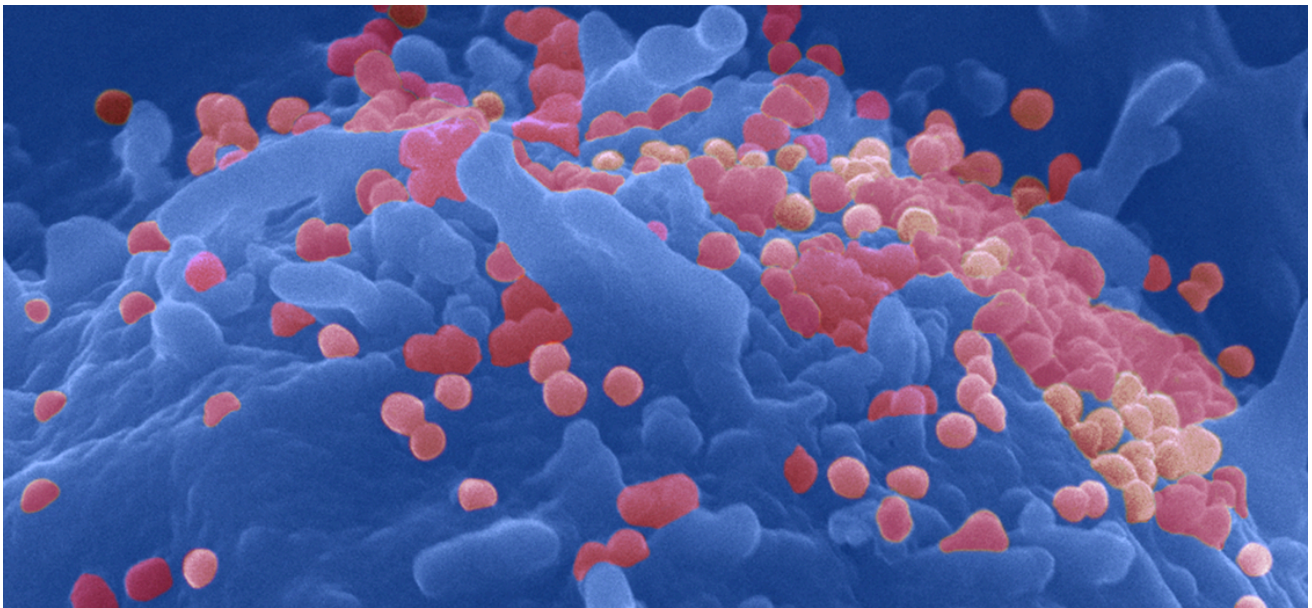


# AIDS Research at the Institut Pasteur



JULY 2017

press kit

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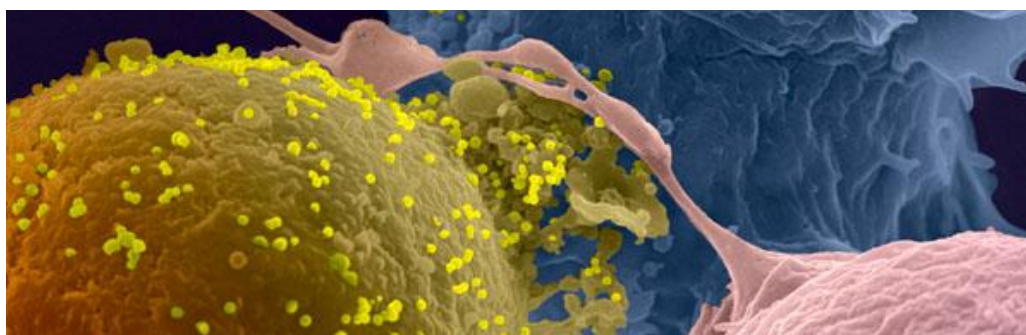
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Cover page : Colored scanning electron micrograph (SEM) of HIV virus particles at the surface of a lymphocyte T CD4 . © Institut Pasteur

# I - AIDS research – a priority for the Institut Pasteur

Today, 34 years after Institut Pasteur scientists discovered HIV-1 – a breakthrough that was awarded the Nobel Prize in Medicine in 2008 – AIDS remains a major public health problem, affecting the poorest countries and people in particular: 37 million people live with HIV/AIDS in the world, half of whom do not have access to treatment, and there are over 2 million new cases every year. HIV is the leading cause of death in women of child-bearing age and the second cause of death in adolescents around the world. In addition, in some regions, Europe in particular, the number of new cases is rising. In France, regrettably, there are still over 6,000 new cases a year with no sign of a slowdown (see "AIDS in terms of numbers").

*Transmission of HIV-1 from cell to cell. An HIV-1 infected lymphocyte (in pseudo-color yellow) in contact with non-infected lymphocyte (blue and pink). The viral particles are light yellow. Photo by scanning electron microscopy.  
© Institut Pasteur*



Regarding the significant progress made in recent years, tritherapy has proved particularly effective in controlling the virus and reducing its transmission. The latest findings show that it is crucial for patients to receive treatment as early as possible after their infection. This is because the virus attacks the immune system in the early weeks of infection and this damage cannot be reversed if treatment begins too late. Despite this progress, HIV triggers chronic inflammation that remains, albeit to a lesser degree, in treated individuals. This inflammation is linked to a higher risk of diseases, such as cancer, cardiovascular diseases and diabetes. There is therefore an urgent need to develop a vaccine to put an end to this epidemic.

In this context, HIV/AIDS research still constitutes one of the main objectives of the Institut Pasteur in Paris and the Institut Pasteur International Network, in countries particularly affected by the epidemic.

**A dozen teams have been mobilized in Paris. The lines of research cover most of the current main fields of investigation. They concern studies on the development of the epidemic, HIV entry and multiplication mechanisms in human cells, virus transmission, pathophysiology of the infection, human immune response to the virus, natural protection in humans, the roll out of treatment in countries with limited resources, research into curing HIV infection, and of course vaccine candidates.**

*This work is being carried out in close partnership with the French National Agency for AIDS Research (ANRS), and in cooperation with the Institut Pasteur International Network, hospitals in France and national and international partner laboratories.*



## II – HIV/AIDS research at the Institut Pasteur

Remarkable progress in academic and clinical research, and in treatment and prevention, has prevented the escalation of the pandemic since 2012. However, with over 37 million individuals infected in the world, AIDS is still a major public health problem today and the research effort must continue. It is essential to improve fundamental knowledge of HIV infection to advance therapeutic and vaccine research in the long term. At the Institut Pasteur, numerous studies are being carried out on virus-host interactions, treatment of the infection, and vaccine candidates.

### 1 - Epidemiology, evolution of the virus and development of the pandemic

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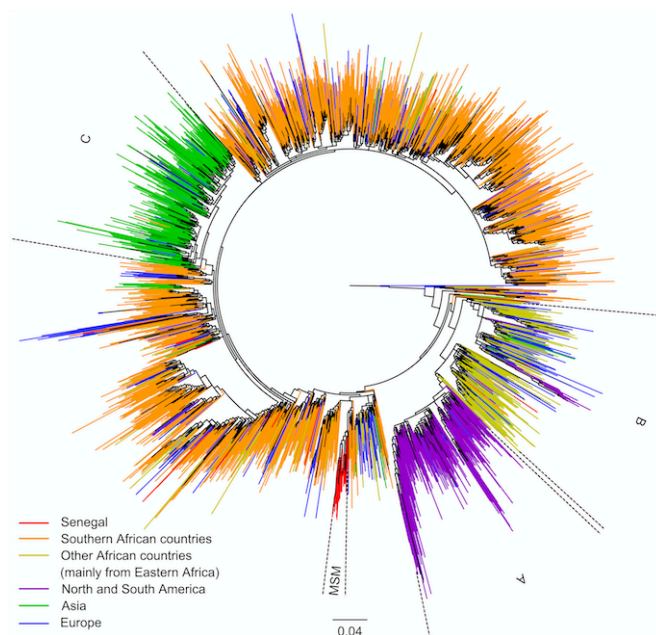


*Olivier Gascuel  
directs the  
Evolutionary  
Bioinformatics Unit.  
© Institut Pasteur*

HIV evolves extremely rapidly. Approximately 0.5% of its genome mutates each year. This flexibility enables it to evade the host immune system and develop resistance to antiretroviral therapy. It also gives rise to a variability that enables researchers to reconstruct its evolution. We also know that HIV first developed in monkeys before coming into contact with the human population several times. Only one of these introductions gave rise to the global pandemic – contact with the HIV-1 M group. Regarding the main stages of this pandemic, scientists have been able to trace its origin back to the early 20th century in Central Africa, its development in the Democratic Republic of the Congo from the 1950s and 1960s, and finally its spread across the world in the 1980s.

Olivier Gascuel's Evolutionary Bioinformatics Unit focuses on methods for understanding this evolution and assessing its effects to help implement preventive policies. This unit is behind widely distributed computer software used to reconstruct viral phylogenies, date them, and monitor their development within risk groups across the world. Using evolutionary studies, these researchers recently formally proved the existence of a tenth HIV-1 gene. It was put forward in the late 1980s but experimental evidence was unconvincing until now. This gene correlates with the spread of the virus and is only present in the M group and its most prevalent sub-types.

*Visualization of the various introductions of HIV-1 subtype C across the world. Obtained thanks to PhyML software which estimates the most likely phylogenies based on the alignments of nucleotide and amino acid sequences. This phylogenetic tree shows that some subtype C introductions were close to unique, such as those which occurred in Asia and in America, as well as in Senegal (specifically in the homosexual community). In Europe, on the contrary, there were several introductions. © M. Jung (CNRS), O. Gascuel (CNRS/Institut Pasteur), M. Peeter (IRD)*



The unit is also interested in resistance mutations, which tend to develop and risk causing major problems, particularly in Africa. Thanks to large-scale analysis of statistical data?, it has demonstrated that these mutations are widely transmitted by untreated patients, hence the emergence of particularly dangerous difficult-to-treat forms, and the need for targeted and active prevention policies in the affected groups.

## 2 - Understanding the mechanisms that naturally control the infection

### The Controllers – patients who do not develop the disease



*Asier Saez-Cirion, group leader within the HIV, Inflammation and Persistence Unit.  
© Institut Pasteur*

Rare individuals infected by HIV-1 control viral replication. These HIV controllers (HIC) have been identified and are monitored in the ANRS CO21 CODEX cohort. These HIV-positive patients, who were infected several years ago, have no detectable virus in their plasma and maintain a high level of CD4 T cells, the immune cells targeted by the virus. They do not therefore develop the disease, and naturally control the infection without therapy.

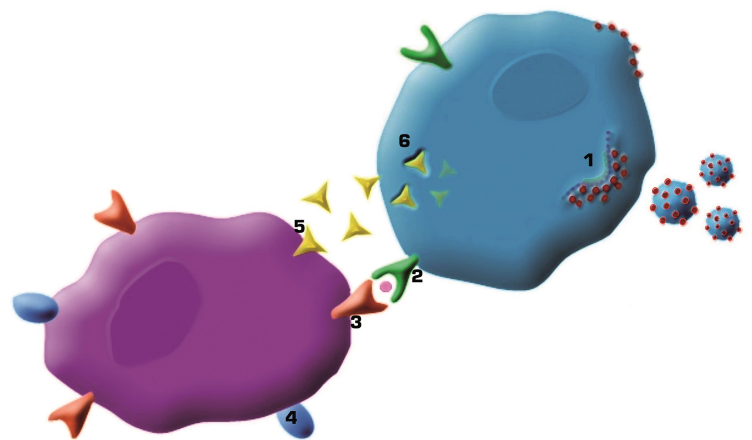
Major breakthroughs have already been made in understanding this protection mechanism. Asier Saez-Cirion's team in the HIV, Inflammation and Persistence Unit, directed by Michaela Müller-Trutwin, has highlighted two factors involved in controlling the infection –particularly effective cells (CD8 T) that recognize other cells infected by HIV-1 and suppress them efficiently, and target cell resistance that limits their HIV infection. Researchers are continuing their work to identify the mechanisms that induce CD8 T suppressor cells to block HIV replication effectively.

Further research shows that "central memory" CD4 lymphocytes play an essential role in HICs and explain the remarkable defenses of these patients, who behave like they have been vaccinated. Lisa Chakrabarti's team (Viral Pathogenesis group) observed that the CD4+ T immune cells in these patients were capable of recognizing tiny quantities of the virus. This highly sensitive detection is dependent on the expression of specific T cell receptors on the surface of immune cells, which target the HIV capsid protein with high affinity. The preferential expression of these receptors appears to keep the immune system on a constant state of alert, thereby enabling the patients to control HIV.

*Research on HIC patients is conducted within a research laboratory consortium, set up by the ANRS. For the first time, scientists can study how the immune system is organized to fight the virus effectively. This work should influence future vaccine and therapeutic strategies.*

*Cytotoxic T CD8 lymphocytes (aka CTL) in HIC patients (HIV Controllers) have preserved their functions, and are therefore able to efficiently eliminate T CD4 lymphocytes which are infected by HIV. © Institut Pasteur*

1. Infected T CD4 lymphocytes produce HIV particles.
2. Viral antigens are exposed at the surface,
3. and recognized by T CD8 lymphocytes
4. which, in HIC patients, present a unique profile (in terms of activation markers) at their surface ; this profile being associated with their ability to control the infection.
5. T CD8 lymphocytes then secrete cytotoxic



## Mucous membranes – key sites for virus transmission and natural control



*Elisabeth Menu heads the MISTIC group, within the HIV, Inflammation and Persistence Unit. © Institut Pasteur*

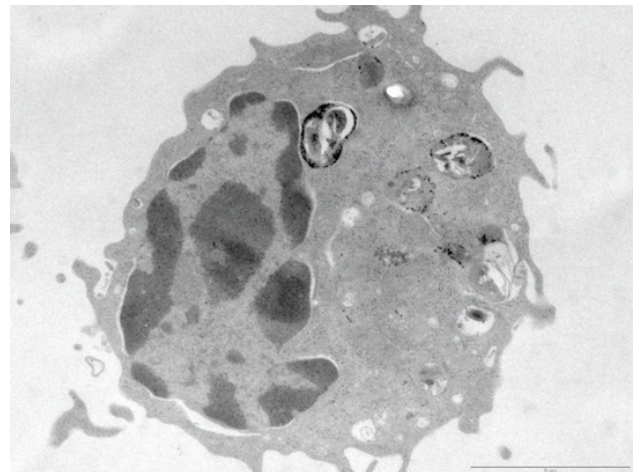
The mucous membranes are the sites favored by HIV for entering the body. Male-to-female heterosexual transmission is the primary route of transmission via the mucous membranes of the female reproductive tract. In addition, 90% of children from HIV-1 positive women are naturally protected against HIV infection during pregnancy. Institut Pasteur scientists have shown that the placenta and its environment play an important role in this protection. Elisabeth Menu's team - MISTIC group of the HIV, Inflammation and Persistence Unit directed by Michaela Müller-Trutwin - has highlighted the role of mucous membrane innate immunity at the mother-child interface in naturally preventing HIV-1 transmission *in utero*.

On the basis of their findings, researchers in this team are currently studying the control of transmission in genital tract mucous membranes of women who are not pregnant. They are particularly investigating innate immune receptors – Toll-like receptors (TLRs) – that recognize the motives of pathogens and trigger immune responses.

They are also studying the impact of seminal fluid during intravaginal exposure on local immune responses and particularly on vaccine responses and inflammation. Finally, they are looking at the role of vaginal microbiota in susceptibility to co-infections and in immune responses.

All this research could lead to the identification of new defense mechanisms against pathogens in barriers formed by mucous membranes.

*Electronic microscopy image of a cell presenting antigens (dAPC CD14+), which is the main target of HIV-1 within the human decidua (uterine lining during pregnancy). ©Institut Pasteur*

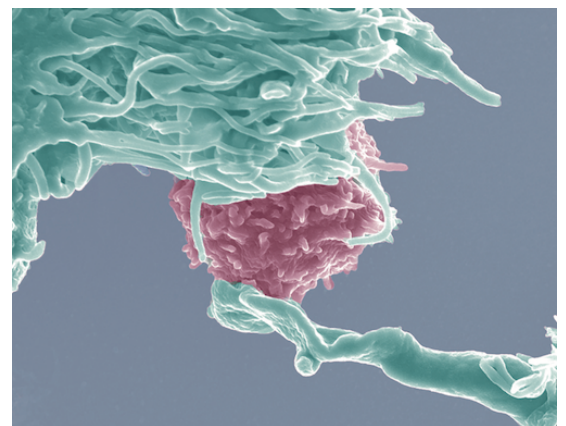


### **Innate immunity, a major mechanism in controlling HIV replication**



*Michaela Müller-Trutwin is chief of the Inflammation and Persistence Unit. © Institut Pasteur*

We know today that activation of innate immune responses is essential for inducing responses specifically mounted against HIV, i.e. antibody and cytotoxic lymphocyte responses. The role of innate immunity against HIV infection constitutes a very active line of research at the Institut Pasteur. Several laboratories are studying the role of dendritic cells, macrophages and natural killer cells in inducing specific immune responses, particularly in the context of vaccine research.



*Interaction between a lymphocyte (in pink) and a dendritic cell (in blue), two cells of the immune system, which are targeted by HIV. Close contact between cells allow them to communicate together. HIV-1 benefits from cell closeness by propagating from one cell to the next. Scale is 1 micron. ©Institut Pasteur*

The virus multiplies mostly in organs, such as the intestine and lymph nodes, particularly in their follicles. Yet, these follicles are major antibody production sites and consequently play a key role in the specific immune response. The high viral replication rate in the lymph node follicles could therefore disrupt the induction of good antibody responses, especially as current tritherapies are not able to

completely control HIV replication in these follicles. The animal model is used to quantify viral replication in the various organs. Thanks to imaging and 3D image building technology, Michaela Müller-Trutwin's team (HIV, Inflammation and Persistence Unit) is analyzing and monitoring innate immune responses within the follicles in this context. These studies shed new light on possibilities for controlling viral replication. They are conducted in partnership with the Infectious Disease Models and Innovative Therapies Center (IDMIT) at the CEA, and supported by the French Vaccine Research Institute (VRI) in Créteil.



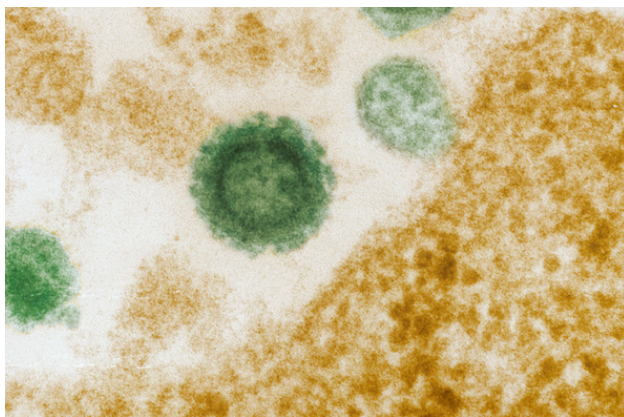
## 3 - Pathophysiology of the infection and immunodeficiency mechanisms

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Numerous analyses have been carried out in animals and in humans (monitoring of HIV-positive patients) to understand how the virus disrupts the immune system, which is to a large extent destroyed during the course of infection.

### Understanding the progression from HIV positive status to the onset of the disease

Michaela Muller-Trutwin's group, formerly part of the Regulation of Retroviral Infections Unit, directed by Françoise Barré-Sinoussi, has demonstrated that it is the chronic inflammation induced by the HIV infection that is responsible for the progression from HIV to AIDS. This



*SIV virus, the causal agent of AIDS in monkeys, belongs to the retrovirus family, and more specifically to the lentivirus genus (slow infection). More than 30 African primate species are naturally infected by strains of SIV. These strains are classified in six phylogenetic groups. The infection is asymptomatic in its natural host, even though the seroprevalence is high. Colorized image.*  
© Institut Pasteur

discovery was made by studying the HIV animal reservoir, the SIV (simian immunodeficiency virus), which is present in African monkeys. African green monkeys are chronic SIV carriers but they maintain their T4 cells and do not develop AIDS. Unlike humans infected with HIV, African monkeys are capable of rapidly overcoming the inflammation induced by the virus and do not present chronic inflammation. The findings in the simian model have been used to focus research on inflammation in humans. Studies are underway in humans to identify the best markers for inflammation associated with poor antiviral response or a higher risk of developing non-AIDS diseases. Other research projects aim to identify the mechanism used to overcome inflammation in African monkeys, which could help to develop and/or find ways to counter chronic inflammation in humans.

### The virus disrupts the contacts between immune system cells and their role in the immune response



*Andrés Alcover*  
©Institut Pasteur

In addition, researchers from the Lymphocyte Cell Biology Unit, directed by Andrés Alcover, and from Olivier Schwartz's Virus and Immunity Unit have discovered a mechanism by which the AIDS virus impairs the immune response. Scientists have demonstrated that HIV infection of the T lymphocytes disrupts contacts between these T lymphocyte cells and other immune system cells. These contacts, known as immunological synapses, are essential for triggering immune responses. The virus slightly alters the location of certain proteins in the T lymphocytes thus disrupting the functions of these cells.

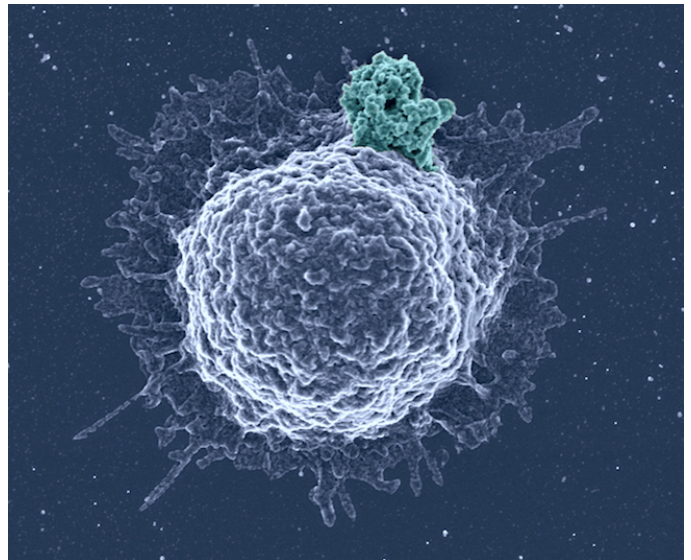
## Long-term immunological effects of infection during childhood



Florence Buseyne  
©Institut Pasteur

Children can be infected with HIV in utero, in late pregnancy or during birth if their mother is HIV-positive. The progression of their disease is very different from that of individuals infected as adults. This is because immune defenses are weaker in children than in adults and therefore less effective in fighting the virus. But, these defenses regenerate themselves more easily and a child's immune system has a higher potential for rebuilding itself than an adult one. Thanks to antiretroviral therapy, children infected at birth can reach adulthood. The first generation of these children, born before the advent of tritherapy, has therefore left pediatric care for adult healthcare services. The question now is whether their immune systems are similar to those of patients infected in adulthood. Florence Buseyne, who leads the Immunity of Human Retroviral Infections group (as part of Antoine Gessain's Oncogenic Virus Epidemiology and Pathophysiology Unit) is working on an answer. Relying on the study of the French cohort of infected children, these research works have shown that CD4 T-lymphocyte regeneration has remained effective in these young people and compensates for the harmful effect of the virus in the long term. Current research aims to demonstrate whether very early treatment of infants (under 6 months of age) is of benefit in the long term.

*Scanning electron micrograph (SEM) image revealing the viral biofilm formed by the T cell of a patient infected by HIV. The viral particles gather in cocoon-like extracellular matrices ; they are produced at the surface of HIV infected cells and help transmit the virus to target cells very effectively.*  
© Institut Pasteur



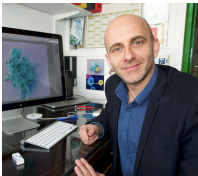


## 4 - How the virus enters, multiplies and spreads in human cells, and how these cells defend themselves

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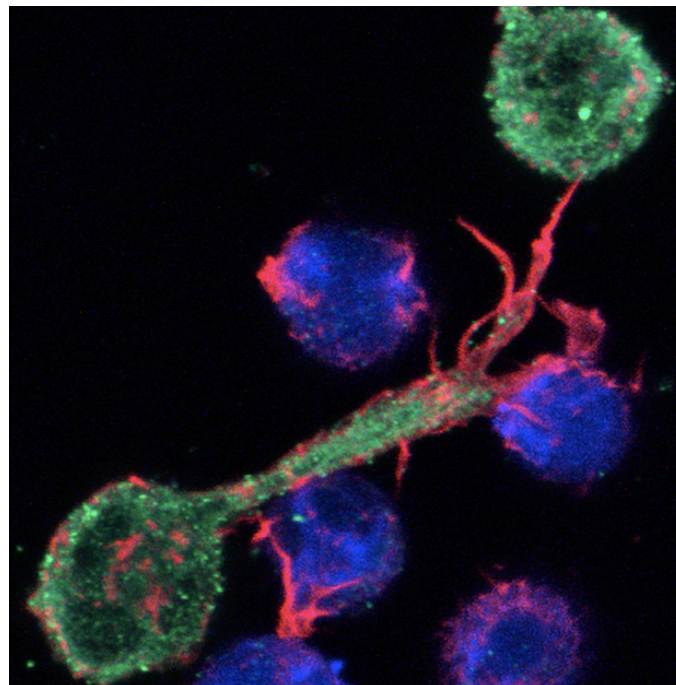
Several Institut Pasteur teams are aiming to decipher the mechanisms by which the virus enters target cells, its integration into the genetic heritage of these cells, the way in which it disrupts cellular functions in order to "reproduce itself" using the cell it infects, and the defense mechanisms used by target cells against the infection.

### The virus spreads from cell to cell



*Olivier Schwartz leads the Virus and Immunity Unit.  
© Institut Pasteur*

Olivier Schwartz and his team (Virus and Immunity Unit) are studying the molecular mechanisms involved in HIV infection and spread in the body, and the immune system response to this infection. This work particularly focuses on HIV mechanisms for spreading from one cell to another – the favored method of propagation for the virus – or the antiviral defense barriers put in place by the cell itself. The HIV virus multiplies effectively by directly progressing from one infected cell to an uninfected target cell. The unit is studying the formation mechanisms behind virological synapses, which enable the virus to spread between cells and probably partly evade the immune system response (antibodies and cytotoxic cells). The role of cell proteins in antiviral activity is also being unraveled. These proteins, called restriction factors, block viral replication at different stages of the viral replication cycle.

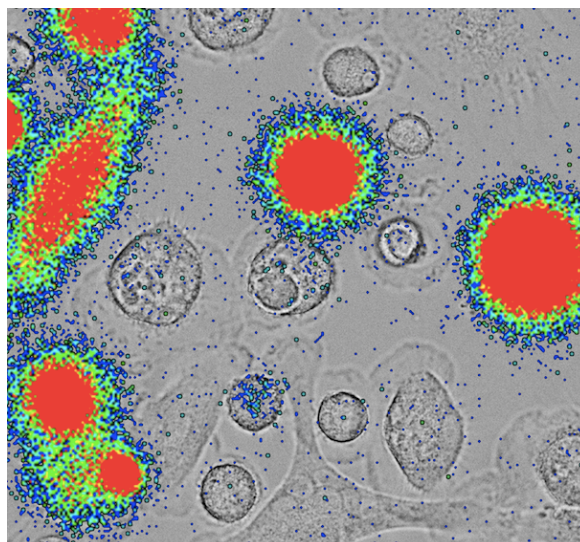


*HIV cell-to-cell transfer (HIV in green, target cell in blue). Jurkat T cell infected with HIV transmitting infection to target Jurkat cell (Far Red DDAO-SE) through pseudopodium-like structure (phalloidin-rhodamine actin staining). © Institut Pasteur*

## Blocking viral replication

The team lead formerly by Gianfranco Pancino and now directed by Asier Saez-Cirion - in the HIV, Inflammation and Persistence Unit - has revealed that activation of macrophages (the main targets of HIV-1 infection along with CD4 T-lymphocytes) blocks viral replication by preventing the virus from establishing a persistent infection. The researchers have identified a cell molecule, called p21, which is responsible for this inhibition.

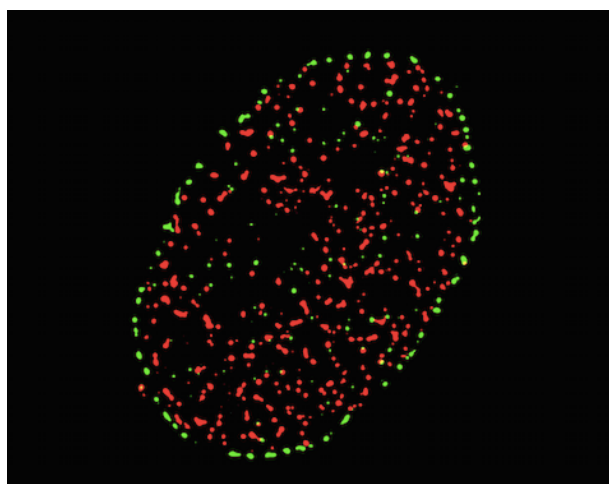
Elisabeth Menu's team, in the same unit, is working on mechanisms that restrict infection in trophoblastic placental cells, human cells that are naturally resistant to HIV-1. These cells could help to control mother-to-child HIV-1 transmission *in utero* (see "*Mucous membranes – key sites for virus transmission and natural control*" above).



*Primary human macrophages exposed to a HIV pseudovirus carrying the luciferase gene. Infection is detected in cells by measuring photon emission by real-time live imaging. Only the infected cells are able to emit photons in presence of the luciferase substrate.*  
© Institut Pasteur

## Cutting-edge imaging techniques help understand how the virus replicates

Christophe Zimmer's Imaging and Modeling Unit uses high-resolution optical imaging techniques to study unknown aspects of HIV interaction with the host cell. Together with Francesca Di Nunzio (from Pierre Charneau's Molecular Virology and Vaccinology Unit), researchers from the unit developed a super-resolution fluorescence microscopy method for studying viral proteins. They therefore viewed HIV in infected cells with a resolution of approximately 30 nm – the diameter of a compacted DNA molecule. Their findings show that, for the most part, the virus remains enclosed by a conical capsid in the cytoplasm of infected cells. More recently, they helped to analyze the role of Tpr (a nuclear pore protein) in the chromosomal integration of the viral genome. With Franscesca Di Nunzio, they were able to show that Tpr guides the viral genome towards active chromosomal regions, and this facilitates HIV expression and replication. As part of a current project, researchers are using cutting-edge imaging methods to study the interaction of the virus with the nuclear pores, microtubules and chromosomes. This work contributes to a better understanding of the HIV replication cycle and may lead to new therapeutic strategies being identified.



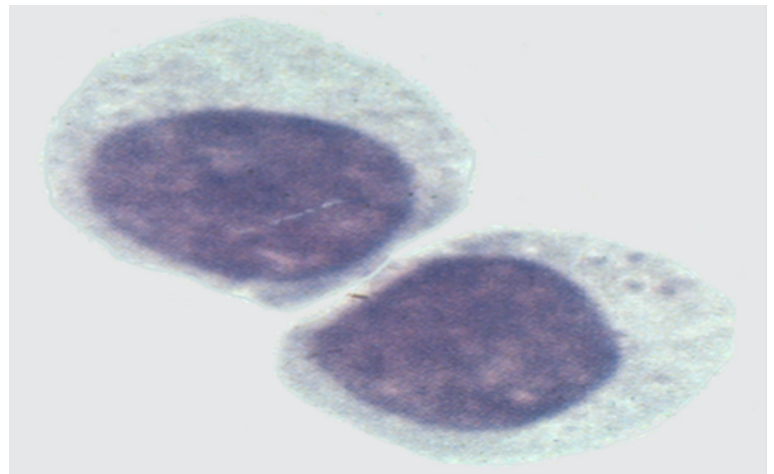
*High resolution optical image (obtained using the STORM technique) of nuclear pores (green) and an active chromatin (red). Researchers have determined the role of the chromatin environment and of nuclear pores in HIV-1 replication.* © Institut Pasteur

## Dialog between immunity cells conducive to viral replication?



*Marie-Lise Gougeon  
directs the Antiviral  
Immunity, Biotherapy and  
Vaccines Unit.  
© Institut Pasteur*

The Antiviral Immunity, Biotherapy and Vaccines Unit, directed by Marie-Lise Gougeon, focused on mechanisms developed by HIV to evade innate immunity, carried in particular by dendritic cells (DCs) and natural killer (NK) cells. The team discovered different viral strategies that, on the one hand, result in the inability of NK cells to eliminate infected DC cells, and on the other, lead to increased viral replication in the DCs. These viral strategies involve a protein, HMGB1 – an inflammatory molecule that is essential for NK-DC dialog, which is itself required for DCs to mature and NKs to be activated in killer cells. In addition, the HMGB1 protein appears to contribute to viral persistence in the central nervous system. Finally, research into the impact of HIV on plasmacytoid dendritic cells (pDCs) has highlighted the ability of HIV to turn pDCs into killer cells. These killer pDCs are thought to play a protective role in the acute phase of the infection (via their ability to destroy infected CD4 T lymphocytes) but they also have a harmful role during the chronic phase as they destroy uninfected cells expressing a specific receptor. These findings contribute to a better understanding of the immune escape mechanisms developed by HIV and open up possibilities for viral eradication strategies.

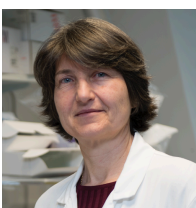


*Blood smear of natural killer cells (NK).  
Cells are able to kill infected cells and  
could potentially secrete inhibitor  
molecules against HIV-1 infection.  
© Institut Pasteur*

## 5 - Improvements in therapies

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### Use of a microbicide gel to control HIV entry into target cells



*Laurence Mulard dirige l'unité  
de Chimie des biomolécules  
© Institut Pasteur*

Collaborative work supported by the ANRS and between teams from the Institut Pasteur (Françoise Baleux in the Chemistry of Biomolecules Unit, directed by Laurence Mulard, and Sylvie Pochet, CNRS-UMR3523, Chemistry and Biocatalysis Unit), the CEA, the CNRS and Joseph Fourier and Paris-Sud 11 universities, led to the development of a molecule capable of blocking HIV entry into its target cells. Initially made up of a CD4 protein mime and a fragment of synthetic heparin, this original molecular structure was then optimized by replacing the heparin fragment with a sulfate peptide. The compound was evaluated in animals as a microbicide gel – a preventive approach designed to protect against HIV infection. Following a vaginal challenge, 83% of animals were protected in this way. As well as its ability to inhibit

infection by free viruses, this family of molecules also inhibits the virus from passing from one cell to another. In addition to their preventive effect, these molecules could also therefore be used as a therapeutic approach.

## Modeling remission

Antiretroviral therapy cannot be stopped in patients treated during the chronic phase for fear of the virus being reactivated. Patients treated very early on after infection and who continue to control the virus after stopping therapy have recently been identified. Research has been conducted on these patients as part of the ANRS VISCONTI study to determine which parameters can lead to long-term remission (Asier Saez-Cirion's team in the HIV, Inflammation and Persistence Unit, directed by Michaela Müller-Trutwin). Based on these discoveries, pre-clinical and clinical trials have begun to test promising new strategies. A phase III multi-center trial evaluating the impact of a combination of antiretrovirals on the viral reservoir (through quantification of HIV-1 DNA in blood cells) of primary HIV infection patients, is currently being conducted by the ANRS in partnership with Institut Pasteur researchers.

## Highly powerful antibodies are used to block the virus and eliminate its reservoir



*Hugo Mouquet leads the Humoral Response to Pathogens group.  
© Institut Pasteur*

Some patients develop extremely effective broadly neutralizing anti-HIV-1 antibodies (bNAbs). Hugo Mouquet's Humoral Response to Pathogens group is currently studying memory B cell and antibody responses to HIV-1 in these individuals to understand how these rare antibodies develop. The researchers are characterizing their various antiviral properties, such as their activity to prevent the virus passing through epithelial cells in the mucosal tissue. They are also trying to unravel the molecular and structural mechanisms responsible for their broadly neutralizing activity against divergent HIV-1 strains. Finally, the group is interested in characterizing the role of antiviral drugs in restoring effective antibody responses in the mucosal sites.

Researchers from Olivier Schwartz's team in the Virus and Immunity Unit (Institut Pasteur/CNRS), co-funded by the Vaccine Research Institute (VRI), and the group directed by Hugo Mouquet, in partnership with Olivier Lambotte's team (Bicêtre Hospital), have shown that bNAbs act in a complementary manner. Firstly, the bNAbs neutralize the spread of the virus, particularly from cell to cell. In addition, the most effective ones are also capable of directly recognizing infected cells and triggering their destruction by Natural Killer (NK) cells – immune system cells that are tasked with eliminating abnormal cells from the body. But, a "viral reservoir" remains in patients receiving antiretroviral therapy and it is responsible for the rapid resumption of viral replication if therapy is stopped. Eliminating or significantly reducing this reservoir represents a potentially interesting strategy for achieving "functional remission", which would enable this therapy to be reduced. With this in mind, the use of antibodies (bNAbs) is a promising approach.

Characterization of these bNAbs is important for various reasons. The way in which they recognize the viral envelope provides valuable information for designing vaccine candidates. Furthermore, it has already been shown that bNAbs can be used in humans. The most effective antibodies are currently undergoing clinical trials in the US, and can significantly reduce the viral load for up to 28 days. These immunotherapy treatments therefore represent promising new therapeutic or preventive strategies.

In addition, Moncef Benkirane's team (Institute of Human Genetics, Montpellier) recently identified "biomarkers", cell molecules that are selectively present on the surface of reservoir cells. Olivier Schwartz's Unit is also testing strategies to eliminate cells presenting these biomarkers to once again reduce the size of the viral reservoir in infected individuals.



## **Trials on new therapies in a humanized mouse model**



*James Di Santo, chief of the Innate Immunity Unit.  
© Institut Pasteur*

By using humanized mouse models for the human immune system (HIS), HIV-1 replication and immune responses can be modeled *in vivo*. These models help to understand the pathophysiology induced by the virus and test immunotherapy to prevent and treat HIV-1, such as broadly neutralizing antibodies (BNabs) and vaccines that stimulate the immune system. In the Innate Immunity Unit, directed by James Di Santo, Guillemette Masse-Ranson has developed a series of new HIS mouse models that improve human innate and adaptive immune responses. In studying these models, she is testing new combination immunotherapy that can potentially target the viral reservoir *in vivo*. These "HIV cure" projects are funded by the Vaccine Research Institute (Yves Lévy) and by Gilead Sciences, Inc (Olivier Schwartz).

## **Using dried blood spot (DBS) blotting paper to measure HIV viral load**



*Fabien Taieb works at the Center for Translational Science.  
© Institut Pasteur*

Early detection of therapy failure is a major challenge when caring for patients receiving antiretroviral therapy (ART) to be able to optimize treatment efficacy, promote good adherence to treatment, prevent the buildup of viral resistance and not compromise future therapeutic possibilities. The recognized technique for detecting therapy failure is based on measuring the HIV viral load. However, in developing countries, patients living in decentralized areas, who represent more than half of patients, have very limited access to this technique. Its complexity, the high cost of the equipment required and the lack of trained staff mean it is only available in a few laboratories located in very large urban areas. Ideally, viral load is measured on a plasma sample but transferring such samples is complicated because viral DNA deteriorates rapidly at room temperature and therefore requires a cold chain. Setting up a permanent plasma transfer system is difficult and costly in developing countries. The use of dried blood spot (DBS) technology, which was set out in the latest WHO recommendations, would overcome sample transfer difficulties.

To promote the use of DBS for accessing the viral load, the MOVIDA (Monitoring Of Viral load In Decentralized Areas) project was developed by researchers from the Institut Pasteur in Paris: Fabien Taieb, Center for Translational Science, and Yoann Madec, Emerging Disease Epidemiology Research and Expertise Unit, directed by Arnaud Fontanet. In Vietnam, two studies have been carried out by virology and epidemiology teams at the National Institute of Hygiene Epidemiology (NIHE) and in HIV treatment centers in Hanoi to train local teams in measuring viral load using dried blood spot (DBS) testing and to assess its different techniques. Thanks to support from the Global Fund, a broader study is due to begin soon in six provinces in North Vietnam to scale up use of the technique in the country. In Cameroon, a study was carried out in 12 decentralized centers from three different regions (Center, East and Northwest). This study was used to virologically assess nearly 1,000 cases and highlight a worrying proportion of patients with virologic failure. It provided precious information regarding individuals, communities and programs. The teams involved in the MOVIDA project now want to assess the scaling up of DBS use in Cameroon.

## 6- Hope for vaccine research

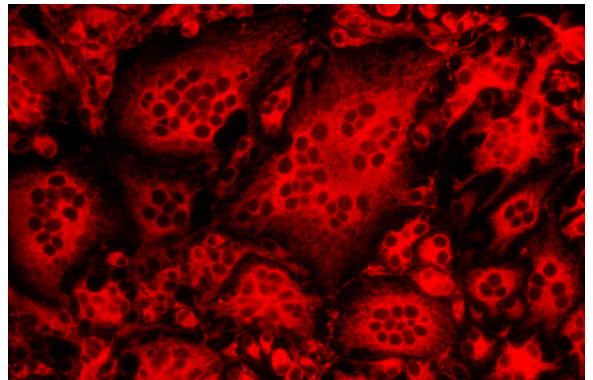
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### A measles-HIV vaccine candidate already tested in humans



*Frédéric Tangy leads the  
Viral Genomics and  
Vaccination Unit.  
© Institut Pasteur*

A "measles-HIV" vaccine candidate has been developed in the Viral Genomics and Vaccination Unit directed by Frédéric Tangy at the Institut Pasteur. An initial version of this vaccine was tested in humans in 2011. This phase I trial demonstrated the harmlessness and immunogenicity of the vaccine in adults who had already been vaccinated against measles. The efficacy of a new, improved version of the vaccine has just been tested in a primate model. The vaccine demonstrated its ability to protect 75% of animals against the establishment of chronic infection. It is a "recombinant" vaccine based on the attenuated measles vaccine virus, which has proved its harmlessness and efficacy on several billion babies vaccinated throughout the world over the last 40 years. The researchers have introduced several HIV genes into the pediatric vaccine virus genome. This combination vaccine could be used to protect against both AIDS and measles.



*T cells infected with next-generation measles/HIVenv  
chimeric vector showing cytopathic effect.  
© Institut Pasteur*

## 7 - Consultations and clinical research projects

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In addition to its academic research, the Institut Pasteur is home to a Medical Center with an infectious disease clinic that receives a significant caseload of HIV-positive patients and can, where necessary, integrate clinical research projects. The Medical Center is involved in including and monitoring patients in national cohorts coordinated by the ANRS. The infectious disease clinic works closely with the Infectious Diseases Department at Necker Hospital (via a shared entity, the Necker-Pasteur Infectiology Center) and can also include patients in clinical trials at Necker.

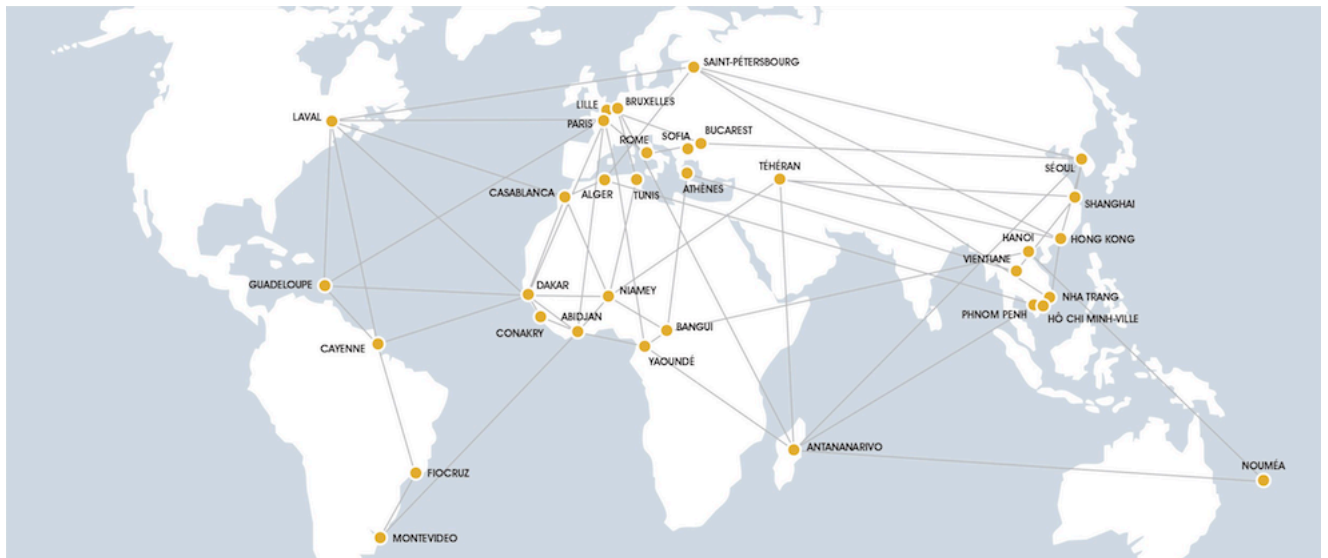
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The Institut Pasteur Group for AIDS research leads joint discussions and organizes exchanges of information on the subject of HIV/AIDS on campus. It provides information, engages in dialog with hospital clinicians and researchers from the Institut Pasteur International Network, and promotes research and public health initiatives.



# III - HIV and AIDS in the Institut Pasteur International Network

Institut Pasteur International Network (IPIN) members are actively involved in work on the AIDS virus and the disease itself. The location of International Network institutes, particularly in Africa and South-East Asia, is especially strategic, given that over 90% of AIDS cases are in the Southern hemisphere. In addition, the vast majority of International Network institutes in Africa and South-East Asia carry out serological and molecular diagnosis of HIV infection, and immunological monitoring (level of CD4+ T lymphocytes) and virological monitoring (viral load and resistance to ARV) of patients, whether or not they are being treated with ARVs.



*The Institut Pasteur international network includes 33 institutions located in 26 countries. © Institut Pasteur*

## Cameroon

### Using dried blood spot (DBS) blotting paper to measure HIV viral load

In Cameroon, the MOVIDA study, jointly coordinated by the Institut Pasteur in Paris, the IRD and various Cameroonian public bodies and associations, was carried out in 12 decentralized centers from three different regions (Center, East and Northwest). This study was used to virologically assess nearly 1,000 patients and highlight a worrying proportion of patients with virologic failure. It provided precious information regarding individuals, communities and programs. The teams involved in the MOVIDA project now want to assess the scaling up of DBS use in Cameroon. A MOVIDA 2 study awaiting funding should involve the Pasteur Center in Cameroon. (see detailed explanation in chapter II.5, Improvements in therapies)

## **Improving early diagnosis and treatment of HIV in infants**



*Mathurin Tejiokem directs the Epidemiology and Public Health Service in the Center Pasteur Cameroon. He is the principal investigator of PEDIACAM projects . © Victor Yene*

Since 2007, the Pasteur Center in Cameroon has been developing and coordinating, as part of the ANRS 12140/12225-Pediacam, a project aiming to improve the diagnosis and treatment of infants infected by HIV. This project has demonstrated that the application of WHO recommendations for preventing mother-to-child transmission of HIV in the operational context of a country with limited resources is feasible and effective. Similarly, this work has shown that routine early antiretroviral treatment is feasible in developing countries, as over 90% of HIV-infected children identified had been treated before the age of 7 months. However, the time between HIV testing and the start of ARV therapy remains long. Light has been shed on the reasons why "mothers fail to return for scheduled appointments" and targeted initiatives are now planned.

As for the ANRS-Pediacam 1b project, planned between 2014 and 2018 with financial backing from the Total foundation, it aims to promote the adoption of research knowledge through the development of simplified data collection tools, to facilitate diagnosis and the instigation of ARV therapy for HIV-infected children.

Thanks to funding from the GSK Foundation, the SIMECAM-FGSK project, launched in 2014, will come to an end in early 2018. Its aim is to assess the impact of including couple-oriented advice in the minimum care package for pregnant women as regards prenatal HIV screening, together with care in semi-urban and rural areas in Cameroon.

## **Improving the long-term follow-up of HIV-infected children who received early treatment**

The Pediacam cohort, one of the rare few in Sub-Saharan Africa, plays a key role in the setting up of research studies which produce numerous data from countries with limited resources regarding the immunovirological response, tolerance and neurocognitive development (ANRS 12322-Pediacamdev study) of HIV-infected children who received early treatment. Hence, this cohort has provided clinical epidemiological and biological data from children who received early treatment, and from control groups.

## **Understanding the humoral response to the measles vaccine according to the child's HIV status**

The aim of this project was to determine whether infants infected with HIV and treated early, or not infected and exposed to HIV, are capable of developing and maintaining an adequate immune response to most antigens used in the Expanded Program on Immunization (EPI) in Cameroon. In the long term, this type of project could help to identify potential indicators of vaccine failure in these children and suggest adjustments to the current vaccination schedule if necessary. The measles vaccine project demonstrated similar protection between infected children, children not infected but born to HIV-positive mothers, and children never exposed to the virus, provided that the vaccination schedules were properly adhered to. Work is continuing for the other antigens.

## Improving diagnosis of tuberculosis in HIV-infected children

It is more difficult to diagnose tuberculosis in children in the event of HIV infection. New Xpert MTB/RIF automated molecular tests, together with alternative bacteriological sample collection methods (nasopharyngeal aspiration, Entero-Test and stools), were assessed as part of a multi-center project (ANRS 12229 – PAANTHER01) coordinated by the Institut Pasteur in Cambodia and involving Cameroon, Burkina Faso and Vietnam. This study began in April 2011 and ended in May 2015. Part of the data has been used to demonstrate that alternative sampling methods are feasible, workable and well tolerated.

## Cambodia

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### An outbreak of HIV and HCV linked to unsafe medical practices in Roka

In the town of Roka (northeast Cambodia), 242 patients were infected with HIV due to unsafe injection practices, i.e. re-use of contaminated syringes or needles by an unqualified health worker. This person was tried and sentenced to 25 years in prison in December 2015. The work carried out by the HIV/Hepatitis team from the Institut Pasteur in Cambodia demonstrated that the individuals were all infected with the same HIV strain, confirming the iatrogenic nature – i.e. caused by a medical intervention – of this outbreak. It also showed that approximately 80% of individuals were co-infected with Hepatitis C (HCV), with 4 HCV viral strains identified. The ANRS 12352 research project, focusing on the prevalence during this nosocomial outbreak, the viral strains and the high risk injection practices, should start in 2017.



*Level 3 biosafety laboratory in the Institut Pasteur of Cambodia, which was inaugurated on April 25th, 2008. HIV and retrovirus research is being carried out in this high security P3 laboratory.*  
© Institut Pasteur

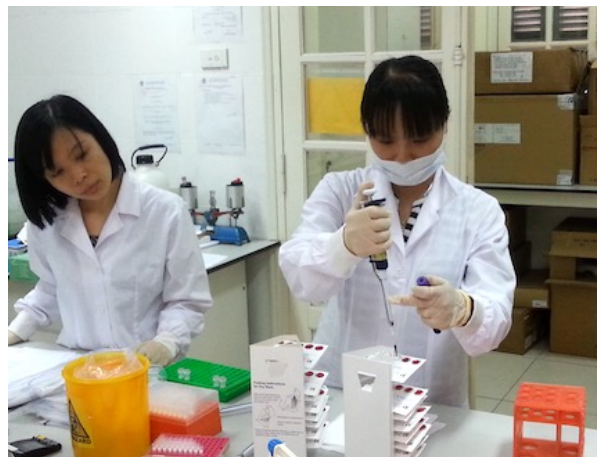
# Vietnam

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## Using dried blood spot (DBS) blotting paper to measure HIV viral load

In Vietnam, two studies have been carried out by virology and epidemiology teams at the National Institute of Hygiene Epidemiology (NIHE), a member institute of the Institut Pasteur International Network, and in HIV treatment centers in Hanoi, to train local teams in measuring the viral load using DBS testing and to assess different techniques for measuring the viral load using DBS technology (studies known as MOVIDA Vietnam phase 1 and 1a). Thanks to support from the Global Fund, a broader study is due to begin soon in six provinces in North Vietnam (MOVIDA Vietnam phase 2 study) to scale up use of the technique in the country.

*Research work being carried out at NIHE, in Hanoi, as part of the MOVIDA study which aims to measure viral charges through the simple use of DBS testing.  
© Institut Pasteur/Yohan Madec*



# Côte d'Ivoire

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## Use of drugs other than antiretroviral therapy by HIV-positive patients

Lead in cooperation with the Pasteur Institute of Côte d'Ivoire, the ANRS 12335 MOTUHS project focuses on describing the use of treatments from mainstream medicine and traditional and complementary medicine, and the use of treatments prescribed in the context of HIV infection. There are three parts to this study – pharmacoepidemiology, socio-anthropology and ethnobotany. It was carried out in six HIV care centers in Côte d'Ivoire (three centers in Abidjan and three inland – Bouaké, San-Pedro and Korhogo). Project participants were aged 18 and over, and had to have been on antiretroviral therapy for at least a year. The study was conducted from October 2015 to March 2017. In total, 1,458 people took part in the study. 48% had taken at least one drug in addition to cotrimoxazole and antiretroviral therapy, and the median number was two drugs. Out of the 1,519 drugs used, the most represented pharmacological classes were nervous system drugs, digestive system and metabolism drugs, antiparasitic drugs and respiratory system drugs. The factors associated with the use of at least one drug in addition to HIV treatment recommendations were – the use of traditional and complementary medicine over the past 30 days, an extra antiretroviral therapy tablet, poor

perception of state of health, high level of education, high income, and the advanced WHO clinical stage on diagnosis. Approximately 31% of participants did not adhere to antiretroviral therapy.

## Central African Republic

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### Free HIV viral load assays by the Global Fund

HIV viral load quantification is still the most effective technique for assessing the therapeutic success of antiretroviral therapy and monitoring the progress of HIV-infected patients receiving treatment. Despite their benefit and the fact they are widely conducted in other African countries, HIV viral load assays were until recently little used in the Central African Republic (CAR) due to their high cost, the inadequate laboratory facilities available in the country, the difficulty in supplying reagents and equipment, and the lack of trained technical staff.



*Bangui, RCA – Health center of the sixth district : a doctor performs a quick HIV screening on a child.  
© Institut Pasteur de Bangui/JM Zokoué*

The medical test laboratory at the Institut Pasteur in Bangui is so far the only facility in the country able to conduct these assays all year round. It even expanded its technical capabilities recently, through the setting-up of a high-tech facility thanks to a grant given to the CAR by the Global Fund to monitor HIV-infected patient. The population has had access to free screening for HIV care for several years now, and HIV viral load quantification has been recently added to the list of tests that are freely available to infected patients. The first patients were therefore seen at the medical test laboratory on 19 April 2017.

# IV - AIDS in terms of numbers

## Worldwide

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Source : Global AIDS Update, ONUSIDA, 2016

Number of people living with HIV/AIDS in the world in 2015:

**36.7 million**

Number of new cases of HIV infection in 2015:

**2.1 million**

Number of deaths from AIDS in 2015:

**1.1 million**

|  | Number of people living with HIV/AIDS in 2015 | Numbers of new cases of HIV in 2015 | Number of deaths from HIV/AIDS in 2015 |
|--|---|-------------------------------------|--|
| Asia and the Pacific                         | 5.1 million                                   | 300,000                             | 180,000                                |
| East and South Africa                        | 19 million                                    | 960,000                             | 470,000                                |
| Eastern Europe and Central Asia              | 1.5 million                                   | 190,000                             | 47,000                                 |
| Latin America and the Caribbean              | 2 million                                     | 100,000                             | 50,000                                 |
| Middle East and North Africa                 | 230,000                                       | 21,000                              | 12,000                                 |
| West and Central Africa                      | 6.5 million                                   | 410,000                             | 330,000                                |
| Western and Central Europe and North America | 2.4 million                                   | 91,000                              | 22,000                                 |
| <b>Total</b>                                 | <b>36.7 million</b>                           | <b>2.1 million</b>                  | <b>1.1 million</b>                     |

## In France

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In France, approximately 150,000 people, including 48,000 women, are living with HIV. Nearly 6,000 people found out they were HIV-positive in 2015, a figure that has been stable since 2011. However, it is estimated that roughly 25,000 people carry the virus without knowing it. Transmission within the male homosexual population is still particularly high, as in the rest of Europe and North America.

- [Find out more > Read the UNISAIDS report](#)



## V – 2008: the Institut Pasteur receives two Nobel prizes for its discovery of the AIDS virus

In 2008, Professors Françoise Barré-Sinoussi and Luc Montagnier received the Nobel Prize in Medicine for their work on the discovery of the retrovirus that causes AIDS, carried out at the Institut Pasteur in 1983. Twenty-five years after the AIDS virus was first isolated, this prize was awarded in recognition of the work accomplished by these two scientists, along with their clinical and research staff. The prize should encourage young scientists to rise to the challenge of tackling a number of ongoing issues in the field, such as the search for a vaccine, virus control, and preventative measures.



*Françoise Barré-Sinoussi and Luc Montagnier in 2008*  
© Institut Pasteur

### **FRANÇOISE BARRÉ-SINOUSSI**

A member of the French Academy of Sciences and Emeritus Director of Research at Inserm, Françoise Barré-Sinoussi directed the Regulation of Retroviral Infections Unit at the Institut Pasteur until 2015. Involved in retrovirology research since the beginning of the 1970s, she is known for her contributions to the field of HIV/AIDS, in particular as the lead author of the paper published in 1983 announcing the discovery of the virus responsible for causing AIDS, later named HIV. This discovery would win her the Nobel Prize for Medicine in 2008. An author and co-author of over 300 publications, Barré-Sinoussi has been and remains a member of a number of high-level scientific committees, both in France and abroad. Through officially retired, Barré-Sinoussi remains active on the international scientific scene. She is a member of the Board of Directors for Sidaction, presides over the Scientific Council of the ANRS and is still Co-President of the IAS initiative "Towards an HIV Cure." An honorary president of the Institut Pasteur International Network, Françoise Barré-Sinoussi continues to play a major role in global health issues.

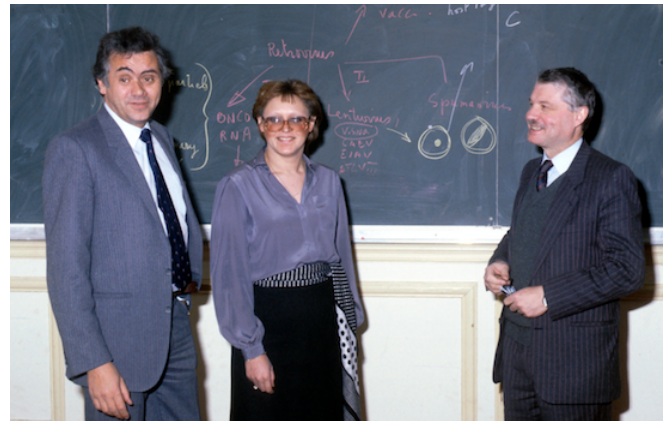
### **LUC MONTAGNIER**

Luc Montagnier is Professor Emeritus at the Institut Pasteur (where he directed the Viral Oncology Unit from 1972 - 2000), Emeritus Research Director at the CNRS and a member of the French Academies of Sciences and Medicine.

He is currently the President of the World Foundation for AIDS Research and Prevention, established in 1993 along with Federico Mayor, a former Director-General of UNESCO.

# VI - Discovery of the AIDS virus in 1983

The first cases of AIDS were documented in the U.S. in 1981. At the time, the phrase "AIDS" (Acquired Immune Deficiency Syndrome) was not yet being used to describe this new and unexplained condition – instead, the disease was dubbed "gay syndrome" as it was initially identified among homosexual men.



Jean-Claude Chermann, Françoise Barré-Sinoussi and Luc Montagnier, co-discoverers of the first virus responsible for AIDS (called LAV in 1983, nowadays named HIV-1) and the second HIV in 1985. © Institut Pasteur

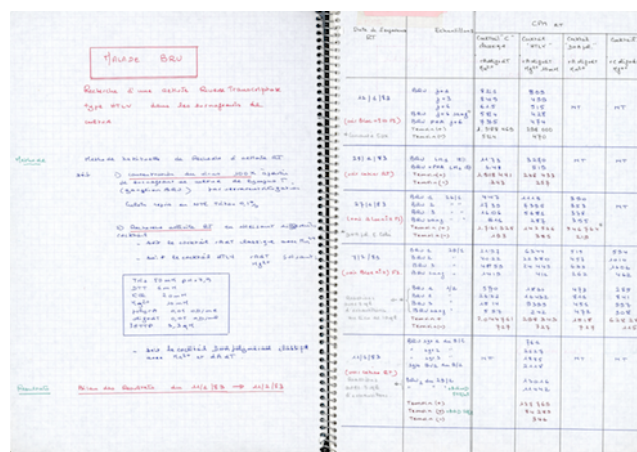
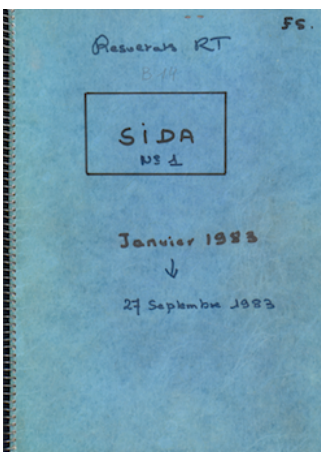
French doctors began to mobilize in 1982, as similar cases were documented in France. A significant number of research initiatives had been undertaken around the world since the first appearance of the disease among the gay community; when the same condition was later observed in hemophiliacs having received blood transfusions, experts were led to suspect that the infectious agent to blame was a virus.

In 1982, having tried in vain to associate this supposed virus with those already known to science, Willy Rozenbaum, a French clinician working at Bichat Hospital, became convinced he was looking at a completely new class of virus. Around the same time, he came to Pasteur Hospital to give a lecture on this new immune deficiency syndrome, hoping to use the opportunity to convince the Institut Pasteur's virologists to come and work with him on the unknown infection. However, no-one took up the call.

Françoise Brun-Vezinet, who worked with Rozenbaum as a clinical virologist, suggested he contact the professors of the retrovirology classes she had attended at the Institut Pasteur: Jean-Claude Chermann (with whom Françoise Barré-Sinoussi was working at the time as an Inserm researcher) and Luc Montagnier. Their research at the Viral Oncology Unit (Institut Pasteur – CNRS – Inserm) looked at the relationships between retroviruses and cancer. Luc Montagnier agreed to help Willy Rozenbaum, and asked Jean-Claude Chermann and Françoise Barré-Sinoussi if they were prepared to join the search for the agent responsible for this newly-

identified disease. As they had access to many of the technological tools needed to work on retroviruses, and given that some of these viruses were known to cause immunodeficiency (particularly in cats), the two scientists accepted.

Thus, the Institut Pasteur joined the search for the virus at the end of 1982. An initial meeting was held at the Institut Pasteur in December 1982, with Willy Rozenbaum and Françoise Brun-Vezinet in attendance,

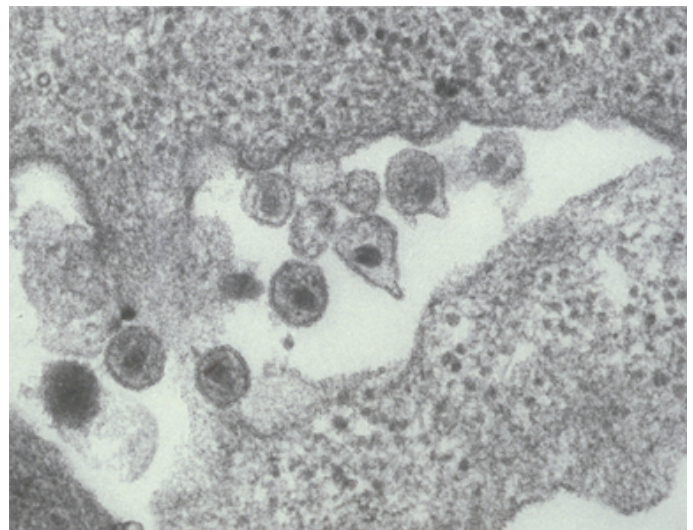


Lab notebook of Françoise Barré-Sinoussi in 1983, which includes the first scientific experiences showing a reverse-transcriptase activity (specific to retroviruses) in cell culture supernatants of patients. © Institut Pasteur

in order to discuss research methods to be undertaken. In January 1983, Rozenbaum sent the first lymph node biopsy from a patient suffering from "generalized lymphadenopathy" (indicating the "pre-AIDS" phase of the disease, before the onset of chronic immunodeficiency), taken at Pitié-Salpêtrière Hospital.

The sample was what the Pasteur team needed, as they already knew that patients who developed the condition saw their CD4 T-cell count plummet, before disappearing almost completely. The team surmised that these CD4 cells were the target for the unknown virus, and that in order to isolate it they would need to still be present in the lymph node biopsy sample. Luc Montagnier cultured the lymph node cells obtained from the biopsy, bringing the supernatant to Françoise Barré-Sinoussi and Jean-Claude Chermann so they could search for the presence of the retrovirus, particularly via the detection of reverse transcriptase activity. Around three weeks later, this type of activity was indeed detected – however, cell death was also observed to be occurring at the same time. This was a worrying moment for the researchers, as they were at risk of losing the virus immediately after having detected it for the first time.

*One of the first photographs  
of the HIV-1 virus which was  
discovered by  
Luc Montagnier's team  
in 1983.  
© Institut Pasteur*



During an emergency meeting, the Institut Pasteur team decided to take white blood cells from blood donors (Pasteur Hospital having its own blood transfusion unit) and reinject them immediately into the cell culture. Retroviral enzymatic activity was observed once again, and once again its observation was followed by a spate of cell death – the team had observed the cytopathogenic effect of the virus for the first time.

Charlie Dauguet, then head of Electron Microscopy within the Viral Oncology Unit, was entrusted with the task of searching for retrovirus-type particles within cell cultures in which retroviral enzymatic activity had been detected. His work required a great deal of patience, but after several days he was finally able to observe the virus under his microscope.

Once the virus had been detected, it then had to be characterized. Researchers from the Viral Oncology Unit consulted Professor Gallo's team at the USA's National Cancer Institute, who had described what was then the only-known human retrovirus: HTLV 1. Prof. Gallo informed the team that he was also searching for the virus that caused what would later be called AIDS, and thought that the culprit might be HTLV-1 (the Human T-Cell Leukemia Virus), which he had discovered in 1980. However, the initial comparisons carried out (particularly immunofluorescence testing by Marie-Thérèse Nugeyre, whose results would later be confirmed) showed that this was not the case.

**And so, in 1983, the first description of the virus that caused AIDS was published in the journal *Science*\*; at the time, the Pasteur team had named it "Lymphadenopathy Associated Virus", or LAV. However, the link between the virus and AIDS still had to be demonstrated.**



From early 1983, research efforts around this newly-identified virus began to intensify. This began an important period for the characterization of the virus and the development of blood tests, along with research aiming to prove a link between the virus and AIDS.

At the Institut Pasteur, the laboratory received further samples from patients in both the pre-AIDS and confirmed AIDS stages. A partnership was formed with hospital-based virologists Françoise Brun-Vezinet and Christine Rouzioux from Bichat Hospital in order to develop diagnostic blood tests for infected patients. These tests went on the market in 1985.

Such partnerships extended to hospital immunologists (Jean-Claude Gluckman and David Klatzman at the Pitié-Salpêtrière) and clinicians such as Dr. Vilmer (Necker Hospital), which enabled the researchers to show, in 1983, that CD4 T cells were the major target for the virus, and that these cells died when infected.



*The 1985 research team with all its members. This team gathered scientists from various research units at Institut Pasteur, including key figures in AIDS research :*

- Professors Luc Montagnier, Françoise Barré-Sinoussi and Jean-Claude Chermann who discovered the AIDS virus (HIV-1 in 1983, HIV-2 in 1985)
  - Marc Alizon, Simon Wain-Hobson, Pierre Sonigo, Olivier Danos who sequenced the HIV-1 genome in 1985 (Stewart Cole who does not appear on the picture)
  - Charlie Dauguet, responsible of the electronic microscopy observations within the unit
  - Ara Hovanessian
  - François Clavel, co-author of the article on the sequencing of the HIV-2 genome in 1987 with Mireille Guyader, Mickael Emerman, Pierre Sonigo, François Clavel, Luc Montagnier et Marc Alizon.
- © Institut Pasteur

The team was also in contact with molecular biologists (Simon Wain-Hobson, Pierre Sonigo, Marc Alizon, and others) in order to analyze the genome of the virus: a year later, their work allowed them to describe the virus sequence. Later in 1983, scientists from the Viral Oncology Unit provided proof that they were indeed dealing with a retrovirus, a theory contested by some at the time.

Characterization of the proteins the virus was made up of was also undertaken in 1983. Protein analysis for the virus also showed that LAV was completely different from the American "suspects", the HTLV-1 and HTLV-2 viruses.

Finally, over the course of the same year, a partnership formed with the CDC in Atlanta used studies of blood serum collected from American and French patients to strengthen the hypothesis for the link between the virus and AIDS, by demonstrating a correlation between the presence of antibodies found in infected patients and that of the virus.

It was also in partnership with the CDC that the first work was undertaken to demonstrate the possibility of viral transmission in chimpanzees.

The reason so many discoveries were able to be made so quickly was due to absolutely exemplary interaction between experts in various disciplines, both distinct and interconnected: clinicians, virologists, immunologists, molecular biologists, and epidemiologists (Jean-Baptiste Brunet), working in both the pure research and clinical fields.

\* Isolation of a T-Lymphotropic Retrovirus from a Patient at Risk for Acquired Immune Deficiency Syndrome ( AIDS), *Science*, 220, 868-871 (1983)

F. Barré-Sinoussi<sup>1</sup>, J.C. Chermann<sup>1</sup>, F. Rey<sup>1</sup>, M.T. Nugeyre<sup>1</sup>, S. Chamaret<sup>1</sup>, J. Gruest<sup>1</sup>, C. Dauguet<sup>1</sup>, C. Axler-Blin<sup>1</sup>, F. Vézinet-Brun<sup>2</sup>, C. Rouzioux<sup>2</sup>, W. Rozenbaum<sup>3</sup>, L. Montagnier<sup>1</sup>.

1- Virology department, Institut Pasteur

2- Central Virology Laboratory, Claude Bernard Hospital

3- Department of Public Health and Tropical Medicine, La Pitié-Salpêtrière Hospital

By the end of 1983, the proof had been provided: the LAV human retrovirus (later renamed the HIV-1 virus) was the agent behind the AIDS epidemic.

In January 1985, an article on sequencing of the LAV virus appeared in the journal *Cell*. This was carried out by:

- Simon Wain-Hobson, then working in the Recombination and Gene Expression Unit (Pasteur – Inserm – CNRS), as team leader;
- Pierre Sonigo, from the same unit;
- Olivier Danos, then working in the Oncovirus Unit (Pasteur – CNRS);
- Stewart Cole, then working in "G3", (*Groupement Génie Génétique*, or Genetic Engineering Group) at the Institut Pasteur;
- Marc Alizon, then working in the Viral Oncology Unit (Pasteur – CNRS – Inserm).

In the same year, Diagnostics Pasteur, following on from work carried out by teams at the Institut Pasteur, developed the first HIV-1 screening test, known as Elavia.

Also in 1985, the Viral Oncology Unit isolated a second AIDS virus, LAV-2 (later renamed HIV-2), using a sample taken from a patient from West Africa who was hospitalized in Portugal (Luc Montagnier, Denise Guétard and François Clavel, working from the Institut Pasteur in collaboration with Portuguese doctors from Egas Moniz Hospital in Lisbon, as well as with doctors and virologists from Claude Bernard Hospital).

Sequences for the second virus would be published in 1987 in the journal *Nature* (the result of a collaboration between the Institut Pasteur and the Viral Oncology Unit, the Recombination and Gene Expression Unit, and the Molecular Biology and Retrovirus Immunology Laboratory, authored by: M. Guyader, M. Emerman, P. Sonigo, F. Clavel, L. Montagnier, M. Alizon).

In 1987, a specific screening test for HIV-2 was developed by Pasteur Diagnostics. A number of collaborations were also formed, in particular with Genetic Systems.