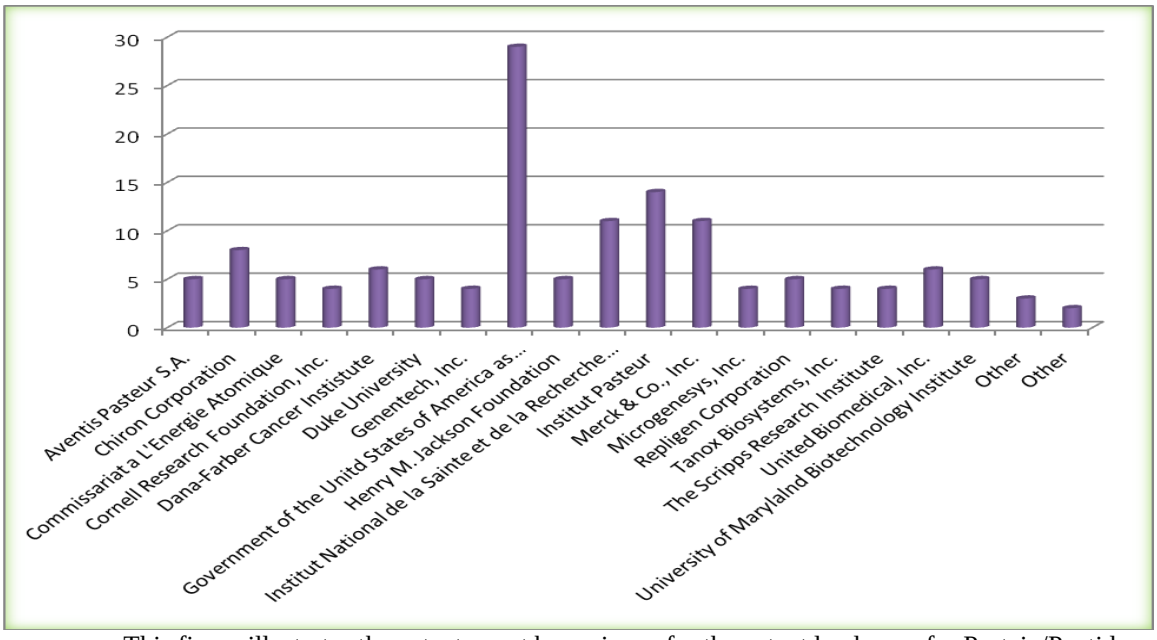
Executive Summary

TOP 10 ASSIGNEES according to MicroPatent®



This figure illustrates the patent count by assignee for the patent landscape for Protein/Peptide Vaccine Technology. The top assignees include Merck & Co., Inc., United Biomedical and Chiron Corp.

TOP 10 ASSIGNEES according to Microsoft Excel®

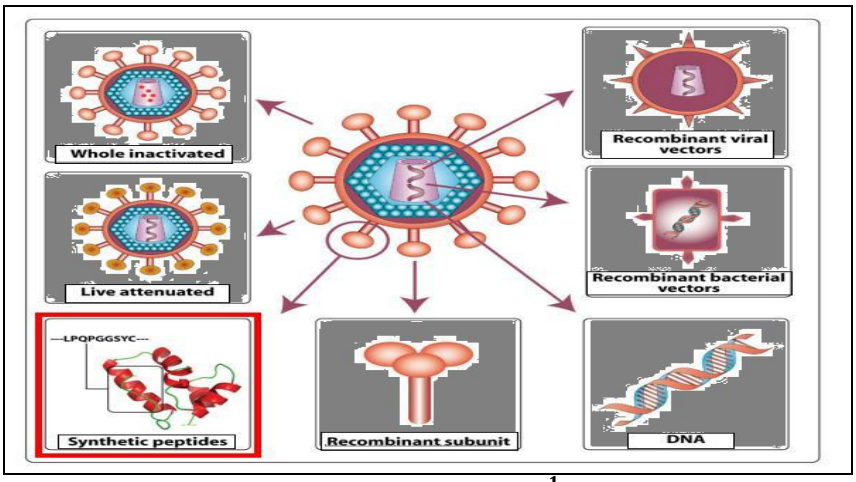


This figure illustrates the patent count by assignee for the patent landscape for Protein/Peptide Vaccine Technology. The top assignees from this analysis, however, reflect a different resulted than those found using MicroPatent®. Instead, Microsoft Excel® indicates that the United States Government and the Institut Pasteur are the two main assignees for this technology.

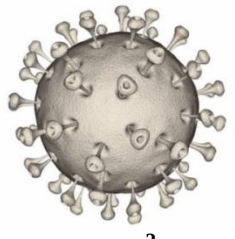
Value Added Features

- Developed more streamlined work flow process between student researchers and Project Director.
- Translation of PCT documents in the French language by team member Alexandre Ferre.
- Further refinement of hybrid iterative search process with more sophisticated use of patent classification codes.
- Enhanced data clean up and manipulation to enhance the integrity of Aureka Theme Maps.
- Enhanced technical capacity with three members holding advanced life science degrees.
- Increased understanding on ways vaccine technology claims are obfuscated with words and claims structure.
- Iterative refinement of Dr. Clarke's five topical categories to ITTI Teams' eleven based on team research and analysis.
- Also, analytics were again included, and one new aspect added was to resolve U.S. patent application assignees (not on cover page) via a USPTO tool which identifies assignees on U.S. Apps. So, this is a new process of refining the U.S. assignee data.

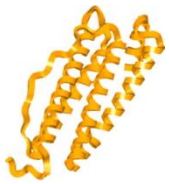
Scope of the Technology Analyzed



Vaccine Strategies[1]



HIV[2]



Peptide: Protein Subunit[3]

Vaccine[4]

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 subunit proteins or epitope-based peptides have emerged as viable candidates for developing effective therapeutic and preventative treatments for HIV. Protein subunits and peptides in a vaccine elicit humoral immune responses by stimulating antibodies to neutralize the native virus. Though a high specificity related to HLA alleles decreases the universal effectiveness of a peptide vaccine approach, many protein subunit and peptide vaccine designs incorporate conjugates or adjuvants to increase their immunogenicity. 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 a subunit protein or peptide based HIV vaccine.

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[1] Various Approaches for HIV Vaccine Development, http://www.retrovirology.com/content/4/1/66/figure/F1 (last visited Mar. 29, 2009).
[2] HIV 101, http://www.aidsdurham.com/Pictures/HIV.JPG (last visited Mar. 29, 2009).
[3] Peptides: Protein Subunits, http://www.chemistry.wustl.edu/~courses/genchem/Tutorials/Ferritin/images/peptide_ribbon.jpg (last visited Mar. 29, 2009).
[4] New HIV vaccine, http://www.topnews.in/health/files/HIV-Vaccine.jpg (last visited Mar. 29, 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 Protein/Peptide vaccines for HIV.

This report is not a list of all potentially relevant patent documents. It is not a Freedom to Operate (FTO) opinion. Furthermore, this report does not reach the level of a FTO analysis, but instead constitutes an educational presentation of potentially relevant information.

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

As the team members are not experts in the field of Protein/Peptide vaccines for HIV, it is also highly possible that the categorization of the patent documents found, coded and compiled are incomplete. The team cannot guarantee that these patent documents were evaluated at the level of expert scientific sophistication.

Due to the limited time frame (~15 weeks) imposed upon this project, the number of patent documents evaluated was established by this constrained schedule, 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, they may not have been considered. Also, certain patents were unable to be examined due to the lack of claims or foreign language restrictions.

Again, this report should not be viewed as a FTO analysis but instead constitutes an educational report.

I. About the Technology

1. Subunit/ Envelope Protein Vaccines

1.A. Obstacles to HIV Vaccines

While a few antiretroviral therapies exist for HIV-1, more than 95% of individuals infected with this disease live in places where access to such therapies is limited due to its high cost. It is because of this that a vaccine is believed to be the best and only real long-term solution to the AIDS pandemic.[5]

The search for a HIV-1 vaccine has proven to be a challenging problem for a number of reasons. First, there has never been a recorded case of natural immunity to HIV. As such, researchers have been unable to "identify immune correlates of protection from natural infection." There is still hope, however, that individuals do exist who have a natural immunity to HIV-1. There have been rumors that female prostitutes in Kenya and Gambia have been exposed to HIV and remain uninfected. It is from these women that researchers have discovered the importance of Cytotoxic T lymphocyte (CTL) activities in vaccine development.[6]

Second, there is no suitable animal model for assessing the effectiveness of any of the proposed vaccines against HIV-1. Chimpanzees present a number of problems to the vaccine trials including: 1) the high cost of their care; 2) the fact that they are an endangered species and are thus not highly accessible; 3) and the fact that while they are susceptible to HIV-1 infection, they do not succumb to its disease except in very few cases. As such, "SIV, which induces AIDS-like symptoms in macaques, has been used widely to model HIV-1 pathogenesis." To overcome some of the problems researchers have encountered using SIV, a chimeric virus of HIV-1 and SIV termed SHIV has been generated. This virus encodes vpu, vpr, rev, env and tat "genes derived from HIV-1 in the backbone of SIV genome." This chimeric virus, however, is limited in that the swift loss of CD4+ T lymphocytes is very different from the slow decline of a HIV-1 infected immune system. Also, SHIV is also limited by the fact that the genome is only partially derived from HIV-1.[7]

The third obstacle to HIV vaccines has been the many ways by which the HIV-1 virus evades the human immune system. "HIV-1 evades humoral immune responses against its envelope glycoprotein in three ways: extensive glycosylation, a high degree of genetic variation, and complex tertiary and quaternary structures." HIV-1 also has a number of means of evading cellular immune responses.[8] This type of invasion includes:

> (1) down regulation of Class I major histocompatibility complex (MHC) molecules by Nef, (2) ability of HIV-1 to integrate into the host genome,

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[5] Michael W. Cho, *Subunit Protein Vaccines: Theoretical and Practical Considerations for HIV-1*, 3(3) CURRENT MOLECULAR MEDICINE 243, 243 (2003).
[6] *Id.*
[7] *Id.* at 244.
[8] *Id.*

which allows the virus to stay dormant for prolonged periods, (3) destruction of CD4+ T lymphocytes, which play a central role in immunity, and (4) immune suppression by Tat.[9]

1.B. Vaccine Strategies Comparison

There are six categories of vaccine strategies including subunit protein, live attenuated, whole-inactivated, DNA, live vector and combinatorial vaccines.[10] Only live attenuated, whole-inactivated and subunit protein vaccines are currently being licensed. Table 1 illustrates the common uses of these vaccines.[11]

Routine childhood vaccination	
Chickenpox (Varicella)	Live attenuated
Hepatitis B virus	**Subunit**
Measles	Live attenuated
Mumps	Live attenuated
Rubella	Live attenuated
Poliovirus	Whole inactivated (Salk vaccine)/ live attentuated (Sabin vaccine)
Vaccines for select population	
Adenovirus	Live attenuated
Japaneses encephalitis virus	Whole inactivated
Hepatitis A virus	Whole inactivated
Influenza virus	Whole inactivated
Rabies	Whole inactivated
Yellow Fever	Live attenuated
Smallpox (Variola virus)	Vaccinia virus ("Jennerian")

Table 1: Viral Vaccines[12]

[9] *Id.*
[10] *Id.* at 244–45.
[11] *Id.* at 245.
[12] *Id.*

1.C. Subunit Protein Vaccines

1.C.1. Introduction to Subunit Vaccines

Subunit vaccines can be composed of either peptides or proteins that are "prepared either from virus, a recombinant source, or synthetically as in the case in the case of peptides." Unlike live attenuated and whole-inactivated vaccines, subunit vaccines are not considered to be dangerous. Based on its modality, subunit protein vaccines are generally considered to better at eliciting both helper T cell responses as opposed to cytotoxic T cell responses and antibody responses.[13]

There are several differences between and characteristics of subunit vaccines based on peptides and those based on whole proteins. (Refer to Figure 1 for a comparison of protein and peptide subunit vaccines). First, peptides can more quickly and easily be obtained in greater amounts than whole proteins. Second, unlike whole proteins, purer forms of peptides can be obtained. Third, peptides may be able to elicit both helper T cell and cytotoxic T cell responses. Fourth, in peptide vaccines, known CTL and helper T cell epitopes can be specifically utilized to direct the immune response. However, peptides vaccines used for one person may not affect or help a different person with a dissimilar HLA haplotype as "T cell epitopes are restricted to the genetic haplotype of the individual person's MHC." Fifth, HIV is likely to more easily escape an immune response based on a peptide vaccine than a whole protein vaccine because peptide vaccines cause immune reactions against less epitopes.[14] Sixth, an advantage of whole proteins over peptides is that no prior studies on the HLA typing and epitope mapping is required. Finally, unlike peptides, proteins are proficient at eliciting potent humoral immune responses.[15]

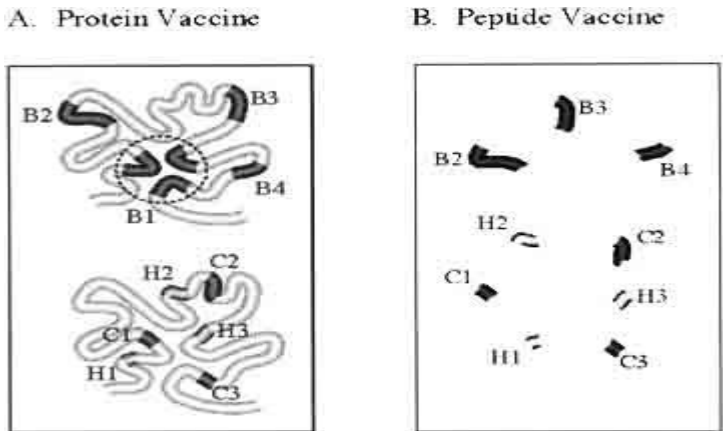

Figure 1: Comparison of protein- and peptide-based subunit vaccines. H= helper T cell, B= B-cell, and C= cytotoxic T cell epitopes.[16]

[13] *Id.*
[14] *Id.* at 246.
[15] *Id.* at 247.
[16] *Id.* at 246.

1.C.2. Protein/Envelope Subunit Vaccines

"Envelope glycoprotein is the only protein that is exposed on the surface of HIV-1 virions and can elicit Nab response."[17] (Refer to Table 2 for vaccine candidates).

"Native" envelopes
gp160 (uncleaved)
gp120
Genetically/biochemically modified envelopes
Oligomeric gp140
gp120/gp41 cleavage site mutants
Intermolecular disulfide linkage (SOS)
Stabilization by GCN4
Variable loop-deleted mutants
Glycosylation site mutants
CD4 independent envelopes
Fusion-competent envelopes
Envelope-CD4 complexes
Envelope with truncated gp41 cytoplasmic domain
Polyvalent envelope vaccines
Large collection of envelopes
Consensus or ancestor sequence(s)
Combinatorial strategies
Live vector gp160 + gp140 or gp120
DNA gp160 or gp140 + gp140 or gp120
Peptides
V3 peptide
Heptad repeat region of gp41
Patient sera-reactive peptides (phage-displayed random peptide library)
IgG b12-binding peptide (phage-displayed random peptide library)

Table 2: Protein and Peptide-based envelope immunogens and vaccine strategies[18]

Because a large portion of the HIV-1 envelope glycoprotein surface is covered with areas that cause either a reduced or an isolated incident antibody response, research has considered strategies of eliciting more broadly reactive Nabs. These strategies include the use of fusion intermediates, glycosylation site-mutated envelopes, CD4-independent envelopes and variable loop-deleted envelopes. (Figure 2 below illustrates these strategies). The fusion intermediate strategy involves the interactions between CD4, envelope glycoprotein and chemokine receptors. The CD4-independent envelope strategy may be able to cause antibody responses "against the conserved coreceptor-binding domain."[19] The theory behind the variable loop-deleted envelopes strategy is that the deletion of variable loops V1/V2 and V3 improves binding of Nabs "directed

[17] *Id.* at 247.
[18] *Id.* at 248.
[19] *Id.* at 249.

against the CD4-binding region." However, as of now, only two variable loop-deleted HIV-1 envelopes have been found to be functional. Finally, the glycosylation site mutant strategy requires the use of "deglycosylated envelope proteins as immunogens" to provide a means of increasing highly reactive Nabs.[20]

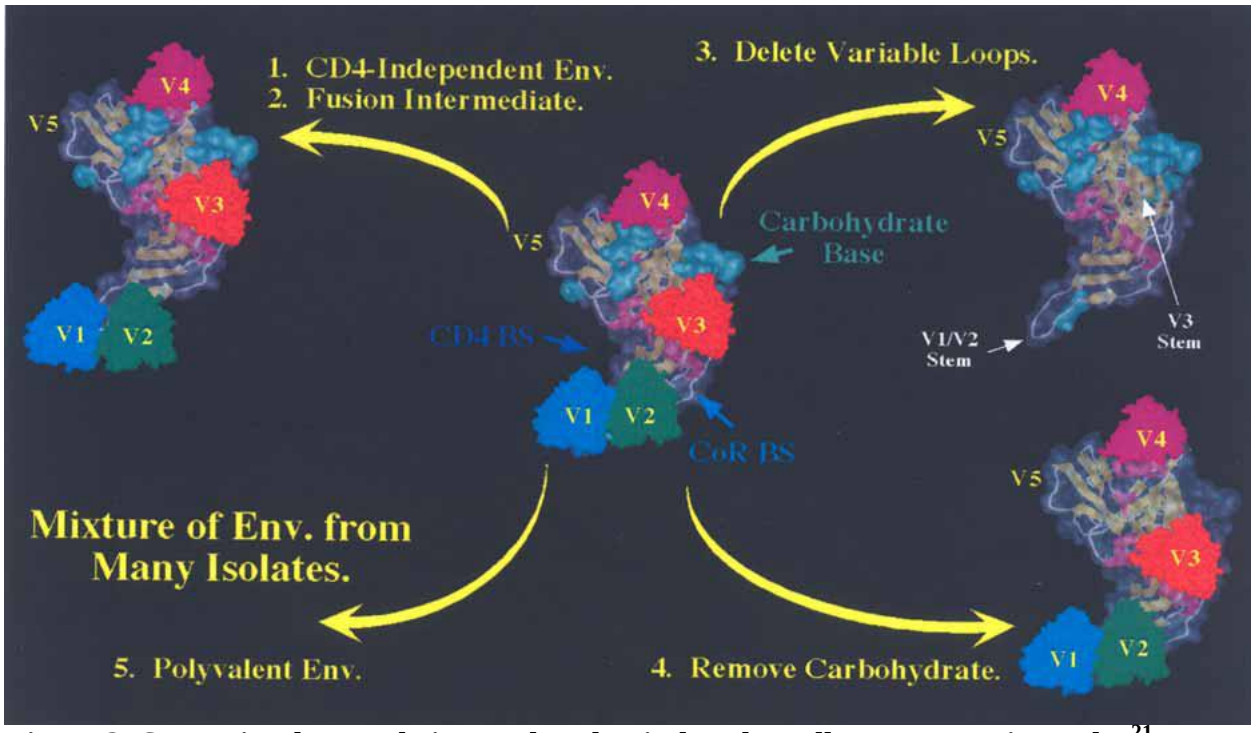

Figure 2: Strategies that are being explored to induce broadly cross-reactive Nabs.[21]

Two alternative strategies to those listed above include polyvalent envelope vaccines and oligomeric envelopes. Polyvalent envelope vaccines cause expand B cells which "target conserved regions of envelope," and hopefully result in more reactive Nabs.[22] Oligomeric envelopes, on the other hand, may potentially serve as superior immunogens than "monomeric forms in eliciting Nabs."[23]

2. Peptides

2.A. Peptide Formulas

A peptide is a series of amino acids linked together by a peptide bond, a chemical bond between the carbonyl group of one amino acid and the amino group of a second amino acid.[24] Polypeptides are large sequences of amino acids; however, a sequence of

[20] *Id.* at 250.
[21] *Id.* at 249.
[22] *Id.* at 251.
[23] *Id.* at 253.
[24] BRUCE ALBERTS ET AL., ESSENTIAL CELL BIOLOGY 74–75 (2d ed. 2004).

more than 50 amino acids is generally considered to be a protein.[25] Below (Figure 3) are the 20 amino acids found in peptides:

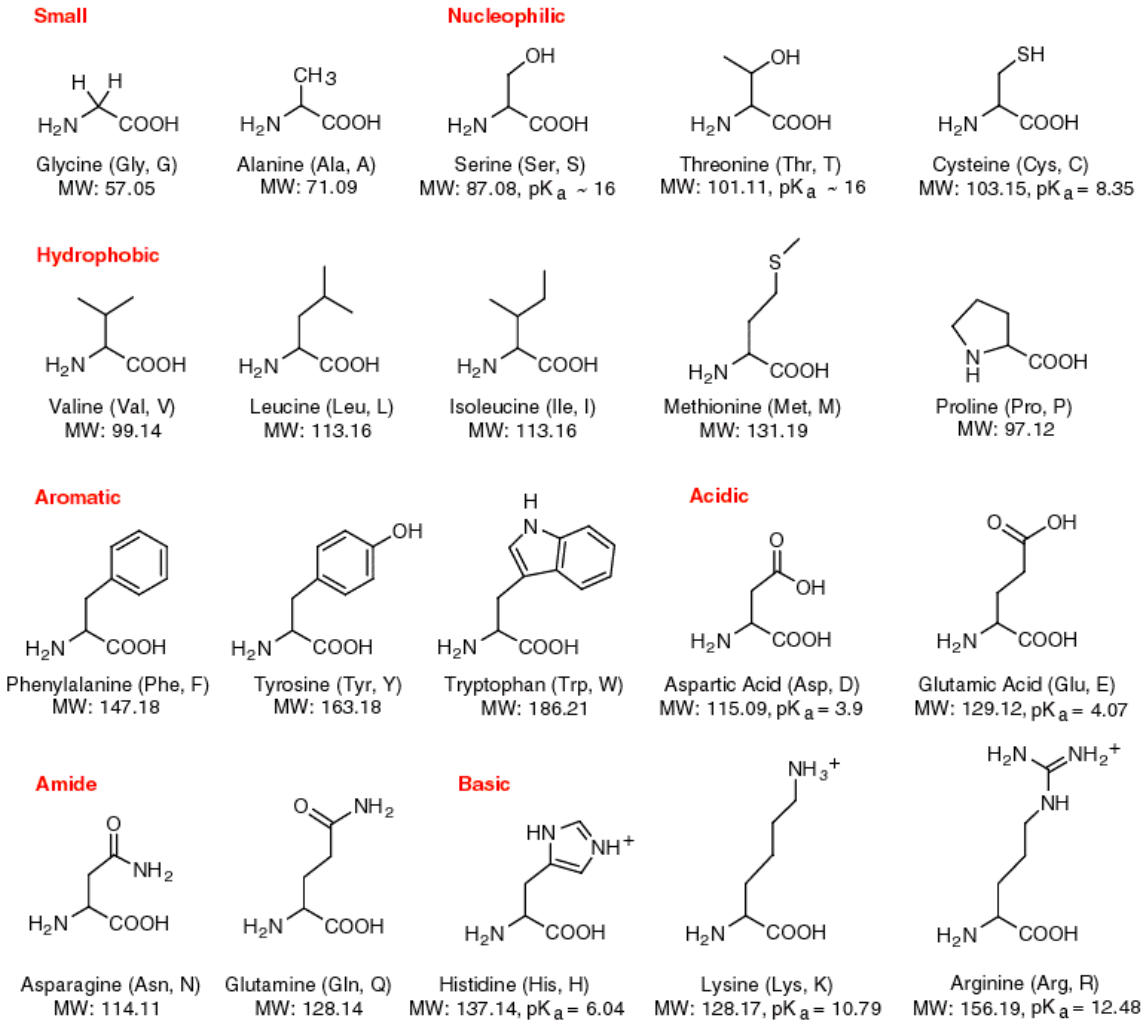

Fig. 3: Amino Acid Structures[26]

Problems using peptides in vaccines against HIV stem from the diversity of HIV, the human leukocyte diversity antigens (HLA), which are associated with presenting antigens to CD8+ and CD4+ T cells, and the ability to stimulate the long-term memory of the immune system.[27] In order to combat these challenges, researchers suggest that therapeutic immunogens should contain multiple epitopes to ensure sufficient potential to target a diversity of virus strains and HLA. Efforts to maximize the number of available epitopes include attempts to artificially string together multiple epitopes as well as

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[25] *Id.* at 120.

[26] New England Biolabs Inc., http://www.neb.com/nebecomm/tech_reference/general_data/amino_acid_structures. asp (last visited Feb. 15, 2009).

[27] Maja Sommerfelt & Birger Sorensen, *Prospects for HIV-1 Therapeutic Immunization and Vaccination: the Potential Contribution of Peptide Immunogens*, 8(6) EXPERT OPINION ON BIOLOGICAL THERAPY 745, 750–51 (2008).

designing compound peptides, a series of 9-mers where potential epitopes have been identified through analysis of proteasome cleave, transporter associated with antigen presentation transport and trimming by peptidases in the endoplasmic reticulum. Problems with these techniques may arise where this leads to functional epitopes that are unrelated to HIV, possibly affecting immunogenicity.[28]

Other strategies to get around the complexity of HIV related immune responses include enhancing the effectiveness of peptide therapeutics by glycosylation, amino-acid-sequence modification, pegylation and cyclization. Additionally, several studies have explored modifications that not only provide subtle conformational changes to the peptide/MHC structure as well as incorporating resistances against proteases. This includes incorporations of β-amino-acids into epitopes to increase the binding affinity of the mimetic for the MHC molecule relative to the wild type peptide.[29] Refer to Figure 4.

Table 2 | **Non-natural amino-acid modifications in peptide vaccines**

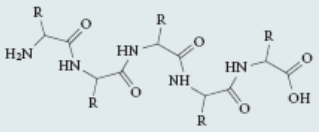
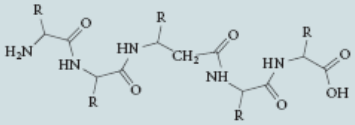
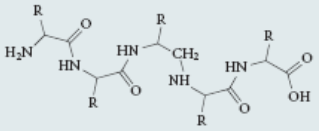
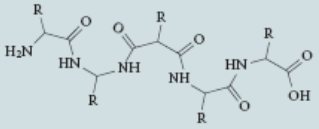
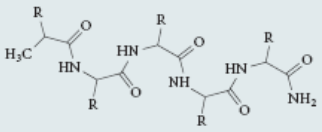
Modification	Structure	Refs
Normal α-peptide		
β-amino-acid substitution		68–70
Backbone reduction		116
Partial retro-inversion		116
N-terminal methylation and C-terminal amidation		72

Figure 4: Non-natural Amino-acid Modifications in Peptide Vaccines[30]

2.B. Epitopes and Epitope Based Vaccines for HIV Infection

With the spread of AIDS still rampant in many parts of the world, there is an urgency to develop a vaccine against HIV. Developing an effective vaccine against the

[28] *Id.* at 750.
[29] Anthony Purcell et al., *More Than One Reason to Rethink the Use of Peptides in Vaccine Design*, 6 NATURE REVIEWS: DRUG DISCOVERY 404, 411 (2007).
[30] *Id.* at 412.

virus has been a scientific challenge.[31] Although advances in molecular biology and biotechnology over the years have enabled the generation of "designer antigens," the ability to transform them into successful vaccine candidates has been limiting.[32]

The development of vaccines and their subsequent use as preventive vaccines was one of the most important developments in medicine.[33] Vaccines make use of the adaptive part of the human immune system to protect from future infections (prophylactic or preventive vaccines) as well as to fight chronic diseases (therapeutic vaccines).[34] Cellular adaptive immunity is triggered by the recognition of immunogenic peptides bound to Major Histocompatibility Complex (MHC) Class I and II molecules by T-cell receptors located on the surface of T cells.[35] These peptides are derived from antigens, i.e., proteins that can cause an immune response, as a result of rather complex antigen processing pathways in vivo. Peptides capable of causing such an immune response are called epitopes and represent the smallest subunits that may be used therapeutically.[36]

An epitope is a localized region on the surface of an antigen that is capable of eliciting an immune response and of combining with a specific antibody to counter that response.[37] Also, an epitope is a short sequence of amino acids, which the immune system can recognize and react against. Such short sequences of amino acids are called peptides. Proteins, by contrast, are very long sequences of amino acids, sometimes with a length of more than a thousand amino acids. A polyepitope is a chain of epitopes.[38] A B cell epitope is an antigenic determinant recognized and bound by the B-cell receptor and isolated on the surface of the antigen.[39] A T-cell epitope is an antigenic determinant recognized and bound by the T-cell receptor and is located in the inner, unexposed side of the antigen, and become accessible to the T-cell receptors after proteolytic processing of the antigen.[40]

The use of epitope based peptide vaccines as therapeutics is a preferable mode because of advances in their delivery, stability and design.[41] As synthetic entities, peptide based vaccines are simple because they can be administered directly without a need for a replicating vector. HIV shows extensive genetic diversity and has the ability to escape immunological pressure through mutation of both potential neutralizing domains for antibody responses as well as cytotoxic T lymphocyte epitopes for cell

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[31] Cho, *supra* note 5, at 243.
[32] *Id.*
[33] Nora C. Toussaint et al., *A Mathematical Framework for the Selection of an Optimal Set of Peptides for Epitope-Based Vaccines*, 4(12) COMPUTATIONAL BIOLOGY 1, 1 (2008).
[34] *Id.*
[35] *Id.*
[36] *Id.*
[37] Epitope, http://www.answers.com/topic/epitope (last visited Feb. 9, 2009).
[38] Epitope Based Vaccines, http://www.pharmexa.com/cms/site.aspx?p=100 (last visited Feb. 9, 2009).
[39] B-Cell Epitope, http://www.online-medical-dictionary.org/B+Cell+Epitope.asp?q=B+Cell+Epitope (last visited Feb. 9, 2009).
[40] T-Cell Epitope, http://www.online-medical-dictionary.org/T-Cell+Epitope.asp?q=T-Cell+Epitope (last visited Feb. 9, 2009).
[41] Purcell et al., *supra* note 29, at 404.

mediated immunity.[42] Hence, there is a growing emphasis on the use of peptides in vaccine design as insights into tissue-specific processing of the immunogenic epitopes of proteins and the discovery of unusually long cytotoxic T-lymphocyte epitopes broaden the range of targets and give clues to enhancing peptide immunogenicity. Peptides can also be synthesized with known post-translational modifications and/or deliberately introduced protease-resistant peptide bonds to regulate their processing independent of tissue-specific proteolysis and to stabilize these compounds *in vivo*.[43]

There are numerous options for constructing a vaccine once a set of potential antigens is known. The antigens or parts thereof can be used as intact proteins, they can be administered as RNA or DNA coding for the antigen or the epitopes contained in the antigens may be used for vaccines.[44] Skilled selection of epitopes can precisely direct the evoked immune response at conserved and highly immunogenic regions of several antigens. Due to these advantages and the applicability in personalized vaccination, EVs have recently been getting more and more attention.[45]

[42] Sommerfelt & Sorensen, *supra* note 27, at 749.
[43] Purcell et al., *supra* note 29, at 404.
[44] Toussaint et al., *supra* note 33, at 1.
[45] *Id.*

2.C. Peptide Conjugate Vaccine and the Immune Response

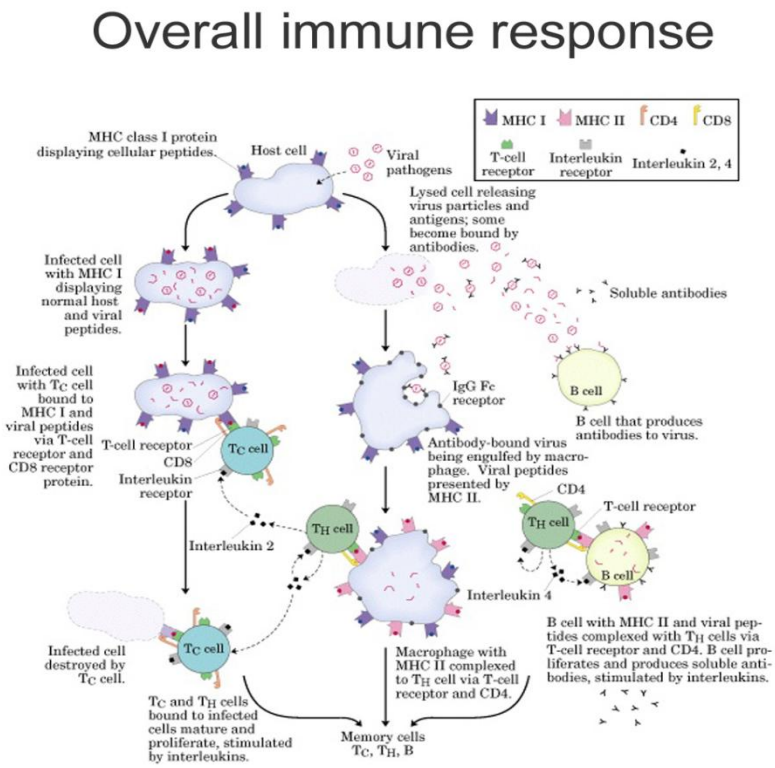

Fig. 5: A Flowchart of Both the Humoral Immune Response and the Cellular Immune Response[46]

A peptide conjugate vaccine is created by covalently attaching a poor antigen to a carrier protein, thereby conferring the immunological attributes of the carrier on the attached antigen. This technique is generally effective to prevent infection of bacteria and viruses. A peptide conjugate vaccine can be used to trigger either a cellular immune response or a humoral immune response.[47]

Normally, an immune response is triggered by an uptake of immunogen or antigen by an antigen presenting cell (APC).[48] The antigen or immunogen undergoes proteolysis to form peptides that bind to Major Histocompatibility Complex class II (MHC II) molecules.[49] This covalent bond moves to the surface of the APC for T-helper (T_h or CD4+) cells to detect. When a T_h cell detects and binds to MHC II on the APC, the T_h sends out signaling molecules that cause proliferation of B cells and cytotoxic T (T_c or CD8+) cells.[50] Interestingly, the immune system can follow two different paths

[46] Dr. Jon Robertus, Overall Immune Response, available at http://courses.cm.utexas.edu/jrobertus/ch339k/overheads-1/ch7_immune-res.jpg.
[47] *Id.*
[48] Purcell et al., *supra* note 29, at 404.
[49] *Id.* at 405.
[50] *Id.* at 407.

after this point. The humoral immune response or the cellular immune response can cause the elimination of virus or bacteria through different mechanisms.

During a humoral immune response, B cells also ingest the antigen by reacting with the B cell's antibody. Inside the B cell, the antigen undergoes proteolysis to form peptides that bind with MHC II and once again move to the surface of the B cell. T_h cells that bind with APCs activate T_h to bind with the MHC II on the B cell. This causes the B cell to proliferate and differentiate into antibody producing plasma cells or B-memory cells. These antibody producing plasma cells will lower the amount of antigen and protect the body.[51]

During a cellular immune response, the virus or bacterial infects a cell. The virus or bacteria is then degraded to form peptides. These peptides then complex to Major Histocompatibility Complex class I (MHC I) molecules and move to the surface of the infected cell. T_c cells interact with the infected cell by recognizing both the antigen and the MHC I molecule. This interaction causes the T_c to release toxins that induce apoptosis in the infected cell. Once the infected cell dies, the T_c cell detaches and looks for another infected cell with MHC I and the antigen displayed on the surface.[52]

A peptide conjugate vaccine takes advantage of the fact that both these processes require peptides to attach to the MHC I or MHC II to display the antigens. Antigens are recognized by the immune system as foreign substances. Antibodies are not made against the entire antigen but specific chemical groups known as antigenic determinants or epitopes. Many antibodies can be made in the body, each antibody reacts with a different epitope. Antigens have different epitopes on their surfaces that bind with a specific antibody.[53]

HIV is a troublesome virus because it is constantly changing and cannot be fully removed by the immune system. A benefit of a peptide conjugate vaccine is that it looks for common peptides/epitopes that exist within HIV infected cell. By knowing which peptide bonds to the binding cleft of MHC I and MHC II, a specific antibody showing specific epitopes can be formed and target HIV infected cells.[54]

Understanding the structure of MHC I and MHC II helps when generating a peptide-conjugate vaccine. An MHC I molecule contains a polymorphic heavy chain and a monomorphic light chain: (β2 microgobulin) and a antigenic peptide ligand. The heavy chain contains an antigen-binding groove that attaches to antigenic peptides, typically 8-10 amino acids in length. Based on specific amino acids that project out of the binding cleft, the specificity of allelic form of bound peptides to MHC can be determined. This allows one to display specific antibodies on the infected cell.[55] On the other hand, the structure of MHC II molecules differs from the structure of MHC I molecules. MHC II

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[51] *Id.* at 405.
[52] *Id.* at 407.
[53] WebMD Antibody. http://dictionary.webmd.com/terms/antibody(ab) (last visited Feb. 15, 2009).
[54] Purcell et al., *supra* note 29, at 405.
[55] *Id.* at 408.

molecules contain two polymorphic heavy chains (α and β) that form a heterodimer (αβ). This heterodimer forms a binding cleft that attaches to the peptide antigen. Peptides that attach to the MHC II are typically longer, 13 amino acids in length. Typically, residues 1, 4, 6 and 9 which attach to the class II bound peptide typically interact with the binding cleft. Generating peptide-epitopes that bind to a specific region of the MHC II will allow for specificity in the humoral immune response.[56]

A synthetic peptide-epitope vaccine offers several advantages such as safety in use and ease of production. However, this type of vaccine also has drawbacks such as poor immunogenicity of the simple peptides and the need to potently stimulate T cells and immunological memory. These peptide vaccines are also limited to specific human leukocyte antigen (HLA) haplotypes which results in vaccine specialized for different types of individuals. Furthermore, there are multiple peptides that are present within the body and hence the modified peptide might not follow the same pathway as a natural peptide of the HIV virus. In order to reduce these issues, different conjugates may be used to covalently attach to the peptide-epitope and increase the ability of the peptide-epitope to attach to either a MHC I or a MHC II compound.[57]

2.D. Peptide Screening

As Peptides can be efficiently processed and presented on MHC class I molecule they have been successfully used to elicit CTL immune response.[58] Peptides have also been shown to "elicit highly protective mucous immunity."[59] Studies show that "V3 loop peptides have been unsuccessful in eliciting broadly reactive Nabs."[60]

In developing a protective HIV-1 vaccine epitopes which are capable of inducing broad neutralizing Ab responses are to be identified and various methods have been made employed to identify these epitopes.[61] "The high mutation rate in HIV-1 envelope proteins and the complex structure of gp120 as an oligomer along with gp41 results in a high degree of antigenic polymorphism."[62] To overcome these obstacles, random peptide libraries are screened using sera from HIV-infected subjects to identify antigenic and immunogenic mimics of HIV-1 epitopes.[63]

[56] *Id.* at 409.
[57] *Id.* at 407.
[58] Cho, *supra* note 5, at 255.
[59] *Id.*
[60] *Id.*
[61] Giuseppe Scala et al, *Selection of HIV-Specific Immunogenic Epitopes by Screening Random Peptide Libraries with HIV-1 Positive Sera*, 162 *J. IMMUNOLOGY* 6155, 6155 (1999).
[62] *Id.*
[63] *Id.*

2.D.1. Eliciting Reactive Nabs Using Phage-Displayed Random Peptide Library (RPL)

Many methods are used for the selection of peptides binding a target molecule by means of screening large RPL.[64] "The objective of screening is to identify antigenic peptides that bind HIV-1-specific antibodies from a large pool of random peptides so that the peptides in turn could be used as immunogens to elicit antibodies with properties similar to the initial antibody used to screen random peptides."[65] Refer to Figure 6 for two approaches to elicit Nabs using random peptide libraries: (A) Peptides that bind immune sera and (B) peptides that bind IgG b12.[66]

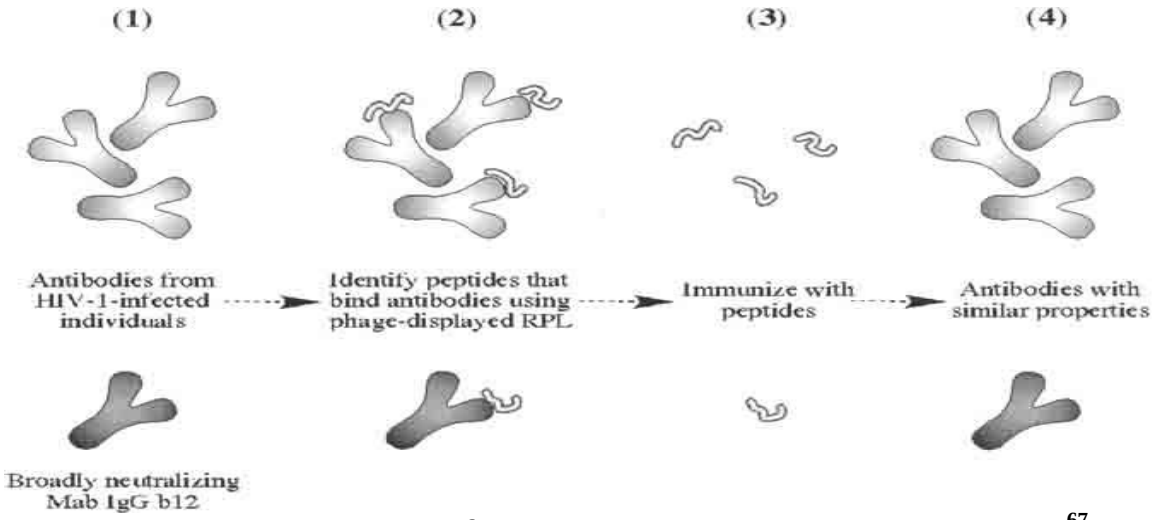

FIG 6: Schematic Diagram of Two Approaches to Elicit Nabs Using RPL[67]

2.D.2. Selecting Peptides from a Phase Displayed RPL

"Phage display is a simple functional genomic methodology for screening and identifying protein–ligand interactions and is widely used in epitope mapping" and in "screening for receptor agonists."[68] Phage display is also used in various forms, "to identify peptide–ligand and protein–ligand interactions that are of importance in infection."[69] Random peptide libraries are screened "using sera from HIV-infected subjects to identify antigenic and immunogenic mimics of HIV-1 epitopes."[70] Further they are counter-screened with HIV-negative sera, peptides specifically recognized by Abs from HIV-1-infected individuals are isolated.[71] Results shows "that pools of HIV-1

[64] Cho, *supra* note 5, at 256.
[65] *Id.*
[66] *Id.* at 255.
[67] *Id.*
[68] Lisa M. Mullen et al, Phage Display in the Study of Infectious Diseases, 14(3) TRENDS IN MICROBIOLOGY 141, 141 (2006).
[69] *Id.*
[70] Scala et al, *supra* note 61, at 6155.
[71] *Id.*

mimotopes can be selected from combinatorial peptide libraries taking advantage of the HIV-specific Ab repertoire induced by the natural infection."[72]

These results infer that the "antigenic polymorphism of HIV can be matched by a collection of epitopes selected for their affinity to human HIV-1 Abs" and also a correlation can be observed "between protection against infection and levels of neutralizing Abs in nonhuman primates infected with HIV-1 or simian HIV (SHIV)".[73] So, "in developing a protective vaccine, it would be advantageous to identify those epitopes that are specifically recognized by Abs generated by HIV- 1-infected subjects."[74]

3. Antibodies to HIV

3.A. Antibodies Overview

Antibodies are blood-borne proteins of the immunoglobulin (Ig) superfamily that play an essential role in the humoral immune response. Antibodies are directed against foreign materials primarily situated outside of the cells of the body such as the protein and polysaccharide components of bacterial cell walls, bacterial toxins, and viral coat proteins.[75] The immune system produces millions of different antibody molecules that have the ability to bind to any type of foreign material to which the body becomes exposed.[76] The antibody reacts specifically with a foreign substance called an antigen which consists of proteins or polysaccharides.[77]

Humoral immunity is mediated by B lymphocytes or B cells. B cells incorporate antibody molecules into their plasma membrane to serve as receptors for antigen. Once an individual is infected with a virus or bacterium, B cells are activated and differentiate into plasma cells that secrete antibodies into the bodily fluids which soon becomes saturated with a high concentration of antibodies capable of reacting with the foreign substance.[78] See Figure 7.

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[72] *Id.*
[73] *Id.*
[74] *Id.*
[75] GERALD KARP, CELL AND MOLECULAR BIOLOGY: CONCEPTS AND EXPERIMENTS 706 (3d ed. 2002).
[76] *Id.* at 712.
[77] *Id.* at 707.
[78] *Id.* at 707.

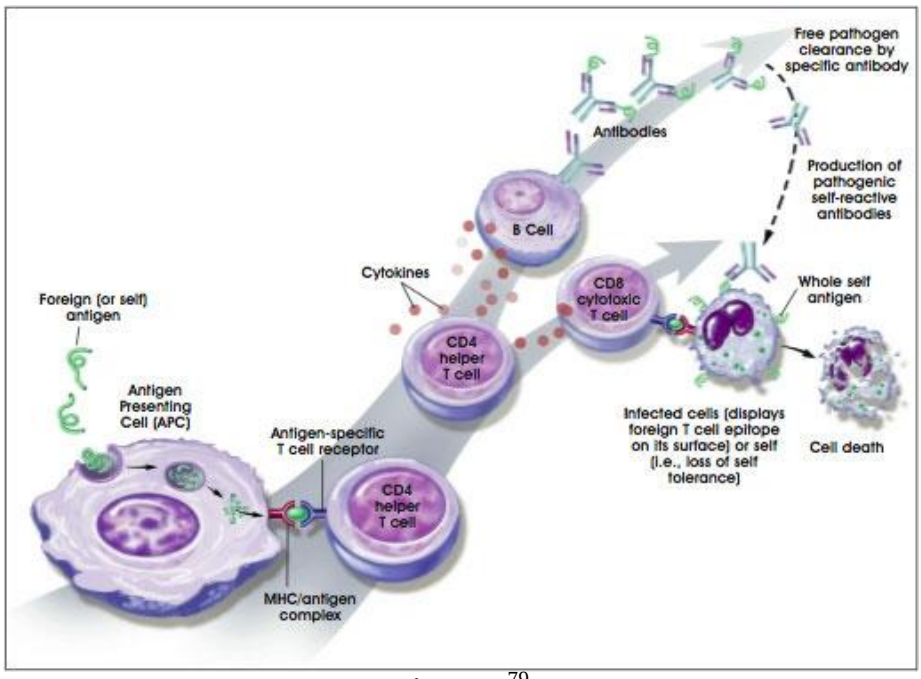

Figure 7[79]

Antibodies are globular proteins built of two types of polypeptide chains, larger heavy chains and smaller light chains. An antibody molecule comprises a structure where two identical light chains and two identical heavy chains are arranged to form a Y-shaped molecule.[80] See Figure 8. Further, the structure contains a variable region and a constant region. [81]

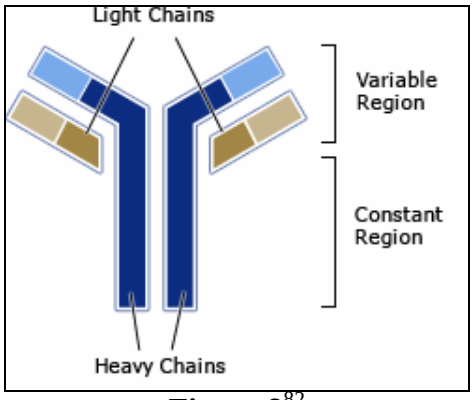

Figure 8[82]

It is the variable portion of the molecule which gives the antibody its specificity. A region which is termed hypervariable is a sub-region especially variable from one

[79] National Institute of Health, http://stemcells.nih.gov/StaticResources/info/scireport/images/figure61.jpg (last visited Feb. 15, 2009).
[80] Karp, *supra* note 75, at 713.
[81] *Id.* at 714.
[82] Structure of Antibodies, http://www.morphosys.com/uploads/antibody-structure.gif (last visited Feb. 15, 2009).

antibody to another.[83] This region forms the structure of the antigen-combining site and the great diversity amongst these regions allows the molecules to bind to antigens of every conceivable shape. This combining site additionally had a complementary stereochemical structure to a particular portion of the antigen, which is termed the antigenic determinant or epitope. An antigen can contain a number of different epitopes that can stimulate the production of a variety of different antibodies.[84]

3.B. Antibodies and Vaccine Design

The most effective vaccines work by generating antibodies that inactivate or neutralize the invading virus.[85] Identifying the antigens or epitopes which the immune system can effectively target is critical for designing the optimal and most effective vaccine and for monitoring the immunological effects of vaccination throughout the development of the vaccine product.[86]

3.B.1. HIV Vaccine Design Problems

The main obstacles to developing an immune response against HIV are the large genetic variation among HIV-1 strains worldwide, the virus' sophisticated shielding mechanisms and a failure thus far to elicit a broadly reactive neutralization against native structures of the virus. Specifically, the virus chronically replicates in the host and evades the humoral immune response through extensive glycosylation of its surface proteins.[87] Further, a large proportion of the HIV-1 envelope protein surface is covered with regions that elicit a poor antibody response.[88] To induce an effective neutralizing antibody response a vaccine must deliver the epitopes that both possess favorable properties for B cell inductive pathways and are available for high affinity antibody binding and esearch indicates that viral epitopes that are conserved among most viral strains are more likely to generate cross-reactive antibodies.[89]

3.B.2. Prophylactic Use of Antibodies

Neutralizing antibodies are more effective as a prophylactic agent rather than a therapeutic agent. Several animal studies indicate that when present in sufficient amounts prior to exposure, neutralizing antibodies can be highly protective. However, it has been extremely difficult to elicit antibodies that are broadly reactive against HIV.[90] A number of strategies are being investigated in order to elicit such a response and

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[83] Karp, supra note 75, at 714.
[84] *Id*. at 715.
[85] David Montefiori et al., *Antibody-Based HIV-1 Vaccines: Recent Developments and Future Directions*, 4 PUBLIC LIBRARY OF SCIENCE 1867, 1867 (2007).
[86] Nikolai Schwabe & Amanda Turner, *Hastening Epitope Discovery for Vaccines*, GENETIC ENGINEERING & BIOTECHNOLOGY NEWS (Feb. 15, 2008), *available at* http://www.genengnews.com/articles/chtitem.aspx?tid=2374&chid=1.
[87] Cho, *supra* note 5, at 244; Montefior et al., *supra* note 85, at 1867.
[88] Cho, *supra* note 5, at 248.
[89] Montefior et al., *supra* note 85, at 1868.
[90] Cho, *supra* note 5, at 247.

include the use of CD4-independent envelopes, fusion intermediates, variable loop-deleted envelopes and glycosylation site-mutated envelopes. These strategies are aimed at using envelope constructs that have exposed conserved regions, like receptor-binding domains, such that they can be targeted by the humoral immune system. [91]

The main targets for eliciting the neutralizing antibodies are the surface gp120 and trans-membrane gp41envelope glycoproteins which mediate receptor and coreceptor binding and subsequent membrane fusion events that facilitate the entry of the virus into cells, such as CD4+ T cells. [92] See Figure 9.

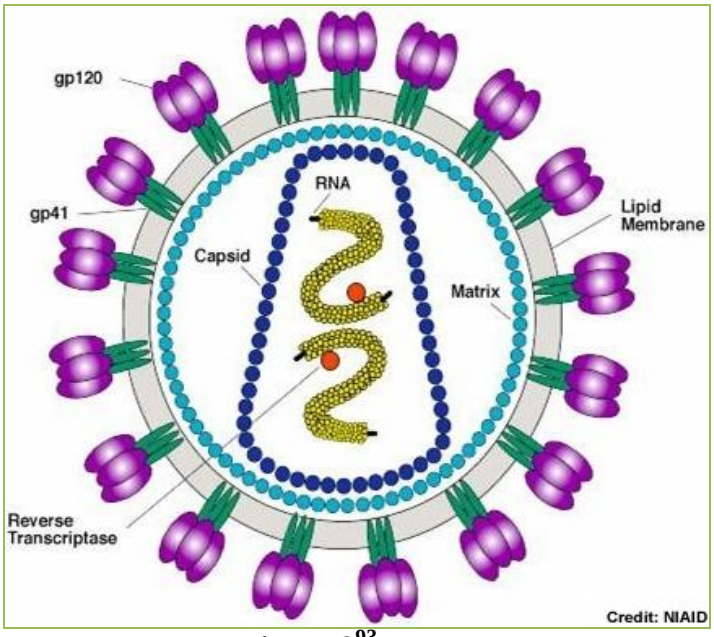

Figure 9[93]

The antibodies neutralize HIV by binding to these constructs and thus blocking the entry of the virus into cells. However, clinical studies have failed to demonstrate that immunization with the gp120 surface unit leads to the induction of broadly reactive neutralizing antibodies.[94] More promising is the membrane proximal ectodomain region (MPER) of the gp41 unit which lies at the base of HIV's envelope protein and is consistent across different strains of the virus.[95] Though research has yet to show a strong neutralizing response for this region, newly discovered features of MPER may be useful future targets for antibody-based vaccines.[96]

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[91] *Id.* at 248.
[92] Montefiori et al., *supra* note 85, at 1867.
[93] HIV-1 Virion, http://www.web-books.com/eLibrary/Medicine/Infectious/Images/HIV.jpg (last visited Mar. 10, 2009).
[94] Montefiori et al., *supra* note 85, at 1867.
[95] New Target For Antibody-based Vaccine Identified (Jan. 10, 2008), http://huehueteotl.wordpress.com/2008/ 01/12/new-target-for-hiv-antibody-based-vaccine-identified.
[96] *Id.*

3.B.3. Therapeutic Use of Antibodies[97]

After years of focusing on adenoviral therapies, the concept of developing a passive immune therapy to combat HIV has been bolstered by animal studies using the macaque model showing that neutralizing antibodies could prevent infection with the chimeric simian-human immunodeficiency virus (SHIV). These animal studies strongly support the idea that neutralizing antibodies may be able to prevent HIV-1 infection in humans when present in sufficient amounts before or shortly after exposure to the virus. However, although animal studies have indicated promise in preventative therapies using neutralizing antibodies, conclusive evidence of a therapeutic use that may be effective in established infections is still lacking.

3.C. Antibodies and Peptide Libraries

To be effective in a vaccine, any peptide component must be immunologically fit; when used as immunogens, the peptides must elicit antibodies that cross-react with the native intact pathogen. For the identification of and measuring effectiveness of peptides for use as immunogens, peptide libraries are a promising tool for subunit vaccine design.[98] From the HIV research perspective, the overall goal of screening peptide libraries is to identify antigenic peptides that bind HIV-1-specific antibodies from a large pool of random peptides. The peptides identified could then be used to elicit antibodies with properties similar to the original antibody used to screen for the random peptides.[99]

A peptide library is a large collection of different peptides consisting of a systematic collection of amino acids and can be synthesized on a solid phase, mostly on resin, which can be a flat surface or beads.[100] There are different types of peptide libraries such as random peptide libraries (RPL) and natural peptide libraries (NPL). Random peptide libraries are those which have phage-displayed peptides encoded by synthetic random degenerate oligonucleotide inserts. Alternatively, natural peptide libraries have phage particle display fragments of natural pathogen proteins encoded by short DNA fragments of the pathogen genome.[101] Peptide libraries have a number of applications such as describing variations of antibody specificity, identifying bioactive peptides, generating synthetic vaccines, and purifying proteins.[102]

For HIV research using random peptide libraries, antibodies with desired properties are prepared from either HIV-1 infected patients or from monoclonal

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[97] Gabriela Stiegler & Hermann Katinger, *Therapeutic Potential of Neutralizing Antibodies in the Treatment of HIV-1 Infection*, 51 J. ANTIMICROBIAL CHEMOTHERAPY 757, 757 (2003).
[98] Leslie J. Matthews et al., *Immunologically Fit Subunit Vaccine Components Via Epitope Discovery From Natural Peptide Libraries*, 169 J. IMMUNOLOGY 837, 837 (2002).
[99] Cho, *supra* note 5, at 256.
[100] Peptide Library, http://en.wikipedia.org/wiki/Peptide_library (last visited Feb. 10, 2009).
[101] Matthews et al, *supra* note 98, at 837.
[102] Princeton BioMolecules, http://www.pbcpeptide.com/Peptide%20Library.htm (last visited Feb. 15, 2009).

antibodies.[103] See Figure 10. The prepared antibodies are then used to select peptides from a phage-displayed random peptide library and the select peptides are used for immunization.[104]

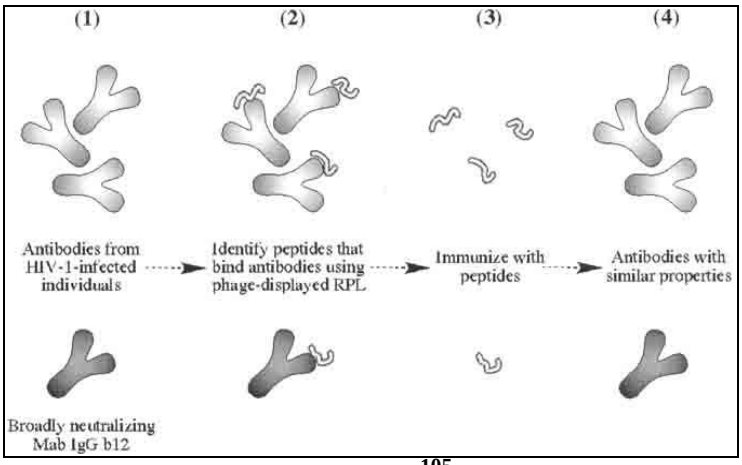

Figure 10[105]

4. Tat-based Vaccines

4.A. HIV Genome

The Genome of HIV is a single-stranded positive sense RNA molecule about 9.5 kb in length. The HIV genome has 9 genes: gag, pol, env, tat, rev, nef, vif, vpr, and vpu. See Figure 1. Among these genes, gag (encoding core proteins), pol (encoding protease, reverse transcriptase, and integrase), and env (encoding envelope protein gp160, which eventually cleaved into an external gp120 subunit and a transmembrane gp41 subunit) are structural genes. The other 6 genes are non-structural genes. Tat and rev are regulatory genes involved in controlling the expression of one or more other genes. Nef, vif, vpr, and vpu are accessory genes. [106]

[103] Cho, *supra* note 5, at 255.
[104] *Id.*
[105] *Id.*
[106] Marc P. Girard et al., *A Review of Vaccine Research and Development: The Human Immunodeficiency Virus (HIV)*, 24 VACCINE 4062, 4069 (2006).

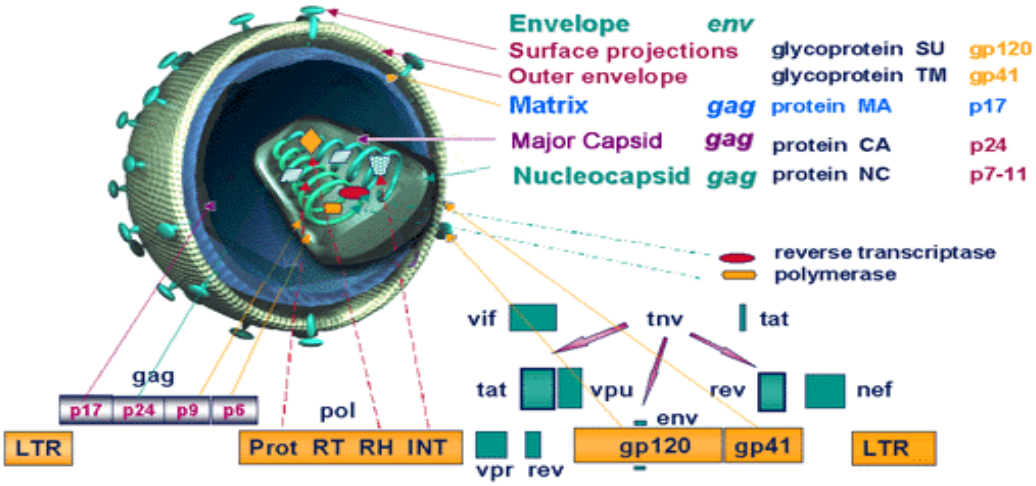

Figure 11[107]

4.B. Tat

"Tat" is short for "transactivator." Tat binds to the Transactivator Active Region (TAR), located at the 5'terminus of HIV RNA strands, and activates the transcription of the remainder of the HIV genome. Regulatory genes, including tat, are crucial to HIV replication in infected cells. In the absence of Tat, HIV is still able to infect the cell, but HIV completely fails to replicate itself. Tat is expressed very early after the HIV infection, even before the virus integrates with the host cell's genetic machinery. Tat is released by acutely HIV-infected T-cells and helps to recruit and activate uninfected cells. This mechanism helps to spread the HIV infection throughout the body.[108]

As shown in Figure 11, Tat protein is encoded by 2 exons located near the center of the viral genome. The wild-type Tat protein is composed of 101 amino acids. Residues 1-72 are encoded by the first exon and residues 73-101 are encoded by the second exon.[109] Tat protein can be subdivided into five distinct functional regions on the basis of its amino acid composition: a N-terminal activation region, a cysteine-rich domain, a core region, a basic region, and a Glutamine-rich region.[110] Exon 2 encodes a well-conserved RGD motif.[111] See Figure 12. The N-terminal region binds to the T-cell activation marker CD26 and T-cell receptor CCR2.[112] This region has also been considered to inhibit important regulators of the immune response and impair the T-cell function.[113] Cysteine-rich region is considered to be involved in metal ion binding.[114]

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[107] *ICTVdB - The Universal Virus Database*, http://www.ncbi.nlm.nih.gov/ICTVdb/ICTVdB/ (then follow "00.061.1.06.009. Human Immunodeficiency virus 1" hyperlink) (last visited Feb. 18, 2009).
[108] Ilia Tikhonov et al., *Tat-Neutralizing Antibodies in Vaccinated Macaques*, 77 J. VIROLOGY 3157, 3157 (2003); HIV-1 TAT Vaccines, http://www.hiv1tat-vaccines.info/index.php (last visited Feb. 18, 2009).
[109] Kuan-Teh Jeang et al., *Multificated Activities of the HIV-1 Transactivator of Transcription, Tat*, 274 THE J. BIOLOGICAL CHEMISTRY 28837, 28837 (1999).
[110] Ilia Tikhonov et al., *supra* note 108, at 3157.
[111] Michael J. Orsini et al., *Extracellular Human Immunodeficiency Virus Type 1 Tat Protein Promotes Aggregation and Adhesion of Cerebellar Neurons*, 16 J. NEUROSCIENCE 2546, 2546 (1996).
[112] Jeang et al., *supra* note 109, 28837.
[113] Bioafrica, http://www.bioafrica.net/proteomics/TATprot.html (last visited Feb. 18, 2009).

Due to the tendency of cystein molecules to bind to themselves to form strong disulphide bonds, this region is considered having great importance for the formation of active structural domains in the protein.[115] Cysteine-rich region has 7 highly conserved cysteines, and it is known that amino acid changes in 6 of the 7 cysteines abolish function of Tat.[116] Core region is highly conserved and is crucial for activation of HIV-transcription. Amino acid residues in this region are considered to form an alpha-helix structure which enhances Tat-TAR binding.[117] The most studied region of Tat is the Basic region, which contains a highly-conserved RKKRRQRRR motif. This peptide motif is essential for binding to the TAR of RNA.[118] The RGD motif in the C-terminal region is proposed to mediate interaction of Tat with cell surface proteins including integrins.[119]

Instead of the wild-type composed of 101 amino acids, an 86-amino acid form of Tat has been frequently used in laboratories. In a few laboratory virus strains of HIV (e.g. LAI, HXB2, pNL4-3), a single nucleotide change at putative residue 87 creates a premature termination codon, which results in a truncated protein. An 86-amino acid version is sufficient for virus replication in vitro. Although residues of 87-101 of Tat might not contribute greatly to the ex vivo replication of HIV, their conservation in the wild-type strains may indicate their biological importance.[120]

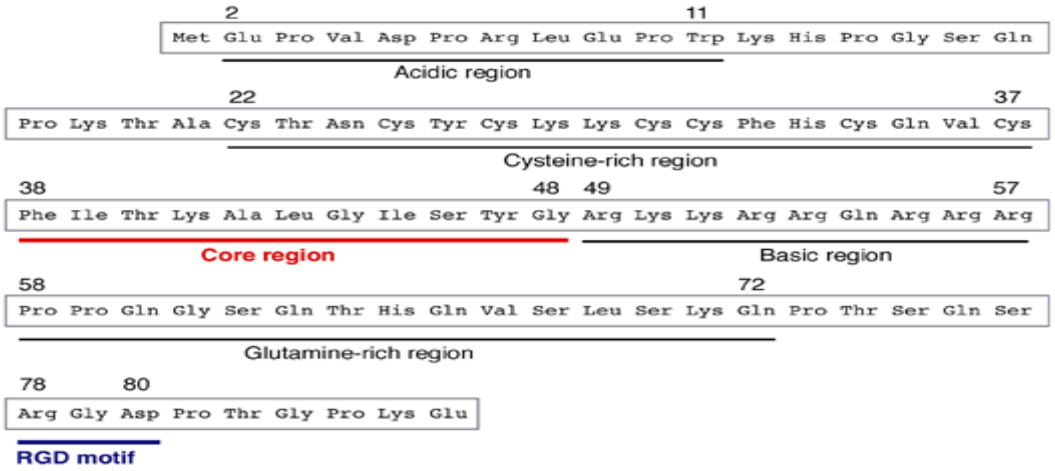

Figure 12[121]

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[114] Jonathan Karn, *Tat, a Novel Regulator of HIV Transcription and Latency*, *available at* http://www.hiv.lanl.gov/content/sequence/HIV/COMPENDIUM/2000/partI/Karn.pdf.
[115] Koken SE et al., *Intracellular Analysis of In Virto Modified HIV Tat Protein*, 269 J. BIOLOGICAL CHEMISTRY 8366, 8373 (1994).
[116] Jeang et al., *supra* note 109, at 28837.
[117] Bioafrica, *supra* note 113.
[118] Kuan-Teh Jeang et al., *supra* note 109, at 28837.
[119] Orsini et al., *supra* note 111, at 2550.
[120] Jeang et al., *supra* note 109, at 28837; Tikhonov et al., *supra* note 108, at 3157.
[121] Kimberly E. Foreman, *The Amino Acid Sequence of Human Immunodeficiency Virus 1 (HIV-1) Tat Protein, available at* http://www-ermm.cbcu.cam.ac.uk/01002769h.htm (last visited Feb. 18, 2009).

4.C. Development of Tat-based Vaccines

Over the past 20 years, Env protein has been used for HIV vaccine development, in an attempt to induce anti-Env antibodies that are capable of neutralizing the HIV infection. However, Env is difficult to neutralize because envelope proteins mutate rapidly and have the extreme cross-clade variability. The HIV infections elicit antibodies to neutralize Env, but these responses tend to be against only to the sequences unique to the Env that triggered the antibody response.[122] This is similar to what happens with influenza each year, but HIV mutates much faster than influenza virus. One study shows that for broadly neutralizing flu monoclonals, 50% neutralization can be achieved with 10-100ng of antibody, while for broadly neutralizing HIV-1 monoclonals, even 50ug of antibody frequently fails to achieve 50% neutralization of the original isolates.[123]

Several features of Tat make it a good candidate for HIV vaccines. First, unlike the structural HIV-1 proteins such as Gag, Pol, and Env, which are expressed later in the viral life cycle, Tat is more frequently found in the early stage of the disease than during the symptomatic stages.[124] Thus, the presence of anti-Tat antibodies seems to protect infected individuals from progressing to AIDS.[125]

Second, anti-Tat cytotoxic (CD8+) T lymphocytes (CTLs) are frequently found in individuals who are infected naturally by HIV. Despite the small size of protein, multiple CTL epitopes have been identified in Tat, and it is considered that Tat is an important target for the T-cell immune response.[126]

Third, the immunogenic regions of Tat are more conserved among the different HIV-1 clades than the Env protein. The parts of the protein that are recognized by the immune system (i.e. epitopes) do not change much over the course of infection. In a study using serum samples from HIV-infected Italian, Ugandan, and South African subjects, it was indicated that the immunogenic and functional domains of Tat were well conserved among distinct HIV-1 subtypes and had a high degree of similarity with the corresponding sequence of Tat from a laboratory isolate.[127] Thus, it is suggested that a Tat vaccine may be useful in different geographic areas of the world.[128]

Fourth, biologically active Tat has immunomodulatory features that make it an attractive adjuvant. An adjuvant is a substance included in a vaccine formulation to

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[122] HIV-1 TAT Vaccines, *supra* note 108.
[123] Harriet L. Robinson, *HIV/AIDS Vaccines*, 82 CLINICAL PHARMACOLOGY & THERAPEUTICS 686, 687 (2007).
[124] Stefano Butto et al., *Sequence Conservation and Antibody Cross-Recognition of Clade B Human Immunodeficiency Virus (HIV) Type 1 Tat Protein in HIV-1-Infected Italians, Ugandans, and South Africans*, 188 J. INFECTIOUS DISEASES 1171, 1171 (2003).
[125] HIV-1 TAT Vaccines, *supra* note 108.
[126] Marylyn M. Addo et al., *The HIV-1 Regulatory Proteins Tat and Rev are Frequently Targeted by Cytotoxic T lymphocytes Derived from HIV-1-Infected Individuals*, 98 PROC. OF THE NAT'L ACAD. OF SCI. U.S. 1781, 1781 (2001).
[127] Butto et al., *supra* note 124, at 1171.
[128] HIV-1 TAT Vaccines, *supra* note 108.

enhance or modify the immune-stimulating properties of a vaccine.[129] In one study using mice, Tat enhanced in vivo epitope-specific T cell responses directed to the HIV-1 Gag and Env. In that study, mice immunized with Gag alone respond to 6 different Gag-derived T cell epitopes, whereas mice immunized with Gag and Tat responded to 11 different T cell epitopes. Similarly, mice vaccinated with Env in combination with Tat responded to 17 peptides, 12 more than mice vaccinated with Env alone.[130] Thus, Tat is not only an antigen, but also a novel and potent adjuvant capable of broadening the spectrum of epitopes recognized by T cells.[131]

Lastly, Tat can be used both as preventive and therapeutic vaccine. Since Tat is necessary for the HIV replication, it may block the initial cycles of virus replication and prevent HIV spread in the organism. It can also be used as a therapeutic one because reduction of viral replication can slow or block disease progression in HIV-infected individuals.[132]

Tat-based vaccines have been tested in pre-clinical studies by using different animal models, including mice, rabbits, and macaques. Immunization with Tat protected macaques against SHIV infection or resulted in attenuated virus replication in the animals.[133] SHIV is a SIV/HIV hybrid virus that is genetically engineered to carry an HIV env envelope and SIV core.[134] A study conducted in SHIV-infected macaques indicated that vaccination with a biologically active Tat protein or tat DNA is safe. Preclinical studies in monkeys also indicate that the Tat/Env combination is safe and enhances the immune-response to the single components.[135]

The Italian National Institute of Health (ISS) has been sponsored Phase I clinical trials in Italy. A Phase I clinical trial of a subunit Tat vaccine was carried out in Italy on HIV seropositive and HIV negative volunteers. The trial showed that the vaccine was well-tolerated and immunogenic.[136] Phase II trials are being prepared in Italy, Uganda, and South Africa. Phase I studies of Tat/Env vaccines are also being prepared by the Italian scientists.[137]

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[129] HIV-1 TAT Vaccines, http://www.hiv1tat-vaccines.info/science_dictionary.htm (then follow "adjuvant") (last visited Feb. 18, 2009).
[130] Riccardo Gavioli et al., *The Tat Protein Broadens T cell Responses Directed to the HIV-1 Antigens Gag and Env: Implications for the Design of New Vaccination Strategies Against AIDS*, 26 VACCINE 727, 727 (2008).
[131] HIV-1 TAT Vaccines, *supra* note 108.
[132] *Id*.
[133] Girard et al., *supra* note 106, at 4068.
[134] HIV-1 TAT Vaccines, supra note 129 (then follow "SHIV") (last visited Feb. 18, 2009)
[135] HIV-1 TAT Vaccines, *supra* note 108.
[136] Girard et al., *supra* note 106, at 4068.
[137] HIV-1 TAT Vaccines, *supra* note 108.

II. Patent Search Methodology and Results

1. Patent Search Methodology

The International Technology Transfer Institute began on January 12, 2009 with a conference call between the clinic members, Professor Jon Cavicchi, Dr. Stanley Kowalski and Dr. Kerri Clark (the clinic contact person at PIPRA). The scope of the project was defined as conducting a patent landscape analysis of technologies pertaining to protein/peptide vaccines applicable to HIV. The team began by reviewing past and recent literature relating to HIV vaccines and, in particular, to developing protein/peptides vaccines.

The seven-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 and present on different aspects of peptide/protein vaccines. The topics were separated into four main categories, each category assigned to a different team member/group. The four categories were:

1) Subunit (envelope)
2) Peptide
   a) Formulae
   b) Epitopes
   c) Conjugates
   d) Screening
3) Antibodies (screening tool)
   a) Antibodies to HIV- Screen peptide library
   b) Antibodies to HIV- as vaccine
4) TAT-based vaccines

Recent literature and articles were utilized to determine keywords, especially keywords specific to each topic. These keywords were then used to do preliminary searches on Delphion and/or the USPTO. Group presentations on the above categories gave team members initial exposure to the research topic and insight into necessary terminology.

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

In addition to a general protein/peptide vaccine search, each group was assigned to search for patents relating to the aspect of antibodies, peptide screening methods and TAT-based vaccines. The search methodology was devised to initially generate a broad set of patents and then to narrow down the results using the "Iterative Search Approach," as promoted by Professor Cavicchi.

These searches utilized keywords derived from the literature reviewed and initial searches to generate useful search strings; the searches also used United States Patent Classifications, International Patent Classifications and Derwent Classifications that were identified through subsequent searches and team meetings. The combination of keywords, inventor/assignee names 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, inventor names, assignee names, and classifications for use in subsequent search strings that became more defined and effective.

The initial keywords used in the four main categories in the subsequent search round were:

- First category (assigned to search for subunit (envelope) proteins):
    - Protein, vaccine, HIV, human immunodeficiency virus, subunit, sequence, formula, inoculation, immunogen, immunogenic composition, immunological composition, envelope, retrovirus, lentivirus.
- Second category (assigned to search for patents relating peptide and sub-category formulae, epitope, conjugate and screening method):
    - Protein, peptide, polypeptide, sequence, formula, HIV, vaccine, immune response, epitope*, HIV, human immunodeficiency virus, vaccine, amino acids, vaccines, human immunodeficiency virus, conjugates, screening.
- Third category (assigned to search for patents relating to antibodies (screening tool)):
    - HIV, human immunodeficiency virus, vaccine, neutralizing antibody, nabs, epitope, screening, peptide, amino acids, cytotoxic, humoral.
- Fourth category (assigned to search for patents relating to TAT-based vaccines):
    - HIV, human immunodeficiency virus, vaccine*, tat, protein, peptide, regulat*, antibody immune* respon*, regulatory, regulator, regulation, env, amino acid, ctl, cytotoxic.

Most of these keywords were searched using the search field of "Title, Abstract Claims" within Delphion since searches under the field of "Description" or "Specification" were found to be too broad. It was useful to limit each search using the most important keywords under the search field of "Claims." The keywords above were then combined with U.S. classifications and subclasses, International patent classifications and subclasses and Derwent classes to generate different sets of search results. Some of the most common classifications used were US Classifications 424/184.1, 435/005, 424/185.1, 424/208.1 and 424/188.1, IPC Codes A61K 39/21, G01N 33/69 and C07K 7/08 and Derwent classes B04 and D16. The top assignees and inventors varied widely with each category.

The search strings gave the team an outcome of more than 2144 patents, which was then de-duplicated using the family option in MicroPatent® into 1200 patents (de-duplication refers to the removal of patents within the same family so as to reduce redundancy in patent coding) and finally manually reduced to 954 patents. The search results were then assembled together and extracted into PDF files for coding and into Excel spreadsheets for data analysis. The subsequent data analyzed were placed into a Master Sheet. The 954 patent documents were divided among the seven team members for coding. Each team member analyzed the claims in the documents and coded under one of the following seven categories.

1. Prime Boost
2. Protein
3. Peptide
4. Peptide Formulas
5. Epitopes
6. Conjugates
7. Peptide Screening
8. Antibodies to HIV
9. Antibodies Screening Library
10. Tat-based Vaccine
11. Therapeutic v. Prophylactic

Each patent was initially coded by individual team members and emphasis was placed on claim language in order to determine whether the patent was relevant to peptide/protein vaccine for HIV. When coding, team members also took consideration of the patent's title, abstract, and additional information (including the assignee, inventor and IPC/US classification codes). Each relevant patent (relevancy determined by the initial team member coding that patent) was then reviewed by the entire team and Dr. Kowalski and each patent was re-coded according to their relevancy. Of the 954 patents, 350 patents were found to be relevant. The coding results were inserted into a Master Sheet demonstrating which categories were relevant to each individual patent.

2. Patent Search Tables

Search Round #1

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	Protein, vaccine, HIV, human immunodeficiency virus, subunit
Classification/ Sub-classification	Not applicable
Search Strings	(((protein) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vaccine) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((HIV or "human immunodeficiency virus") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((subunit) <in> (TITLE,ABSTRACT,CLAIMS)))
Results	Total Results= 230 Total Results Considered= 98

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	Sequence, formula, HIV, immunodeficiency, vaccine, inoculation, immunogen, protein, peptide, polypeptide
Classification/ Sub-classification	Not applicable
Search Strings	(((sequence or formula) <in> CLAIMS) AND ((HIV or immunodeficiency) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vaccine or innoculation or immunogen) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((protein or peptide or polypeptide) <in> (CLAIMS)))
Results	Total Results= 2,123

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	Peptide, polypeptide, sequence, formula, HIV, vaccine, immune response
Classification/ Sub-classification	Not applicable
Search Strings	(((peptide or polypeptide <near> sequence or formula) <in> CLAIMS) AND ((HIV) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vaccine or immune response) <in> CLAIMS))
Results	Total Results= 2,118

Database	Delphion

	(US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	Peptide vaccine, HIV, sequence
Classification/ Sub-classification	Not applicable
Search Strings	(("peptide vaccine") <in> CLAIMS) AND ((HIV) <in> CLAIMS) AND ((sequence) <in> CLAIMS)
Results	Total Results= 6 Total Results Considered= 6

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	Epitope?, HIV, human immunodefi* virus?, protein, peptide, vaccine?
Classification/ Sub-classification	Not applicable
Search Strings	((epitope?) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((HIV or "human immunodefi* virus?") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((protein or peptide) <in> (TITLE,ABSTRACT,CLAIMS)) AND (vaccine?)
Results	Not applicable

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	Epitope, epitopes, HIV, human immunodefi* virus?, protein, peptide, vaccine?
Classification/ Sub-classification	Not applicable
Search Strings	((epitope or epitopes) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((HIV or human immunodefi* virus?) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((protein or peptide) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vaccine?) <in> (TITLE,ABSTRACT,CLAIMS))
Results	Total Results Considered= 59

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	Peptide, amino acids, vaccines, HIV, human immunodeficiency virus, conjugates
Classification/	Not applicable

Sub-classification	
Search Strings	((Peptide or "Amino Acids") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((Vaccines) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((HIV or "Human Immunodeficiency Virus") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((conjugates) <in> (TITLE,ABSTRACT,CLAIMS))
Results	Total Results Considered= 219

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	Peptide, amino acid, vaccines, HIV, human immunodeficiency virus, humoral
Classification/ Sub-classification	Not applicable
Search Strings	((peptide or "amino acid") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vaccines) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((HIV or "Human Immunodeficiency Virus") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((humoral) <in> (TITLE,ABSTRACT,CLAIMS))
Results	Total Results Considered= 93

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, peptide, amino acids, vaccine, cytotoxic
Classification/ Sub-classification	Not applicable
Search Strings	((HIV or "Human immunodeficiency virus") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((peptide or "amino acids") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vaccine) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((cytotoxic) <in> (TITLE,ABSTRACT,CLAIMS))
Results	Total Results Considered= 205

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	Peptide, proteins, HIV, human immunodeficiency virus, screening
Classification/ Sub-classification	Not applicable
Search Strings	(((peptide OR proteins) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((HIV OR "Human immunodeficiency virus") <in>

	(TITLE,ABSTRACT,CLAIMS)) AND ((screening) <in> (TITLE,ABSTRACT,CLAIMS))
Results	Total Results= 789

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	Protein, peptide, HIV, human immunodeficiency virus, screening, vaccine
Classification/ Sub-classification	Not applicable
Search Strings	(((Protein OR Peptide) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((HIV OR "Human immunodeficiency virus") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((Screening) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vaccine) <in> DESCRIPTION))
Results	Total Results= 311 Total Results Considered= 58

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, vaccine, antibody, epitope
Classification/ Sub-classification	Not applicable
Search Strings	((hiv or human immunodeficiency virus) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vaccine) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((antibody) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((epitope) <in> (TITLE,ABSTRACT,CLAIMS))
Results	Total Results= 597

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, vaccine, neutralizing antibody, epitope
Classification/ Sub-classification	Not applicable
Search Strings	((hiv or human immunodeficiency virus) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vaccine) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((neutralizing antibody) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((epitope) <in>

	(TITLE,ABSTRACT,CLAIMS))
Results	Total Results= 131 Total Results Considered= 110

Database	United States Patent and Trademark Office
Keywords	HIV, epitope, peptide
Classification/ Sub-classification	Not applicable
Search Strings	TTL/(hiv) and ABST/(epitope and peptide)
Results	Total Results= 16 patents & 14 applications

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, vaccine, peptide
Classification/ Sub-classification	Not applicable
Search Strings	(HIV and vaccine) <in> TI and peptide <in> AB
Results	Total Results= 83

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, tat, env, vaccine*
Classification/ Sub-classification	Not applicable
Search Strings	((hiv or "human immunodeficiency virus") <in> TI) AND ((tat or env) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vaccin*) <in> (TITLE,ABSTRACT,CLAIMS))
Results	Total Results= 369

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, AIDS, tat, regulatory, regulator
Classification/ Sub-classification	Not applicable
Search Strings	((HIV or AIDS) <in> TI) AND ((tat) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((regulatory or regulator) <in> (TITLE,ABSTRACT,CLAIMS))
Results	Total Results= 59

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, vaccin*, tat, protein, peptide, regulatory, regulator, regulation
Classification/ Sub-classification	Not applicable
Search Strings	((hiv or "human immunodeficiency virus") <in> TI) AND ((vaccin*) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((tat <near/10> protein or peptide) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((regulatory or regulator or regulation) <in> (TITLE,ABSTRACT,CLAIMS))
Results	Total Results= 54

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, vaccine*, immune*, tat, protein, peptide, regulatory, regulator, regulation
Classification/ Sub-classification	Not applicable
Search Strings	((((hiv or "human immunodeficiency virus") <in> TI) AND ((vaccin* and immun*) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((tat <near/10> protein or peptide) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((regulatory or regulator or regulation) <in> (TITLE,ABSTRACT,CLAIMS))))
Results	Total Results= 43

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, vaccine*, immune* respon*, tat, protein, peptide, regulatory, regulator, regulation
Classification/ Sub-classification	Not application
Search Strings	((((hiv or "human immunodeficiency virus") <in> TI) AND ((vaccin* and immun* <near> respon*) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((tat <near/10> protein or peptide) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((regulatory or regulator or regulation) <in> (TITLE,ABSTRACT,CLAIMS))))
Results	Total Results Considered= 24

Database	Delphion

	(US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, vaccine*, tat, protein, peptide, regulat*, antibody
Classification/ Sub-classification	Not applicable
Search Strings	(((hiv or "human immunodeficiency virus") <in> TI) AND ((vaccin*) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((tat <near/10> protein or peptide) <in> (CLAIMS)) AND ((regulat*) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((antibody) <in> (TITLE,ABSTRACT,CLAIMS)))
Results	Total Results Considered= 26

Search Round #2

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, protein, peptide, envelope, vaccine, immunogenic composition, immunological composition
Classification/ Sub-classification	Not applicable
Search Strings	(((HIV or "human immunodeficiency virus") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((protein or peptide) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((envelope) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vaccine or "immunologic composition" or "immunological composition") <in> (TITLE,ABSTRACT,CLAIMS)))
Results	Total Results= 643

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, protein, peptide, envelope, vaccine, immunogenic composition, immunological composition, nabs, neutralizing antibodies
Classification/ Sub-classification	Not applicable
Search Strings	((((HIV or "human immunodeficiency virus") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((protein or peptide) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((envelope) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vaccine or "immunologic composition" or "immunological composition") <in> (TITLE,ABSTRACT,CLAIMS))) AND ((nabs or "neutralizing antibodies") <in> (TITLE,ABSTRACT,CLAIMS)))
Results	Total Results= 53

	Total Results Considered= 53

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, protein, peptide, envelope, vaccine, immunogenic composition, immunological composition, lentivirus, retrovirus
Classification/ Sub-classification	Not applicable
Search Strings	((((HIV or "human immunodeficiency virus") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((protein or peptide) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((envelope) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vaccine or "immunologic composition" or "immunological composition") <in> (TITLE,ABSTRACT,CLAIMS))) AND ((lentivirus or retrovirus) <in> (TITLE,ABSTRACT,CLAIMS)))
Results	Total Results= 136 Total Results Considered= 104

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	Peptide, vaccine, HIV, epitope
Classification/ Sub-classification	Not applicable
Search Strings	(((peptide <near> vaccine) <in> CLAIMS) AND ((HIV) <in> CLAIMS) AND ((epitope) <in> CLAIMS))
Results	Total Results Considered= 362

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	Peptide, formula, vaccine, elicit immune response, HIV
Classification/ Sub-classification	Not applicable
Search Strings	(((peptide <near> formula) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vaccine or elicit <near> immune response) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((hiv) <in> (TITLE,ABSTRACT,CLAIMS)))
Results	Total Results Considered= 216

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	Epitope, vaccine, protein, peptide, HIV, human immunodeficiency virus
Classification/ Sub-classification	Not applicable
Search Strings	((epitope) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vaccine) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((protein or peptide) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((HIV or Human Immunodeficiency Virus) <in> (TITLE,ABSTRACT,CLAIMS))
Results	Total Results= 955

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	Epitope, HIV, human immunodeficiency virus, subunit, protein, peptide, vaccine
Classification/ Sub-classification	Not applicable
Search Strings	((epitope) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((HIV or "Human Immunodeficiency virus") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((subunit or protein or peptide) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vaccine) <in> (TITLE,ABSTRACT,CLAIMS))
Results	Total Results= 975

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	Epitope, HIV, human immunodeficiency virus, subunit, protein, peptide, vaccine
Classification/ Sub-classification	Not applicable
Search Strings	(((epitope) <in> (CLAIMS)) AND ((HIV or "Human Immunodeficiency virus") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((subunit or protein or peptide) <in> (CLAIMS)) AND ((vaccine) <in> (TITLE,CLAIMS)))
Results	Total Results= 669

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	Epitope, HIV, human immunodeficiency virus, subunit, protein, peptide, vaccine, A61K

Classification/ Sub-classification	A61K
Search Strings	(((epitope) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((HIV or "Human Immunodeficiency virus") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((subunit or protein or peptide) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vaccine) <in> (TITLE,ABSTRACT,CLAIMS))) AND ((A61K) <in> IC)
Results	Total Results= 890 Total Results Considered= 890

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	Peptide, amino acid, vaccines, HIV, human immunodeficiency virus, MHC-I, MHC-II
Classification/ Sub-classification	Not applicable
Search Strings	((peptide or "amino acid") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vaccines) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((HIV or "Human Immunodeficiency Virus") <in> (TITLE,ABSTRACT,CLAIMS)) AND (("MHC I" or "MHC II") <in> (TITLE,ABSTRACT,CLAIMS))
Results	Total Results= 28 Total Results Considered= 28

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, peptide, amino acids, conjugate, Merck
Classification/ Sub-classification	Not applicable
Search Strings	(("Human immunodeficiency virus" or HIV) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((peptide or "amino acids") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((conjugate) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((merck) <in> PA)
Results	Total Results= 29 Total Results Considered= 29

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	Protein, peptide, HIV, human immunodeficiency virus, screen*, random peptide library, RPL, natural peptide library, NPL, random antigenic peptide, NAP
Classification/	Not applicable

Sub-classification	
Search Strings	(((protien OR peptide) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((HIV OR "Human immunodeficiency virus") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((Screen*) <in> (TITLE,ABSTRACT,CLAIMS)) AND (("Random Peptide Library" OR RPL OR "natural peptide library" OR NPL OR "random antigenic peptide" OR NAP) <in> DESCRIPTION))
Results	Total Results= 45 Total Results Considered= 45

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, vacci*, epitope, antige*, peptide, peptide library
Classification/ Sub-classification	Not applicable
Search Strings	(((HIV or human immunodeficiency virus) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vacci*) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((epitope or antige* or peptide) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((peptide library) <in> (TITLE,ABSTRACT,CLAIMS)))
Results	Total Results= 13 Total Results Considered= 13

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, vacci*, epitope, antige*, peptide, peptide library*, screen*
Classification/ Sub-classification	Not applicable
Search Strings	(((HIV or human immunodeficiency virus) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vacci*) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((epitope or antige* or peptide) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((peptide librar* or screen*) <in> (TITLE,ABSTRACT,CLAIMS)))
Results	Total Results= 25 Total Results Considered= 22

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, vacci*, peptide, protein, envelope protein, neutraliz* antibod*
Classification/	Not applicable

Sub-classification	
Search Strings	(((HIV or human immunodeficiency virus) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vacci*) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((peptide or protein) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((envelope protein or neutraliz* antibod*) <in> (TITLE,ABSTRACT,CLAIMS)))
Results	Total Results= 528

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, vacci*, peptide, protein, envelope protein
Classification/ Sub-classification	Not applicable
Search Strings	(((HIV or human immunodeficiency virus) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vacci*) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((peptide or protein) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((envelope protein) <in> (TITLE,ABSTRACT,CLAIMS)))
Results	Total Results= 85 Total Results Considered= 71

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, vacci*, peptide, protein, envelope protein, neutraliz* antibody*
Classification/ Sub-classification	Not applicable
Search Strings	(((HIV or human immunodeficiency virus) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vacci*) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((peptide or protein) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((envelope protein and neutraliz* antibod*) <in> (TITLE,ABSTRACT,CLAIMS)))
Results	Total Results= 38 Total Results Considered= 30

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, peptide, protein, amino acid, vaccine, immune*
Classification/ Sub-classification	Not applicable
Search Strings	((hiv or "human immunodeficiency virus") <in> TI) AND ((peptide

	or protein or "amino acid") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vaccine or immun*) <in> (TITLE,ABSTRACT,CLAIMS))
Results	Total Results= 2283

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, peptide, protein, amino acid, vaccine, immune*
Classification/ Sub-classification	Not applicable
Search Strings	(((hiv or "human immunodeficiency virus") <in> TI) AND ((peptide or protein or "amino acid") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vaccine or immun*) <in> (CLAIMS)))
Results	Total Results= 1526

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, peptide, protein, amino acid, vaccine, immune*, CTL, cytotoxic activity, cytotoxic response
Classification/ Sub-classification	Not applicable
Search Strings	(((hiv or "human immunodeficiency virus") <in> TI) AND ((peptide or protein or "amino acid") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vaccine or immun*) <in> AB) AND (((CTL or cytotoxic) <near/5> (activity or response)) <in> AB))
Results	Total Results= 48 Total Results Considered= 48

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, Assignee codes (828528, 833513, 793660 and 178210)
Classification/ Sub-classification	Not applicable
Search Strings	hiv or "human immunodeficiency virus") <in> TI) AND ((828528 <OR> 833513) <in> assigneecode) OR ((793660 <OR> 178210) <in> assigneecode)
Results	Total Results= 36

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO

	Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, Assignee codes (828528, 833513, 793660 and 178210), vaccine*
Classification/ Sub-classification	Not applicable
Search Strings	((hiv or "human immunodeficiency virus") <in> TI) AND ((828528 <OR> 833513) <in> assigneecode) OR ((793660 <OR> 178210) <in> assigneecode) AND ((vaccin*) <in> (TITLE,ABSTRACT,CLAIMS))
Results	Total Results= 8 Total Results Considered= 8

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus
Classification/ Sub-classification	435/005, 424/188.1, 424/208.1, 530/326, 530/325, 424/185.1, 530/350
Search Strings	((hiv or "human immunodeficiency virus") <in> TI) AND ((435/005 or 424/188.1 or 424/208.1 or 530/326 or 530/325 or 424/185.1 or 530/350) <in> NC)
Results	Total Results= 633

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, vaccine*, immune*
Classification/ Sub-classification	435/005, 424/188.1, 424/208.1, 530/326, 530/325, 424/185.1, 530/350
Search Strings	((hiv or "human immunodeficiency virus") <in> TI) AND ((435/005 or 424/188.1 or 424/208.1 or 530/326 or 530/325 or 424/185.1 or 530/350) <in> NC) AND ((vaccin* or immun*) <in> (TITLE,ABSTRACT,CLAIMS))
Results	Total Results= 515

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, vaccine*, immune*, peptide, protein, amino acid, polypeptide, sequence
Classification/ Sub-classification	435/005, 424/188.1, 424/208.1, 530/326, 530/325, 424/185.1, 530/350
Search Strings	((hiv or "human immunodeficiency virus") <in> TI) AND ((435/005 or 424/188.1 or 424/208.1 or 530/326 or 530/325 or 424/185.1 or 530/350) <in> NC) AND ((vaccin* or immun*) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((peptide or protein or

	"amino acid" or polypeptide or sequence) <in> CLAIMS)
Results	Total Results= 469

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, vaccin*, immune*, peptide, protein, amino acid, polypeptide, sequence, env, gag, pol, tat, nef, rev, vif, vpr, vpu, vpx
Classification/ Sub-classification	435/005, 424/188.1, 424/208.1, 530/326, 530/325, 424/185.1, 530/350
Search Strings	(((((hiv or "human immunodeficiency virus") <in> TI) AND ((435/005 or 424/188.1 or 424/208.1 or 530/326 or 530/325 or 424/185.1 or 530/350) <in> NC) AND ((vaccin* or immun*) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((peptide or protein or "amino acid" or polypeptide or sequence) <in> CLAIMS)) AND ((env or gag or pol or tat or nef or rev or vif or vpr or vpu or vpx) <in> CLAIMS)))
Results	Total Results= 198

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, vaccin*, immune*, peptide, protein, amino acid, polypeptide, sequence, env, gag, pol, tat, nef, rev, vif, vpr, vpu, vpx
Classification/ Sub-classification	435/005, 424/188.1, 424/208.1, 530/326, 530/325, 424/185.1, 530/350
Search Strings	(((((hiv or "human immunodeficiency virus") <in> TI) AND ((435/005 or 424/188.1 or 424/208.1 or 530/326 or 530/325 or 424/185.1 or 530/350) <in> NC) AND ((vaccin* or immun*) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((peptide or protein or "amino acid" or polypeptide or sequence) <in> CLAIMS)) AND ((env or gag or pol or tat or nef or rev or vif or vpr or vpu or vpx) <in> CLAIMS) AND (therap* or treat*) <in> (TITLE,ABSTRACT,CLAIMS)))
Results	Total Results= 73 Total Results Considered= 73

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, vaccin*
Classification/ Sub-classification	A61K*, C07K*, C12Q*, G01N*, C12N*, C07H*
Search Strings	(((hiv or "human immunodeficiency virus") <in> TI) AND

	((A61K* or C07K* or C12Q* or G01N* or C12N* or C07H*) <in> (ICINV,MC)) AND ((vaccin*) <in> (TITLE,ABSTRACT,CLAIMS)))
Results	Total Results= 1373

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, vaccin*, peptide, protein, amino acid, polypeptide
Classification/ Sub-classification	A61K*, C07K*, C12Q*, G01N*, C12N*, C07H*
Search Strings	((((hiv or "human immunodeficiency virus") <in> TI) AND ((A61K* or C07K* or C12Q* or G01N* or C12N* or C07H*) <in> (ICINV,MC)) AND ((vaccin*) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((peptide or protein or "amino acid" or polypeptide) <in> (TITLE,ABSTRACT,CLAIMS))))
Results	Total Results= 926

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, vaccin*, peptide, protein, amino acid, polypeptide
Classification/ Sub-classification	A61K*, C07K*, C12Q*, G01N*, C12N*, C07H*, 435/005, 424/188.1, 424/208.1, 530/326, 530/325
Search Strings	(((((hiv or "human immunodeficiency virus") <in> TI) AND ((A61K* or C07K* or C12Q* or G01N* or C12N* or C07H*) <in> (ICINV,MC)) AND ((vaccin*) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((PEPTIDE OR PROTEIN OR "AMINO ACID" OR POLYPEPTIDE) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((435/005 or 424/188.1 or 424/208.1 or 530/326 or 530/325) <in> NC))))
Results	Total Results= 151

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, vaccin*, peptide, protein, amino acid, polypeptide
Classification/ Sub-classification	A61K*, C07K*, C12Q*, G01N*, C12N*, C07H*, 435/005, 424/188.1, 424/208.1, 530/326, 530/325
Search Strings	((((((hiv or "human immunodeficiency virus") <in> TI) AND ((A61K* or C07K* or C12Q* or G01N* or C12N* or C07H*) <in> (ICINV,MC)) AND ((vaccin*) <in> (CLAIMS)) AND ((PEPTIDE

	OR PROTEIN OR "AMINO ACID" OR POLYPEPTIDE) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((435/005 or 424/188.1 or 424/208.1 or 530/326 or 530/325) <in> NC)))))
Results	Total Results= 66 Total Results Considered= 66

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, vaccin*, peptide, protein, polypeptide
Classification/ Sub-classification	B04, D16, B14-A02B1, B14-S11A
Search Strings	(((hiv or "human immunodeficiency virus") <in> TITLETERMS) and ((B04 or D16) <in> DERWENTCLASS) and ((B14-A02B1 or B14-S11A) <in> MANUALCODES) and ((vaccin* and (protein or peptide or polypeptide)) <in> TITLETERMS))
Results	Total Results= 121

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, vaccin*, peptide, protein, polypeptide
Classification/ Sub-classification	B04, D16, B14-A02B1, B14-S11A
Search Strings	(((hiv or "human immunodeficiency virus") <in> TITLETERMS) and ((B04 or D16) <in> DERWENTCLASS) and ((B14-A02B1 or B14-S11A) <in> MANUALCODES) and ((vaccin* <near/3> (peptide or protein or polypeptide)) <in> TITLETERMS))
Results	Total Results= 42 Total Results Considered= 42

Search Round #3

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, protein, peptide, envelope, vaccine, immunologic composition, immunological composition
Classification/ Sub-classification	B04, D16
Search Strings	(((((HIV or "human immunodeficiency virus") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((protein or peptide) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((envelope) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vaccine or "immunologic composition" or "immunological composition") <in>

	(TITLE,ABSTRACT,CLAIMS)))) and ((B04 or D16) <in> DERWENTMAINCLASS))
Results	Total Results= 287

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, protein, peptide, envelope, vaccine, immunologic composition, immunological composition
Classification/ Sub-classification	B04, D16, A61K, C07K, G01N, C12N, C12Q, C07H, A91N, A61P
Search Strings	(((((((HIV or "human immunodeficiency virus") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((protein or peptide) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((envelope) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vaccine or "immunologic composition" or "immunological composition") <in> (TITLE,ABSTRACT,CLAIMS))))) and ((B04 or D16) <in> DERWENTMAINCLASS)))) and ((A61K or C07K or G01N or C12N or C12Q or C07H or A91N or A61P) <in> MAINCLASS)
Results	Total Results= 281 Total Results Considered= 226

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	Vaccine, peptide
Classification/ Sub-classification	424/188.1
Search Strings	((vaccine) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((4241881) <in> NC) AND ((peptide) <in> (TITLE,ABSTRACT,CLAIMS))
Results	Total Results Considered= 114

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, peptide, protein, vaccine
Classification/ Sub-classification	424/184.1
Search Strings	((4241841) <in> NC) AND ((HIV) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((peptide or protein) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vaccine) <in> (TITLE,ABSTRACT,CLAIMS))
Results	Total Results Considered= 102

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO

	Granted, EPO Applications, Abstracts of Japan)
Keywords	Vaccine, peptide, HIV, immunodeficiency
Classification/ Sub-classification	424/188.1
Search Strings	((4241881) <in> NC) AND ((vaccine <near> peptide) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((HIV or immunodeficiency) <in> (TITLE,ABSTRACT,CLAIMS))
Results	Total Results Considered= 71

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	Vaccine, peptide, polypeptide
Classification/ Sub-classification	424/208.1
Search Strings	((4242081) <in> NC) AND ((vaccine) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((peptide or polypeptide) <in> (TITLE,ABSTRACT,CLAIMS))
Results	Total Results Considered= 155

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	Epitope, HIV, human immunodeficiency virus, protein, peptide, vaccine, immunological composition or immunogenic composition
Classification/ Sub-classification	Not applicable
Search Strings	(((((epitope) <in> (CLAIMS)) AND ((HIV or "Human Immunodeficiency virus") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((protein or peptide) <in> (CLAIMS)) AND ((vaccine or immunological composition or immunogenic composition) <in> (CLAIMS)))))
Results	Total Results= 701

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	Epitope, HIV, human immunodeficiency virus, protein, peptide, vaccine, immunological composition, immunogenic composition
Classification/ Sub-classification	Not applicable
Search Strings	(((((epitope) <in> (CLAIMS)) AND ((HIV or "Human Immunodeficiency virus") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((protein or peptide) <in> (CLAIMS)) AND ((vaccine or immunological composition or immunogenic composition) <in>

	(TITLE, ABSTRACT,CLAIMS)))))
Results	Total Results= 861

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	Epitope, mimotope, antigen determinant, antigenic repertoire, HIV, human immunodeficiency virus, protein, peptide, vaccine, immunological composition, immunogenic composition
Classification/ Sub-classification	Not applicable
Search Strings	(((((epitope or mimotope or antigen determinant or antigenic repertoire) <in> (CLAIMS)) AND ((HIV or "Human Immunodeficiency virus") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((protein or peptide) <in> (CLAIMS)) AND ((vaccine or immunological composition or immunogenic composition) <in> (TITLE, ABSTRACT,CLAIMS)))))
Results	Total Results= 876 Total Results Considered= 190

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	Amino acid, peptide, HIV, human immunodeficiency virus, conjugate, vaccine
Classification/ Sub-classification	424/184.1
Search Strings	(("amino acid" or "peptide") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((HIV or "human immunodeficiency virus") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((conjugate or vaccine) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((4241841) <in> NC)
Results	Total Results= 121 Total Results Considered= 93

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	Amino acid, HIV, human immunodeficiency virus, conjugate, vaccine
Classification/ Sub-classification	424/188.1
Search Strings	((("amino acid" or "peptide") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((HIV or "human immunodeficiency virus") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((conjugate or vaccine) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((4241881) <in> NC))
Results	Total Results= 159

	Total Results Considered= 159

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	Amino acid, peptide, HIV, human immunodeficiency virus, conjugate, vaccine
Classification/ Sub-classification	435/005
Search Strings	((("amino acid" or "peptide") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((HIV or "human immunodeficiency virus") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((conjugate or vaccine) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((435005) <in> NC))
Results	Total Results= 179

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, peptide, protein, vaccine
Classification/ Sub-classification	435/005, 435/006, 530/350
Search Strings	(((HIV OR "human immunodeficiency virus") <in> (TITLE,ABSTRACT,CLAIMS)) AND (((peptide OR protien) AND screening) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vaccine) <in> DESCRIPTION) AND ((435/005 OR 435/006 OR 530/350) <in> NC))
Results	Total Results= 19 Total Results Considered= 19

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, peptide, protein, vaccine, screening, screen*
Classification/ Sub-classification	Not applicable
Search Strings	((((HIV OR "Human Immunodeficiency virus") <in> AB) and ((peptide OR protein) <in> AB) and ((vaccine) <in> AB) and ((screening) <in> AB))or((("human Immunodeficiency virus" OR HIV) <in> AB) and ((protien OR peptide) <in> AB) and ((vaccine) <in> AB) and ((screen*) <in> AB)))
Results	Total Results= 202 Total Results Considered= 185

Database	Delphion

	(US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, vaccin*
Classification/ Sub-classification	530/387.1
Search Strings	((HIV or human immunodeficiency virus) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vaccin*) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((5303871) <in> NC)
Results	Total Results= 18 Total Results Considered= 18

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, vaccin*, peptide, epitope
Classification/ Sub-classification	530/387.1
Search Strings	(((HIV or human immunodeficiency virus) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vaccin*) <in> (TITLE,ABSTRACT,CLAIMS)) AND (peptide or epitope) <in> (TITLE,ABSTRACT,CLAIMS) AND ((5303871) <in> NC))
Results	Total Results= 14 Total Results Considered= 11

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, peptide, epitope, immunogen
Classification/ Sub-classification	424/184.1
Search Strings	(((4241841) <in> NC) AND ((HIV or human immunodeficiency virus) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((peptide or epitope or immunogen) <in> (TITLE,ABSTRACT,CLAIMS)))
Results	Total Results= 210

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, peptide, epitope, immunogen, antibod*
Classification/ Sub-classification	424/184.1
Search Strings	((4241841) <in> NC) AND ((HIV or human immunodeficiency virus) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((peptide or epitope or immunogen) <in> (TITLE,ABSTRACT,CLAIMS)) AND

	((antibod*) <in> (TITLE,ABSTRACT,CLAIMS))
Results	Total Results= 92 Total Results Considered= 76

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus
Classification/ Sub-classification	435/005, 424/185.1, 424/188.1, 424/208.1
Search Strings	((hiv or "human immunodeficiency virus") <in> AB) AND ((435/005 or 424/185.1 or 424/188.1 or 424/208.1) <in> CNC)
Results	Total Results= 644

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, Not(DNA, gene, vector)
Classification/ Sub-classification	435/005, 424/185.1, 424/188.1, 424/208.1
Search Strings	((hiv or "human immunodeficiency virus") <in> AB) AND ((435/005 or 424/185.1 or 424/188.1 or 424/208.1) <in> CNC) AND NOT ((dna or gene or vector) <in> TI)
Results	Total Results= 598

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, peptide, protein, polypeptide, Not (DNA, gene, vector)
Classification/ Sub-classification	435/005, 424/185.1, 424/188.1, 424/208.1
Search Strings	((hiv or "human immunodeficiency virus") <in> AB) AND ((435/005 or 424/185.1 or 424/188.1 or 424/208.1) <in> CNC) AND NOT ((dna or gene or vector) <in> TI) AND ((peptide or protein or polypeptide) <in> CLAIMS)
Results	Total Results= 479

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, peptide, protein, polypeptide, Not (DNA, gene, vector)
Classification/ Sub-classification	435/005, 424/185.1, 424/188.1, 424/208.1, A61K 39/21, G01N 33/69, C07K 7/08
Search Strings	(((hiv or "human immunodeficiency virus") <in> AB) AND (

	(435/005 or 424/185.1 or 424/188.1 or 424/208.1) <in> CNC) AND NOT ((dna or gene or vector) <in> TI) AND ((peptide or protein or polypeptide) <in> CLAIMS) AND ((A61K 39/21 or G01N 33/69 or C07K 7/08) <in> IC))
Results	Total Results= 326

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, vaccin*, immun*, Not (DNA, gene, vector, nucleic acid, nucleotide)
Classification/ Sub-classification	435/005, 424/185.1, 424/188.1, 424/208.1, A61K 39/21, G01N 33/69, C07K 7/08
Search Strings	(((hiv or "human immunodeficiency virus") <in> AB) AND ((435/005 or 424/185.1 or 424/188.1 or 424/208.1) <in> CNC) AND NOT ((dna or gene or vector or "nucleic acid" or nucleotide) <in> TI) AND ((peptide or protein or polypeptide) <in> CLAIMS) AND ((vaccin* or immun*) <in> CLAIMS) AND ((A61K 39/21 or G01N 33/69 or C07K 7/08) <in> IC))
Results	Total Results= 227

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, vaccin*, immun*, peptide, protein, polypeptide, Not (DNA, gene, vector, nucleic acid, nucleotide)
Classification/ Sub-classification	435/005, 424/188.1, A61K 39/21, G01N 33/69, C07K 7/08
Search Strings	(((hiv or "human immunodeficiency virus") <in> AB) AND ((435/005 or 424/188.1) <in> CNC) AND NOT ((dna or gene or vector or "nucleic acid" or nucleotide) <in> TI) AND ((peptide or protein or polypeptide) <in> CLAIMS) AND ((vaccin* or immun*) <in> CLAIMS) AND ((A61K 39/21 or G01N 33/69 or C07K 7/08) <in> IC))
Results	Total Results= 151 Total Results Considered= 151

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	Assignee codes (276480, 798240, 822976, 820290, 820256, 724068, 276470, 921251, 809486, 276475, 884707, 917261), HIV, human immunodeficiency virus, vaccin*, immun*
Classification/ Sub-classification	Not applicable

Search Strings	((276480 <OR> 798240 <OR> 822976 <OR> 820290 <OR> 820256 <OR> 724068 <OR> 276470 <OR> 921251 <OR> 809486 <OR> 276475 <OR> 884707 <OR> 917261) <in> assigneecode) AND ((hiv or "human immunodeficiency virus") <in> AB) AND ((vaccin* or immun*) <in> CLAIMS)
Results	Total Results= 76

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	Assignee codes (276480, 798240, 822976, 820290, 820256, 724068, 276470, 921251, 809486, 276475, 884707, 917261), HIV, human immunodeficiency virus, vaccin*, immun*, protein, peptide, amino acid, polypeptide, subunit, sequence
Classification/ Sub-classification	Not applicable
Search Strings	((276480 <OR> 798240 <OR> 822976 <OR> 820290 <OR> 820256 <OR> 724068 <OR> 276470 <OR> 921251 <OR> 809486 <OR> 276475 <OR> 884707 <OR> 917261) <in> assigneecode) AND ((hiv or "human immunodeficiency virus") <in> AB) AND ((vaccin* or immun*) <in> (TITLE,ABSTRACT,CLAIMS)) AND (((protein or peptide or "amino acid" or polypeptide or subunit) <near> sequence) <in> CLAIMS)
Results	Total Results= 39

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	Assignee codes (276480, 798240, 822976, 820290, 820256, 724068, 276470, 921251, 809486, 276475, 884707, 917261), HIV, human immunodeficiency virus, vaccin*, immun*, protein, peptide, amino acid, polypeptide, subunit, sequence, Not (DNA, gene, nucleotide)
Classification/ Sub-classification	Not applicable
Search Strings	(((276480 <OR> 798240 <OR> 822976 <OR> 820290 <OR> 820256 <OR> 724068 <OR> 276470 <OR> 921251 <OR> 809486 <OR> 276475 <OR> 884707 <OR> 917261) <in> assigneecode) AND ((hiv or "human immunodeficiency virus") <in> AB) AND ((vaccin* or immun*) <in> (TITLE,ABSTRACT,CLAIMS)) AND (((protein or peptide or "amino acid" or polypeptide or subunit) <near> sequence) <in> CLAIMS) AND NOT ((dna or gene or nucleotide) <in> TI))
Results	Total Results= 25 Total Results Considered= 25

Search Round #4

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	Protein, vaccine, immunogenic composition, immunological composition, subunit, envelope
Classification/ Sub-classification	B04, D16
Search Strings	((protein) <in> TI) and ((B04 or D16) <in> DERWENTMAINCLASS) and ((vaccine or immunogenic composition or immunological composition) <in> TI) and ((subunit or envelope) <in> TI)
Results	Total Results= 220 Total Results Considered= 70

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, inoculation, vaccine
Classification/ Sub-classification	CO7K 014005
Search Strings	(((C07K 014005) <in> IC) AND ((HIV) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((inoculation or vaccine) <in> (TITLE,ABSTRACT,CLAIMS)))
Results	Total Results= 1611

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	Peptide, polypeptide, vaccine, inoculation, HIV, immunodeficiency
Classification/ Sub-classification	CO7K 014005
Search Strings	(((C07K 014005) <in> IC) AND ((peptide or polypeptide <near> vaccine or inoculation) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((HIV or immunodeficiency) <in> (TITLE,ABSTRACT,CLAIMS)))
Results	Total Results= 2257

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	Peptide, polypeptide, HIV, vaccine, sequence, formula
Classification/ Sub-classification	C07K 01416
Search Strings	(((C07K 01416) <in> IC) AND ((peptide or polypeptide) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((HIV <near> vaccine) <in>

	(TITLE,ABSTRACT,CLAIMS)) AND ((sequence or formula) <in> (TITLE,ABSTRACT,CLAIMS)))
Results	Total Results= 526

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	Peptide, polypeptide, HIV, vaccine, sequence, formula
Classification/ Sub-classification	C07K 014005
Search Strings	(((C07K 014005) <in> IC) AND ((peptide or polypeptide) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((HIV <near> vaccine) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((sequence or formula) <in> (TITLE,ABSTRACT,CLAIMS)))
Results	Total Results= 624

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	Epitope, HIV, human immunodeficiency virus, vaccine, immunogenic composition, immunological composition, peptide
Classification/ Sub-classification	Not applicable
Search Strings	((epitope) <in> CLAIMS) AND ((HIV or "human immunodeficiency virus") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vaccine or "immunogenic composition" or "immunological composition") <in> CLAIMS) AND ((peptide) <in> CLAIMS)
Results	Total Results= 463

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	Epitope, mimotope, antigen determinant, HIV, human immunodeficiency virus, vaccine, immunogenic composition, immunological composition, peptide
Classification/ Sub-classification	Not applicable
Search Strings	((((epitope or mimotope or "antigen determinant") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((HIV or "human immunodeficiency virus") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vaccine or "immunogenic composition" or "immunological composition") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((peptide) <in> (TITLE,ABSTRACT,CLAIMS))))
Results	Total Results= 715

Database	Delphion

	(US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	Epitope, mimotope, antigen determinant, HIV, human immunodeficiency virus, vaccine, immunogenic composition, immunological composition, peptide
Classification/ Sub-classification	Not applicable
Search Strings	(((epitope or mimotope or "antigen determinant") <in> CLAIMS) AND ((HIV or "human immunodeficiency virus") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vaccine or "immunogenic composition" or "immunological composition") <in> CLAIMS) AND ((peptide) <in> CLAIMS))
Results	Total Results= 468

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	Epitope, mimotope, antigen determinant, HIV, human immunodeficiency virus, vaccine, immunogenic composition, immunological composition, peptide
Classification/ Sub-classification	A61K 39/21, C07K 7/08
Search Strings	((((((epitope or mimotope or "antigen determinant") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((HIV or "human immunodeficiency virus") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vaccine or "immunogenic composition" or "immunological composition") <in> (CLAIMS)) AND ((peptide) <in> (CLAIMS)))))) AND ((A61K 39/21 or C07K 7/08) <in> (ICINV,MC))
Results	Total Results= 162 Total Results Considered= 162

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	Epitope, mimotope, antigen determinant, HIV, human immunodeficiency virus, vaccine, immunogenic composition, immunological composition, peptide
Classification/ Sub-classification	435*, 424*
Search Strings	((((((epitope or mimotope or "antigen determinant") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((HIV or "human immunodeficiency virus") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vaccine or "immunogenic composition" or "immunological composition") <in> (CLAIMS)) AND ((peptide) <in> (CLAIMS)))))) AND ((435* or 424*) <in> NC)
Results	Total Results= 143

	Total Results Considered= 143

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	Human immunodeficiency virus, HIV, conjugate, adjuvants, peptide, amino acid, vaccine, immunological agent
Classification/ Sub-classification	Not applicable
Search Strings	(("human immunodeficiency virus" or HIV) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((conjugate or adjuvants) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((peptide or "amino acid") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vaccine or "immunological agent") <in> (TITLE,ABSTRACT,CLAIMS))
Results	Total Results= 857

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	Human immunodeficiency virus, HIV, conjugate, adjuvants, peptide, amino acid, vaccine, humoral, cytotoxic
Classification/ Sub-classification	Not applicable
Search Strings	(((((("human immunodeficiency virus" or HIV) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((conjugate or adjuvants) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((peptide or "amino acid") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vaccine) <in> (TITLE,ABSTRACT,CLAIMS))) AND (((humoral or cytotoxic) <in> (TITLE,ABSTRACT,CLAIMS)))))
Results	Total Results= 194 Total Results Considered= 170

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, peptide, protein, vaccine, screen*
Classification/ Sub-classification	C12N 15/*
Search Strings	((((HIV OR "Human Immunodeficiency virus") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((peptide OR protein) AND ((C12N 15/*) <in> (ICINV,MC)) AND(TITLE,ABSTRACT,CLAIMS)) AND ((vaccine) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((screen*) <in> (TITLE,ABSTRACT,CLAIMS))))
Results	Total Results= 145

	Total Results Considered= 145

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, peptide, protein, vaccine, screen*
Classification/ Sub-classification	A61K 39/21, C07K 7/08
Search Strings	(((HIV OR "Human Immunodeficiency virus") <in> (TITLE,ABSTRACT,CLAIMS)) AND ((peptide OR protein) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((A61K 39/21 OR C07K 7/08) <in> (ICINV,MC)) AND ((vaccine) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((screen*) <in> (TITLE,ABSTRACT,CLAIMS)))
Results	Total Results= 65 Total Results Considered= 65

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, peptide, protein, vaccine, immunogenic, immunology, screening
Classification/ Sub-classification	Not applicable
Search Strings	((HIV) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((Peptide OR protien) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((vaccine OR immunogenic OR immunology) <in> (TITLE,ABSTRACT,CLAIMS)) AND ((screening) <in> CLAIMS)
Results	Total Results= 193 Total Results Considered= 193

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, vaccin*, antibod*
Classification/ Sub-classification	D16, B04
Search Strings	(((HIV or human immunodeficiency virus) <in> AB) and ((vaccin*) <in> AB) and ((antibod*) <in> AB) and ((D16 or B04) <in> DERWENTCLASS))
Results	Total Results= 1030

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)

Keywords	HIV, human immunodeficiency virus, vaccin*, antibod*, peptide, subunit, epitope
Classification/ Sub-classification	D16, B04
Search Strings	(((HIV or human immunodeficiency virus) <in> AB) and ((vaccin*) <in> AB) and ((antibod*) <in> AB) and ((D16 or B04) <in> DERWENTCLASS) and ((peptide or subunit or epitope) <in> AB))
Results	Total Results= 499

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, vaccin*, neutraliz* antibod*, peptide, subunit, epitope
Classification/ Sub-classification	D16, B04
Search Strings	(((HIV or human immunodeficiency virus) <in> AB) and ((vaccin*) <in> AB) and ((neutraliz* antibod*) <in> AB) and ((D16 or B04) <in> DERWENTCLASS) and ((peptide or subunit or epitope) <in> AB))
Results	Total Results= 59 Total Results Considered= 51

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, vaccin*, immun*, gag, pol, env, tat, rev, nef, vif, vpr,vpu
Classification/ Sub-classification	Not applicable
Search Strings	((hiv or "human immunodeficiency virus") <in> AB) and ((vaccin* or immun*) <in> AB) and ((gag or pol or env or tat or rev or nef or vif or vpr or vpu) <in> AB)
Results	Total Results= 805

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, vaccin*, immun*, gag, pol, env, tat, rev, nef, vif, vpr,vpu, Not (DNA, gene, nucleotide, vector)
Classification/ Sub-classification	Not applicable
Search Strings	((hiv or "human immunodeficiency virus") <in> AB) and ((vaccin* or immun*) <in> AB) and ((gag or pol or env or tat or rev or nef or vif or vpr or vpu) <in> AB) and not ((dna or gene or nucleotide or

	vector) <in> TI)
Results	Total Results= 509

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, vaccin*, immun*, gag, pol, env, tat, rev, nef, vif, vpr,vpu, Not (DNA, gene, nucleotide, vector)
Classification/ Sub-classification	Not applicable
Search Strings	((hiv or "human immunodeficiency virus") <in> TI) and ((vaccin* or immun*) <in> AB) and ((gag or pol or env or tat or rev or nef or vif or vpr or vpu) <in> AB) and not ((dna or gene or nucleotide or vector) <in> TI)
Results	Total Results= 343

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, vaccin*, immun*, protein, peptide, polypeptide, amino acid, gag, pol, env, tat, rev, nef, vif, vpr,vpu, Not (DNA, gene, nucleotide, vector)
Classification/ Sub-classification	Not applicable
Search Strings	(((hiv or "human immunodeficiency virus") <in> TI) and ((vaccin* or immun*) <in> AB) and ((protein or peptide or polypeptide or "amino acid") <in> AB) and ((gag or pol or env or tat or rev or nef or vif or vpr or vpu) <in> AB) and not ((dna or gene or nucleotide or vector) <in> TI))
Results	Total Results= 282

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, vaccin*, immun*, protein, peptide, polypeptide, amino acid, gag, pol, env, tat, rev, nef, vif, vpr,vpu, Not (DNA, gene, nucleotide, vector)
Classification/ Sub-classification	Not applicable
Search Strings	(((hiv or "human immunodeficiency virus") <in> TI) and ((vaccin* or immun*) <in> TI) and ((protein or peptide or polypeptide or "amino acid") <in> AB) and ((gag or pol or env or tat or rev or nef or vif or vpr or vpu) <in> AB) and not ((dna or gene or nucleotide or vector) <in> TI))
Results	Total Results= 237

Database	Delphion (US Applications, US Patents, WIPO PCT Publications, EPO Granted, EPO Applications, Abstracts of Japan)
Keywords	HIV, human immunodeficiency virus, vaccin*, immun*, protein, peptide, polypeptide, amino acid, gag, pol, env, tat, rev, nef, vif, vpr,vpu, Not (DNA, gene, nucleotide, vector)
Classification/ Sub-classification	B04, D16, S03, A61K 39/21, C07K 7/08
Search Strings	((((hiv or "human immunodeficiency virus") <in> TI) and ((vaccin* or immun*) <in> TI) and ((protein or peptide or polypeptide or "amino acid") <in> AB) and ((gag or pol or env or tat or rev or nef or vif or vpr or vpu) <in> AB) and not ((dna or gene or nucleotide or vector) <in> TI))) AND ((B04 or D16 or S03) <in> DERWENTCLASS) AND ((A61K 39/21 or C07K 7/08) <in> CLASS)
Results	Total Results= 128 Total Results Considered= 113

3. Patent Search Results Spreadsheet Summary
3.1. Categorization Summary

Patent documents on peptide vaccines generally fall into 11 categories:

(1) Prime Boost
(2) Protein
(3), Peptide
(4) Peptide Formulation
(5) Epitopes
(6) Conjugates
(7) Peptide Screening
(8) Antibodies to HIV
(9) Antibodies Screening Library
(10) Tat-based Vaccine
(11) Therapeutic v. Prophylactic.

1. The "**Prime Boost**" category contains patent documents[138] that are classified as peptide vaccines which enhance the immune response to HIV by repeated administration, a phenomenon called boosting. Typically, the first administration of the vaccine is "prime" element where you infect the patient with an initial dose. The following treatments of vaccine are classified as the "boost" element of the vaccine. This method is usually used when a single administration of a peptide vaccine is not sufficiently strong or sustained to provide effective protection. Interestingly, priming a patient with a live attenuated HIV is generally considered too risky for uninfected people because there is an increasing chance of becoming infected with HIV. However, many studies show that it is possible to develop a preventative vaccine using prime boosting of components of a partially split HIV, rather than the live attenuated virus.[139]

2. The "**Proteins**" category contains patents that are defined as whole proteins that are utilized in a protein vaccine for HIV. Generally, protein vaccines incorporate proteins that are utilized to induce an autoimmune response to HIV. These patents are limited to only proteins and not polypeptides. Although it may be difficult to determine when a polypeptide can be large enough to be classified as a protein, for the purposes of this report this group is limited to only whole proteins described in patent that induce an immune response for HIV.

3. The "**Peptide**" category is comprised of patents that claim either peptides, polypeptides or a composition that comprises a chain of amino acids for peptide vaccines. Peptides are short chains of amino acids linked together by peptide

[138] Patent documents include US patents; US patent applications; WIPO PCT applications; Japanese patents; European patents, European patent applications.
[139] Laurence Peiperl, Why Prime-Boost?, http://chi.ucsf.edu/vaccine/vaccines?page=vc-05-01 (last visited April 19, 2009).

bonds.[140] Generally, peptides have fewer than 40 amino acids and can act as hormones and neurotransmitters. Polypeptides are generally longer chains of at least 50 amino acids. For the development of a useful peptide vaccine, a potential candidate peptides are identified through either cytolysis or by an APC (Antigen Presenting Cells) ingesting a HIV and breaking it down. For the purposes of this report, polypeptides are classified under the "**Peptide**" rather than under the "**Protein**" section.

4. "**Peptide/Protein Formulation**" category contains patents that claim a combination of peptides or proteins are used as a peptide or protein vaccine. These patents generally suggest that one or more peptides or proteins can be used in conjunction to create a peptide or protein vaccine. Typical claim language will characterize a peptide/protein formula as at least one peptide that can be used in any combination thereof.

5. "**Epitopes**" category contains patents pertaining to a region on the surface of an antigen molecule which the antibody attaches itself.[141] HIV has both good and bad epitopes.[142] Bad epitopes waste the immune response reaction while good epitopes promote a correct response to HIV.[143] Since HIV is rapidly mutating, a good epitope can be found in regions where the virus maintains the same structure. Furthermore, HLA-HIV associations[144] can also suggest the location of good epitopes to use for peptide vaccines for HIV.[145]

6. The "**Conjugate**" category contains patents that claim a covalently attached protein carrier that elicit a sufficient immune response. Typically, peptides alone are too small to induce a sufficient immune response.[146] Therefore, carrier proteins, such as KLH[147], BSA[148] and OVA[149] that contain many epitopes are used to generate T-helper cells, which induce the B-cell response.[150] This group is limited to only fusion proteins and carriers and does not include any common

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[140] Peptides http://www.vitaminstuff.com/definitions/definitions41.html (last visited April 19, 2009).
[141] Epitope. http://www.thefreedictionary.com/Epitopes (lasted visited April 19, 2009).
[142] David Heckerman et al., Graphical Models for HIV vaccine design, *available at* https://velblod.videolectures.net/2007/pascal/icml07_corvallis/heckerman_david/icml07_heckerman_gmhi_01.pptx (2007).
[143] *Id.*
[144] HLA (Human Leukocyte Antigens) is a genetic designation for the human major histocompatibility complex. There are two types: class I and class II. A HLA-HIV Association is the binding of these major histocompatibility complexes with the peptides from a HIV vaccine.
[145] Id.
[146] Peptides for Immunization. http://www.thermo.com/eThermo/CMA/PDFs/Various/File_9276.pdf (lasted visited April 19, 2009).
[147] Keyhole Lipet Hemocyanin (KLH) is a copper containing, non-heme protein found in arthropods and mollusca and is a commonly selected carrier for immunization. *Id.*
[148] Bovine Serum Albumin (BSA) is a stable and highly soluble plasma protein form cattle. SO it is a popular carrier protein for vaccines. *Id.*
[149] Ovalbumin (OVA) is a protein isolated form the egg whites and is a good choice for a carrier protein to verify antibodies specific for peptides. *Id.*
[150] *Id.*

adjuvants, which are commonly used molecules that promote a response in for any type of vaccine.

7. The "**Peptide Screening or Library**" category includes patents that claim a process or method to detect peptides for HIV or patents that compiled a peptide library for HIV. These patents should not included any diagnostic test done to determine whether a mammal has HIV.

8. The "**Antibodies to HIV**" category contains patents that claim antibodies specific to HIV. Antibodies are B- cell proteins that recognize and attach to specific sites on antigens to block their effect.[151] When triggering an immune response, a vaccine would most likely promote the production of antibodies. During this study, patents that claim antibodies that are specific for HIV or released as a result of the vaccine will be relevant to this group. These antibodies will recognize HIV antigens and will block their effected.

9. The "**Antibodies Screening or Library**" category consists of patents that claim either the process to detect antibodies specific to HIV or claim an antibody library for HIV.

10. The "**Tat-based Vaccine**" category contains patent that pertain to Tat-based vaccines for HIV. Tat-based vaccine are generally vaccine that based on a native Tat protein, which is a early regulatory protein key for HIV replication and AIDS pathogenesis, highlights the importance of targeting the virus very early after infection.[152] One benefit of Tat based vaccine is that modify the virus-host interactions at the very beginning of infection, thus containing the depletion of critical immune cells and the progression of HIV.[153]

11. The final group in this report categorizes patents that are classified as "**Therapeutic v. Prophylactic.**" In this category, the patent will claim methods that are either prophylactic or therapeutic to HIV. A prophylactic peptide vaccine is a vaccine that will prevent HIV from infecting an individual. A therapeutic composition will treat HIV after a patent has been diagnosed with the virus. For the purposes of this report, when a vaccine is only claimed within the patent, the patent will be assumed to be under the prophylactic category because an HIV vaccine will prevent the infection.

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[151] Carol & Richard Eustice, What are Antibodies?, http://arthritis.about.com/od/arthritislearnthebasics/g/antibody.html (last visited April 19, 2009).
[152] Antonella Caputo et al., *Recent Advances in the Development of HIV-1 Tat-Based Vaccines*, 2(4) Current HIV Research 357 (Oct. 2004).
[153] *Id.*

3.2 Master Spreadsheet

Patent Number	Prime Boost	Protein	Peptide	Peptide Formulation	Epitopes	Conjugates	Peptide Screening	Antibodies to HIV	Antibodies Screening Library	TAT-base Vaccine	Therapeutic v.	Title	Assignee/ Applicant
EP1487484B1	N	N	N	N	N	N	N	N	N	N	P	Use of Mixtures of Lipopeptides for Vaccine Protection	Centre National de la Recherche Scientifique (CNRS); Universite de Lille II; Institut National de la Sante et de la Recherche Medicale (Inserm)
EP199301A1	N	Y	N	N	N	N	N	Y	N	N	P	Recombinant acquired immune deficiency syndrome (AIDS) viral envelope protein and method of testing for AIDS	Hoffmann- La Roche & Co.; Government of the United States of America as represented by the Secretary of the Department of Health and Human Services
EP265785A2	N	Y	N	N	N	N	N	Y	Y	N	N	Polypeptides derived from the envelope gene of human immunodeficiency virus in recombinant baculovirus infected insect cells	Microgenesys, Inc.
EP272858A2	N	N	Y	N	N	N	N	N	Y	N	P	Recombinant HIV envelope proteins produced in insect cells	Repligen Corporation
EP279688A2	N	N	Y	N	Y	Y	N	Y	N	N	T/P	Methods and compositions for the use of HIV env polypeptides and antibodies thereto	Genentech, Inc.
EP280468A2	N	N	Y	N	N	N	N	Y	Y	N	P	Methods and materials for hiv detection and therapy	Nissin Shokuhin Kabushiki Kaisha
EP298633A2	N	N	Y	N	N	N	N	Y	N	N	T/P	Synthetic polypeptides	Proteus Biotechnology Limited
EP306219A2	N	Y	Y	N	N	N	N	N	N	N	P	Novel HIV proteins and peptides useful in the diagnosis, prophylaxis or therapy of AIDS	Repligen Corporation
EP317804A2	N	N	Y	Y	N	N	N	N	N	N	P	HIV peptides and methods for detection of HIV	Abbott Laboratories
EP327180A2	N	Y	N	N	N	N	N	N	N	N	P	Vaccine containing polypeptides derived from the envelope gene of human immunodeficiency virus type 1	Microgenesys, Inc.

3.2 Master Spreadsheet

Patent Number	Prime Boost	Protein	Peptide	Peptide Formulation	Epitopes	Conjugates	Peptide Screening	Antibodies to HIV	Antibodies Screening Library	TAT-base Vaccine	Therapeutic v.	Title	Assignee/ Applicant
EP330359A2	N	N	Y	Y	N	N	N	Y	N	N	P	Composition useful in the diagnosis and treating of HIV-1 infection	Bio-Rad Laboratories, Inc.
EP339504A2	N	N	Y	N	N	Y	N	N	Y	N	T/P	Human immunodeficiency virus (HIV) env-coded peptide capable of eliciting HIV-inhibiting antibodies in mammals	E.I. Du Pont de Nemours & Co.
EP354109A1	N	N	Y	N	Y	N	N	Y	N	N	P	Recombinant HBsAg hybrid particles having morphological characteristics ofthe HBsAg antigen and containing an immunogenic sequence which induces neutralizing antibodies directed against HIV or susceptible of being recognized by such antibodies. Nucle	Institut Pasteur; Institut National de la Sante et de la Recherche Medicale (Inserm)
EP356007A2	N	N	Y	Y	N	N	N	Y	N	N	P	Antigenic determinants	Medical Research Council
EP373070A1	N	N	N	N	N	N	Y	N	N	N	N	Preparation of a library of peptidic antigenic determinants, new peptides built from or containing these determinants and use thereof, namely for diagnosis	Centre National de la Recherche Scientifique (CNRS)
EP400245A1	N	Y	N	N	N	N	N	Y	N	N	N	Proteins and glycoproteins of the HIV-2 EHO retrovirus antiobodies directed against them - application for the diagnosis	Institut Pasteur
EP402088A2	N	N	N	N	N	Y	N	N	N	N	P	Conjugate immunogen for aids	Merck & Co., Inc.
EP421626A1	N	Y	N	N	N	Y	N	N	N	N	T/P	Vaccine for aids and hepatitis B	Merck & Co., Inc.
EP426314A2	N	N	Y	Y	N	N	N	N	N	N	T/P	HIV related peptides	Viral Technologies, Inc.; The George Washington University

3.2 Master Spreadsheet

Patent Number	Prime Boost	Protein	Peptide	Peptide Formulation	Epitopes	Conjugates	Peptide Screening	Antibodies to HIV	Antibodies Screening Library	TAT-base Vaccine	Therapeutic v.	Title	Assignee/ Applicant
EP448095A1	N	N	Y	N	Y	N	N	N	N	N	N	Subregion of the retroviral ENV protein, DNA sequences encoding it and compositions for the diagnosis, prevention or therapy of retrovirus infections	Prof. Dr. Hans Joachim Wolf
EP459842A1	N	N	Y	N	N	N	N	N	N	N	P	Process for the production of retroviral immunogenes and vaccines against retroviral infections, especially HIV, and immunogens and vaccines thereof	Pasteur Merieux Serums & Vaccins
EP467699A2	N	N	Y	Y	N	N	N	N	N	N	N	Cyclic HIV principal neutralizing determinant peptides	Merck & Co., Inc.
EP467701A2	N	N	Y	Y	N	N	N	N	N	N	T	Cyclic HIV principal neutralizing determinant peptides	Merck & Co., Inc.
EP471453A2	N	N	Y	Y	N	N	N	N	N	N	N	Cyclic HIV principal neutralizing determinant peptides	Merck & Co., Inc.
EP498905A1	N	N	Y	Y	Y	N	N	N	N	N	P	Conformational epitopes of human immunodeficiency virus envelope glycoprotein gp120	New York Blood Center, Inc.
EP516135A2	N	N	Y	Y	N	N	N	Y	Y	N	P	Human immunodeficiency virus-related immune preparation	Juridical Foundation The Chemo-Sero-Therapeutic Research Institute
EP519554A1	N	N	Y	N	N	Y	N	N	N	N	N	Conjugates of the class II protein of the outer membrane of neisseria meningitidis and of HIV-1 related peptides	Merck & Co., Inc.
EP551689A2	N	N	Y	N	N	Y	N	N	N	N	P	Cyclic HIV principal neutralizing determinant (PNP) peptides	Merck & Co., Inc.
EP572737A2	N	Y	N	N	N	N	N	N	N	N	P	HIV Gag-env fusion antigen	The Research Foundation for Microbial Diseases of Osaka University

3.2 Master Spreadsheet

Patent Number	Prime Boost	Protein	Peptide	Peptide Formulation	Epitopes	Conjugates	Peptide Screening	Antibodies to HIV	Antibodies Screening Library	TAT-base Vaccine	Therapeutic v.	Title	Assignee/ Applicant
EP588750A2	N	N	Y	Y	N	Y	N	Y	Y	N	P	Method for the production of recombinant polypeptides bearing epitopes from different hiv isolates, and their uses as immunogens and in the detectionof antibodies against hiv	Centro de Ingenieria Genetica Y Biotecnologia
US20010007017A1	N	N	Y	N	N	Y	N	Y	N	N	T/P	Peptides which react with antibody representing the prognostic marker for HIV disease progression	
US20010009667A1	N	N	Y	N	N	N	N	N	N	N	N	Method of detecting nucleic acid encoding a retrovirus using polymerase chain reaction (PCR)	
US20010036461A1	N	N	N	N	N	N	N	N	N	N	P	Human immunodeficiency virus vaccine	Haynes Barton F.; Liao Hua-Xin
US20010043932A1	N	N	N	N	N	N	N	N	N	N	P	Method of inducing cell-mediated protective immunity against HIV using low doses of immunogens	Government of the United States of America as represented by the Secretary of the Department of Health and
US20020044948A1	N	N	N	N	N	N	N	N	N	N	T/P	Methods and compositions for co-stimulation of immunological responses to peptide antigens	Khleif Samir; Berzofsky Jay
US20020081576A1	N	N	N	N	Y	N	N	Y	N	N	T	Antibodies directed against binding-associated epitopes	Ramot University for Applied Research and Industrial Development Ltd.
US20020094523A1	N	N	Y	N	N	N	N	N	N	N	N	Chimeric retroviral gag genes and screening assays	Government of the United States of America as represented by the Secretary of the Department of Health and Human Services and the National Institute of Health (NIH)

3.2 Master Spreadsheet

Patent Number	Prime Boost	Protein	Peptide	Peptide Formulation	Epitopes	Conjugates	Peptide Screening	Antibodies to HIV	Antibodies Screening Library	TAT-base Vaccine	Therapeutic v.	Title	Assignee/ Applicant
US20020127238A1	N	Y	N	N	N	N	N	N	N	N	P	HIV-1 vaccines and screening methods therefor	Chiron Corporation
US20020146683A1	Y	N	Y	N	N	N	N	N	N	N	P	Modified HIV Env polypeptides	Chiron Corporation
US20020182222A1	N	N	Y	N	N	N	N	N	N	N	P	HIV vaccine candidate peptides	Groot Anne De
US20020192227A1	N	N	N	N	N	N	N	N	N	N	T/P	Vaccines against cancer and infectious diseases	Immunomedics, Inc.
US20030049604A1	N	Y	Y	N	N	N	N	Y	N	N	N	Nucleotide sequences of HIV-1 group (or subgroup) O retroviral antigens	Institut Pasteur
US20030068615A1	N	N	Y	N	N	N	Y	N	N	N	N	Polypeptides that bind HIV gp120 and related nucleic acids, antibodies, compositions, and methods of use	Government of the United States of America as represented by the Secretary of the Department of Health and Services
US20030082521A1	N	N	Y	N	N	Y	N	Y	N	N	P	Polypeptide inducing antibodies neutralizing HIV	Aventis Pasteur S.A.
US20030108562A1	Y	N	Y	Y	N	N	N	N	N	N	T/P	Immune responses to hiv	Medical Research Council
US20030124143A1	N	N	Y	N	Y	N	Y	N	N	N	P	Methods for selecting immunogenic polypeptides	Phalipon Armelle; Sansonetti Philippe; Felici Franco; Cortese Riccardo; Kraehenbuhl Jean Pierre
US20030138445A1	N	N	Y	N	N	Y	N	N	N	N	P	gp41 antigen	Aventis Pasteur S.A.
US20030157115A1	N	N	N	N	N	Y	N	Y	N	N	T/P	Multiple antigen gylcopeptide carbohydrate vaccine comprising the same and use thereof	Institut Pasteur
US20030158134A1	Y	N	N	N	N	N	N	N	N	Y	P	Vaccine for the prophylactic or therapeutic immunization against hiv	Smithkline Beecham Biologicals S.A.
US20030161834A1	N	N	N	N	N	N	N	N	N	N	P	Vaccines	Smithkline Beecham Biologicals S.A.
US20030165542A1	N	Y	N	N	N	N	N	N	N	N	T/P	Methods and compositions for promoting immunopotentiation	Arch Development Corp.
US20030180759A1	N	N	Y	N	N	N	N	Y	N	N	P	HIV-1 group O antigens and uses thereof	Innogenetics N.V.

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Patent Number	Prime Boost	Protein	Peptide	Peptide Formulation	Epitopes	Conjugates	Peptide Screening	Antibodies to HIV	Antibodies Screening Library	TAT-base Vaccine	Therapeutic v.	Title	Assignee/ Applicant
US20030191076A1	Y	N	N	N	N	N	N	N	N	N	N	Prime-boost vaccination strategy	Alfred Hospital; Commonwealth Scientific and Industrial Research Organisation; University of Melbourne; The Australian National University
US20030206900A1	N	N	Y	N	N	N	N	Y	N	N	P	Vectors derived from antibodies for transferring substances into cells	Institut Pasteur; Universite Pierre et Marie Curie
US20030215797A1	N	N	Y	N	N	N	N	N	N	Y	T/P	Vaccines and immunotherapeutics derived from the human immunodeficiency virus (HIV) trans-activator of transcription protein for the treatment and prevention of HIV disease	Inist, Inc.
US20030219378A1	N	N	Y	N	N	Y	N	N	N	Y	N	Membrane-permeant peptide complexes for medical imaging, diagnostics, and pharmaceutical therapy	The Washington University
US20030219452A1	N	N	Y	Y	N	N	N	N	N	N	T/P	HIV envelope V3-CCR5 binding site immunogen	Los Alamos National Security, LLC
US20030224021A1	N	N	N	N	N	N	Y	N	N	N	P	Methods of using epitope peptides of human pathogens	Regents of the University of Minnesota
US20040001845A1	N	N	N	N	N	N	N	N	N	N	P	Cytotoxic T-cell epitopes of HIV-1 virus	Altfeld Marcus; Yu Xu; Walker Bruce D.; Addo Maryln
US20040005330A1	Y	Y	N	N	N	N	N	N	N	Y	T/P	Mutated HIV Tat	Aventis Pasteur S.A.
US20040006001A1	N	Y	N	N	N	Y	N	N	N	Y	T/P	Ferritin fusion proteins for use in vaccines and other applications	New Century Pharmaceuticals, Inc.
US20040018207A1	Y	N	N	N	N	N	N	N	N	N	P	Preventive and therapeutic AIDS vaccines	Chen Qun
US20040043033A1	N	N	Y	N	N	N	N	N	N	N	T/P	Method and vaccine for the prevention of AIDS	Green Lorrencce H.

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Patent Number	Prime Boost	Protein	Peptide	Peptide Formulation	Epitopes	Conjugates	Peptide Screening	Antibodies to HIV	Antibodies Screening Library	TAT-base Vaccine	Therapeutic v.	Title	Assignee/ Applicant
US20040057968A1	N	N	Y	N	N	N	N	N	N	N	T/P	T cell binding ligand peptides, peptide constructs containing same and use thereof for treatment of immunological disorders	Zimmerman Daniel H.
US20040072162A1	N	N	N	N	Y	N	Y	N	N	N	P	Hiv peptides and nucleic acids encoding them for diagnosis and control of hiv infection	Statens Serum Institut
US20040096458A1	N	Y	N	N	N	N	N	N	N	N	P	Fusion protein construct and method for inducing HIV-specific serum IgG and secretory IgA antibodies in-vivo	Weissenhorn Winfried; Wiley Don; Mantis Nicholas; Neutra Marian R.; Kozlowski Pamela
US20040106105A1	N	N	Y	N	N	N	N	Y	N	N	P	Vaccine	Consejo Superior de Investigaciones; Pharmacia Spain
US20040115615A1	N	N	Y	N	N	N	N	Y	Y	N	P	Hiv peptides antigens, vaccine compositions, immunoassay kit and a method of detecting antibodies induced by hiv	Bionor Immuno A.S.
US20040115622A1	N	N	Y	Y	N	N	N	N	N	N	P	Mixture of peptides originating from a Nef protein and applications thereof	Commissariat a L'Energie Atomique;Institut National de la Sante et de la Recherche Medicale (Inserm)
US20040137010A1	N	Y	N	N	N	N	N	N	N	N	T/P	Prophylactic and therapeutic HIV aptamers	Archemix Corporation
US20040170606A1	N	N	Y	N	N	Y	N	N	N	N	P	Production of peptides in plants as viral coat protein fusions	Large Scale Biology Corporation
US20040191269A1	N	Y	N	N	N	N	N	N	N	N	P	Polyvalent, primary HIV-1 glycoprotein DNA vaccines and vaccination methods	Advanced Bioscience Laboratories
US20040223977A1	N	N	N	N	N	N	N	N	N	N	P	Fusion peptide HIV vaccines	City of Hope
US20040241641A1	N	N	Y	N	N	N	N	Y	N	N	P	Peptides mimicking a cryptic epitope of gp41 hiv-1	Polymun Scienc Immunologische

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Patent Number	Prime Boost	Protein	Peptide	Peptide Formulation	Epitopes	Conjugates	Peptide Screening	Antibodies to HIV	Antibodies Screening Library	TAT-base Vaccine	Therapeutic v.	Title	Assignee/ Applicant
US20040249124A1	N	N	Y	N	N	Y	N	Y	N	N	P	Isolated polypeptides based on the neutralizing epitope of the p17 protein of hiv useful as vaccines, and neutralizing anti-p17 antibodies which specifically recognize said neutralizing epitope	Medestea Internazionale S.R.L.
US20050031639A1	N	N	N	N	N	N	Y	N	N	N	N	Materials and methods for immunizing against FIV infection	University of Florida Research Foundation, Inc.
US20050036985A1	N	N	N	N	N	N	N	N	N	Y	N	Use of biologically active hiv-1 tat, fragments or derivatives thereof, to target and/or to activate antigen-presenting cells, and/or to deliver cargo molecules for preventive or therapeutic vaccination and/or to treat other diseases	Istituto Superiore di Sanita
US20050053616A1	N	N	Y	N	N	N	N	Y	N	N	T/P	Hiv regulatory and auxiliary peptides, antigens, vaccine compositions, immunoassay kit and a method of detecting antibodies induced by hiv	Bionor Immuno A.S.
US20050058657A1	N	N	Y	N	N	N	N	N	N	N	T/P	Vaccine comprising gp120 and nef and/or tat for the immunisation against hiv	Glaxosmithkline Biologicals S.A.
US20050058983A1	N	N	N	N	N	N	N	Y	N	N	N	Use of transgenic mice for the efficient isolation of novel human monoclonal antibodies with neutralizing activity against primary HIV-1 strains and novel HIV-1 neutralizing antibodies	Public Health Research Institute

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Patent Number	Prime Boost	Protein	Peptide	Peptide Formulation	Epitopes	Conjugates	Peptide Screening	Antibodies to HIV	Antibodies Screening Library	TAT-base Vaccine	Therapeutic v.	Title	Assignee/ Applicant
US20050074751A1	N	N	N	N	N	N	N	Y	N	N	N	Assays and therapies for latent viral infection	Oklahoma Medical Research Foundation
US20050080240A1	N	N	Y	N	N	N	N	N	N	N	T/P	Anti-idiotypic antibody inducing hiv-1 neutralizing antibodies	Polymun Scienc Immunologische
US20050089526A1	N	Y	N	N	N	N	N	N	N	N	N	Human immunodeficiency virus envelope clycoprotein mutants and uses thereof	Cornell Research Foundation, Inc.
US20050089840A1	Y	N	Y	N	N	Y	N	N	N	N	N	Peptide derivative fusion inhibitors of HIV infection	Frontier Biotechnologies Co., Ltd.
US20050106160A1	N	Y	N	N	N	N	N	N	N	N	P	Hiv-1 envelope glycoproteins stabilized by flexible linkers as potent entry inhibitors and immunogens	Dimitrov Dimiter S.; Chow Yen Hung; Phogat Sanjay K.; Broder Christopher C.
US20050107322A1	N	N	N	N	N	N	N	N	N	N	P	Compositions for inducing immune responses	O'Hagan Derek; Singh Manmohan
US20050112140A1	N	N	N	N	N	N	N	N	N	N	P	Immunogenic composition and method of developing a vaccine based on portions of the HIV matrix protein	NMK Research, LLC
US20050124540A1	N	N	Y	N	N	Y	N	Y	N	N	P	Novel synthetic peptide vaccines for HIV: the CBD epitope as an effective immunogen to elicit broadly neutralizing antibodies against HIV	Institut Pasteur; Centre National de la Recherche Scientifique (CNRS)
US20050163796A1	N	N	Y	Y	N	N	N	Y	N	N	N	Identification of new cd8 epitopes from hiv-1 proteins with therapeutical and vaccinal properties against hiv infections	Institut Pasteur; Institut National de la Sante et de la Recherche Medicale (Inserm)
US20050164164A1	N	N	N	N	N	N	N	Y	N	Y	P	Hiv-1 virus tat-protein mutants	Biomerieux S.A.
US20050175627A1	Y	N	Y	N	N	N	N	N	N	N	T/P	HIV pharmaccines	Oxxon Therapeutics Ltd.

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Patent Number	Prime Boost	Protein	Peptide	Peptide Formulation	Epitopes	Conjugates	Peptide Screening	Antibodies to HIV	Antibodies Screening Library	TAT-base Vaccine	Therapeutic v.	Title	Assignee/ Applicant
US20050176929A1	N	N	Y	N	N	N	N	N	N	Y	T/P	Hiv-1 subtype isolate regulatory/accessory genes, and modifications and derivatives thereof	The South African Medical Research Council; University of Cape Town
US20050180984A1	N	N	Y	N	N	N	N	N	N	N	N	Modulating vaccine against HIV-1 Nef protein induced lymphocyte depletion	Bond Vincent C.; Powel Michael; Huang Ming B.; James Cleve
US20050221288A1	N	Y	N	N	N	N	N	Y	N	Y	N	Variant tat proteins and methods for use thereof	University of Medicine and Denistry of New Jersey
US20050271686A1	N	Y	N	N	N	N	N	N	N	N	T/P	HIV vaccine	The University of Western Ontario
US20060094017A1	N	N	Y	N	N	Y	N	N	N	N	P	Immunogens for hiv vaccine	Merck & Co., Inc.
US20060121538A1	N	N	Y	N	N	N	Y	N	N	N	P	Peptides having affinity for the gp120 viral protein and use thereof	Commissariat a L'Energie Atomique
US20060153865A1	N	N	Y	Y	N	N	N	N	Y	N	N	Antigenic peptides	State Research Center of Virology and Biotechnology
US20060188884A1	N	Y	Y	N	N	Y	N	N	N	N	T/P	Enhanced hiv-1 vaccines and methods for their use	Government of the United States of America as represented by the Secretary of the Department of Health and Human Services and the National Institute of Health (NIH)
US20060204514A1	N	N	Y	N	Y	N	N	N	N	N	P	Expression of hydrophobic proteins	CSL Limited; The Council of the Queensland Institute of Medical Research
US20060210588A1	N	N	Y	Y	Y	Y	N	N	N	N	N	Hiv-peptide-carrier-conjugates	Cytos Biotechnology A.G.
US20060229432A1	N	N	Y	Y	N	N	N	Y	N	N	T/P	Gp120 specific antigens and uses thereof	Sloan-Kettering Institute for Cancer Research
US20060241027A1	N	N	Y	N	N	N	N	N	N	N	P	Hiv inhibiting proteins	Novozymes Delta Limited

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Patent Number	Prime Boost	Protein	Peptide	Peptide Formulation	Epitopes	Conjugates	Peptide Screening	Antibodies to HIV	Antibodies Screening Library	TAT-base Vaccine	Therapeutic v.	Title	Assignee/ Applicant
US20060246088A1	N	Y	N	N	N	N	N	N	N	N	P	Use of HIV-1 gp120 and gp160 proteins modified in the V3 loop for the preparation of vaccine compositions and formulations containing the same	La Fondation Mondiale Recherche et Prevention Sida
US20060275309A1	N	N	Y	N	Y	Y	Y	Y	Y	N	T	Peptide oligomers for use as hiv vaccines	University of Nottingham
US20060292167A1	N	N	Y	Y	N	N	N	N	N	N	N	Therapeutic Peptides and Vaccines	Rapid Pharmaceuticals, A.G.
US20070009549A1	N	Y	N	N	N	N	N	Y	Y	N	N	Expression and characterization of HIV-1 envelope protein associated with a broadly reactive neutralizing antibody response	Henry M. Jackson Foundation
US20070014814A1	N	Y	Y	N	Y	Y	N	Y	N	N	N	Webbed HIV envelope immunogens, methods for production and use of same	Aeras Global TB Vaccine Foundation
US20070042977A1	N	N	Y	N	N	Y	N	N	N	N	N	Vaccine	
US20070072225A1	N	N	N	N	N	N	N	Y	Y	N	N	Antibodies with simultaneous subsite specificities to protein and lipid epitopes	
US20070092525A1	N	N	Y	N	N	Y	N	Y	N	N	T/P	Polypeptide derived from gp41, a vaccine composition comprising said polypeptide, and uses for treating an infection by an hiv virus in an individual	Institut National de la Sante et de la Recherche Medicale (Inserm); Assistance Publique Hopitaux de Paris
US20070178532A1	N	N	N	N	N	N	Y	N	N	N	N	Identification, quantification, and characterization of t cells and t cell antigens	Government of the United States of America as represented by the Secretary of the Department of Health and Human Services

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Patent Number	Prime Boost	Protein	Peptide	Peptide Formulation	Epitopes	Conjugates	Peptide Screening	Antibodies to HIV	Antibodies Screening Library	TAT-base Vaccine	Therapeutic v.	Title	Assignee/ Applicant
US20070190524A1	N	N	N	N	N	N	N	Y	N	N	N	Non-M, non-O HIV-1 strains, fragments and uses	Institut National de la Sante et de la Recherche Medicale (Inserm); Assistance Publique Hopitaux de Paris; Institute Pasteur
US20070224211A1	N	N	Y	N	N	N	N	Y	N	N	T	HIV-1 glycopeptides and derivatives; preparation and applications thereof	University of Maryland Biotechnolgy Institute
US20070224212A1	N	N	Y	N	N	Y	N	N	N	N	P	Stable Peptide Mimetic of Hiv Gp41 Fusion Intermediate	Istituto di Ricerche di Biologia Molecolare P. Angeletti S.P.A.
US20070243203A1	N	N	Y	N	N	N	N	N	N	N	N	Vaccine for Prevention and Treatment of Hiv-Infection	
US20070248613A1	N	N	N	N	N	N	N	Y	N	N	T/P	Human Antibodies Interacting with Hiv Gp41	Cambridge Antibody Technology Limited
US20070292390A1	N	N	N	N	Y	N	Y	Y	N	N	P	Broadly Cross-Reactive Hiv-1 Neutralizing Human Monoclonal Antibodies	Government of the United States of America as represented by the Secretary of the Department of Health and Human Services
US20080102073A1	Y	N	N	N	N	N	N	N	N	N	P	Antigen-Antibody Complexes as HIV-1 Vaccines	International AIDS Vaccine Initiative
US20080124352A1	N	N	N	N	N	N	N	N	N	N	P	Methods to bypass CD4+ cells in the induction of an immune response	Mannkind Corporation
US20080131451A1	N	N	Y	Y	N	N	N	N	N	N	N	Epitope escape mutations	General Hospital Corporation
US20080146499A1	N	N	Y	N	N	N	N	N	N	N	T	Identification of the Precise Amino Acid Sequence of the Epitope Recognized by the Potent Neutralizing Human Anti-Hiv-1 Monoclonal Antibody Igg1b12	University of Manitoba

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Patent Number	Prime Boost	Protein	Peptide	Peptide Formulation	Epitopes	Conjugates	Peptide Screening	Antibodies to HIV	Antibodies Screening Library	TAT-base Vaccine	Therapeutic v.	Title	Assignee/ Applicant
US20080160010A1	N	N	Y	N	N	N	N	Y	N	N	N	Peptide That Elicits Neutralizing Antibodies Targeting the Hiv Co-Receptor	Government of the United States of America as represented by the Secretary of the Department of Health and Human Services
	N	N	Y	N	N	N	N	N	N	N	N	Inhibition of Hiv-1 Replication by Disruption of the Processing of the Viral Capsid-Spacer Peptide 1 Protein	V.I. Technologies, Inc.; Government of the Unitd States of America as represented by the Secretary of the Department of Health and Human Services
US20080206264A1	N	N	Y	N	N	N	Y	N	N	N	P	Constrained Hiv V3 Loop Peptides as Novel Immunogens and Receptor Antagonists	New York University
US20080220008A1	N	N	N	N	N	N	Y	Y	N	N	T/P	Mutated Hiv Nef For Modulating Immunity	Institut Gustave Roussy; Centre National de la Recherche Scientifique (CNRS)
US20080233131A1	N	N	N	N	N	N	N	N	N	N	P	Vaccine	National Institute for Biological Standards and Control
US20080248063A1	N	Y	N	N	N	N	N	N	N	N	P	Hetero-Oligomeric Hiv Envelope Proteins	Seattle Biomedical Research Institute
US20080260766A1	N	N	N	N	Y	N	N	N	N	N	T/P	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	Fundacao de Amparo A Pesquisa do Estado de Sao Paulo; Fundacao Zerbini; Universidade de Sao Paulo-USP

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Patent Number	Prime Boost	Protein	Peptide	Peptide Formulation	Epitopes	Conjugates	Peptide Screening	Antibodies to HIV	Antibodies Screening Library	TAT-base Vaccine	Therapeutic v.	Title	Assignee/ Applicant
US20080279879A1	Y	Y	N	N	N	N	N	N	N	N	P	Induction of broadly reactive neutralizing antibodies by focusing the immune response on V3 epitopes of the HIV-1 gp120 envelope	New York University
US20080317779A1	N	Y	N	N	N	N	N	N	N	Y	P	Hiv Tat-Cd4 Hybrid Molecules and Methods of Use Thereof	Novartis Vaccines and Diagnostics, Inc.
US20090023164A1	N	N	Y	N	N	N	N	N	N	N	N	Compositions and methods for the detection of HIV-1/HIV-2 Infection	Government of the United States of America as represented by the Secretary of the Department of Health and Human Services
US4735896A	N	N	Y	N	N	N	N	N	N	N	N	Synthetic peptide and process of using same for the detection and diagnosis of AIDS and pre-AIDS conditions	United Biomedical, Inc.
US4772547A	N	N	Y	N	N	N	N	Y	N	N	N	HTLV-III envelope peptides	Hoffmann- La Roche & Co.
US4833072A	N	N	Y	N	N	N	N	N	N	N	N	Antigentic peptides and process for their preparation	Spoea, Spojene Podniky
US4957737A	N	N	Y	N	N	N	N	N	N	N	N	HTLV-III (LAV) envelope peptides	Hoffmann-La Roche Inc.
US4983387A	N	N	Y	N	N	Y	N	N	N	N	N	HIV related peptides, immunogenic antigens, and use therefor as subunit vaccine for AIDS virus	Viral Technologies, Inc.
US5030449A	N	N	Y	N	N	N	N	N	N	N	N	Synthetic vaccine against AIDS virus	The United States of America as represented by the Secretary of the Department of Health and Human Services

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Patent Number	Prime Boost	Protein	Peptide	Peptide Formulation	Epitopes	Conjugates	Peptide Screening	Antibodies to HIV	Antibodies Screening Library	TAT-base Vaccine	Therapeutic v.	Title	Assignee/ Applicant
US5039522A	N	N	Y	N	N	N	N	N	N	N	P	Immunogens containing peptides with an attached hydrophobic tail for adsorption to hepatitis B virus surface antigen	New York Blood Center, Inc.
US5043262A	N	Y	N	N	N	N	N	N	N	N	N	Protein, sequences containing the VPU gene therefore, vectors, methods of preparation and use	Dana-Farber Cancer Institute
US5051496A	N	N	Y	N	N	N	N	N	N	N	N	Peptides related to human immunodeficiency virus II (HIV-2)	Institut Pasteur
US5075211A	N	N	Y	N	N	N	N	N	N	N	N	Synthetic antigen for the detection of AIDS-related disease	Genetic Systems Corporation
US5142025A	N	Y	N	N	N	N	N	N	N	N	N	Recombinant HTLV-III proteins and uses thereof	Repligen Corporation
US5260189A	N	N	Y	Y	N	Y	N	N	N	N	N	Synthetic HIV-like peptides their compositions and uses	Immunodiagnostics, Inc.
US5443828A	N	N	Y	N	N	N	N	N	N	N	N	Chimeric HIV-2 gag particles	Korea Green Cross Corporation
US5459238A	N	N	Y	N	N	N	N	N	N	N	N	Peptide fragments of HIV	United Biomedical, Inc.
US5464933A	N	N	Y	N	N	N	N	N	N	N	N	Synthetic peptide inhibitors of HIV transmission	Duke University
US5476765A	N	N	Y	N	N	N	N	N	N	N	N	Synthetic peptide compositions with immunoreactivities to antibodies to HTLV and as vaccines	United Biomedical, Inc.
US5480966A	N	N	Y	Y	N	N	N	N	N	N	N	Peptides derived from the envelope glycoprotein of HIV viruses, their applications to the detection of infection caused by these viruses and to the vaccination against AIDS	Clonatec, S.A.

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Patent Number	Prime Boost	Protein	Peptide	Peptide Formulation	Epitopes	Conjugates	Peptide Screening	Antibodies to HIV	Antibodies Screening Library	TAT-base Vaccine	Therapeutic v.	Title	Assignee/ Applicant
US5576000A	Y	N	Y	N	N	N	N	N	N	N	P	Molecular clones of HIV-1 viral strains MH-ST1 and BA-L, and uses thereof	Government of the United States of America as represented by the Secretary of the Department of Health and Human Services
US5580563A	N	N	Y	Y	N	N	N	N	N	N	P	Multiple antigen peptide system having adjuvant properties, vaccines prepared therefrom and methods of use thereof	Rockefeller University
US5589175A	N	N	Y	Y	N	N	N	N	N	N	N	Peptides for induction of neutralizing antibodies against human immunodeficiency virus	Syntello Vaccine Development KB
US5606030A	N	N	N	N	N	Y	N	N	N	N	N	Coconjugates of OMPC, HIV related peptides and anionic moieties	Merck & Co., Inc.
US5614612A	N	Y	N	N	N	N	N	N	N	N	N	Purified gp120 compositions retaining natural conformation	Haigwood, Nancy L.; Scandella, Carl
US5639854A	N	N	Y	N	N	N	N	N	N	N	N	Tandem synthetic HIV-1 peptides	Connaught Laboratories Limited
US5652333A	N	N	Y	N	N	N	N	N	N	N	N	gC1q receptor, HIV-1 gp120 region binding thereto, and related peptides and targeting antibodies	Tanox Biosystems, Inc.
US5688914A	N	N	Y	N	N	Y	N	N	N	N	P	Composition containing a B epitope of the envelope glycoprotein of a retrovirus and a T epitope of another distinct protein of this retrovirus	Institut Pasteur; Universite Pierre et Marie Curie
US5709879A	N	Y	N	N	N	N	N	N	N	N	P	Vaccine compositions containing liposomes	Chiron Corporation
US5756666A	N	N	Y	N	N	N	Y	N	N	N	P	Peptides capable of inducing immune response to HIV	Ajinomoto Co., Inc.

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Patent Number	Prime Boost	Protein	Peptide	Peptide Formulation	Epitopes	Conjugates	Peptide Screening	Antibodies to HIV	Antibodies Screening Library	TAT-base Vaccine	Therapeutic v.	Title	Assignee/ Applicant
US5763160A	N	N	Y	N	N	N	N	N	N	N	T/P	Synthetic peptides and process of using same for the detection of antibodies to human immunodeficiency virus (HIV) gp120 envelope protein, diagnosis of AIDS and pre-AIDS conditions and as vaccines	United Biomedical, Inc.
US5763574A	N	N	Y	N	N	Y	N	N	N	N	N	HIV-specific synthetic antigens and their use	Merck & Co., Inc.
US5807979A	N	N	Y	N	N	N	N	N	N	N	N	Synthetic, three-dimensionally stabilized polypeptide mimics of HIV	The Scripps Research Institute
US5817315A	N	Y	N	N	N	N	N	N	N	N	T/P	Recombinant vaccine	Andrew Atkin
US5817316A	N	N	Y	N	N	N	N	N	N	N	N	Immunogenic peptides, antibodies and uses thereof relating to CD4 receptor binding	Dana-Farber Cancer Instistute
US5817318A	N	N	Y	N	N	N	N	N	N	N	N	Synthetic peptides for an HIV-1 vaccine	Connaught Laboratories Limited
US5853724A	N	N	Y	N	Y	Y	N	N	N	N	N	Dampening of an immunodominant epitope of an antigen for use in plant, animal and human vaccines and immunotherapies	Government of the United States of America as represented by the Secretary of the Department of Health and Human Services
US5861243A	N	N	Y	N	N	N	N	N	N	N	N	Vaccine for protection against HIV infections, process for preparing same and their use as diagnostic and agent immunotherapeutic agent	Chemotherapeutisches Forschunginstitut Georg Speyer-Haus Zu Frankfurt A.M.
US5871746A	N	N	Y	N	N	N	N	N	N	N	N	Cytotoxic T lymphocyte-inducing lipopeptides and use as vaccines	Institut National de la Sainte et de la Recherche Medicale (INSERM); Institut Pasteur

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Patent Number	Prime Boost	Protein	Peptide	Peptide Formulation	Epitopes	Conjugates	Peptide Screening	Antibodies to HIV	Antibodies Screening Library	TAT-base Vaccine	Therapeutic v.	Title	Assignee/ Applicant
US5871933A	N	N	Y	N	N	N	N	N	N	N	P	HTLV-I and HTLV-II peptide antigens and methods	Genelabs Technologies, Inc.
US5876724A	Y	Y	N	Y	N	N	N	N	N	N	P	Induction of neutralizing antibody against viral infection by synergy between virus envelope glycoprotein and peptides corresponding to neutralization epitopes of the glycoprotein	Institut Pasteur
US5891994A	N	N	Y	Y	N	Y	N	N	N	N	N	Methods and compositions for impairing multiplication of HIV-1	Thymon L.L.C.
US5911989A	N	N	N	N	N	N	N	Y	N	N	N	HIV-vaccines	Polymun Scienc Immunologische
US5952474A	N	Y	N	N	N	N	N	N	N	N	N	Fusion glycoproteins	Public Health Research Institute
US5961970A	N	Y	Y	N	N	N	N	N	N	N	P	Submicron emulsions as vaccine adjuvants	Pharmos Corporation; The United States of America as represented by the Secretary of the Army
US5965135A	N	N	Y	N	N	N	N	N	N	N	N	HIV-1 virus isolates of a subtype and its differential diagnostics	Chemotherapeutisches Forschungsinstitut
US5968514A	N	N	Y	N	N	N	N	N	N	N	P	Methods for stimulating immune responses in a host through the administration of superantigen peptides derived from human immunodeficiency virus type 1 Nef	University of Florida
US5972339A	Y	N	Y	N	N	N	N	N	N	N	P	Method of eliciting anti-HIV-1 helper T cell responses	General Hospital Corporation
US5980900A	N	N	Y	Y	N	N	N	N	N	N	N	Amino acid DNA sequences related to genomic RNA of human immunodeficiency virus (HIV-1)	Institut Pasteur; Centre National de la Recherche Scientifique (CNRS)
US5981170A	N	N	Y	N	N	N	N	N	N	N	N	Peptides, artificial antigens and immunoassay kits	Ferring AB

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Patent Number	Prime Boost	Protein	Peptide	Peptide Formulation	Epitopes	Conjugates	Peptide Screening	Antibodies to HIV	Antibodies Screening Library	TAT-base Vaccine	Therapeutic v.	Title	Assignee/ Applicant
US5994516A	N	Y	N	N	N	N	N	N	N	N	N	Mutated proteins encoded by a lentivirus mutated env gene, peptide fragments and expression vectors	Centre National de la Recherche Scientifique (CNRS)
US6017537A	N	Y	N	N	N	N	N	N	N	N	P	Formyl methionyl peptide vaccine adjuvant	Connaught Laboratories Limited
US6039957A	N	N	N	N	N	N	N	N	N	N	P	Oligomeric HIV-1 envelope glycoproteins	Government of the United States of America as represented by the Secretary of the Department of Health and Human Services
US6042831A	N	N	Y	N	Y	N	N	N	N	N	P	Human immunodeficiency virus type 1 (HIV-1) GP160 epitopes that are immunologically homologous to epitopes located in the class I major histocompatibility complex (MHC) heavy chain .alpha.-1 domain	La Fondation Mondiale Recherche et Prevention Sida
US6042836A	N	N	Y	N	N	N	N	N	N	N	N	HIV envelope polypeptides	Genentech, Inc.
US6056963A	N	Y	N	N	N	N	N	N	N	N	N	Immunogenic compositions comprising glycosylated and deglycosylated monomeric and dimeric forms of HIV-2 enveloped glycoproteins	Institut Pasteur; Centre National de la Recherche Scientifique (CNRS)
US6090392A	N	N	Y	N	N	N	N	N	N	N	N	HIV envelope polypeptides and vaccine	Genentech, Inc.
US6132721A	N	Y	N	N	N	N	N	N	N	Y	P	Non-Toxic immunogens derived from a retroviral regulatory protein, antibodies, preparation method therefor, and pharmaceutical compositions containing same	Neovacs

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Patent Number	Prime Boost	Protein	Peptide	Peptide Formulation	Epitopes	Conjugates	Peptide Screening	Antibodies to HIV	Antibodies Screening Library	TAT-base Vaccine	Therapeutic v.	Title	Assignee/ Applicant
US6140059A	N	Y	N	N	N	N	N	N	N	N	N	Methods for the obtention of human immunodeficiency virsus Type 1 envelope glycoproteins in native and oligomeric form employing recombinant chimeric antigens containing collagenase recognition sites.	Manfred Schawaller
US6149910A	N	N	Y	N	N	N	N	N	N	N	N	Peptides for the detection of HIV-1 group O	Ortho-Clinical Diagnostics, Inc.
US6210873B1	N	N	N	N	N	N	N	N	N	N	P	Methods and compositions for the priming of specific cytotoxic T-lymphocyte response	Board of Regents, The University of Texas System
US6235881B1	N	N	Y	N	N	N	N	N	N	N	N	Polypeptides encoded by novel HIV-2 proviruses	The Regents of the University of California
US6284252B1	N	Y	N	N	N	N	N	N	N	Y	N	Transdominant TAT variants of the human immunodeficiency virus	Transgene S.A.
US6287568B1	N	N	N	N	N	N	Y	N	N	N	P	Methods relating to immunogenic dextran-protein conjugates	The Trustees of Columbia University in the City of New York
US6290963B1	N	N	Y	N	N	N	N	N	N	N	P	Anti-HIV compositions containing native and recombinant peptides	Government of the United States of America as represented by the Secretary of the Department of Health and Human Services
US6335183B1	N	Y	Y	N	N	N	N	N	N	N	P	Stress proteins and uses therefor	Whitehead Institute for Biomedical Research
US6420141B1	N	Y	N	N	N	N	N	N	N	Y	T/P	Anti-HIV immunogens (toxoids), preparation methods and use for preventing and treating aids	Neovacs
US6451325B1	N	Y	N	N	N	N	N	N	N	N	N	Adjuvant formulation comprising a submicron oil droplet emulsion	Chiron Corporation

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US6455265B1	N	N	Y	N	N	N	N	N	N	N	P	Method for obtaining vaccines for preventing the pathogenic effects related to a retroviral infection	Mymetics S.A.
US6534064B1	N	Y	N	N	N	N	N	N	N	N	T/P	Stabilized protein particles for inducing cellular immune responses	Chiron Corporation
US6534285B1	N	N	Y	N	N	N	N	N	N	N	N	Molecularly cloned acquired immunodeficiency syndrome polypeptides and their methods of use	Genentech, Inc.
US6596497B1	N	N	N	N	N	N	N	N	Y	N	N	Screening of antiviral compounds targeted to the HIV-1 gp41 core structure	New York Blood Center, Inc.
US6706859	N	N	Y	N	N	N	N	N	N	N	N	HIV peptides, antigens, vaccine compositions, immunoassay kit and a method of detecting antibodies induced by HIV	Bionor Immuno A.S.
US6818627	N	N	N	N	N	Y	N	N	N	N	N	Functional fragments of HIV-1 Vpr protein and methods of using the same	The Trustees of the University of Pennsylvania
US6911527	N	N	Y	N	N	N	N	N	N	N	N	HIV related peptides	Government of the United States of America as represented by the Secretary of the Department of Health and Human Services
US6927031	N	N	N	N	N	N	Y	N	N	N	N	Methods for identifying polypeptide factors interacting with RNA	Rigel Pharmaceuticals, Incorporated
US7118751	N	N	Y	N	N	N	N	N	N	N	N	DNA vaccines encoding antigen	Trubion Pharmaceuticals, Inc.
US7179468	N	Y	N	N	N	N	N	N	N	N	N	Antigen for developing neutralizing antibodies to human immunodeficiency virus	Cornell Research Foundation, Inc.

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Patent Number	Prime Boost	Protein	Peptide	Peptide Formulation	Epitopes	Conjugates	Peptide Screening	Antibodies to HIV	Antibodies Screening Library	TAT-base Vaccine	Therapeutic v.	Title	Assignee/ Applicant
WO 2007112079A2	N	N	N	N	Y	Y	N	N	N	N	T	Multivalent Immunogen	Duke University
WO1988008718A1	N	N	N	N	N	N	N	N	N	N	P	Intranasal immunization against viral infection using viral glycoprotein subunit vaccine	Molecular Engineering Associates, Inc.
WO1988009181A2	N	N	Y	N	N	Y	N	Y	N	N	T/P	Monoclonal antibodies neutralizing HIV-1	Tanox Biosystems, Inc.; Baylor College of Medicine
WO1989005821A1	N	N	N	N	N	Y	N	Y	N	N	P	HIV-related antigens and antibodies	Arch Development Corporation
WO1989009618A1	N	N	Y	N	N	N	N	N	N	N	P	Method for controlling HIV infectivity and vaccines for use therein	Vanderbilt University
WO1990002568A1	N	N	Y	N	N	N	N	N	N	N	P	HIV-1 envelope nuteins lacking hypervariable domains	Chiron Corporation
WO1990003984A1	N	N	Y	N	Y	N	N	N	N	N	T/P	HIV proteins and peptides useful in the diagnosis, prophylaxis or therapy of AIDS	Repligen Corporation
WO1990015078A1	N	N	N	N	N	N	N	Y	Y	N	T	Human monoclonal antibodies to HIV-1MN gp120	Scott, Charles, F., Jr.; Carson, Helen, F.; White-Scharf, Mary, E.; Silver, Sandra; Rusche, James, R.
WO1991001996A1	N	N	Y	Y	N	N	N	N	N	N	T/P	Peptide fragments of HIV	Medical Research Council; The Chancellor, Masters and Scholars of the…; McMichael, Andrew James; Nixon, Douglas, Fraser; Townsend, Alain, Robert, Michael
WO1991004051A1	N	N	Y	Y	N	N	N	N	N	N	T	Peptides including CTL epitopes of HIV proteins and use thereof	Medimmune, Inc.; Government of the United States of America as represented by the Secretary of the Department of Health and Human Services; Fuerst, Thomas; Koenig, Scott

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Patent Number	Prime Boost	Protein	Peptide	Peptide Formulation	Epitopes	Conjugates	Peptide Screening	Antibodies to HIV	Antibodies Screening Library	TAT-base Vaccine	Therapeutic v.	Title	Assignee/ Applicant
WO1991004273A2	N	N	Y	Y	Y	N	N	Y	Y	N	N	Novel peptides associated with the CD4 binding region of gp120 and their methods of use	IDEC Pharmaceuticals Corp.
WO1991007425A1	N	Y	N	N	N	N	N	N	N	N	T	Non-replicating recombinant-made retroviral particles used as antiviral agents and immunogens	Oncogen Limited Partnership
WO1991009625A1	N	N	Y	N	N	N	N	Y	N	N	P	Monoclonal antibodies which neutralize HIV-1 infection and their anti-idiotypes	Tanox Biosystems, Inc.; Chang, Tse, Wen; Fung, Michael, S., C.; Sun, Cecily, R., Y.; Sun, Bill, N., C.; Chang, Nancy, T.
WO1991009869A1	N	N	Y	Y	N	N	N	N	N	N	T/P	HIV-1 core protein fragments	Medical Research Council; The Chancellor, Masters and Scholars of the …; McMichaell, Andrew, James; Nixon, Douglas, Fraser; Townsend, Alain, Robert, Michael; Gotch, Frances, Margaret
WO1991009872A1	N	N	Y	N	N	Y	N	Y	N	N	T/P	Polypeptides slectively reactive with antibodies against human immunodeficiency virus and vaccine comprising the polypeptides	Univax Biologics, Inc.; Shafferman, Avigdor
WO1991011198A1	N	N	N	N	Y	N	N	Y	N	N	T/P	Neutralizing and/or ADCC mediating monoclonal HIV antibody	Wahren, Britta; Broliden, Per, Anders; Morein, Bror; Åkerblom, Lennart
WO1991012332A1	N	N	N	N	N	N	N	Y	N	N	N	Monoclonal antibodies for recognizing a peptide linked to a major histocompatibility antigen	Institut National de la Sante et de la Recherche Medicale (Inserm); Huynh Thien Duc, Guy; Rucay, Pierre; Kourilsky, Philippe
WO1991013909A1	N	N	Y	Y	N	N	N	Y	N	N	T/P	Synthetic polypeptides	Proteus Molecular Design Limited; Fishleigh, Robert, Vincent; Robson, Barry

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Patent Number	Prime Boost	Protein	Peptide	Peptide Formulation	Epitopes	Conjugates	Peptide Screening	Antibodies to HIV	Antibodies Screening Library	TAT-base Vaccine	Therapeutic v.	Title	Assignee/ Applicant
WO1991013910A1	N	N	N	N	N	N	N	N	N	N	N	Peptides stimulating cytotoxic T cells immune to HIV RT	Government of the United States of America as represented by the Secretary of the Department of Health and Human Services
WO1991015224A1	N	Y	N	N	N	N	N	N	N	Y	T	Inhibition of disease associated with immunodeficiency virus infection	Smithkline Beecham Biologicals S.A.; Debouck Christine, Marie; Brake, David, Alan
WO1992000098A1	N	N	N	N	N	Y	N	N	N	N	T/P	Methods of inducing immune response to AIDS virus	Zagury, Daniel; Imbert, Jean-Claude; Salaun, Jean-Jacques; Zirimwamba, Lurhuma
WO1992000997A1	N	N	Y	Y	N	N	N	Y	Y	N	T	Synthetic peptides and mixtures thereof for detecting HIV antibodies	IAF Biochem International Inc.
WO1992007878A1	N	N	Y	N	N	N	N	Y	Y	N	T/P	Neutralizing human monoclonal antibodies specific for the V3 loop and CD-4 binding site of HIV-1 gp120	The Public Health Research Institue; Tilley, Shermaine, A.; Pintner, Abraham
WO1992008491A1	N	N	N	N	Y	N	N	N	N	N	P	Conjugates of anti-idiotype antibodies and carriers and their use in epitope-directed immunization	Tanox Biosystems, Inc.
WO1992022572A1	N	N	Y	Y	N	N	Y	N	N	N	P	New HIV-1 gag and env peptides, diagnostic	Replico Medical AB; Blomberg, Jonas; Pipkorn, Rüdiger
WO1992022579A1	N	N	Y	N	N	N	Y	N	N	N	P	Mimic peptides of gp120	Immulogic Pharmaceutical Corporation
WO1992022654A1	Y	N	N	N	N	N	N	N	N	N	P	Vaccine and treatment method of human immunodeficiency virus infection	Microgenesys, Inc.
WO1993003766A1	N	N	Y	Y	Y	Y	N	N	N	N	P	Multiple antigen peptides for use as HIV vaccines	Repligen Corporation; The Rockefeller University

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Patent Number	Prime Boost	Protein	Peptide	Peptide Formulation	Epitopes	Conjugates	Peptide Screening	Antibodies to HIV	Antibodies Screening Library	TAT-base Vaccine	Therapeutic v.	Title	Assignee/ Applicant
WO1993013201A1	N	N	N	N	N	N	N	N	N	N	N	Lipopolysaccharide binding opsonin inhibitor and methods of use thereof	The Rockefeller University
WO1993017705A1	N	Y	N	N	N	N	N	Y	N	N	T/P	Selectively deglycosylated human immunodeficiency virus type 1 envelope vaccines	President and Fellows of Harvard College
WO1993018160A1	N	N	N	N	N	Y	N	N	N	N	T	Anti-viral fusion peptides	Prendergast, Kenneth, Francis
WO1993020103A2	N	N	Y	N	N	N	N	N	N	N	P	Peptides of an antigen, capable of recognition by or induction of cytotoxic T lymphocytes, and method of their identification	Isis Innovation Limited; Hill, Adrian, Vivian, Sinton; Gotch, Frances, Margaret; Elvin, John; McMichael, Andrew, James; Whittle, Hilton, Carter
WO1993020104A1	N	N	Y	N	N	N	N	Y	N	N	P	Monoclonal antibodies against a carbohydrate-dependent epitope related to the V2 region of HIV-1 gp120	The Public Health Research Institute; Tilley, Shermain; Pinter, Abraham
WO1993020840A1	Y	Y	Y	Y	N	N	N	N	N	N	T/P	Induction of CTL responses	British Bio-Technology Limited; Layton, Guy, Timothy; Burns, Nigel, Robert; Adams, Sally, Elizabeth; Kingsman, Alan, John; Kingsman, Susan, Mary; Harris, Stepehn, John; Gearing, Andrew, John, Hubert
WO1993021218A1	N	N	Y	Y	N	Y	N	Y	N	N	P	Synthetic polypeptides derived from the HIV envelope glycoprotein	Proteus Molecular Design Limited; Fishleigh, Robert, Vincent; Robson, Barry; Aston, Roger
WO1993025680A1	N	N	Y	N	N	Y	N	Y	N	N	P	Endogenous ligands for CDR4 of T-cell receptor "beta" chains and genes encoding the same	Colorado State University Research Foundation
WO1994002614A1	N	N	Y	N	N	N	N	Y	N	N	T/P	Peptides that mimic gp120 HIV epitope	Medical Research Council; Butler, Peter, Jonathan, Gasking; Hacking, Graeme, Norman, Varey

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Patent Number	Prime Boost	Protein	Peptide	Peptide Formulation	Epitopes	Conjugates	Peptide Screening	Antibodies to HIV	Antibodies Screening Library	TAT-base Vaccine	Therapeutic v.	Title	Assignee/ Applicant
WO1994002626A1	N	N	N	N	Y	Y	Y	N	N	N	N	Immunological conjugates of OMPC and HIV-specific selected principal neutralization epitopes	Merck & Co., Inc.; Keller, Paul, M.; Conley, Anthony, J.; Shaw, Alan, R.; Arnold, Beth, A.
WO1994003487A1	N	N	Y	N	N	N	N	Y	N	N	P	New Peptides, antibodies raised against peptides and means for blocking said antibodies application as medicaments, pharmaceutical compositions and utilization methods	Zagury, Jean-François
WO1994022477A1	N	Y	N	N	N	N	N	Y	N	N	T/P	HIV-1 vaccines, antibody compositions related thereto, and therapeutic and prophylactic uses thereof	Progenics Pharmeceuticals Inc; Hasel Karl W; Maddon Paul J
WO1994026776A1	N	Y	N	N	N	N	N	N	N	N	T/P	Therapeutic Compounds	Biomolecular Research Institute Ltd.; MacFarlane Burnet Centre for Medical Research Ltd.; Commonwealth Scientific and Industrial Research Organisation; Azad, Ahmed, Abdullah; Curtain, Cyril, C.; Greenway, Alison, Louise; McPhee, Dale, Alan; MacReadie, Ian
WO1995011998A1	N	N	Y	Y	N	N	Y	N	N	N	T/P	Structured synthetic antigen libraries as diagnostics, vaccines and therapeutics	United Biomedical, Inc.
WO1995026361A1	N	Y	N	N	N	N	N	Y	Y	N	T/P	VPR and VPX proteins of HIV	Biomolecular Research Institute, Ltd.
WO1995032000A1	N	Y	N	N	Y	N	N	N	N	N	P	HIV polyprotein immunogens	Microgenesys, Inc.
WO1996019584A1	Y	N	N	N	N	N	N	Y	N	N	P	Chimeric antibodies comprising antigen binding sites and B and T cell epitopes	Mount Sinai School of Medicine of the City University of New York

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Patent Number	Prime Boost	Protein	Peptide	Peptide Formulation	Epitopes	Conjugates	Peptide Screening	Antibodies to HIV	Antibodies Screening Library	TAT-base Vaccine	Therapeutic v.	Title	Assignee/ Applicant
WO1996020006A1	N	N	Y	N	N	Y	N	N	N	N	T/P	Vaccine against AIDS comprising a peptide sequence of HIV	Medical Research Council; Rowland-Jones, Sarh; Gotch, Frances; McMichael, Andrew, James
WO1997046697A2	N	N	N	N	N	N	N	Y	N	N	N	Antibodies against a complex of CD4 and a chemokinen receptor domain, and their use against HIV infections	United Biomedical, Inc.
WO1998000535A2	N	Y	Y	N	N	N	N	N	N	N	P	Method for inhibiting HIV-1 infection, drug screens, and methods of diagnosis and prognosis of susceptibility ot HIV infection	Dana-Farber Cancer Institute; Leukosite Inc.; Sodroski Joseph G; Newman Walter; Choe Hye Ryun; Wu Lijun; Gerard Norma; Gerard Craig
WO1998000695A2	N	N	Y	N	N	N	Y	N	N	Y	T	TAT-SF: Cofactor for stimulation of transcriptional elongation by HIV-1 Tat	Massachusetts Inst Technology; Sharp Phillip A; Zhou Qiang
WO1998022589A2	N	N	N	N	N	N	N	N	N	N	T	Survivin, a protein that inhibits cellular apoptosis, and its modulation	Yale University
WO1998023960A1	N	N	Y	N	Y	N	N	N	N	N	N	Assay method for peptide specific T-cells	Isis Innovation Limited
WO1998041536A1	N	Y	N	N	N	N	N	Y	N	N	P	Glycosylation deficient SIV and HIV envelope glycoproteins	President and Fellows of Harvard College
WO1998050423A3	N	N	Y	N	N	N	N	N	N	N	N	Peptide Analogues, and their uses in particular in pharmaceutical compositions and for diagnosis	Muller, Sylviane
WO1999016466A2	N	N	N	N	N	N	N	N	N	N	P	Vaccine compositions and methods of enhancing vaccine efficacy	Beth Israel Deaconess Medical Center

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Patent Number	Prime Boost	Protein	Peptide	Peptide Formulation	Epitopes	Conjugates	Peptide Screening	Antibodies to HIV	Antibodies Screening Library	TAT-base Vaccine	Therapeutic v.	Title	Assignee/ Applicant
WO1999016883A2	N	Y	N	N	N	N	N	N	N	N	P	Stabilization of envelope glycoprotein trimers by disulfide bonds introduced into a gp41 glycoprotein ectodomain	Dana-Farber Cancer Institute
WO1999027958A2	N	Y	N	N	N	N	N	N	N	Y	T/P	HIV-1 TAT, or derivatives thereof for prophylactic and therapeutic vaccination	Istituto Superiore di Sanita
WO1999053033A1	N	N	Y	N	N	N	N	N	N	N	P	Methods and compositions for high yield production of eukaryotic proteins	Vanderbilt University
WO1999066046A1	N	N	Y	N	N	Y	N	N	N	N	T/P	HIV virus mimotopes	Pasteur Merieux Serums & Vaccins
WO2000008043A2	N	N	N	N	Y	N	N	Y	N	N	P	Prevention and treatment of viral disease	The University of Montana
WO2000027880A2	N	N	Y	N	N	N	N	N	N	N	T/P	Rantes-derived peptides with anti-HIV activity	Primm S.R.L.
WO2000049038A2	N	N	Y	N	N	N	N	N	N	N	T/P	Synthetic peptide of regularoty virus protein R (VPR) of human immunodeficiency virus type 1 (HIV-1) and the utiliazation thereof	Wray, Victor
WO2000061067A2	N	Y	N	N	N	N	Y	N	N	Y	P	Anti-HIV-1 vaccine comprising the entire or part of the TAT HIV-1 protein	Centre National de la Recherche Scientifique (CNRS)
WO2000062067A1	N	N	N	N	N	Y	N	N	N	N	P	Novel transduction molecules and methods for using same	The Washington University
WO2000075181A1	N	N	Y	N	N	N	N	N	N	N	P	Polyepitopic proteinic fragments of the HIV nef protein, production and use thereof in vaccinations	Institut National de la Sante et de la Recherche Medicale (Inserm)

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Patent Number	Prime Boost	Protein	Peptide	Peptide Formulation	Epitopes	Conjugates	Peptide Screening	Antibodies to HIV	Antibodies Screening Library	TAT-base Vaccine	Therapeutic v.	Title	Assignee/ Applicant
WO2000078969A1	N	N	Y	N	N	N	N	N	Y	N	P	HIV TAT peptides and multiple peptide conjugate system	Government of the United States of America as represented by the Secretary of the Department of Health and Human Services
WO2001000648A1	N	N	N	N	N	N	N	Y	N	N	N	Proteins and uses thereof	Research Centre
WO2001011048A2	N	N	Y	Y	N	N	N	N	N	N	T/P	Therapeutic polypeptides and methods for using same	University of Maryland Biotechnology Institute
WO2001019958A2	N	Y	N	N	N	N	N	N	N	N	P	Stabilized soluble glycoprotein trimers	Dana-Farber Cancer Institute; The Trustees of Columbia University in the City of New York; Sodroski, Joseph, G.; Wyatt, Richard; Yang, Xinzhen; Farzan, Michael; Kwong, Peter, D.
WO2001025254A2	N	N	Y	N	N	N	N	N	N	N	P	Novel adjuvant comprising a lipopolysaccharide antagonist	University of Maryland Biotechnology Institute; Hone, David; Crowley, Richard; Shata, Mohamed
WO2001027294A1	N	N	Y	N	N	N	N	Y	Y	N	P	Virus coat proteinn/receptor chimeras and methods of use	University of Maryland Biotechnology Institute; University of Maryland Biotechnology Institute; Devico, Anthony, Louis; Fouts, Timonthy R.; Tuskan, Robert, G.
WO2001029233A2	N	N	N	N	N	N	N	N	N	N	N	Chimeric immunogenic compositions and nucleic acids encoding them	The Johns Hopkins University School of Medicine; Wu, Tzyy-Choou; Hung, Chien-Fu
WO2001030814A1	N	Y	N	N	N	N	N	N	N	N	P	Deglycosylated env/CD4 complex and the use thereof for vaccination against HIV	Aventis Pasteur S.A.; Boudet, Florence; Chevalier, Michel; Dubayle, Jean; El Habib, Raphaëlle
WO2001032712A2	N	Y	N	N	Y	N	N	Y	N	N	P	Antibody diversity generation	Maxygen, Inc.

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Patent Number	Prime Boost	Protein	Peptide	Peptide Formulation	Epitopes	Conjugates	Peptide Screening	Antibodies to HIV	Antibodies Screening Library	TAT-base Vaccine	Therapeutic v.	Title	Assignee/ Applicant
WO2001049711A2	N	N	Y	N	N	N	N	N	N	N	T/P	Nucleic acids encoding (poly)peptides having chips activity	Jari Pharmaceuticals B.V.
WO2001082963A2	N	N	Y	N	Y	N	N	N	N	N	T	Eptitope synchronization in antigent presenting cells	CTL Immunotherapies Corp.
WO2001083535A2	N	N	Y	N	N	Y	N	N	N	N	P	Peptides for use as a vaccine and/or treatment for HIV infection	Simon Fraser University; The Scrips Research Institute
WO2002024149A2	N	Y	Y	N	N	Y	Y	N	N	N	P	Immungen	Duke University
WO2002026254A2	N	N	N	N	Y	Y	N	N	N	N	T	Non-replicative particulate vaccine delivery system and methods of making and using same	The UAB Research Foundation
WO2002034909A2	N	N	Y	N	N	N	N	Y	Y	N	N	Engineered chimera of protein fragments and methods of use thereof	Abbott Laboratories
WO2002051865A2	N	N	Y	N	N	N	N	N	N	N	T/P	Proteinic antigens inducing antibodies neutralising HIV virus	Aventis Pasteur S.A.
WO2002069691A2	N	N	Y	N	N	N	N	N	N	N	P	Immunogenic HIV peptides for use as reagaents and vaccines	Government of the United States of America as represented by the Secretary of the Department of Health and Human Services, Centers for Disease Control and Prevention, Technology Transfer Office; Brown University Research Foundation
WO2002074795A2	N	N	N	N	N	N	N	N	N	N	N	Recombinant oligomeric protein complexes with enhanced immunogenic potential	Vlaams Interuniversitair Instituut Voor Biotechnologie VZW
WO2003006056A2	N	Y	N	N	N	N	N	N	Y	N	P	End-locked five-helix protein	Zhou, Genfa

3.2 Master Spreadsheet

Patent Number	Prime Boost	Protein	Peptide	Peptide Formulation	Epitopes	Conjugates	Peptide Screening	Antibodies to HIV	Antibodies Screening Library	TAT-base Vaccine	Therapeutic v.	Title	Assignee/ Applicant
WO2003025002A2	N	N	Y	N	N	N	N	N	N	N	T/P	Method and compositions of defensin-antigen fusion proteins and chemokine-antigen fusions proteins as vaccines for tumors and viral infection	Government of the United States of America as represented by the Secretary of the Department of Health and Human Services
WO2003033646A2	N	N	Y	N	N	N	N	Y	N	N	P	Compositions and methods for the modulation of viral maturation	Proteologics, Inc.
WO2003033666A2	N	N	N	N	N	N	N	Y	Y	N	N	Broadly cross-reactive neautralizing antibodies against human immunodeficiency virus selected by env-CD4-CO-Receptor Complexes	Government of the United States of America as represented by the Secretary of the Department of Health and Human Services; The Scripps Research Institute
WO2004009785A2	N	N	Y	N	N	Y	N	N	N	N	P	IgG Fc/HIV-gp120/C3d fusion protein	Duke University
WO2004014945A1	N	N	Y	N	N	N	N	Y	N	N	T/P	gp41 epitope and uses thereof for the treatment of HIV infections	Fondazione Centro S. Raffaele del Monte Tabor; Istituto Superiore di Sanita; Universita Delgli Studi di Milano
WO2004037847A2	Y	N	Y	N	N	N	N	Y	N	N	N	HIV envelope CD4 complexes and hybrids	Chiron Corporation
WO2004041310A1	N	Y	N	N	N	N	N	N	N	N	P	Preparation of chemically well-defined carbohydrate dendrimer conjugates	Danmarks Fodevare- OG Veterinaerforskning
WO2004046168A2	N	Y	Y	N	N	N	N	N	N	N	T/P	Recombinant HIV-1 subclass D envelope glycoproteins	Henry M. Jackson Foundation
WO2004053100A2	N	N	Y	N	N	N	N	Y	N	N	T/P	Immunogenic mutant human immunodeficiency virus gp120 polypeptides, and methods of using same	The Scripps Research Institute

3.2 Master Spreadsheet

Patent Number	Prime Boost	Protein	Peptide	Peptide Formulation	Epitopes	Conjugates	Peptide Screening	Antibodies to HIV	Antibodies Screening Library	TAT-base Vaccine	Therapeutic v.	Title	Assignee/ Applicant
WO2005018666A1	N	N	Y	N	N	N	N	Y	N	N	N	Polypeptide multimers having antiviral activity	Government of the United States of America as represented by the Secretary of the Department of Health and Human Services
WO2005035555A1	N	N	Y	N	N	Y	N	N	N	N	P	HIV/SIV env chimeras that promote trimerization and maintain targerts of neutralizing antibodies	Government of the United States of America as represented by the Secretary of the Department of Health and Human Services
WO2005039631A1	Y	Y	Y	N	N	N	N	N	N	Y	P	Vaccines containing the HIV Tat protein as an adjuvant for the enhancement of cytotoxic T-cell responses	Istituto Superiore di Sanita
WO2005047483A2	Y	Y	N	N	N	Y	N	N	N	N	P	Renta: An HIV immunogen and uses thereof	Medical Research Council; International AIDS Vaccine Initiative; University of Nairobi
WO2005062871A2	N	N	Y	N	Y	Y	N	N	N	Y	P	TAT linear epitope peptides and conjugates thereof for use in therapeutic compositions and assays	University of Marylalnd Biotechnology Institute
WO2005075679A2	N	N	Y	Y	N	N	Y	N	N	N	P	Method of antigenic peptide identification and relative use for the preparation of a vaccine anti HIV-1	Universita'Degli Studi di Roma "Tor Vergata" (70%); Universita'Delgi Studi di Palermo (20%); Consiglio Nazionale delle Richerche (10%)
WO2005111065A2	N	N	Y	Y	N	N	N	N	N	Y	T/P	Epitope-enhancement of a human CD4 HIV epitope	Government of the United States of America as represented by the Secretary of the Department of Health and Human Services
WO2006026508A2	N	Y	N	N	N	Y	N	Y	N	N	T/P	Modified HIV-1 envelope proteins	Henry M. Jackson Foundation; Institute of Tropical Medicine
WO2006027468A2	N	N	Y	Y	N	Y	N	N	N	N	T/P	HLA-DP4 restricted T CD4+ DU VIH epitopes and the use thereof	Commissariat a L'Energie Atomique

3.2 Master Spreadsheet

Patent Number	Prime Boost	Protein	Peptide	Peptide Formulation	Epitopes	Conjugates	Peptide Screening	Antibodies to HIV	Antibodies Screening Library	TAT-base Vaccine	Therapeutic v.	Title	Assignee/ Applicant
WO2006029338A2	N	Y	N	N	N	Y	N	Y	N	N	P	Modified HIV-1 envelope proteins	Henry M. Jackson Foundation
WO2006044410A2	N	Y	N	N	N	Y	N	N	N	N	P	A32 monoclonal antibody fusion proteins for use as HIV inhibitors and vaccines	Government of the United States of America as represented by the Secretary of the Department of Health and Human Services
WO2006067506A2	N	N	Y	N	N	N	Y	N	N	N	T/P	Resistance genes	Immunoclin Ltd.; Osaka Industrial Promotion Organization; Toppan Printing Company Limited
WO2006085959A2	Y	N	N	N	N	Y	N	N	N	N	P	Fusion proteins comprising CD4 minimal modules and methods of use thereof	Chiron Corporation
WO2006091455A2	N	N	Y	N	N	Y	N	N	N	N	P	Molecular scaffolds for HIV-1 immunogens	UAB Research Foundation
WO2006092046A1	N	Y	Y	N	N	N	N	N	N	N	P	HIV vaccine composition	Variation Biotechnolgies Inc.
WO2006102098A2	N	N	Y	N	Y	N	N	N	N	N	T/P	Immunogens for vaccines against antigenically variable pathogens and diseases	Primex Clinical Laboratories, Inc.
WO2006105993A2	N	N	N	N	N	Y	N	N	N	N	P	Method for shielding functional sites or epitopes on proteins	Istituto di Richerche di Biologia Molecolare P Angeletti Spa
WO2006110728A2	N	N	N	N	N	N	N	N	N	N	N	Immunogenic tegument aggregates	The UAB Research
WO2006110831A2	N	Y	Y	N	N	N	N	N	N	N	P	Method of inducing neutralizing antibodies to human immunodeficiency virus	Duke University
WO2006116475A2	N	N	Y	Y	N	Y	N	N	N	N	P	Immunostimulatory compositions	3M Innovative Properties Company
WO2006117584A1	N	N	N	N	N	N	N	Y	N	N	T/P	Antibody or a fragment thereof, having neutralizing activity against HIV	Institut National de la Sante et de la Recherche Medicale (Inserm)

3.2 Master Spreadsheet

Patent Number	Prime Boost	Protein	Peptide	Peptide Formulation	Epitopes	Conjugates	Peptide Screening	Antibodies to HIV	Antibodies Screening Library	TAT-base Vaccine	Therapeutic v.	Title	Assignee/ Applicant
WO2006117586A1	N	N	N	N	N	N	N	Y	N	N	T/P	Antibody or a fragment thereof, having neturalizing activity against HIV but not against IL2	Mymetics S.A.; Institut National de la Sante et de la Recherche Medicale (Inserm))
WO2006123256A2	N	Y	Y	N	Y	Y	Y	N	N	N	P	HIVCON: an HIV Immunogen and uses thereof	Medical Research Council
WO2007025178A2	N	N	Y	N	N	N	N	N	N	N	T	Rolyvalent multimeric compositions containing active polypeptides, pharmaceutical compositions and methods of using the same	New York University
WO2007025276A2	N	N	N	N	N	N	N	Y	N	N	T/P	Use of HIV envelope/CD4 complexes for the generation antibodies and as immunogenic complexes	Government of the United States of America as represented by the Secretary of the Department of Health and Human Services
WO2007030518A2	N	N	Y	N	N	N	N	N	N	N	T/P	Conformationallly Stabilized HIV envelope immunogens and triggering HIV-1 envelope to reveal cryptic V3-loop epitopes	Government of the United States of America as represented by the Secretary of the Department of Health and Human Services; Dana-Farber Cancer Institute
WO2007037265A1	N	N	N	N	N	N	N	N	N	N	N	DNA vaccine composition	National Hospital Organization; Jichi Medical University; Genomidea Inc.
WO2007039458A2	N	N	Y	N	N	Y	N	N	N	N	T/P	HIV peptide conjugates and uses thereof	Cytos Biotechnology A.G.
WO2007047916A2	N	N	Y	N	N	N	N	N	N	N	N	Multivalent HIV vaccines	Novartis Vaccines and Diagnostics, Inc.
WO2007062656A2	Y	Y	N	N	N	N	N	N	N	N	N	A nucleotide vaccine	Copenhagen University
WO2007066236A2	N	Y	N	N	N	N	N	Y	N	N	T/P	Chimeric HIV-1 glycoproteins and their biological applications	Institut de la Recherche pour le Developpement (IRD); Commissariat a L'Energie Atomique; Immunoclin Ltd.

3.2 Master Spreadsheet

Patent Number	Prime Boost	Protein	Peptide	Peptide Formulation	Epitopes	Conjugates	Peptide Screening	Antibodies to HIV	Antibodies Screening Library	TAT-base Vaccine	Therapeutic v.	Title	Assignee/ Applicant
WO2007104932A2	N	N	Y	N	N	N	N	N	N	N	T/P	Peptide sequencs and compositions	Peptcell Limited
WO2007107597A2	N	Y	N	N	N	N	N	N	Y	N	T	Immunogenic construct and a method for the prophylactic or therapeutic treatment of AIDS	Bundersrepublik Deutschland, Vertreten Durch Das Bundesministerium fur Gesundheit, Dieses Vertereten Durch Das Robert-Koch-Institut
WO2007126856A2	N	Y	Y	N	N	N	N	N	N	N	N	Covalenttly-linked complexes of HIV TAT and env proteins	Novartis Vaccines and Diagnostics, Inc.
WO2007127290A2	N	Y	N	N	N	N	N	N	N	N	T/P	Method of producing viral vaccine and therapeutic peptide antigens	Protelix, Inc.
WO2007133573A1	N	Y	N	N	N	N	N	N	N	N	P	HIV-1 immunogenic compositions	Henry M. Jackson Foundation
WO2007135684A2	N	N	Y	N	N	Y	N	N	N	N	P	Method of treatment of anti-CD4 autoimmunity	Hadasit Medical Research Services & Development Limited
WO2007144685A1	N	N	N	N	N	Y	N	N	N	N	N	CD4 mimic peptides and their uses	Commissariat a L'Energie Atomique; Sauvage-Vita Mireille; Vita, Fabio; Vito, Elena
WO2007147630A2	N	N	Y	N	N	N	N	N	N	N	T/P	Peptides regulating the surface expression of the T cell receptor	Max-Delbruck-Centrum fur Molekulare Meizin
WO2007149491A2	Y	Y	N	N	N	N	N	N	N	N	T/P	Soluble stabilized trimeric HIV env proteins and uses thereof	Progenics Pharmaceuticals Inc.; Cornell Research Foundation, Inc.
WO2008010930A2	N	N	Y	N	N	N	N	Y	N	N	T/P	HIV-1 peptides, nucleic acids, and compositions and uses thereof	University of Medicine and Dentistry of New Jersey
WO2008021295A2	N	N	N	N	N	N	N	N	N	Y	P	Compositions and methods for the treatmentn and prophylaxis of mulitple strains and subtypes of HIV-1	Thymon L.L.C.

3.2 Master Spreadsheet

Patent Number	Prime Boost	Protein	Peptide	Peptide Formulation	Epitopes	Conjugates	Peptide Screening	Antibodies to HIV	Antibodies Screening Library	TAT-base Vaccine	Therapeutic v.	Title	Assignee/ Applicant
WO2008025015A2	Y	N	N	N	N	N	N	N	Y	N	N	Epitope-transplant scaffolds and their use	Government of the United States of America as represented by the Secretary of the Department of Health and Human Services; The University of Washington
WO2008049643A2	N	N	Y	N	N	N	N	N	N	N	N	GD2 peptide mimotopes, their production and use	Charite-Universitatsmedizin Berlin
WO2008099284A2	Y	Y	N	N	N	N	N	N	N	N	T/P	HIV combination vaccine and prime boost method	The University of Western Ontario
WO2008100061A1	N	N	N	N	N	N	N	N	N	N	T/P	Novel use of HIV NC protein	Avexgen Inc.
WO2008103428A2	Y	Y	Y	N	N	N	N	N	N	N	T/P	Demannosylated HIV-1 gp120 envelope gylcoproteins, compositions thereof and methods relating thereto	Progenics Pharmaceuticals Inc.; Cornell Research Foundation, Inc.
WO2008109059A2	N	N	Y	N	N	N	N	N	N	N	P	Conserved-element vaccines and methods for designing conserved-element vaccines	The University of Washington
WO2008115199A2	N	Y	N	N	N	N	N	N	N	N	N	Chimeric virus vaccines	The University of North Carolina at Chapel Hill
WO2008133652A2	N	N	Y	N	N	N	N	N	N	N	N	Binary epitope antibodies and b cell superantigen immune stimulants	Paul Sudhir; Nishiyama Yasuhiro; Planque Stephanie
WO2008151633A2	N	N	N	N	N	N	N	N	N	N	T/P	Vectors for HIV-1 vaccine	Skau Aps

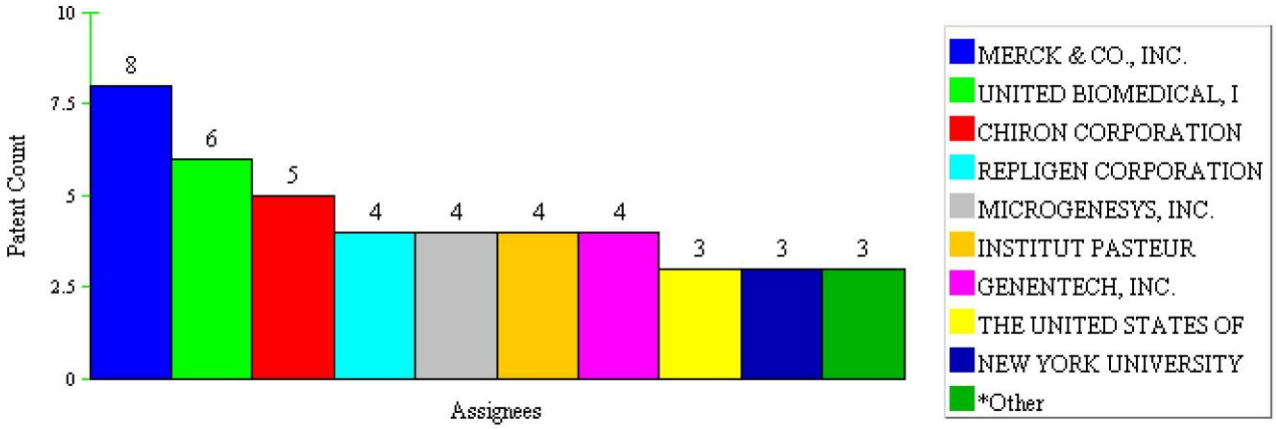
4. Patent Search Analytics

The following results reflect an analysis of the 351 relevant patents. This analysis was performed using multiple commercial analytic tools including Microsoft Excel®, Micropatent® and Aureka®.

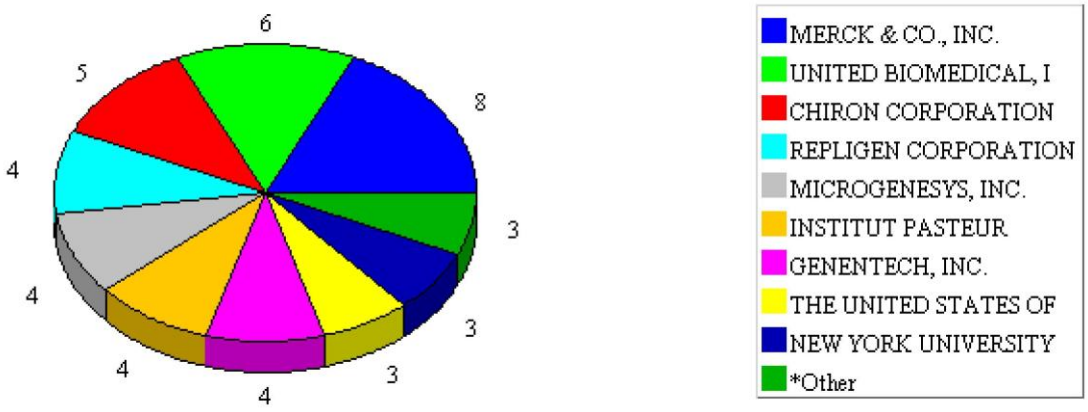
4.A. Search Analysis through MicroPatent®, Aureka® and Microsoft Excel®

4.A.1. Micropatent® Results

2D Bar Count (Patent count vs. Assignee)

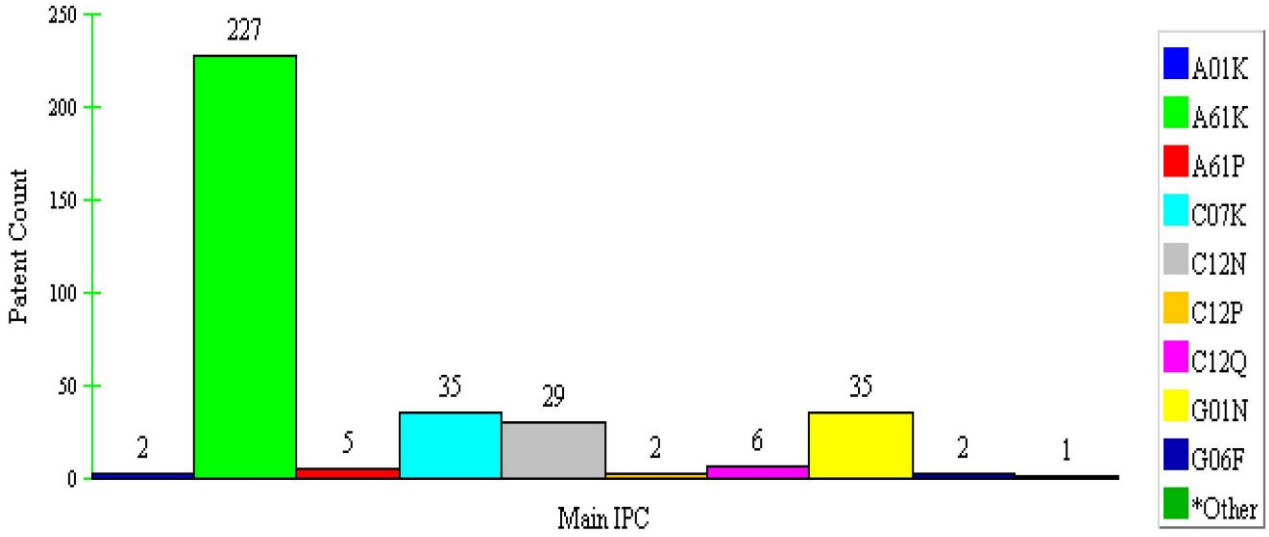


Pie Chart (Patent count vs. Assignee)

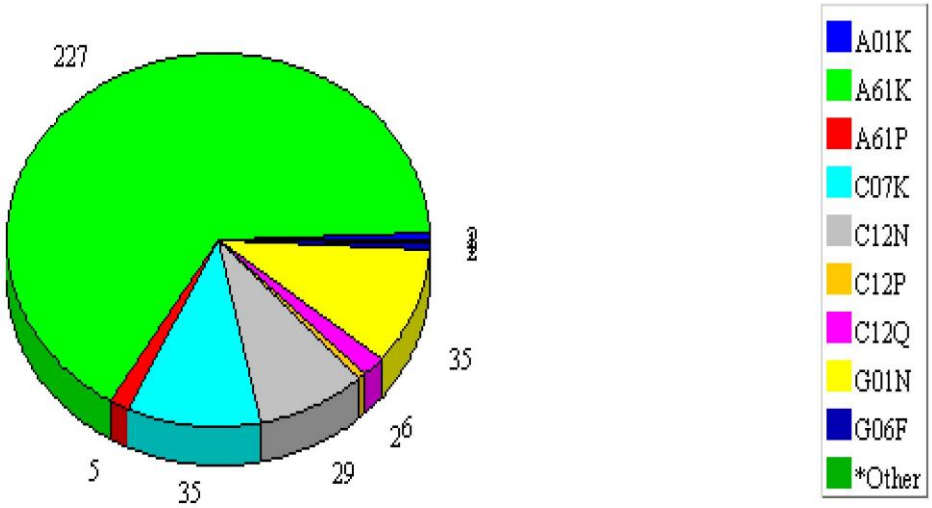


According to the above charts, Merck & Co., United Biomedical and Chiron Corporation are three top assignees in field of Protein/Peptide Vaccines.

2D Bar Chart (Patent Count vs. Main IPC Class)

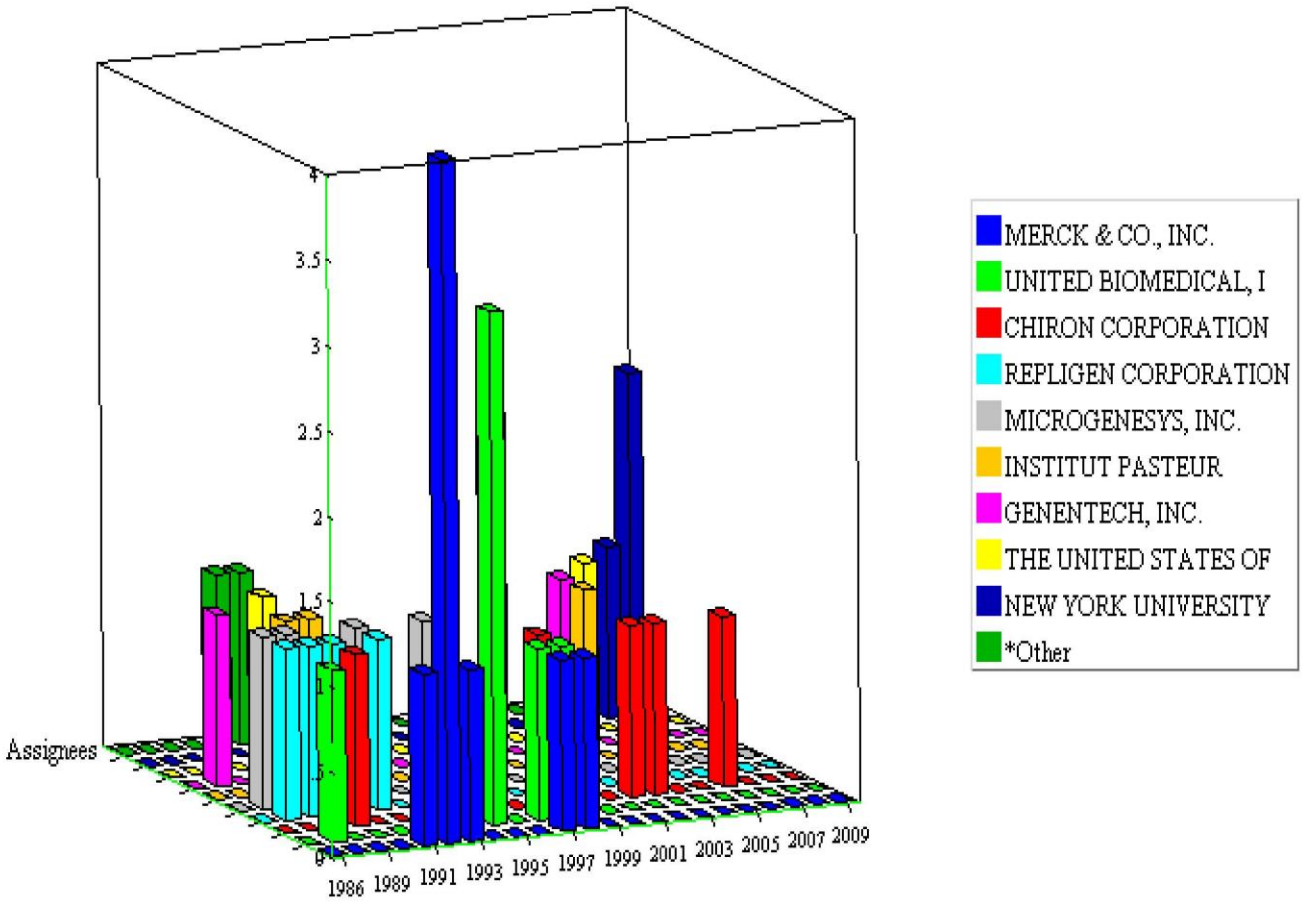


Pie Chart (Patent Count vs. Main IPC Class)



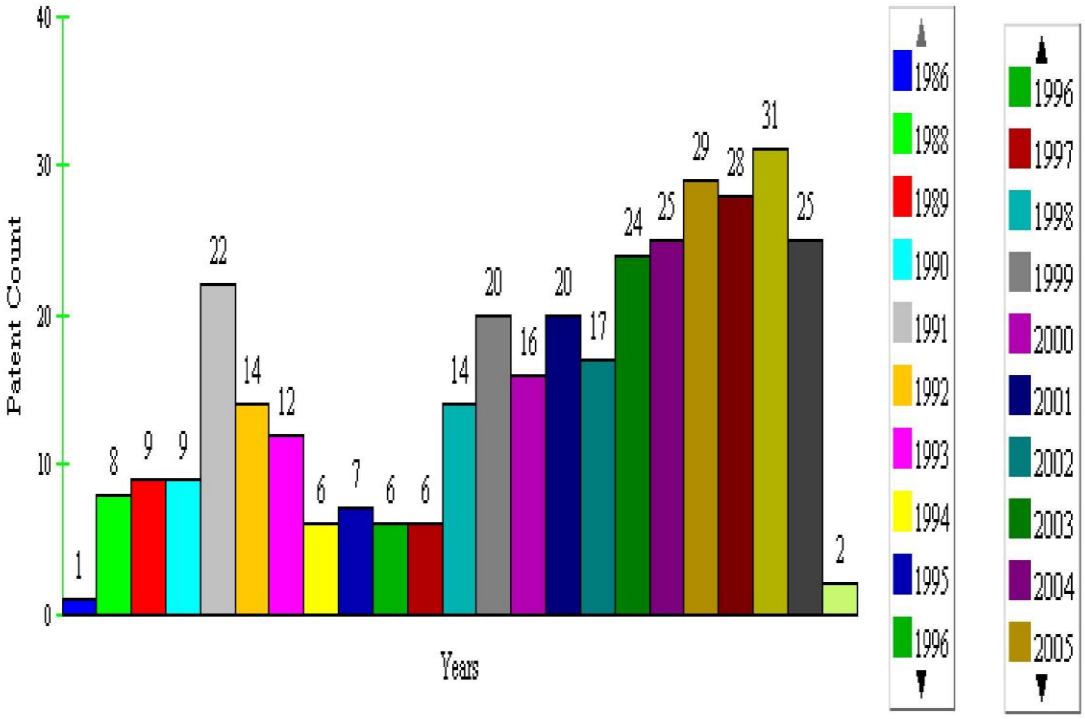
According to the above charts, the Main IPC Class in the field of Protein/Peptide Vaccines is A61K. This result was discovered early on in the patent searching process and was utilized in narrowing our results. C07K, C12N and G01N were also three Main IPC cited very frequently in patent applications.

3D Bar Count (Patent Count vs. Assignee vs. Publication Date)



According to the above chart, Merck & Co, Inc. and Chiron Corporation started filing patents in the field of Protein/Peptide Vaccines in the early 90's. United Biomedical, however, started filing patents on the same technology in late 80's.

2D Bar Chart (Patent Count v. Year)



According to the above chart, patents in the field of Protein/Peptide Vaccines have increased in frequency since the outset in the mid-80's. During the early 90's, the technology saw a marked increase but decreased until the late 90's where the technology experienced a marked increase in patent applications.

4.A.2. Aureka® ThemeMap® Results

Aureka® was utilized to generate preliminary Aureka® ThemeMaps® for HIV Protein/Peptide Vaccine Landscape. These ThemeMaps® were generated from the 351 relevant patents/patent applications using language from the claims, title and abstract and title, abstract and claims. Maps therefore represent a very broad view of the representative technologies which are embodied in the entire patent landscape. As such, these ThemeMaps® provide an overview of potentially applicable technologies. For example, from the Claims Map, it appears that a large portion of the claimed technology is in the area of peptides, TAT and nef. Additionally, unlike the results suggested by Micropatent®[154], the Title, Abstract and Claims Map suggests that the United States Government is a key assignee in the field of protein/peptide vaccines

[154] Unlike Micropatent® which only uses the information available on the US patent apps., Aureka® allows for the input of information not found on the US patent apps. As such, prior to running analytics in Aureka®, the team was able to ascertain assignees for various US patent apps. which were not available for analysis in Micropatent®. This likely accounts for the differences between the Micropatent® and Aureka® top assignee results.

Aureka ThemeMap® 1: ThemeMap® based on the language from the <u>title and abstract</u> in the 351 patents.

Aureka ThemeMap® 2: ThemeMap® based on the language from the <u>claims</u> in the 351 patents.

Aureka ThemeMap® 3: ThemeMap® based on the language from the <u>title, abstract and claims</u> in the 351 patents and illustrates where the top six assignees (based on data inputted into Aureka®) are clustered in relation to the technology.

4.A.3. Microsoft Excel®

As mentioned above, we found that the commercial tools utilized in this project did not reflect the slight variation in the assignee's names. First, with regard to United States Patent Applications, the assignee name is not listed on the application itself so the inventor name tends to be inserted into the assignee category. Second, with regard to assignee names, there are slight variations not recognized by commercial tools such as Corp. as opposed to Corporation. To fix this problem, we used the United States Patent and Trademark website to determine the names of assignees not listed. Then, using our Master Spreadsheet in Excel®, we generated additional graphs and charts.

4.A.3.i. Patent Count vs. Country

(A)

Country	Patent Count
WO	139
US	178
EP	33
Total	267

(B)

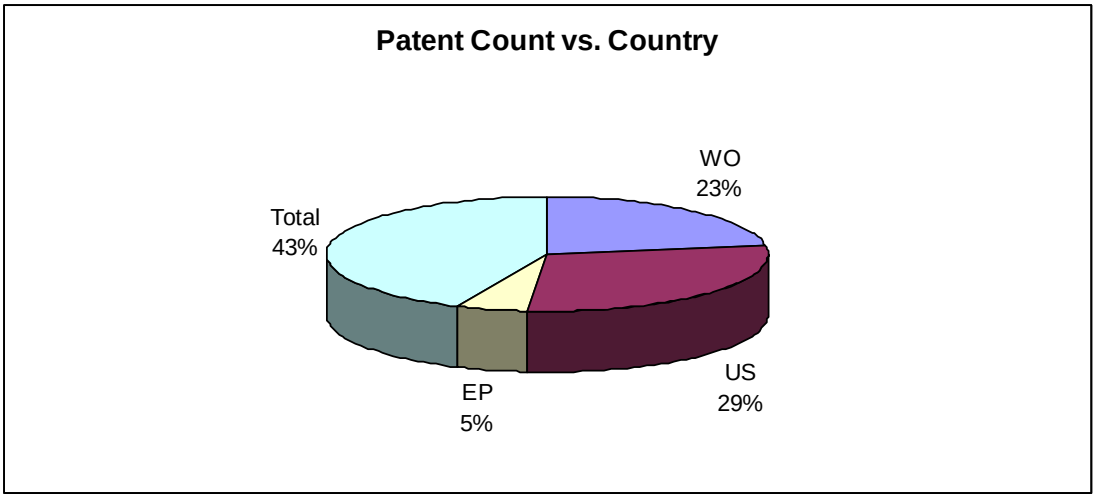


Figure 1: Patent counts according to publication country. Shown in a table (A) and a pie chart (B)

4.A.3.ii. Patent Count vs. Publication date

(A)

Year of Publication	Patent Count
1986	1
1987	0
1988	8
1989	9
1990	9
1991	22
1992	14
1993	12
1994	6
1995	7
1996	6
1997	6
1998	14
1999	20
2000	16
2001	20
2002	17
2003	24
2004	25
2005	29
2006	28
2007	31
2008	24

(B)

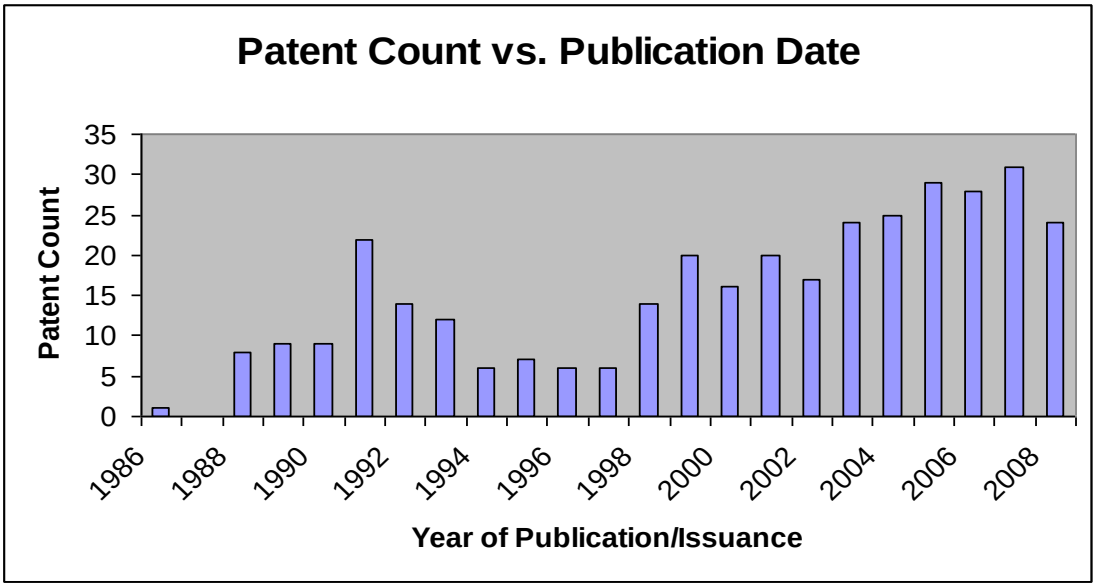


Figure 2: Patent counts according to publication date. Shown in table (A) and a bar graph (B).

4.A.3.iii. Patent Count vs. Filing date

(A)

Year of Filing	Patent Count
1986	5
1987	3
1988	11
1989	13
1990	12
1991	18
1992	15
1993	12
1994	11
1995	19
1996	5
1997	13
1998	11
1999	8
2000	21
2001	18
2002	28
2003	30
2004	19
2005	27
2006	23
2007	18
2008	6

(B)

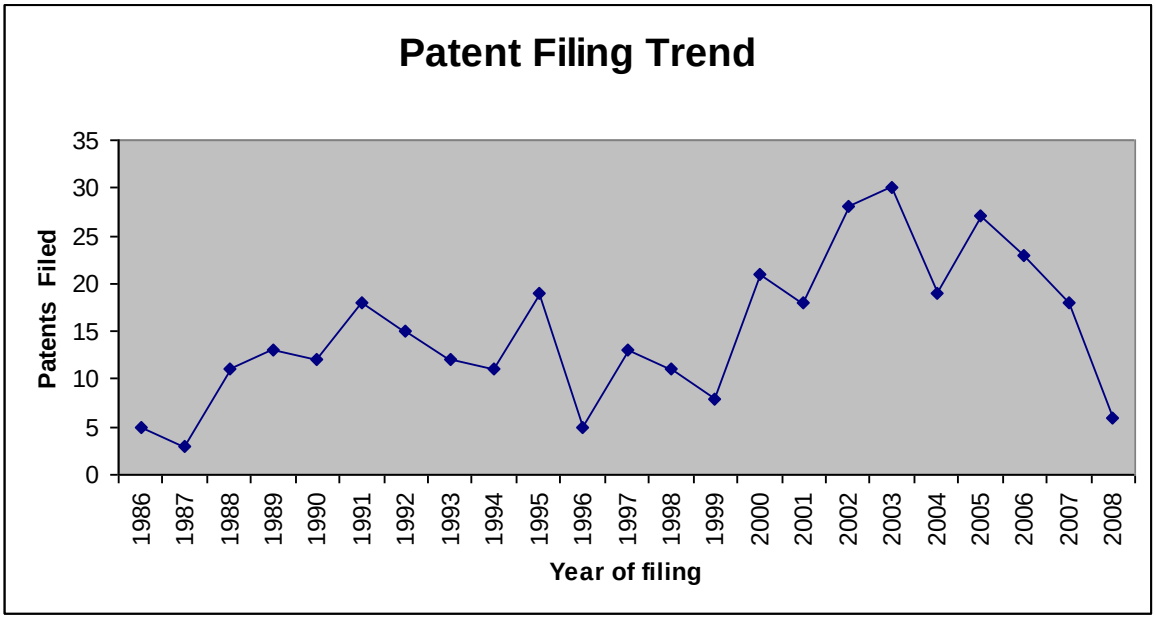
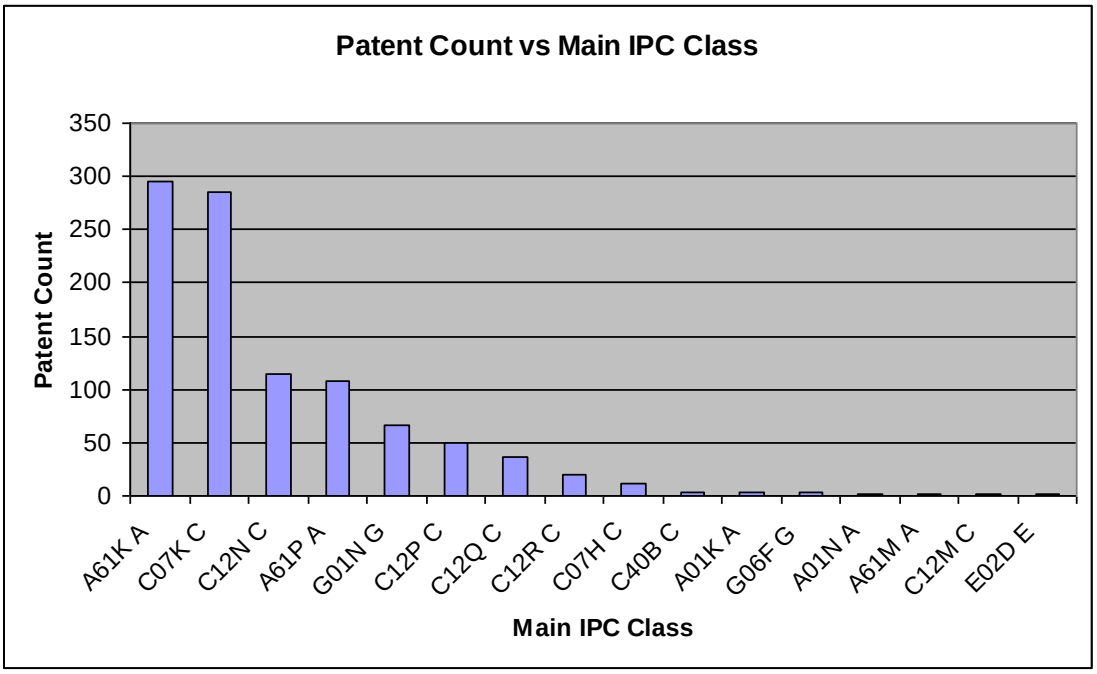


Figure 3: Patent counts according to the filing date. Shown in a table (A) and a line graph (B)

4.A.3.iv. Patent Count vs. Main IPC Class
(A)

IPC Code- 4 digit	Patent Count
A61K A — Human Necessities; Medical or Veterinary Science	296
C07K C — Chemistry; Metallurgy; Organic Chemistry	285
C12N C — Chemistry; Metallurgy; Biochemistry;	114
A61P A — Human Necessities; Medical or Veterinary Science	108
G01N G — Physics; Measuring (counting G06M);	67
C12P C — Chemistry; Metallurgy; Biochemistry;	49
C12Q C — Chemistry; Metallurgy; Biochemistry;	36
C12R C — Chemistry; Metallurgy; Biochemistry;	20
C07H C — Chemistry; Metallurgy; Organic Chemistry	12
C40B C — Chemistry; Metallurgy; Combinatorial Technology	4
A01K A — Human Necessities; Agriculture; Forestry;	3
G06F G — Physics; Computing; Calculating;	3
A01N A — Human Necessities; Agriculture; Forestry;	1
A61M A — Human Necessities; Medical or Veterinary Science;	1
C12M C — Chemistry; Metallurgy; Biochemistry;+A2	1
E02D E — Fixed Constructions; Hydraulic Engineering; Foundation	1

(B)



(C)

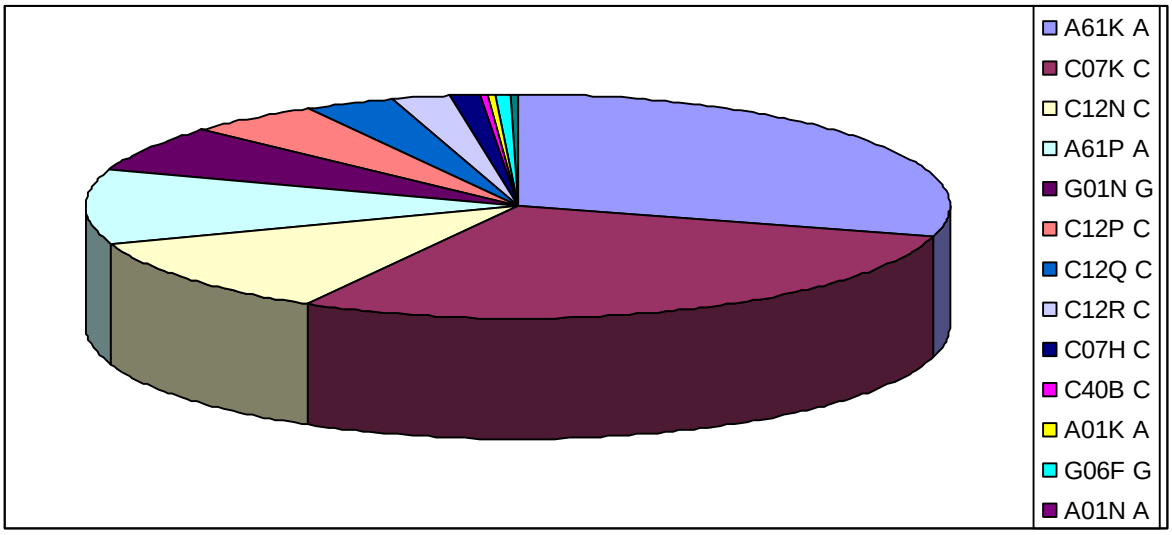


Figure 4: Patent Counts according to IPC Classification. Shown in table (A), a bar graph (B), and a pie chart (C).

4.A.3.v. Patent Count vs. Derwent Main Class

(A)

Top 5 Derwent Main Class	Patent Count
B04 Natural products and polymers.	338
D16 Fermentation industry.	325
S03 Scientific Instrumentation.	84
A96 Medical, dental, veterinary, cosmetic.	23
C06 Biotechnology - including plant genetics and veterinary vaccines.	18

(B)

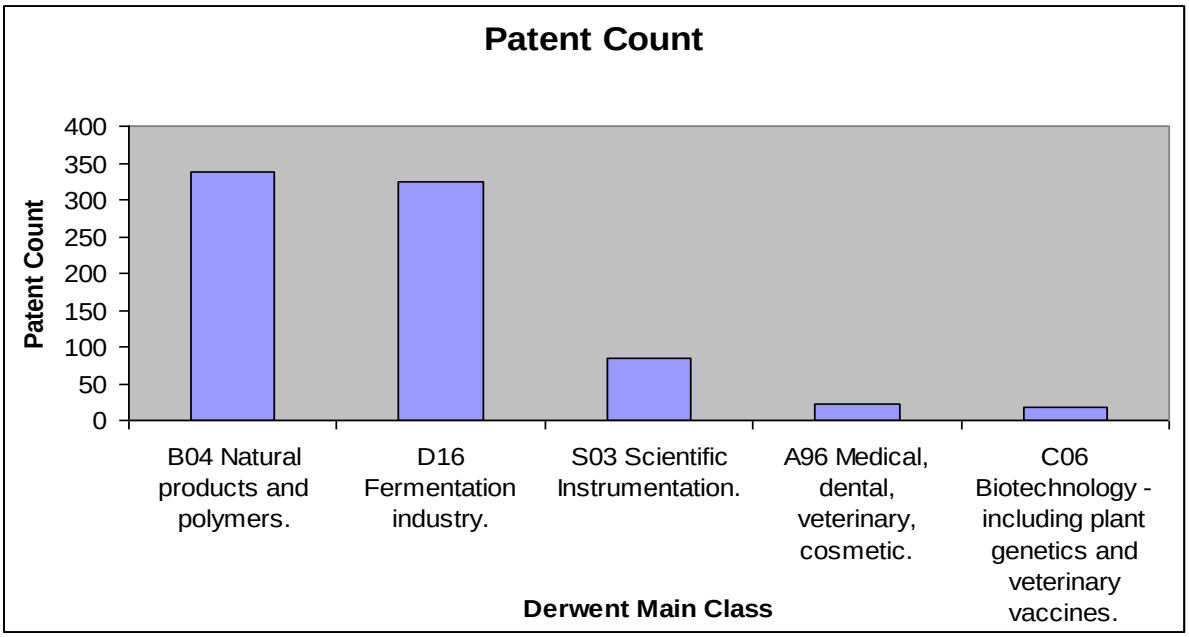


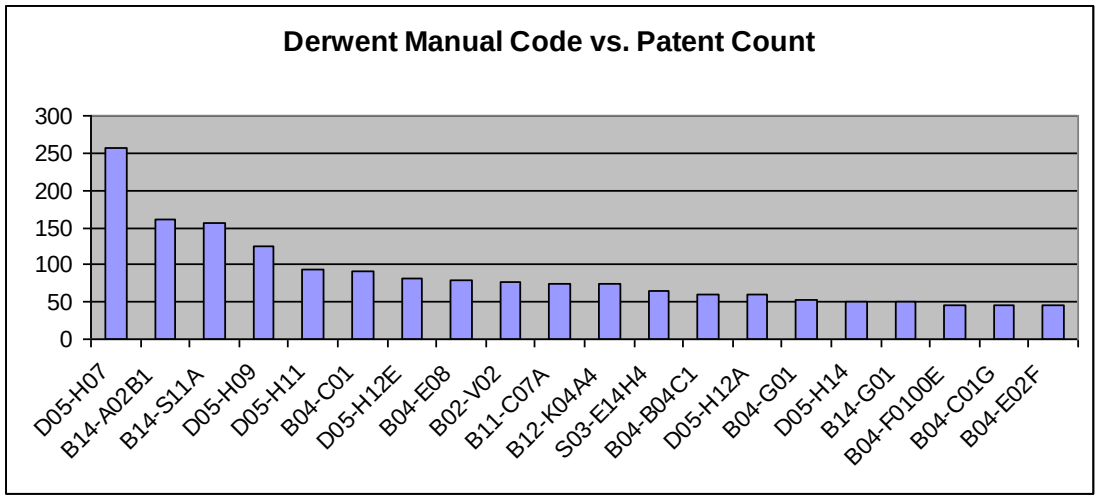
Figure 5: Patent counts according to Derwent Main classification. Shown in tables (A) and a bar graph (B)

4.A.3.vi. Patent Count vs. Derwent Manual Code

(A)

Top 20 Derwent Manual Code	Patent Count
D05-H07 Fermentation industry: Production of vaccines, antigens	256
B14-A02B1 Pharmaceutical activities: Retrovirus	160
B14-S11A Pharmaceutical activities: Antiviral Vaccine	157
D05-H09 Fermentation Inudstry: Testing and detection (exc. Bacteria, fungi, viruses)	125
D05-H11 Fermentation industry: Antibodies	93
B04-C01 Natural products (or genetically engineered), polymers: Polypeptides (general)	91
D05-H12E Fermentation industry: Vectors	82
B04-E08 Natural products (or genetically engineered), polymers: vectors, plasmids, cosmids, transposons	79
B02-V02 Antibotics: Vaccines	76
B11-C07A Processes, apparatus: Antigen - antibody reaction (general)	74
B12-K04A4 Diagnostics and formulation types (therapeutic, pesticidal, herbicidal): Diagnosis of microbial infections	74
S03-E14H4 Scietific instrumentation: Immunoassay	65
B04-B04C1 Natural products (or genetically engineered), polymers: Microbial antigen	59
D05-H12A Fermentation industry: wild-type coding sequences	59
B04-G01 Natural products (or genetically engineered), polymers: Antibody defined in terms of antigen general and other	54
D05-H14 Fermentation industry: Recombinant	51
B14-G01 Pharmaceutical activities: Immunostimulant general and others	50
B04-F0100E Natural Products (or genetically engineered), polymers: Cells, microorganisms, transformants, hosts, cell lines, tissue	46
B04-C01G Natural products (or genetically engineered), polymers: Polypeptides with 31 or more alpha amino acid residues	45
B04-E02F Natural products (or genetically engineered), polymers: Encoding other protein/polypeptide	45

(B)



(C)

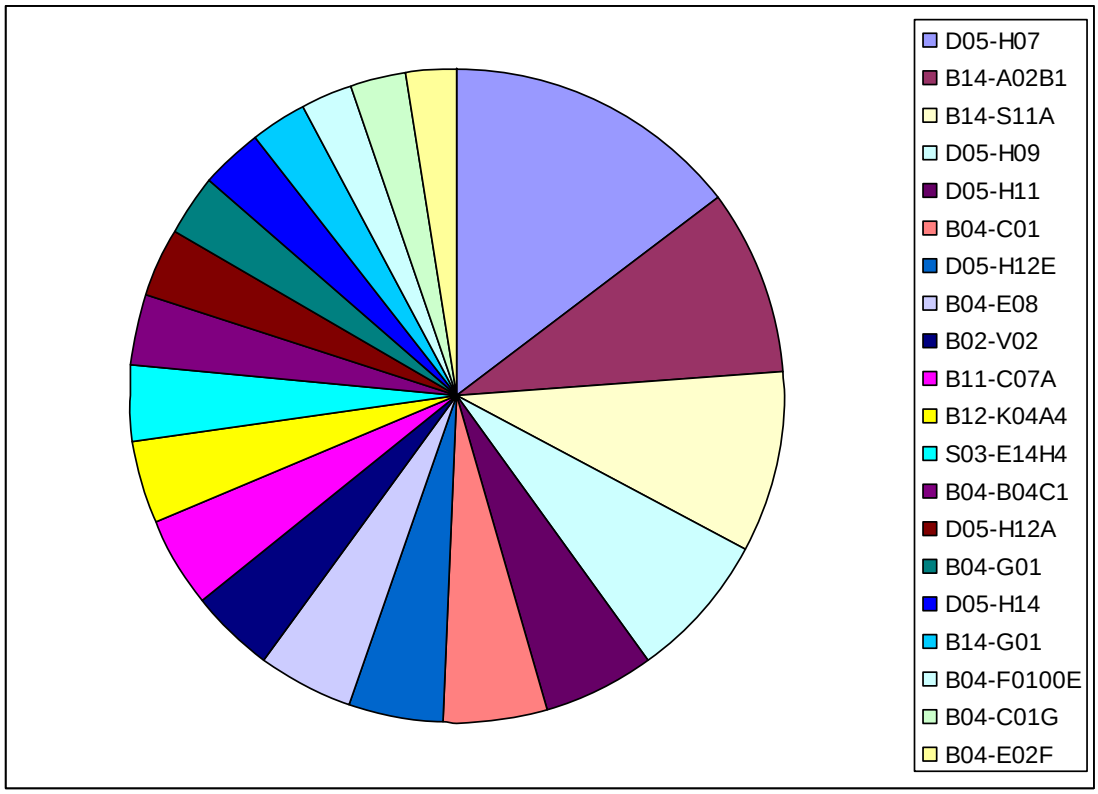


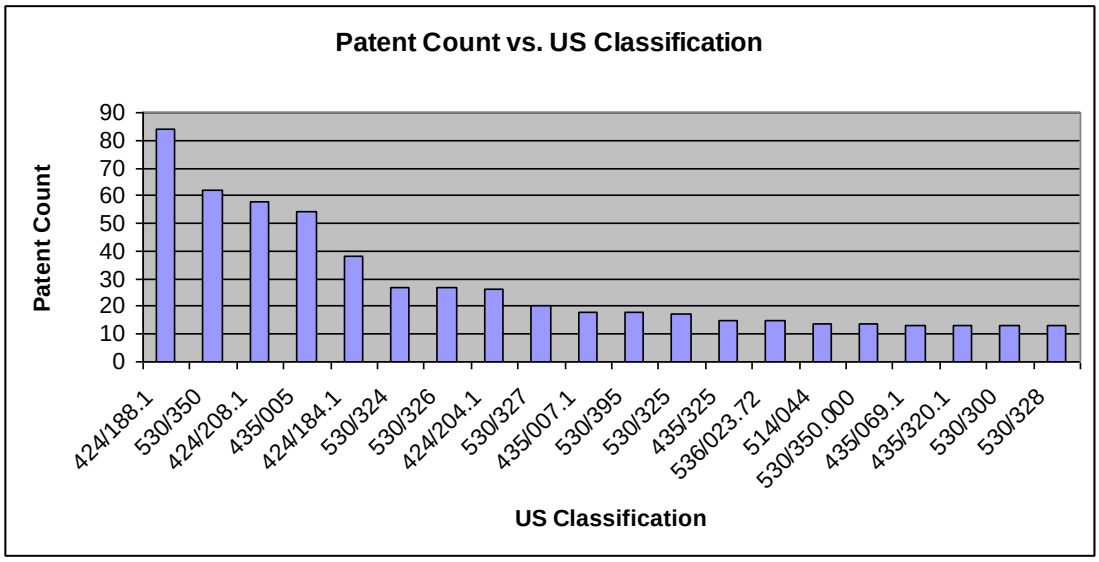
Figure 6: Patent counts according to Top 20 Derwent Manual Code. Shown in a table (A), a bar graph (B), and a pie chart (C).

4.A.3.vii. Patent Count vs. US Classification

(A)

Top 20 US Classification	Patent Count
424/188.1	84
530/350	62
424/208.1	58
435/005	54
424/184.1	38
530/324	27
530/326	27
424/204.1	26
530/327	20
435/007.1	18
530/395	18
530/325	17
435/325	15
536/023.72	15
514/044	14
530/350.000	14
435/069.1	13
435/320.1	13
530/300	13
530/328	13

(B)



(C)

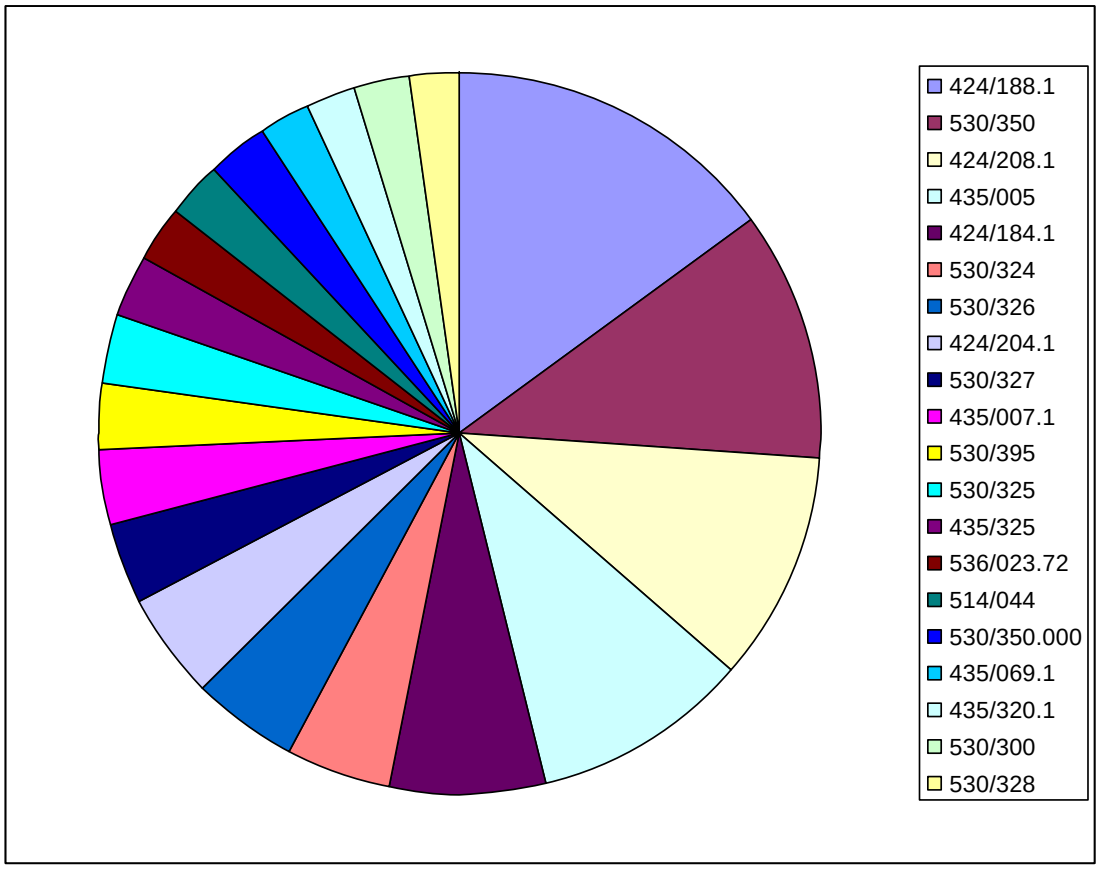


Figure 7: Patent counts according to Top 20 US class-subclass. Shown in a table (A), a bar graph (B), and a pie chart (C).

4.A.3.viii. Patent Count vs. Assignee

(A)

Assignee	Patent Count
Aventis Pasteur S.A.	5
Chiron Corporation	8
Commissariat a L'Energie Atomique	5
Cornell Research Foundation, Inc.	4
Dana-Farber Cancer Instistute	6
Duke University	5
Genentech, Inc.	4
Government of the Unitd States of America as represented by the Secretary of the Department of Health and Human Services	29
Henry M. Jackson Foundation	5
Institut National de la Sainte et de la Recherche Medicale (INSERM)	11
Institut Pasteur	14
Merck & Co., Inc.	11
Microgenesys, Inc.	4
Repligen Corporation	5
Tanox Biosystems, Inc.	4
The Scripps Research Institute	4
United Biomedical, Inc.	6
University of Marylalnd Biotechnology Institute	5
Other	3
Other	2

(B)

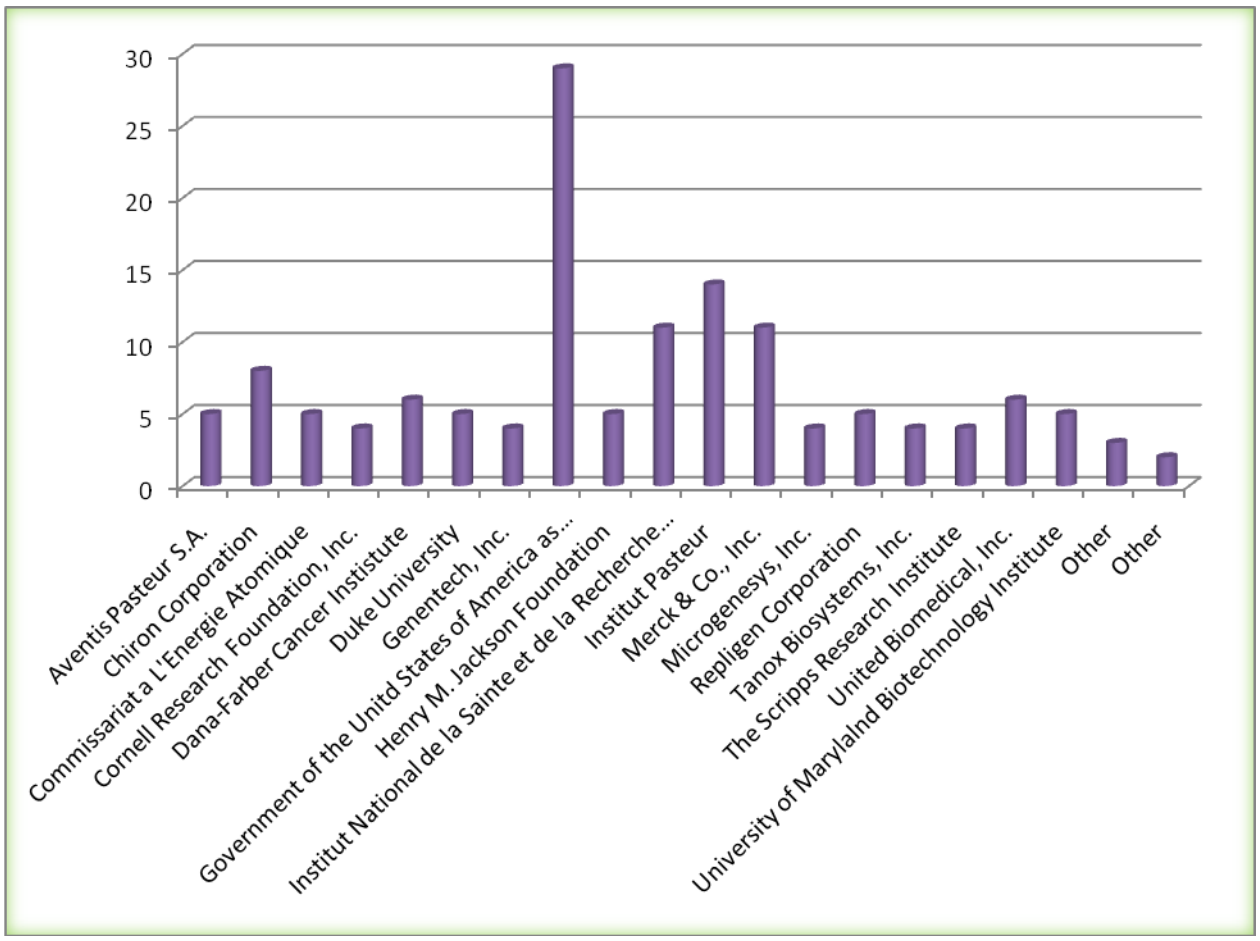


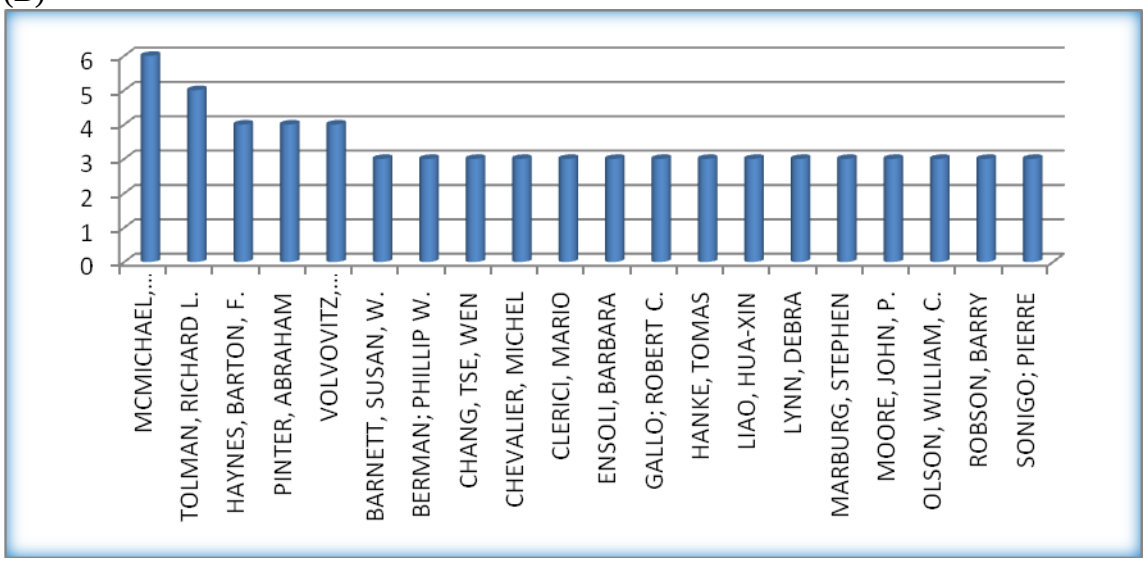
Figure 8: Patent counts according to Top 20 Assignees. Shown in a table (A) and a bar graph (B).

4.A.3.viv. Patent Count vs. Inventor

(A)

Inventors	Patent Count
MCMICHAEL, ANDREW, JAMES	6
TOLMAN, RICHARD L.	5
HAYNES, BARTON, F.	4
PINTER, ABRAHAM	4
VOLVOVITZ, FRANKLIN	4
BARNETT, SUSAN, W.	3
BERMAN; PHILLIP W.	3
CHANG, TSE, WEN	3
CHEVALIER, MICHEL	3
CLERICI, MARIO	3
ENSOLI, BARBARA	3
GALLO; ROBERT C.	3
HANKE, TOMAS	3
LIAO, HUA-XIN	3
LYNN, DEBRA	3
MARBURG, STEPHEN	3
MOORE, JOHN, P.	3
OLSON, WILLIAM, C.	3
ROBSON, BARRY	3
SONIGO; PIERRE	3

(B)



APPENDIX A: Scientific Papers

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

1. Curr Mol Med. 2003 May;3(3):243-63.

Subunit protein vaccines: theoretical and practical considerations for HIV-1.

Cho MW

With the spread of AIDS still rampant in many parts of the world, there is a global urgency to develop a vaccine against HIV-1. Without a doubt, developing an effective vaccine against the virus has been a monumental scientific challenge. Although advances in molecular biology and biotechnology over the years have enabled us to generate "designer antigens," our ability to transform them into successful vaccine candidates has been limiting. This review will be divided into three sections: First, the theoretical benefits and limitations of subunit protein vaccine strategy will be presented. Secondly, recent progress in our understanding of immune responses against AIDS vaccine candidates that incorporate recombinant proteins or peptides will be reviewed, mainly those that are designed to elicit humoral immune responses. Finally, some of the factors that must be considered in designing and evaluating future vaccine candidates will be discussed.

2. Expert Opin Biol Ther. 2008 Jun;8(6):745-57.

Prospects for HIV-1 therapeutic immunisation and vaccination: the potential contribution of peptide immunogens.

Sommerfelt MA, Sørensen B

Human immunodeficiency virus (HIV)-1 infection continues to challenge the development of antigen-specific immune-based strategies for the management (therapeutic immunisation) and prevention (vaccination) of HIV-1 infection. OBJECTIVE: This review aims to assess current prospects for HIV-1 therapeutic immunisation with particular emphasis on the contribution of peptide-based immunogens. METHODS: The potential for therapeutic immunisation to provide immunological support that can allow for prolonged safe ART-free periods is discussed in light of the Strategies for Management of Antiretroviral Therapy (SMART) study. Different approaches to peptide design are considered including the quality of T-cell responses desired. RESULTS/CONCLUSION: Synthetic peptide immunogens are amenable to modification to improve immunogenicity and reactivity to multiple virus subtypes. Ideally peptide immunogens should incorporate combinations that target restricted, relevant polyfunctional epitopes to regions of HIV-1 associated with control of infection. Peptides showing a beneficial effect following therapeutic immunisation may provide the basis for a future preventative vaccine.

3. Nat Rev Drug Discov. 2007 May;6(5):404-14.

More than one reason to rethink the use of peptides in vaccine design.

Purcell AW, McCluskey J, Rossjohn J

The use of peptides as therapeutics is experiencing renewed enthusiasm owing to advances in delivery, stability and design. Moreover, there is a growing emphasis on the use of peptides in vaccine design as insights into tissue-specific processing of the immunogenic epitopes of proteins and the discovery of unusually long cytotoxic T-lymphocyte epitopes broaden the range of targets and give clues to enhancing peptide immunogenicity. Peptides can also be synthesized with known post-translational modifications and/or deliberately introduced protease-resistant peptide bonds to regulate their processing independent of tissue-specific proteolysis and to stabilize these compounds in vivo. We discuss the potential of peptide-based vaccines for the treatment of chronic viral diseases and cancer, and review recent developments in the field of peptide-based vaccines.

4. PLoS Comput Biol. 2008 Dec;4(12):e1000246. Epub 2008 Dec 26.

A mathematical framework for the selection of an optimal set of peptides for epitope-based vaccines.

Toussaint NC, Dönnes P, Kohlbacher O

Epitope-based vaccines (EVs) have a wide range of applications: from therapeutic to prophylactic approaches, from infectious diseases to cancer. The development of an EV is based on the knowledge of target-specific antigens from which immunogenic peptides, so-called epitopes, are derived. Such epitopes form the key components of the EV. Due to regulatory, economic, and practical concerns the number of epitopes that can be included in an EV is limited. Furthermore, as the major histocompatibility complex (MHC) binding these epitopes is highly polymorphic, every patient possesses a set of MHC class I and class II molecules of differing specificities. A peptide combination effective for one person can thus be completely ineffective for another. This renders the optimal selection of these epitopes an important and interesting optimization problem. In this work we present a mathematical framework based on integer linear programming (ILP) that allows the formulation of various flavors of the vaccine design problem and the efficient identification of optimal sets of epitopes. Out of a user-defined set of predicted or experimentally determined epitopes, the framework selects the set with the maximum likelihood of eliciting a broad and potent immune response. Our ILP approach allows an elegant and flexible formulation of numerous variants of the EV design problem. In order to demonstrate this, we show how common immunological requirements for a good EV (e.g., coverage of epitopes from each antigen, coverage of all MHC alleles in a set, or avoidance of epitopes with high mutation rates) can be translated into constraints or modifications of the objective function within the ILP framework. An implementation of the algorithm outperforms a simple greedy strategy as well as a previously suggested evolutionary algorithm and has runtimes on the order of seconds for typical problem sizes.

5. J Immunol. 1999 May 15;162(10):6155-61.

Selection of HIV-specific immunogenic epitopes by screening random peptide libraries with HIV-1-positive sera.

Scala G, Chen X, Liu W, Telles JN, Cohen OJ, Vaccarezza M, Igarashi T, Fauci AS

Efforts to develop a protective HIV-1 vaccine have been hindered by difficulties in identifying epitopes capable of inducing broad neutralizing Ab responses. In fact, the high mutation rate occurring in HIV-1 envelope proteins and the complex structure of gp120 as an oligomer associated with gp41 result in a high degree of antigenic polymorphism. To overcome these obstacles, we screened random peptide libraries using sera from HIV-infected subjects to identify antigenic and immunogenic mimics of HIV-1 epitopes. After extensive counterscreening with HIV-negative sera, we isolated peptides specifically recognized by Abs from HIV-1-infected individuals. These peptides behaved as antigenic mimics of linear or conformational HIV-1 epitopes generated in vivo in infected subjects. Consistent with these findings, sera of simian HIV-infected monkeys also recognized the HIV-specific epitopes. The selected peptides were immunogenic in mice, where they elicited HIV-specific Abs that effectively neutralized HIV-1 isolates. These results demonstrate that pools of HIV-1 mimotopes can be selected from combinatorial peptide libraries by taking advantage of the HIV-specific Ab repertoire induced by the natural infection.

6. Trends Microbiol. 2006 Mar;14(3):141-7. Epub 2006 Feb 7.

Phage display in the study of infectious diseases.

Mullen LM, Nair SP, Ward JM, Rycroft AN, Henderson B

Microbial infections are dependent on the panoply of interactions between pathogen and host and identifying the molecular basis of such interactions is necessary to understand and control infection. Phage display is a simple functional genomic methodology for screening and identifying protein-ligand interactions and is widely used in epitope mapping, antibody engineering and screening for receptor agonists or antagonists. Phage display is also used widely in various forms, including the use of fragment libraries of whole microbial genomes, to identify peptide-ligand and protein-ligand interactions that are of importance in infection. In particular, this technique has proved successful in identifying microbial adhesins that are vital for colonization.

7. PLoS Med. 2007 Dec;4(12):e348.

Antibody-based HIV-1 vaccines: recent developments and future directions.

Montefiori D, Sattentau Q, Flores J, Esparza J, Mascola J; Working Group convened by the Global HIV Vaccine Enterprise

8. J Antimicrob Chemother. 2003 Apr;51(4):757-9. Epub 2003 Mar 13.

Therapeutic potential of neutralizing antibodies in the treatment of HIV-1 infection.

Stiegler G, Katinger H

9. The Journal of Immunology, 2002, 169: 837-846.

Immunogenically Fit Subunit Vaccine Components Via Epitope Discovery from Natural Peptide Libraries

Leslie J. Matthews, Robert Davis and George P. Smith

Antigenic peptides that bind pathogen-specific Abs are a potential source of subunit vaccine components. To be effective the peptides must be immunogenically fit: when used as immunogens they must elicit Abs that cross-react with native intact pathogen. In this study, antigenic peptides obtained from phage display libraries through epitope discovery were systematically examined for immunogenic fitness. Peptides selected from random peptide libraries, in which the phage-displayed peptides are encoded by synthetic degenerate oligonucleotides, had marginal immunogenic fitness. In contrast, 50% of the peptides selected from a natural peptide library, in which phage display segments of actual pathogen polypeptides, proved very successful. Epitope discovery from natural peptide libraries is a promising route to subunit vaccines.

10. Vaccine. 2006 May 8;24(19):4062-81. Epub 2006 Feb 28.

A review of vaccine research and development: the human immunodeficiency virus (HIV).

Girard MP, Osmanov SK, Kieny MP

Since the discovery of AIDS in 1981, the global spread of HIV has reached pandemic proportions, representing a global developmental and public health threat. The development of a safe, globally effective and affordable HIV vaccine offers the best hope for the future control of the pandemic. Significant progress has been made over the past years in the areas of basic virology, immunology, pathogenesis of HIV/AIDS and the development of antiretroviral drugs. However, the development of an HIV vaccine faces formidable scientific challenges related to the high genetic variability of the virus, the lack of immune correlates of protection, limitations with the existing animal models and logistical problems associated with the conduct of multiple clinical trials. More than 35 vaccine candidates have been tested in Phase I/II clinical trials, involving more than 10,000 volunteers, and two Phase III trials have been completed, themselves involving more than 7500 volunteers. Multiple vaccine concepts and vaccination strategies have been tested, including DNA vaccines, subunit vaccines, live vectored recombinant vaccines and various prime-boost vaccine combinations. This article reviews the state of the art in HIV vaccine development, summarizes the results obtained so far and discusses the challenges to be met in the development of the various vaccine candidates.

11: J Virol. 2003 Mar;77(5):3157-66.

Tat-neutralizing antibodies in vaccinated macaques.

Tikhonov I, Ruckwardt TJ, Hatfield GS, Pauza CD

The human immunodeficiency virus Tat protein is essential for virus replication and is a candidate vaccine antigen. Macaques immunized with Tat or chemically modified Tat toxoid having the same clade B sequence developed strong antibody responses. We compared these antisera for their abilities to recognize diverse Tat sequences. An overlapping peptide array covering three clade B and two clade C Tat sequences was constructed to help identify reactive linear epitopes. Sera from Tat-immunized macaques were broadly cross-reactive with clade B and clade C sequences but recognized a clade B-specific epitope in the basic domain. Sera from Tat toxoid-immunized macaques had a more restricted pattern of recognition, reacting mainly with clade B and with only one clade B basic domain sequence, which included the rare amino acids RPPQ at positions 57 to 60. Monoclonal antibodies against the amino terminus or the domain RPPQ sequence blocked Tat uptake into T cells and neutralized Tat in a cell-based transactivation assay. Macaques immunized with Tat or Tat toxoid proteins varied in their responses to minor epitopes, but all developed a strong response to the amino terminus, and antisera were capable of neutralizing Tat in a transactivation assay.

12. J Biol Chem. 1999 Oct 8;274(41):28837-40.

Multifaceted activities of the HIV-1 transactivator of transcription, Tat.

Jeang KT, Xiao H, Rich EA

13. J Neurosci. 1996 Apr 15;16(8):2546-52.

Extracellular human immunodeficiency virus type 1 Tat protein promotes aggregation and adhesion of cerebellar neurons.

Orsini MJ, Debouck CM, Webb CL, Lysko PG.

Recombinant human immunodeficiency virus (HIV-1) Tat protein added to the culture medium of rat cerebellar neurons promoted aggregation and formation of spoke-like neurites in a dose-dependent manner. Tat proteins containing mutations in the Arg-Gly-Asp (RGD) cell adhesion motif or a deletion of the cysteine-rich domain had no effect on neuronal morphology. In contrast, a Tat protein that contained a deletion of the proline-rich domain promoted neuronal aggregation. Aggregation of neurons was inhibited by the addition of monoclonal antibodies directed against the RGD and basic domains of Tat, but not against the proline-rich domain. The same domains of Tat required to induce aggregation also mediated adhesion of neurons to Tat-coated substrates. The HIV-2 Tat protein, which lacks an RGD sequence but contains cysteine-rich and basic domains similar to HIV-1 Tat, induced aggregation and acted as a substrate for adhesion when added at higher concentrations than HIV-1 Tat. Vitronectin, fibronectin, and RGD-containing peptides did not induce morphological changes in neurons or act as substrates

for adhesion. The ability of Tat to induce morphological changes and promote adhesion was independent of the ability of Tat to transactivate HIV gene expression. Our results suggest that extracellular Tat protein most likely alters neuronal morphology and mediates adhesion by acting in a manner similar to an extracellular matrix protein.

14 J Biol Chem. 1994 Mar 18;269(11):8366-75.

Intracellular analysis of in vitro modified HIV Tat protein.

Koken SE, Greijer AE, Verhoef K, van Wamel J, Bukrinskaya AG, Berkhout B

Human immunodeficiency viruses HIV-1 and HIV-2 encode a Tat protein that specifically activates transcription from the viral long terminal repeat. To characterize the properties of the Tat proteins, we have expressed them in Escherichia coli. The purified Tat protein was biochemically analyzed and tested for activity upon electroporation into human cell lines. This protein electroporation was used for the intracellular analysis of in vitro modified Tat protein. Our results indicate that the transcriptionally active form of the Tat protein is a monomer. Furthermore, we found that Tat activity is dramatically inhibited by preincubation of the protein with strongly reducing agents. In contrast, no inhibitory effect was measured upon incubation with metal-chelating reagents. These results suggest that the cysteine residues of Tat are involved in the formation of intramolecular disulfide bonds.

15. Clinical Pharmacology & Therapeutics 686, 687 (2007).

HIV/AIDS Vaccines

Harriet L. Robinson

16 J Infect Dis. 2003 Oct 15;188(8):1171-80. Epub 2003 Sep 30.

Sequence conservation and antibody cross-recognition of clade B human immunodeficiency virus (HIV) type 1 Tat protein in HIV-1-infected Italians, Ugandans, and South Africans.

Buttò S, Fiorelli V, Tripiciano A, Ruiz-Alvarez MJ, Scoglio A, Ensoli F, Ciccozzi M, Collacchi B, Sabbatucci M, Cafaro A, Guzmán CA, Borsetti A, Caputo A, Vardas E, Colvin M, Lukwiya M, Rezza G, Ensoli B; Tat Multicentric Study Group

We determined immune cross-recognition and the degree of Tat conservation in patients infected by local human immunodeficiency virus (HIV) type 1 strains. The data indicated a similar prevalence of total and epitope-specific anti-Tat IgG in 578 serum samples from HIV-infected Italian (n=302), Ugandan (n=139), and South African (n=137) subjects, using the same B clade Tat protein that is being used in vaccine trials. In particular, anti-Tat antibodies were detected in 13.2%, 10.8%, and 13.9% of HIV-1-infected individuals from Italy, Uganda, and South Africa, respectively. Sequence analysis results indicated a high similarity of Tat from the different circulating viruses with BH-10 Tat, particularly in the 1-58 amino acid region, which contains most of the immunogenic epitopes. These data indicate an effective cross-recognition of

a B-clade laboratory strain-derived Tat protein vaccine by individuals infected with different local viruses, owing to the high similarity of Tat epitopes.

17. Proc Natl Acad Sci U S A. 2001 Feb 13;98(4):1781-6.

The HIV-1 regulatory proteins Tat and Rev are frequently targeted by cytotoxic T lymphocytes derived from HIV-1-infected individuals.

Addo MM, Altfeld M, Rosenberg ES, Eldridge RL, Philips MN, Habeeb K, Khatri A, Brander C, Robbins GK, Mazzara GP, Goulder PJ, Walker BD; HIV Controller Study Collaboration

The HIV-1 regulatory proteins Rev and Tat are expressed early in the virus life cycle and thus may be important targets for the immune control of HIV-1-infection and for effective vaccines. However, the extent to which these proteins are targeted in natural HIV-1 infection as well as precise epitopes targeted by human cytotoxic T lymphocytes (CTL) remain to be defined. In the present study, 57 HIV-1-infected individuals were screened for responses against Tat and Rev by using overlapping peptides spanning the entire Tat and Rev proteins. CD8+ T cell responses against Tat and Rev were found in up to 19 and 37% of HIV-1-infected individuals, respectively, indicating that these regulatory proteins are important targets for HIV-1-specific CTL. Despite the small size of these proteins, multiple CTL epitopes were identified in each. These data indicate that Tat and Rev are frequently targeted by CTL in natural HIV-1 infection and may be important targets for HIV vaccines.

18. Vaccine. 2008 Jan 30;26(5):727-37. Epub 2007 Dec 4.

The Tat protein broadens T cell responses directed to the HIV-1 antigens Gag and Env: implications for the design of new vaccination strategies against AIDS.

Gavioli R, Cellini S, Castaldello A, Voltan R, Gallerani E, Gagliardoni F, Fortini C, Cofano EB, Triulzi C, Cafaro A, Srivastava I, Barnett S, Caputo A, Ensoli B.

We have previously shown that the biologically active Tat protein targets and efficiently enters dendritic cells, and increases the proteolytic activities of the immunoproteasome, thereby favoring the generation and presentation of the subdominant MHC-I binding CTL epitopes of heterologous antigens. In the present study, we demonstrate that Tat broadens in vivo epitope-specific T cell responses directed to heterologous antigens including HIV structural proteins. Specifically, co-immunization of mice with OVA and Tat proteins induces CTL responses against subdominant and cryptic OVA-derived epitopes, which are not detected in mice vaccinated with OVA alone. Similarly, mice vaccinated with the HIV-1 Gag, Env or V2-deleted Env antigens in combination with Tat show Th1-type and CTL responses directed to a larger number of T cell epitopes, as compared to mice vaccinated with these proteins in absence of Tat. In contrast, Tat did not affect Th2-type responses to these structural HIV proteins. These results indicate that Tat is not only an antigen but also a novel Th1-type adjuvant capable of broadening in vivo the spectrum of epitopes recognized by T cells, and suggest that Tat can be considered an optimal co-antigen in the development of novel vaccination strategies against AIDS.

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

Platform Name– Aureka

General information

- Aureka is a Thomson Reuters product
- Full text data coverage: United States (US) patents and applications, European (EP) patents and applications, World Intellectual Property Organization (WO) PCT applications, German (DE) patents, applications, and utility models, French (FR) applications, British (GB) applications, and Japanese (JP) applications
- Updated to accommodate IPC-R (International Patent Classification Reform) codes

Searches

- Boolean searching allows users to search specified topics or patent fields and to narrow or broaden the search results as needed
- Two wildcards (* and ?) can be used to account for US and English spelling
- Patent and non−patent citations are associated with every publication record
- Ability to search for a range of PCT publication dates
- Ability to sub-search a hit list to narrow your searches
- US litigation data is displayed in records and is available in the Legal Status view, although it is not searchable
- Includes non−patent citation, such as journal articles, book chapters, technical reports, etc. from US, EP, WO, GB, and DE
- Document lists are the results of a search or series of searches, listed with the data and in the preferred order

Analysis and mapping

- Clustering tool (Vivismo) extracts and groups records by like concepts into hierarchically organized folders for a quick snapshot
- Vovismo can cluster Aureka document lists of up to 1,000 average length documents in less than a few minutes.
- In Aureka, only the titles and abstracts of patent documents are analyzed
- Useful text−mining module called ThemeScape, which helps companies compare portfolios using pseudo−3D maps with contoured hills representing the patent themes identified
- Citation trees visually depict all reference and referenced patents to a source document in an interactive tool that captures the history, competitive activity and future of a technology up to five generations
- Can import non−patent literature to analyze alongside patent information
- Users can post messages to make announcements or provide information with co-collaborators

Platform Name– Patent Insight Pro

General information

- Supports US, EP, WIPO, JP, GB, CA and other countries patents
- Users can submit a list of patent numbers in an Excel or CSV file; the software will download them one−by−one

- Full Claims section can be separately captured in original PDF format and exported to Word documents
- The Tabular Word/Excel Export function allows the export of patent summaries with images to Excel and Word documents
- Automatic language detection of patents with preset nine languages stop−word lists for segmentation according to the detected language
- Includes Automated Patent term cleanup using Thesaurus

Search and view

- The Patent Viewer allows quick browsing of patents within the portfolio and includes multiword highlighting capabilities
- Provides the ability to conduct advanced Boolean searching through patent sets
- The Classification Browser allows users to view US Class and IPC−R details and to reverse search for appropriate Class Codes based on the technology name
- The Claims Tree and Claims Comparison Viewer allows users to generate complete claims trees that show all the dependencies within the claims of a patent and allow the comparison of independent claims of different patents in a side−by−side viewer

Analysis and mapping

- Offers patent mapping, patent alerts, text clustering and auto- categorization, natural language searching, similarity searching, patent landscaping, and concurrency analysis

Platform Name– Westlaw

General Information

- Westlaw is a Thomson Company product.
- Flexible pricing plans (i.e., large company or single attorney)
- The Westlaw database contains full text information of patents before 1972, whereas other services just have bibliographic information.

Searching

- The value-added services can be accessed from the "Patent Practitioner" tab of the user's account after login. This tab includes links useful to facilitate research in patent literature, cases, statutes, and regulations, court records and litigation tracking. It also provides information on recent developments, litigation practice guides, prosecution practice guides, and forms.
- "KeyCite" covers all patents granted by the USPTO since 1976. "KeyCite" also offers access to reissued patents, defensive publications, and statutory invention registrations. To view KeyCite information for a document, users can click a status flag on the document or click "Full History" or "Citing References" links on the "Links" tab
- Citing references provide relevant previous patent literatures
- Citing references are available for U.S. patents only
- Provides access to the Derwent World Patent Index as well as relevant sources, including cases and statutes, patents and patent treatises, and post issuance information, such as KeyCite for patents.
- Includes a link to Delphion which provides access to the full text of US and European patents and patent applications, PCT applications, and abstracts from Japanese patents and patent applications

- Has ability to search full- text patent documents, each has a link to display the full original patent, including drawings in PDF format.
- U.S. patent file histories are available in PDF format, with handwritten comments and time stamps intact.
- Using certain truncations and connectors is difficult when using the Westlaw database
- Hybrid searches often generate a large number of irrelevant results

Analysis

- No patent landscaping tools are available

Platform Name– Delphion

General Information

- Delphion gives patent collections & searching options inside the world's important patent databases.
- Data coverage:
    - United States Patents - Applications and Granted
    - Derwent World Patents Index (DWPI)
    - European Patents - Applications (EP- A) and Granted (EP-B)
    - German Patents - Applications and Granted
    - INPADOC Family and Legal Status
    - Patent Abstracts of Japan (JP)
    - Switzerland (CH) patents
    - WIPO PCT publications (WO)

Search and view

- Quick/Number searching and Boolean searching are available
- Corporate Tree facilitates targeted Assignee name searching
- Patent images can be viewed in both high and low resolution.
- 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.
- 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
- Data Extract exports key bibliographic fields in common formats
- Alerts automatically run Saved Searches and email the user the results on a desired frequency
- PDF Express bulk downloads of up to 500 PDFs and create a zip archive of the PDFs
- Patent viewing options include the Delphion Integrated View, both high resolution and low resolution image options, and a variety of download and delivery options.

Analytical tools

- Snapshot allows quick online analysis of the search results. Users can view top 10 assignees, inventors, US classes, IPC codes, and more.
- Citation Link creates graphical maps of forward and backward reference

Database Name– Derwent World Patent Index

General Information

- Can be accessed via Delphion
- Most comprehensive database of international patent information
- DWPI covers inventions from over 40 patent issuing authorities
- Documents are read in their native language. Titles and abstracts are then rewritten in English to create a DWPI record
- 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.
- There are 36.2 million patent documents currently in the database and over 2.5 million patents are added each year.
- A Derwent record has the followings:
    - Derwent title
    - Link to the original patent; users can ieemdiately access to the full text of the basic patent in PDF
    - Derwent classes
    - Derwent abstract showing novelty, use, and advantage
    - Legal status information from INPADOC
    - Claims from the basic patent
- $ 4.00 for a search performed, and $ 6.00 for each full Derwent Record viewed

Searches

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

Platform Name– MicroPatent Family Option

In the "Reduce to One Member per Family" option, the WorkSheet retains only one family member and deletes the other patents from the list. The representing family member is selected by using the default order; US-WO-EP-JP-GB-DE-FR.

This feature gives the user the basis for analysis of patents by family, eliminating the distortion that results from counting the same invention in each country.

A PDF report includes bibliographic information and claims of selected patents in a common format. Selected patents are bookmarked on the left side of the report.

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 most frequently found classes are underlined.

- **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-diated immunity, imunospecific 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 424/204.1: Virus or component thereof
    - Class 424/208.1: Immunodeficiency virus (e.g., HIV, etc.)

- **Class 435: Chemistry: Molecular Biology and Microbiology**
    - Class 435/005: Involving virus or bacteriophage
    - Class 435/006: Involving nucleic acid
    - 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 435/320.1: Vector, per se (e.g., plasmid, hybrid plasmid, cosmid, viral vector, bacteriophage vector, etc.)

- **Class 514: Drug, Bio-Affecting and Body Treating Compositions**
    - Class 514/044: 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 530/325: 24 amino acid residues in defined sequence
    - Class 530/326: 15 to 23 amino acid residues in defined sequence
    - Class 530/350: Proteins, i.e., more than 100 amino acid residues

- **Class 544: Organic Compounds – Part of the Class 532-570 Series**
    - Class 544/238: 1,2-diazines which contain an additional hetero ring

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

Classification Codes applicable for this report

The most frequently found codes are underlined.

- **Section A: Human Necessities**
    - A61K: Preparations for Medical, Dental, or Toilet Purposes
        - 39/21: Retroviridae, e.g. equine infectious anemia virus
    - A61P: Therapeutic Activity of Chemical Compounds or Medical Preparations

- **Section C: Chemistry; Metallurgy**
    - C07H: Organic Chemistry
    - C07K: Peptides
        - 7/08: Having 12 to 20 amino acids
        - 14/005: From viruses
    - C12N: Micro-Organisms or Enzymes; Compositions Thereof; Propagating, Preserving, or Maintaining Micro-Organisms; Mutation or Genetic Engineering; Culture Media
    - 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

- **Section G: Physics**
    - G01N: Investigation or Analyzing Materials by Determining Their Chemical or Physical Properties
        - 33/68: Involving proteins, peptides or amino acids

APPENDIX E: Derwent Classifications

(http://www.delphion.com/derwent/docs/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 we 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 our subject experts, and no strict correspondence is claimed.

Classification Codes (applicable for this report)

- **Class D16:** Fermentation industry – including fermentation equipment, brewing, yeast production, production of pharmaceuticals and other chemicals by fermentation, microbiology, production of vaccines and antibodies, cell and tissue culture and genetic engineering.
- **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.
- **Class S03:** Scientific Instrumentation – Photometry, calorimetry. Thermometers. Meteorology, geophysics, measurement of nuclear or X-radiation. Investigating chemical or physical properties.

APPENDIX F: Chemical Patents Index (CPI) Manual Codes

(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 by categories
- 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)

- Antiviral
    - B14-A02B1 retrovirus
    - (Including leuco- and oncoviruses, Tcell leukemia virus, HIV, Rous sarcoma. Non-antiviral AIDS treatment is coded B14-G01B).
- Vaccine
    - B14-S11A antiviral activity

APPENDIX G: Author's *Curriculum Vitae*

MICHELLE WINDOM
mwindom@piercelaw.edu

EDUCATION

Franklin Pierce Law Center, Concord, NH
Candidate for Juris Doctor, 2009
Member, Pierce Law Review
Member, Student Bar Association Finance Committee 1L Representative
Member, Student Intellectual Property Organization

Franklin Pierce Law Center, Concord, NH
Masters of Intellectual Property, 2006
Member, Student Bar Association Finance Committee MIP Representative
Member, Student Intellectual Property Organization

Tulane University, New Orleans, LA
Masters of Engineering, Biomedical Engineering, 2004

Louisiana State University, Baton Rouge, LA
Bachelor of Science, Biological Engineering, 2002
Member, Biological Engineering Society
Member, Zeta Tau Alpha Sorority

EXPERIENCE

Fall 2009	**Oliff & Berridge, PLC** *Associate*
Summer 2008	**Oliff & Berridge, PLC** *Summer Associate*
Summer 2007	**Duane Morris LLP** (Philadelphia, PA) *Summer Associate*
Summer 2006	**Tulane University Office of Technology Transfer** *Intern*

PUBLICATIONS

Michelle Windom et al., *Educational Report of the Patent Landscape of DNA Vaccines for HIV*, Franklin Pierce Law Center, May 2008.

Michelle Windom et al., *Educational Report of the Patent Landscape of Adenoviral Vector Vaccines for HIV*, Franklin Pierce Law Center, December 2008.

ALEXANDRE FERRE

37 Alice Drive, Unit 96 **email : aferre@piercelaw.edu**
Concord, NH 03303 **Tel : (603)892 2156**

EDUCATION

Franklin Pierce Law Center, Concord, NH
Candidate for Juris Doctor, 2010

Virginia Commonwealth University (VCU) Richmond, VA
Bachelor of Science in Chemistry and Minor in Biology, Cum Laude 2007

PAST EXPERIENCE

Attorney Melanie Bell Spring 2009
Research/ motion drafting assistant
I assisted a solo practitioner in a variety of legal matters, including the defense of a client against a copyright infringement lawsuit. I was responsible for working independently and research legal issues that Mrs. Bell asked me about, as well as write memo's analysis case law with the facts of the case. I was also responsible for drafting several motions in federal court.

Dr. Stan Kowalski, Franklin Pierce Law Center, NH Spring 2009
International Technology Transfer Institute Patent Landscape Analysis Clinic (ITTI) – Team leader
A team leader's responsibilities include supervision of team members for the duration of the semester to make sure the project was completed on time and for quality control. Worked on protein-peptide vaccines.

Professor Tom Field, Jr., Franklin Pierce Law Center, NH Spring 2009
Teaching Assistant – Fundamentals of Intellectual Property
Responsibilities include mastery of material sufficient to hold extra sessions outside of class, supervising the students while they take their quizzes and being a liaison between the students and professor.

Dr. Stan Kowalski, Franklin Pierce Law Center, NH Summer/Fall 2008
International Technology Transfer Institute Patent Landscape Analysis Clinic (ITTI) – Team member
The ITTI Clinic provides instruction in professional skills related to the various responsibilities patent lawyers encounter when preparing patent landscape analysis search reports in biotechnological fields. Legal skills gained: participation in interdisciplinary teams working at the intersection of law and technology, approaches to interviewing and counseling the organizations the ITTI Clinic serves and preventative lawyering. Worked on adenovirus vector vaccines.

Dr. Qibing Zhou, VCU assistant professor**,** Richmond, VA Fall 2005
Lab Assistant
Volunteered in an organic chemistry lab to work on synthesis of potential anti-cancer drugs. Focused firstly on the effects of natural polyterpene quinone methides derivatives on DNA and secondly on the development of a latent DNA alkylating agent that can be activated through target recognitions.

Mr. Jason Cotrell, VCU co-director of the Campus Learning Center 2005-2006
Tutor and Supplemental Instruction instructor
Tutored and taught courses that students were having difficulty with. Responsibilities included paying attention to individual learning needs, grading assignments and other teach assistant responsibilities.

PATENT TOOLS

Extremely proficient with patent searching tools such as Delphion, Aureka, Dialog, Total Patent, USPTO.gov. Proficiency with some patent analytics program (Aureka, Total Patent, MicroPatent)

LANGUAGES AND COMPUTER SKILLS

Fluent in French and English; Conversational in Spanish and Chinese; Extremely proficient with MS Office products

M.V. RAMINI, Ph.D.
8 Celtic Street, Apt #6
Concord, NH 03301
(612) 203-0674

EDUCATION

Juris Doctor/Masters in Intellectual Property, 2011
Franklin Pierce Law Center, Concord, NH

PhD Chemical Engineering, 1992
Indian Institute of Science, Bangalore, India

Patent Information Specialist, The Hague, The Netherlands, 2004

Postgraduate Diploma in Intellectual Property Right, National Law School of India University, Bangalore, India, 2005

Indian Patent Agent, 2005
Indian Trademark Agent, 2007

EXPERIENCE

IP Counsel, *2004-2008*

Philips Electronics India Ltd., Bangalore, India

- Responsible for IP Creation for Centre of Competency, Singapore.
- Drafted patent applications in the fields of Molecular Diagnostics, Personal Health Care and Domestic Appliances.
- Carried out prosecution with Indian and European Patent Offices.
- Undertook Identification projects to identify the possible infringement of Philips products by third parties.
- Conducted risk assessment projects to advise the business to develop/introduce new products.
- Carried out validity and novelty searches using various databases.

Lead Engineer, *2000-2004*

GE India Technology Centre, Bangalore, India

Suggested optimum operating conditions based on mathematical modeling to result in savings of $1 Million to GE Phenol Plant, USA.

Led the team of engineers / scientists to reduce the raw material usage significantly in Crystalline business, USA. Significantly contributed to the Crystalline business in a key decision of retrofitting the existing plant, by estimating fundamental kinetics, generating solubility, and vapor liquid equilibrium data for the processes involved.

Authored seven confidential Technical Reports related to various monomer/polymer process technologies.

Six sigma Green Belt certified and DFSS facilitator and Coach.

Assistant Professor *1995-2000*
Dayananda Sagar College of Engineering, Bangalore, India.

Research Associate *1992-1995*
National Aerospace Laboratories, Bangalore, India

Patents

1. **Ramani, M.V.** Online detection kit for bio-contamination of aviation fuels.(Invention disclosure submitted to Aeronautical Research and Development Board, Ministry of Defence, India)

2. Fulmer John, Pramod Kumbhar, **Ramani, M.V**, Bharat Singh. System and method for purifying Cumene Hydroperoxide cleavage products .US Patent No. **6573408**

List of Publications

1. **Ramani, M.V.,** Kumar, R, Gandhi, K.S., 1992, A Model for static foam drainage. *Chemical Engineering Science*, **48**, 3, 455-465.

2. **Ramani, M.V.,** Kumar, R, Gandhi, K.S., 1992, Drainage and separation factors for static foams containing agglomerates of microbial cells. *Chemical Engineering Science*, **48**, 10, 1819-1831.

3. **Ramani, M.V.,** Patrawalla, 1998, How safe is aviation fuel from bio-contamination. *Aviators*, **2**, 6, 32-34.

4. **Ramani, M.V.,** Veena, B.R. 1999, Anaerobic digestion of Parthenium hysterophorus. *J l. Environmental Studies and Policy*, **2**, 1, 23-28.

5. **Ramani, M.V.,** Utpal Vakil, M., R, Deepak, Swayajith, S, 2004, Vapor Liquid Equilibrium for polymer – diluent systems from melting point depression. *Ind. Eng. Chem..Res, **43,*** 1144-1149.

6. **Ramani, M.V.,** Sekhar Krishnan, Prashant Tatake, 2004, Novel Energy Saving method of rectification, *Chemical Engineering Communications*, **191** (6).

Technical Reports

1. **Ramani, M.V.,** Sridhar, M.K. *Recovery of solvent used in the polymerization of paraphenelyne terephthalamide.* Technical report PD MT 9411, March ,1994

2. Bharat Singh, **Ramani, M.V**., P.Kumbhar, John Fulmer. *Hydroxy acetone removal from phenol plant aqueous stream.* GE Technical report, 2001JFWTC002, May, 2001.

3. G.L.Tulasi, **Ramani, M.V**. *Phosgene reactor modeling*. GE Technical report 2003GRC277, March, 2004.

CHIKA TERANISHI

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EDUCATION

Franklin Pierce Law Center Concord, NH
Candidate for Juris Doctor Expected May 2010

- Member of International Technology Transfer Institute Clinic, Spring 2009
- Intellectual Property Summer Institute, Summer 2008

Kyoto University Kyoto, Japan
Master of Agriculture in Applied Bioscience 2006

- Specialized in Population Genetics
- Conducted research on DNA polymorphism; delivered research presentations

Bachelor of Agriculture in Bio-Production Science and Technology 2004

- Studied DNA polymorphism at a disease resistance gene of wild rice species

EXPERIENCE

TMI Associates Tokyo, Japan
Summer Associate Summer 2009

Management of Technology in Medical Sciences, Kyoto University Kyoto, Japan
Research Associate 2006-2007

- Studied patent, copyright, and contract law; management and entrepreneurship.

Plant Genetics Lab, Kyoto University Kyoto, Japan
Teaching Assistant 2004-2006

- Instructed undergraduate students how to conduct biological experiments. Prepared and modeled experiments; answered students questions.

PUBLICATIONS

Chika Teranishi, Kentaro Yoshida, Naohiko T. Miyashita, *DNA Polymorphism in the SUPERWOMAN1 (SPW1) Locus of the Wild Rice Oryza rufipogon and its Related Species*, 83 Genes & Genetic Systems, pp. 403-15 (2008). (Co-author)

Publicized rice DNA sequences at GenBank, National Center for Biotechnology Information (NCBI) (www.ncbi.nlm.nih.gov/Genbank/): accession numbers AB255631-AB255637 (2006).

Chika Teranishi, Kentaro Yoshida, Naohiko T. Miyashita, *Analysis of DNA Polymorphism at the MADS-box Gene (SUPERWOMAN1) Locus of the Wild Rice Oryza rufipogon*, 80 Genes & Genetic Systems, p. 444 (2005).

CERTIFICATIONS

Japanese Patent Attorney (*Benrishi*), currently unregistered

Kristal M. Wicks

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(615) 513-0367
kwicks@piercelaw.edu

Education

Franklin Pierce Law Center, Concord, NH
Juris Doctor candidate, 2010
Patent Bar Eligible

Belmont University, Nashville, TN
Bachelor of Science, 2006
Major: Biochemistry and Molecular Biology, Minor: Journalism

Experience

Jan. 2009-present — International Technology Transfer Institute/ Patent Landscape Analysis Clinic
Franklin Pierce Law Center

- Prepare patent landscape analysis from patent searching
- Author technical background for a published volume in the Patent Landscape Educational Report Series
- Aid client organizations in achieving effective strategies for application of biotechnology for the global public interest

July 2006-August 2008 — Vanderbilt University Medical Center, Nashville, TN
Research Assistant I, Department of Biochemistry

- Provided support for research projects with vascular smooth muscle cells
- Performed Western blot analysis, RNA microarray, and tissue culture
- Assisted in general laboratory operation and inventory

May 2005-August 2005 — Washington Internship Program /Student Conservation Association, Arlington, VA
Strategic Initiatives Intern

- Conducted research on funding opportunities for invasive plant removal
- Drafted documents for proposed partnerships with conservation organizations
- Assisted with general office duties

Other Experience

Jan. 2009 — Advanced Licensing Institute-CLE
Franklin Pierce Law Center

- Attended sessions relating to biotechnology licensing, cross licensing preparation, government licensing, IP misuse and antitrust law, merchandising, negotiation strategies and mining patent portfolios

July 2008 — e-Law Summer Institute
University College Cork, Ireland

- Completed coursework with focus on regulation of the internet, cyber crime, data protection, online contracting, and the European Union legal and political system

Skills and Interests

Patent searching with Delphion, PATFT, USPTO class search; legal research with LexisNexis, Westlaw; hiking, fishing, developing a law and technology blog, cartooning, cribbage, Minnesota Twins baseball

PRAVIN CONDA

38 Jackson St | Concord, NH | 848-391-7375 | pconda@piercelaw.edu

SKILLS

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

EDUCATION

FRANKLIN PIERCE LAW SCHOOL
Juris Doctorate May 2010

RUTGERS UNIVERSITY • School of Engineering
Bachelor of Science in Biomedical Engineering May 2005

LEGAL EXPERIENCE

Griffith Hack 2008 to August 2008
Summer Legal Assistant *North Sydney, Australia*

- Researched about the regulations on Microorganisms 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) 2008 to August 2008
Research Scientist *Piscataway, NJ*

- Conducted Mass Transfer and kLa studies on various experimental Wave Cellbags®
- Verified multiple tubing types and sizes on the Sterile Tube Fuser Compact, Sterile Tube Fuser Wet Weld, and Hot Lips II to create a comprehensive chart of workable tubing
- Validated various pH probes to be inserted into the Wave Cellbags® and located programming bugs on the WavePod

GBSC, CentoCor (Johnson & Johnson's Family Company) May 2005 to October 2006
Research Scientist *Raritan, NJ*

- Acquired knowledge in the field of Biological Process Sciences – Bioreactor's functionality, valve assemblies and monitoring PLC trends.
- Analyzed PLC trends to understand effects of Fed Batch Supplementation to ongoing process of developing antibodies in a 200 L Bioreactor
- Designed and Implemented a protocol utilizing disposable Wave Cellbags® to upstream erythropoietin producing CHO cells, while observing the effect of Pluronic F-68 on CHO cells in shaker flasks

SWETHA MALADKAR

82 North State Street, Concord, NH 03301

248.924.0670(cell), shweta.maladkar@gmail.com

EDUCATION

Franklin Pierce Law Center, Concord, NH
Expected May 2009
Masters in Intellectual Property (MIP),
Coursework: Patent Practice & Procedure I & II, Patent Law, Legal Writing, Legal Research & Litigation, Intellectual Property Management, Technology Licensing, Mining Patent Information, Advertising Law, Inter Partes in the USPTO and Research paper on "Licensing in Pharmaceutical Industry" (Profitable IP).

Visveswaraiah Technological University, Karnataka, India September 2001 - June 2005
Bachelors of Chemical Engineering
Major project (Central Power Research Institute, Bangalore, India): Studied the heat transfer characteristics of oxide layer formed in boiler tubes. Boiler tubes with oxide scale of varying thickness were collected from thermal power plant and laboratory scale concentric tube heat exchangers was design and fabricated.

EXPERIENCE

International Technology Transfer Institute Patent Landscape Analysis Clinic (ITTI), Franklin Pierce Law Center, Concord, NH**.**
Jan 2009 – present

Working on "Primary Landscape Analysis of Patents Related to Peptide Protein vaccine for HIV", to populate publicly available web based database in collaboration with the Public Intellectual Property Resource for Agriculture (PIPRA).

R.K. Dewan & Company, Pune, India. Feb 2007 – July 2008
Patent Research Associate
Drafted and filed patent application for domestic and global client before Indian Patent Office. Conducted searches in online patent databases like USPTO, EPO, JPO, Delphion and WIPO – IPLD and advised clients on issues of patentability, freedom to operate, validity and infringement. Drafted amendments and responded to Office actions received by the Indian Patent Office, USPTO and EPO.

Legaline, Bangalore, India. Aug 2005 – Dec 2006
Patent Engineer
Conducted Global patent search and analysis of Internet databases including USPTO, WIPO, EPO, Performed novelty searches and prepared patentability search report based on the patentability criteria and on the details provided. Prepared background report for drafting patent

applications. Reviewed and analyzed the technology trends in alternative energy sources like fuel cell, batteries, photovoltaic, bio fuels and micro turbines.

AdMats, Advanced Materials Consultant, Bangalore, India. Aug 2006 – Dec 2006

Development Engineer

Engineering materials were tested using Pin-on -Disc mechanism. Coating adhesion and effective friction coefficient were measured using Scratch Adhesion Tester and Optical Microscopy study of wear and friction.

Languages: English (Advanced), Marathi (Advanced), Hindi (Advanced), Kannada (Advanced), Sanskrit (Intermediary).

Certificates:

- General Course on Intellectual Property (DL-101e) by **World Intellectual Property Organization,** Geneva, Switzerland (November 2008).
- Proficiency Course in Intellectual Property and Protection at **Indian Institute of Science** (**IISc**), Bangalore (Jan-May 2006).

APPENDIX H: MicroPatent Summary Report of Relevant Patents

(see following pages)