



→ A national infrastructure
for infectious disease models
and innovative therapies to provide
the academic and industrial scientific
communities with highly innovative
technologies for:

Preclinical research

- Understanding host-pathogen interactions
- Innovative technologies for monitoring infections and host responses
- Developing and testing new vaccines and therapeutic approaches

THE FOUNDERS



The teams of Life Sciences Division at the CEA have demonstrated their ability to combine their skills and infrastructures to focus on issues of importance to society, such as Energy and Health. Its Division of Immuno-Virology, which co-ordinates IDMIT, carries out internationally recognised cutting-edge research on human viral diseases, including in particular those caused by HIV and emerging viruses. In addition to its substantial immunological know-how, IDMIT has unique expertise in the use of non-human primate (NHP) models of human infectious diseases; these models are essential for the evaluation of vaccination strategies and approaches to the treatment of infection, accelerating progress towards clinical research in humans. The SIV teams make major contributions to several international research networks and to national and European research programmes.



Institut Pasteur

Institut Pasteur is an international leader for research into infectious diseases, to which it devotes almost half its resources. It has placed its scientific expertise in this domain and in vaccination at the disposal of this project. It also contributes its knowledge and experience in the use of animal models of human diseases. With its internationally renowned teaching activities, Institut Pasteur also makes a major contribution to the training activities implemented within this infrastructure. Several Institut Pasteur scientists are involved in the governance of IDMIT, including, in particular, Professor Françoise Barré-Sinoussi, who won the Nobel Prize for Medicine in 2008 and holds the posts of Professor at Institut Pasteur and of President of the Executive Board of IDMIT.



Université Paris-Sud houses many medicine, pharmacy and science faculty laboratories, together with highly respected laboratories working in the domains of the physics, and fundamental and structural chemistry, of infectious diseases. This research focuses, in particular, on the control mechanisms governing host-pathogen interactions both in vitro and in vivo, and clinical research on human cohorts. The university is also involved in other excellence initiatives, such as LERMIT (laboratory of excellence in the domain of research on drugs and innovative treatments, particularly for infectious diseases) and VRI (the Vaccine Research Institute).



INSERM, the French National Health and Medical Research Institute, is responsible for biomedical research. Its Institute of Microbiology and Infectious Diseases is responsible for co-ordinating studies on infectious diseases, vaccine biology and prevention strategies. The principal goals of the IMMI are to support research on viruses, bacteria and parasites and to characterise human infectious diseases through studies of host-pathogen relationships, anti-infection agents and vaccine escape. This research requires appropriate facilities for studying NHPs, at a suitable confinement level, to strengthen investigations of the fundamental mechanisms underlying infectious diseases, their transmission and innovative therapeutic and preventive strategies.



ANRS, The French National Agency for Research on AIDS and Viral Hepatitis, has strongly supported NHP models of AIDS research in the last 25 years, funding research projects as well as animal facilities at Institut Pasteur and CEA. In 2007, ANRS urged leading investigators from these institutions to constitute a unique steering committee of their animal facilities as well as a scientific committee to promote interactions between basic, clinical and pre-clinical aspects of AIDS research. Thus, the ANRS Group “NHP Models for AIDS Research” paved the way for the IDMIT. Since then, ANRS has funded 30 peer-reviewed NHP research projects, including vaccine studies. In addition to its contributions to IDMIT as a founder partner, the ANRS will support all research programs eligible for grants.



Bertin Pharma, a service company, supplies a large range of preclinical and clinical services for R&D for drug candidates, in a quality environment (GLP, Good Laboratory Practice; GMP, Good Manufacturing Practice, GDP, Good Distribution Practice) or with high levels of security (levels 2 and 3). Bertin Pharma and CEA have established a functional private/public sector partnership that has functioned effectively for more than 20 years. Through their common platform, “PharmImmune”, they provide access to diverse cell and animal models and immunomonitoring solutions for evaluating the efficacy of biodistribution and/or the safety of new therapeutic approaches. In addition to its skills in the development and validation of new tools and as an industrial operator, Bertin Pharma provides expertise for contract management and quality assurance projects.

IDMIT is a national infrastructure for biology and health dedicated to preclinical research on infectious diseases. It benefits from the considerable expertise and know-how of its founders, world leaders in this domain: the CEA, Institut Pasteur, Université Paris-Sud, INSERM, ANRS and Bertin Pharma. Its goals: to provide the scientific community with exceptional resources for studying and understanding infectious diseases and to develop and evaluate innovative preventive and therapeutic strategies.

“IDMIT has unique resources, combining internationally recognised expertise in preclinical research with cutting-edge technological platforms, particularly in the domains of immunology and in vivo imaging. It provides the scientific community with access to exceptional resources, in a professional environment, for the development of the vaccines and drugs of the future”.

Dr Roger Le Grand

Director of the Division of Immunovirology*
Executive Director of IDMIT

* The Division of Immunovirology is one of the divisions of the Institute of Emerging Diseases and Innovative Therapies, part of the Life Sciences Division of the French Alternative Energies and Atomic Energy Commission.

RESEARCH DOMAINS

Characterising host-pathogen interactions

IDMIT has at its disposal technologies for the real-time monitoring, in relevant animal models, of the dynamics of the spread of pathogenic agents in the body and of the host response; these technologies are adapted to HIV, HBV, alphaviruses, flaviviruses, influenza viruses, Plasmodium and mycobacteria.

In vivo near infrared fluorescence imaging of lymphatic draining of fluorescent-labelled anti-langerin-HIVgag vaccine in NHP.
© Nina Salabert, CEA

The use of innovative technologies to study the innate and adaptive responses induced in the systemic and mucosal compartments. Genomics, flow cytometry, mass cytometry, confocal and intravital microscopy, positron emission tomography (PET), fluorescence imaging.

Multiparametric cellular staining analysis by flow cytometry.
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Preclinical studies of innovative vaccines and therapeutic strategies

IDMIT is developing new preclinical models in NHPs for testing vaccines, microbicides and treatments for infectious diseases in humans:

- ⇒ AIDS, dengue, hepatitis, yellow fever, seasonal and pandemic flu, SARS, Chikungunya,
- ⇒ Malaria, leishmaniasis, Chlamydia infection.
- ⇒ Tuberculosis.

Improving the bioavailability of vaccines and treatments

- ⇒ Developing and optimising delivery systems for compounds
- ⇒ Evaluating new adjuvants and immunomodulators
- ⇒ Studying new routes of administration

Expression of a vaccine antigen (green) in macaque skin after intradermal injection of a DNA vector. © Slobodan Culina, CEA

Characterising host immune responses to vaccines

- ⇒ Characterising the dynamics of cellular and molecular events after vaccination
- ⇒ Developing new tools for monitoring humoral and cellular responses
- ⇒ Improving the real-time monitoring of immune responses by in vivo imaging

Immunohisto-fluorescence microscopy of lymph node draining the vaccination site. © Lucille Adam, CEA

Determining the pharmacokinetics and pharmacodynamics of new drugs in infected hosts, by new in vivo imaging methods, including in particular PET-CT.

Evaluating the efficacy of new intervention strategies in experimental models of infection. Identifying biomarkers associated with vaccine -or treatment-mediated protection.

Experimental infection of primate in BSL3 conditions.
© L. Soufflet/CEA

Assessing safety of vaccines and treatments

IDMIT is developing new programmes for biomarker identification, and evaluation of the safety of vaccines and innovative treatments.

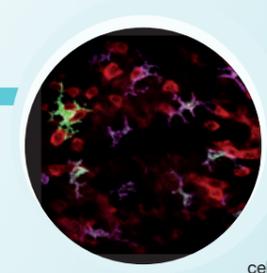
Characterising the biodistribution of vaccines and treatments and their activation of the immune system.

- ⇒ Evaluating the concentration, life time and pharmacokinetics of compounds in biological tissues and fluids
- ⇒ Characterising immune activation and biomarkers of inflammation
- ⇒ Testing the immunogenicity and safety of compounds



In vivo imaging

- ⇒ Multimodal in vivo molecular imaging in NHPs
- ⇒ Optical imaging (near-infrared fluorescence, bioluminescence, confocal endomicroscopy)
- ⇒ Magnetic resonance imaging, tomodesitometry, confocal microscopy
- ⇒ Positron emission tomography and two-photon excitation microscopy in BSL3 conditions



Confocal videomicroscopy of primate epidermal cells.
© Biliiana Todorova, CEA



Biological resource center.
© P.Stroppa/CEA

Biological resource center

- ⇒ Centre fulfilling OECD criteria
- ⇒ Access to biological samples from primates
- ⇒ Storage of pathogenic strains for experimental infections
- ⇒ Frozen sample storage at -80°C and -135°C
- ⇒ Storage of dedicated reagents for NHPs

EQUIPEMENT AND EXPERTISE

IDMIT provides its academic and industrial partners with access to all its facilities and cutting-edge equipment for their R&D projects. Its infrastructure, covering an area of more than 5 000 m², includes research laboratories and animal houses dedicated to primates. In collaboration with MIRCen – the Molecular Imaging Research Center, a DSV platform specialising in the domain of neurosciences – IDMIT is developing in vivo imaging techniques for use in biosafety level 3 conditions

- ⇒ Biosafety level 2 and 3 research and animal experimentation facilities
- ⇒ Provision of services, with quality assurance, in collaboration with Bertin Pharma

Animal experimentation

- ⇒ Genotyping
- ⇒ Housing in biosafety level 2 and 3 conditions
- ⇒ Programmes for improving the welfare of animals in captivity
- ⇒ Development of methods for non-invasive interventions (telemetry, in vivo imaging)



Multiparameter cell analysis

- ⇒ Complex single-cell phenotyping (up to 18 parameters): FACS Canto II®, LSR-II® and Fortessa®
- ⇒ Cell sorting in biosafety level 3 conditions: FACS Aria®
- ⇒ Mass cytometry (up to 100 parameters at the single-cell scale): CyTOF®

FACS Aria, flow cytometry, cell sorting in BSL3 conditions.
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Designing, validating and conducting efficacy trials in NHPs



Carrying out studies in accordance with the constraints imposed by the professionals developing drugs, through partnership between CEA and Bertin Pharma with the PharmImmune platform.

- ⇒ Quality assurance
- ⇒ Reports compliant with Regulatory Affairs
- ⇒ Respect for deadlines
- ⇒ Simplification of contractualisation

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