MYMETICS CORP
Form 10-K
March 30, 2007

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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 10-K

[X] ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

FOR THE FISCAL YEAR ENDED DECEMBER 31, 2006

[ ] TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

FOR THE TRANSITION PERIOD FROM _____ TO _____

COMMISSION FILE NUMBER 000-25132

MYMETICS CORPORATION
(Exact name of Registrant as specified in its charter)

DELAWARE	25-1741849
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)

European Executive Office
14, rue de la Colombiere
CH-1260 Nyon (Switzerland)
(Address of principal executive offices)

REGISTRANT'S TELEPHONE NUMBER, INCLUDING AREA CODE: 011 41 22 363 13 10
SECURITIES REGISTERED PURSUANT TO SECTION 12(b) OF THE ACT: NONE
SECURITIES REGISTERED PURSUANT TO SECTION 12(g) OF THE ACT:
COMMON STOCK, $0.01 PAR VALUE
(Title of Class)

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes [ ] No [X]

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes [ ] No [X]

If this report is a an annual or transition report, indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934. Yes [ ] No [X]

Indicate by check mark whether the registrant (1) has filed all reports required to be filed be Section 13 or 15(d) of the Securities Exchange Act of

1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes [X] No [ ]

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (Section 229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. [ ]

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, or a non-accelerated filer. See definition of "accelerated filer and large accelerated filer" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer [ ] Accelerated filer [ ] Non-accelerated filer [X]

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes [ ] No [X].

The aggregate market value of the voting common stock held by non-affiliates of the Registrant (assuming officers and directors are affiliates) was approximately U.S. $1,454,563 as of June 30, 2006, computed on the basis of the average of the bid and ask prices on such date. The Registrant has no non-voting common stock.

As of March 19, 2007, there were 135,627,464 shares of the Registrant's Common Stock outstanding.

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USE OF EUROS

The financial information contained in this Form 10-K is provided in Euros (E) (except in "Item 5. Market for Registrant's Common Equity and Related Stockholder Matters" which is provided in United States Dollars, and except as expressly indicated otherwise herein). See Note 1 to the Consolidated Financial Statements contained in this Form 10-K for further explanation. As of March 17, 2007, 1 Euro was convertible into 1.33 United States Dollars.

FORWARD-LOOKING STATEMENTS

The Private Securities Litigation Reform Act of 1995 provides a "safe harbor" for forward-looking statements, which are identified by the words "believe," "expect," "anticipate," "intend," "plan" and similar expressions. The statements contained herein which are not based on historical facts are forward-looking statements that involve known and unknown risks and uncertainties that could significantly affect our actual results, performance or achievements in the future and, accordingly, such actual results, performance or achievements may materially differ from those expressed or implied in any forward-looking statements made by or on our behalf. These risks and uncertainties include, but are not limited to, risks associated with our ability to successfully develop and protect our intellectual property, our ability to raise additional capital to fund future operations and compliance with applicable laws and changes in such laws and the administration of such laws. These risks are described below and in "Item 1. Business," "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations," and "Item 7A. Quantitative and Qualitative Disclosures About Market Risk" included in this Form 10-K. Readers

are cautioned not to place undue reliance on these forward-looking statements which speak only as of the date the statements were made.

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PART I

ITEM 1. BUSINESS

THE CORPORATION

OVERVIEW

We are a biotechnology research and development company devoted to fundamental and applied research in the area of human biology and medicine conducting our business from our European offices located in Lausanne and Nyon (near Geneva), Switzerland. We were incorporated in July 1994 pursuant to the laws of the Commonwealth of Pennsylvania under the name "PDG Remediation, Inc." In November 1996, we reincorporated under the laws of the State of Delaware and changed our name to "ICHOR Corporation." In July 2001, we changed our name to "Mymetics Corporation."

We own all of the outstanding voting stock of 6543 Luxembourg S.A., a joint stock company organized in 2001 under the laws of Luxembourg, and 99.9% of Mymetics S.A. (formerly Hippocampe S.A.), a company organized in 1990 under the laws of France ("Mymetics S.A."), which is a subsidiary of 6543 Luxembourg S.A. In this document, unless the context otherwise requires, "Mymetics" and the "Corporation" refer to Mymetics Corporation and its subsidiaries.

We currently do not make, market or sell any products or services, and thus, we have no revenues. We believe, however, that our research and development activities will result in strong intellectual property that can generate revenues for us in the future. Our business model is to conduct our research and development far enough to sign a partnership agreement with one or more major pharmaceutical companies active in either or both the fields of HIV-AIDS preventive vaccines and therapies.

DEVELOPMENT OF THE COMPANY

From our inception in 1990 to December 1997, we operated in the environmental services industry, focusing on thermal treatment, remediation services and waste oil recycling. In February 1995, we completed an initial public offering. In 1998 and 1999, after disposing of our environmental services businesses, we provided consulting services to an industrial customer in Europe. In June 1999, we acquired a majority interest in Nazca Holdings Ltd., whose business involved the exploration for and development of groundwater resources in Chile. Following the disposal of our interest in Nazca in July 2000, we did not have an operating business.

In March 2001, we acquired 99.9% of the outstanding shares of Mymetics S.A. in consideration for shares of our common stock and shares of Class B Exchangeable Preferential Non-Voting Stock of 6543 Luxembourg S.A., or Preferential Shares, which are convertible into shares of our common stock. In 2002, we acquired all but 0.01% of the remaining outstanding common stock of Mymetics S.A. pursuant to share exchanges with the remaining stockholders of Mymetics S.A. The terms of these share exchanges were substantially similar to the terms of the share exchange that occurred in March 2001. In 2004, all the remaining convertible shares of 6543 Luxembourg S.A. not already held by Mymetics Corporation were converted into shares of Mymetics Corporation.

MYMETICS CORPORATION

Mymetics's primary objective is to develop vaccines and therapies to prevent and treat the effects of certain retroviruses, including the human immunodeficiency virus, or HIV, the virus that leads to acquired immunodeficiency syndrome, or AIDS. Additional applications of Mymetics's research include potential treatments and/or vaccines for human oncoviral leukemias, multiple sclerosis, and organ transplantation.

Prior to 2002, our activities such as design of the prototype molecules, synthesis, and in vitro testing, had been conducted exclusively in Europe. During the second quarter of 2002, we launched programs in the United States in

an attempt to reinforce our intellectual property portfolio and to accelerate the commercialization of our technology. Our previous management believed that expanding

our operating activities in the United States offered numerous advantages, including greater access to expertise, grants, subsidies, intellectual property and public and private research teams. Due to financial constraints, it decided to limit these activities in January 2003. Following the management changes of July 2003, our activities have again been conducted exclusively in Europe, with certain pre-clinical tests being performed in the United States by the National Institutes of Health (NIH).

Under our "best of class" R&D model, the overall research strategy, as well as most original ideas, are defined and contributed by our own scientific team, including Dr. Sylvain Fleury, Ph.D. (Chief Scientific Officer) and Professor Marc Girard, DVM, D.Sc. (Head of Vaccine Development). Any given project is first subdivided into "technology modules" which are then subcontracted to "best of class" teams from academia, public or private laboratories or industry, all chosen for their high standards and specific knowledge. For example, if we need rabbits to be bred, we will outsource this work on a commercial basis to the best company we can find. Most of the work that we outsource is available through other vendors and to date there have not been any providers that are the only source of expertise that we require. We believe that having such specialized expertise in-house would make us dependent on the staff required to carry out such tasks. We believe we benefit from the established relationships with our partners and that it is a cost effective approach to achieving our business plan. Mymetics pays for and coordinates the work, consolidates the results and retains all intellectual property associated with it. In certain limited cases, we will sign partnership agreements with companies offering technologies that can enhance or add value to our own products under development. An example of this approach is the scientific collaboration agreement with Pevion AG, a small Swiss company that granted us an exclusive license to use their Virosome vaccine delivery technology in conjunction with our AIDS preventive vaccine under development. Under this model, Mymetics retains all intellectual property rights in the combined research and applies for domestic and international patents whenever justified. In limited cases, the patent ownership is shared with certain partners such as the French INSERM (Institut National de la Sante Et de la Recherche Medicale). In this case, Mymetics nevertheless received an exclusive license for the eventual exploitation of the shared patents.

Our business model is to sign a partnership agreement with at least one of the few major pharmaceutical companies presently active in the preventive vaccine against HIV-AIDS as soon as our human clinical Phase I trials are completed. We are trying to achieve this by June 2008. We expect that partnership agreement to be typical in the world of biotechnology: an initial cash payment, followed by a series of payments associated with specific milestones and finally, royalties on any sales of end products, assuming these will have been approved by the various regulatory authorities involved, such as the Food and Drug Administration. We would not expect this to occur prior to 2010-2011.

LUXEMBOURG 6543 S.A.

Our Luxembourg subsidiary, Luxembourg 6543 S.A., was founded in 2001 in connection with the acquisition of Mymetics S.A. by Mymetics Corporation as a vehicle to allow the former French shareholders of Hippocampe S.A. to defer French taxes due on the exchange of their Hippocampe S.A. shares for Mymetics

Corporation shares. Luxembourg 6543 S.A. is dormant. We intend to liquidate it as soon as Mymetics S.A. is dissolved following its emergence from its receivership status discussed below.

MYMETICS S.A.

Our French subsidiary, Mymetics S.A. (formerly, Hippocampe S.A.), founded in 1990, is a biotechnology research and development company devoted to fundamental and applied research in the area of biology and medicine. The company is the legal owner of our initial key patents, which were applied for prior to it being acquired by Mymetics Corporation. At this time, it is not possible to transfer these patents to any non-French legal entity without the French tax authorities' approval. This approval requires an assessment of the actual economic value of the patents, which the French tax authorities will only accept as resulting from one or more arms-length transactions in which the technology protected by the patents is licensed or sold to one or more third parties. Mymetics S.A. is presently inactive. Its last salaried employee completed her assignment and had her employment contract terminated on January 31, 2005. We do not intend to hire new staff in France in the

foreseeable future, and all R&D will be conducted by Mymetics Corporation. We intend to liquidate Mymetics S.A. as soon as it emerges from receivership, discussed below.

On February 7, 2006, the Tribunal de Commerce in Lyon, France placed Mymetics S.A., under receivership ("Redressement Judiciaire") as a result of an ongoing dispute between Mymetics Corporation and a former officer and director, Dr. Pierre-Francois Serres, who obtained an initial judgment against Mymetics S.A. in France in the amount of E173,000 for an alleged wrongful termination by the Company's prior management during 2003, which judgment was reversed on appeal. The court appointed two judges to oversee the case, a lawyer to represent the creditors and a judicial administrator to manage Mymetics S.A., all of whom are considered agents of the court. The court further imposed a two-month "observation period" during which management and the administrator should strive to find a solution to the crisis. This period has been extended several times, the last time until May 7, 2007. We expect to arrive at a viable solution before the end of this observation period.

Under the order of the French court, Mymetics S.A. recently sold its patents to Lomastar Technologies for E80,000 in order to pay its creditors and the administration costs of the case. We do not believe that the sale of the patents is significant to us since they expire in 2017 and 2018, the dates we first expect to be selling the vaccine. To protect the value of our intellectual property, however, we are negotiating an exclusive worldwide perpetual license with Lomastar Technologies with respect to these patents that we hope to conclude in the next several weeks. There can be no assurance, however, that we will be successful in achieving this result, which could limit the value of our intellectual property and the potential value of our company to a prospective purchaser.

TECHNOLOGY

CURRENT APPROACHES

Current drug treatments in HIV focus on slowing or impeding the progress of the virus once it has infected the body's host cells. Recent approaches seek to develop therapies that prevent the virus from fusing with host cells. If the

virus cannot fuse, it cannot enter inside the cell(infect) and reproduce, thereby facilitating the successful fight of the body's immune system against the invasion.

HIV transmission generally occurs through sexual contact. Indeed, semen and cervico-vaginal secretions may potentially transmit HIV to the gastrointestinal, anorectal and genitourinary tracts because these fluids contain cell-free HIV particles and numerous HIV-infected cells. Contracting HIV infection may be subdivided into two main events. The first event, considered as a very early step, corresponds to viral translocation across mucosal surfaces that facilitates virus penetration and spreading into the body. The second event, which usually takes place after virus translocation such as by transcytosis, represents the infection step that leads to virus entry into target cells (ex. CD4+ T lymphocytes). Therefore, the HIV vaccine should ideally elicit immune responses not only in the blood but most importantly, also at the primary entry site, which corresponds to two important anatomically compartments: genital-reproductive tracts and intestine/rectal mucosal tissues. Therefore, vaccines or therapies for preventing this very early event of HIV translocation at the mucosa levels (ex. Transcytosis) became another important research aspect.

Until recently, vaccine development was focusing on clade B strains, which dominate the epidemic in industrialized countries but cause only about 12% of infections globally. Development of non-clade B candidates, having clade C as a key target became a priority and Mymetics seriously intends to invest all its research effort in developing its "universal" vaccine, with a primary interest for the clade C because of its world dominance, especially in countries under development like Africa, India and Asia.

MYMETICS'S APPROACH

Mymetics proposes an innovative AIDS vaccine that could prevent or reduce HIV entry at the mucosal level (primary entry: early event) as well as preventing cell infection by HIV (late event). To achieve this goal, Mymetics has combined three important concepts in the vaccine design for eliciting different sets of antibodies:

1- Preferential induction of mucosal antibodies for protecting various anatomical compartments

Mymetics postulates that the induction of protective mucosal antibodies such as IgA and secretory IgA might block the early event of HIV entry across the genito-reproductive and intestinal tracts. These mucosal antibodies could also contribute to prevent the HIV infection of target cells located just under the mucosal epithelium, thus preventing HIV entry and spreading in the body. Neutralizing blood antibodies (systemic) such as IgG will also be elicited by Mymetics's vaccine candidate. These blood antibodies will likely act on later events that may take place into secondary lymphoid organs, which consist to prevent the infection of target cells in the periphery, outside of the mucosal system. These mucosal (mostly IgA) and blood (mostly IgG) antibodies should act synergistically for optimal protection against HIV transmission and they may circulate from one compartment to another one, especially blood antibodies migrating to the mucosa levels.

2- Focused antibody response against relevant conserved gp41 regions

To achieve this objective, Mymetics's HIV vaccine candidate is constituted of

gp41 peptides and recombinant proteins that are devoid of immunodistractive and useless areas. Generally, the immune system develops immune responses toward all possible regions of the foreign antigens (peptides, proteins, etc.). However, antigens are often harbouring several immunodominant regions, each eliciting an immune response of different magnitude (low, intermediate or strong recognition/affinity by the immune system) and frequency (region rarely, sometimes or often recognized by the immune system). Therefore, it is common to observe an immune response that preferentially recognizes some protein areas (immunodominant), while others are neglected. Furthermore, viruses have developed antigens that contain often immunodominant regions for distracting the immune system. These immunodistractive regions may have little or no function for the pathogen protein but may blind the immune system. Consequently, immune responses against the pathogen might be sometimes useless. Mymetics is developing vaccines that contain different antigens expressing limited and useful immunodominant regions, while useless immunodistractive regions have been removed or altered with minimal effect on the immunogenicity of the viral antigen. Using this approach, it forces the antibody response to focus on relevant viral protein regions.

3- Minimal mimicry

This concept is intended to remove in part or entirely the human protein homologies naturally present in many HIV proteins that serve as a vaccine component. To achieve that objective, Mymetics intends to use as a candidate vaccine the smallest engineered viral antigen sequence for two main reasons. First, the smaller the protein, the more limited are the homologies with human proteins. Second, it is easier to remove human homologies into a small viral protein or peptide because of their limited distribution. Using this approach, Mymetics believes that an HIV vaccine constituted of viral antigens or genes encoding viral antigens with minimal human homologies should reduce the risk of developing potential long-term autoimmunity side-effects after HIV vaccination.

How to trigger the protective immune response?

Mymetics's vaccine uses the technology of Virosomes(R), a lipid-like structure highly efficient for delivering the vaccine's active ingredients.

The virosome-based vaccine is constituted of two types of virosomes, each with surface anchored gp41-derived conserved antigens, each eliciting different antibodies not mutually exclusive with a broad activity spectrum:

- Virosomes with peptides corresponding to the conserved Membrane Proximal Region (MPR) of gp41 for triggering protective mucosal antibodies (mostly IgA) against a broad spectrum of HIV isolates.

- Virosomes with soluble/stable recombinant gp41 without the MPR for eliciting complementary neutralizing IgA and IgG antibodies.

This Virosomes(R) technology is already market approved in more than 40 countries with excellent safety profile and no mucosal adjuvant is required for triggering mucosal antibodies.

We executed an exclusive License Agreement dated March 1, 2007 with Pevion Biotech for the use of Virosomes(R) in the production of our HIV vaccine. We believe that our exclusive agreement with Pevion Biotech provides a competitive advantage by allowing us to avoid using an adjuvant for our HIV vaccine. We believe that adjuvants have not sufficiently advanced to allow clinical testing

for our HIV vaccines.

By carefully modifying parts of the HIV gp41 molecule, Mymetics has obtained vaccine subunits such as gp41 peptides and engineered recombinant gp41 molecules that:

- May form stable dimers, trimers or tetramers and the protein folding isclose to the native protein;
- Are soluble in the absence of detergent and can be incorporated into an artificial lipidic membrane, which is more suitable for in vivo work;
- Can be chemically synthesized or easily produced by recombinant bacterialike E. coli;
- Have been stripped of immunodominant areas that generates numerous non-neutralizing antibodies, which may fool the immune response.
- Have been stripped of its key IL-2-like sequence and other human homologies, minimizing the important potential cross-reaction with host proteins that may contribute to the destruction of the immune system seen in HIV patients;

This type of new engineered gp41 molecules should be able to elicit antibodies with a broad spectrum of action (cross-clade neutralization like A, B and C): blocking virus translocation across the mucosal barrier and/or to inhibit cell infection, thus preventing HIV-1 infection.

Based on our recent research results, we believe that Mymetics's HIV vaccine candidate and strategies definitely place us amongst the most advanced teams devoted to AIDS prophylactic vaccine research that aims to prevent HIV transmission across the mucosal barrier.

Mymetics's findings further apply to a range of additional diseases, including certain oncoviruses often associated with leukemia.

THE IMMUNE RESPONSE

Normally, the body's immune system responds to the invasion of pathogens. In the case of HIV, for example, an infected host cell alerts the immune system by secreting interleukine-2 (IL-2), a special protein (called a cytokine) that acts as a key messenger for many cells of the immune system.

IL-2 acts as a T cell growth factor, promotes NK proliferation and stimulates B cell growth (cells that produce antibodies). Together, these "soldier cells" attack foreign pathogens like viruses, and help to destroy them. From the first encounter with the invader, the immune system keeps a memory of what happened and specialized "memory" T and B cells are established as guardians in the host's body. The next time the invaders try to enter, they will be swiftly attacked and disarmed.

HIV AND AIDS

The HIV (human immunodeficiency virus) is a retrovirus that gradually destroys the immune system and ultimately leads to AIDS, is famously the most genetically diverse viral pathogen known, specially in Africa where HIV is also rapidly mutating. Indeed, HIV exists under many different versions like members of a large family, they are different from, but related to each other.

By sequencing the viral genomes (genes), researchers have been able to map out the family tree of HIV. At the root of the tree, there are three groups called

M, N and

O, group M being responsible for the current AIDS pandemic. Group M is split into nine genetic subtypes, also called nine clades (designated A through K, with no E or I). The original definition of clades was based on short genomic sequences, mostly within the HIV envelope protein (Env: gp160).

These nine clades have uneven geographic distribution patterns. Clade C circulates in South Africa, India and parts of China. Clade A and D are common in East Africa and clade B is common in North & South America and Western Europe. Looking at the global numbers, it emerges that four clades (A, B, C and D) plus two recombinant forms called CRFs 01 and 02 (both of which are about 70% clade A) account for over 90% of all infections worldwide. From this perspective, diversity can be mostly limited to 4 key major clades, plus small contributions from the non-A segments of these two CRFs. According to the statistics, clade C represents the world's most dominant HIV (>50%).

HIV attaches itself to the target host cell using a harpoon-like surface protein called gp160. This protein spears the host cell's membrane, drawing them together so that the virus can fuse with the host cell. Once attached, the virus penetrates the cell and commandeers the cell's machinery. Then it rapidly replicates itself.

HIV-1 is lethal since it targets the most central cell of the immune system, the CD4+ T cells which produce the IL-2 cytokine, a key messenger for immune cells. These cells usually coordinate the cellular and humoral responses that are directed to thwart the pathogen (HIV). When the number of such CD4+ T cells decreases significantly over time, the amount of IL-2 becomes too low for an efficient immune attack orchestration. Consequently, HIV as well as other pathogens evade the activity of the immune system, leaving the host vulnerable to disease.

HIV proves itself an elusive target because it:

- Reproduces itself at an extraordinary rate (several million new virus particles are created daily)

- Mutates rapidly: as it reproduces itself, it makes mistakes that produce new virus particles that are slightly different; these differences make the virus harder to target by the immune system.

MYMETICS AND HIV-AIDS

Normally, the immune system would respond to this attack: IL-2 would be secreted mostly by activated CD4+ T cells to signal the alarm to the other T-Cells subtypes and B-cells. With HIV, this approach backfires. Why?

Mymetics has discovered a peculiar inter-reactivity between part of the virus's "harpoon" and the host cell's "alarm" (IL-2). We call it "mimicry". Several other homologies between HIV and human proteins have been reported. It has also been reported that most of HIV infected subjects develop auto-antibodies (antibodies attacking your own proteins), even in early phase of the infection. It has been postulated that some mimicries must exist between HIV and human proteins, which could lead to such autoimmunity problems.

The shaft of the virus' harpoon, called gp41, actually appears to "mimic" the host cell's IL-2. This dynamic enables the virus to attach itself to the host

cell membrane at a precise portal. An unusual consequence: when the "soldiers" (antibodies against the viral gp41 protein) arrive to battle the virus, they can potentially "confuse" the virus's gp41 with the host cell IL-2 and attack and destroy them both.

As the immune system methodically kills its own soldiers, the HIV continues to replicate swiftly. The equilibrium shifts and the HIV outpace our body's defenses. Such events likely contribute to the development of AIDS, a fatal disease that affects an increasing number of people worldwide. In light of these reported observations, Mymetics is using this information to develop a safer HIV vaccine that would be constituted of vaccine subunits having minimal human homologies.

WHERE ARE WE AND WHERE ARE WE GOING?

From 1997 to 2001, Mymetics's R&D has documented the existence of an important three-dimensional molecular mimicry between the gp41 glycoprotein of HIV-1 and the human interleukin-2 (IL-2) cytokine, a mimicry also found in lentiviruses causing AIDS in other animal species. Mymetics has explored this mimicry as the starting point for developing a safe HIV-1 candidate vaccine capable of eliciting protective antibodies, while preventing potential harmful cross-reactivities toward host proteins such as the human IL-2 (Mymetics US Patent 6,455,265). We believe that this innovative concept may render vaccines from the 21st century as efficacious as those from the 20th century, in addition to being safer.

Together with Protein'eXpert S.A. (Grenoble, France), we have succeeded in engineering and producing in bacteria E. Coli the first gp41 generation in September 2003, which forms soluble and stable gp41 trimers that closely resembles the native gp41 found on HIV-1. This first generation of gp41 immunogen is devoid of the cluster I and 2F5/4E10 epitopes, in addition of being mutated in one important IL-2 mimicry area. The design of the first gp41 generation was intended to identify new important epitopes as well as to focus the immune response on possible neutralizing epitopes different from the 2F5/4E10 previously identified by other teams.

In 2004, we started a collaboration with Dr. Morgane Bomsel(Cochin Institute, Paris, France), a renowned scientist in the field of HIV transcytosis and mucosal immunity. Dr Bomsel had few monoclonal IgA antibodies obtained from a phage display libraries issued from B cells of HIV resistant women. These monoclonal IgA antibodies were found later capable of preventing HIV transcytosis and HIV infection of primary isolates. Interestingly, these IgA have recognized epitopes on our gp41 first generation devoid of the 2F5/4E10 epitopes, meaning that other potential neutralizing epitopes exist and they are not limited to IgG isotypes.

From January to August 2004, the first gp41 generation was tested in rabbits for it's capacity to elicit neutralizing antibodies toward HIV-1. Such antibodies were obtained in large quantities and their neutralizing potential was evaluated by our academic collaborators. Thus, Dr. Morgane Bomsel obtained 60% inhibition of HIV-1 transcytosis with primary strains. Sera were also tested in the laboratory of Dr Christiane Moog (Institut Pasteur, Strasbourg, France), a well acclaimed specialist in neutralizing antibodies in the HIV field. In the performed assay, primary T cells infection by primary HIV-1 strains from clade B (Bx-08 and SF-162) and clade C (TV1) were respectively neutralized at 70%, 80% and 90% by low sera dilutions. When total rabbit antibodies were purified from the serum, a neutralizing activity of 80% was obtained with an antibody

concentration of 20ug/ml, using three primary HIV-1 strains. These results are similar to those obtained with the 2F5 monoclonal antibody (>90% inhibition), one of the most potent neutralizing antibodies so far identified. Infection of primary human macrophages by primary HIV-1 strains was also strongly inhibited (>90%) with a low antibody concentration (