

**Monday, 17
October 2016
Chicago Ballroom X
9:00 – 10:30**

**SATELLITE TITLE:
➤ FROM BASIC
TO POPULATION
SCIENCES: HOW
TO UNDERSTAND
AND PREVENT HIV
TRANSMISSION:
VACCINES
AND SEXUAL
TRANSMISSION**



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DESCRIPTION

Ending HIV infection requires a better understanding of HIV transmission at cellular, clinical and social level, with a comprehensive and innovative approach. Here outcomes and ongoing research results spanning from understanding the physiology of the target cell and the initial processes of infection in mucosal tissues in order to develop blocking antibodies and vaccine antigens, to the use of biodegradable nanoparticles in HIV vaccine development and the effect of male circumcision in South Africa on HIV infection of women at population scale will be presented. The current state of the art in biomedical prevention tools such as PrEP, vaccines and antibodies as well as evidence based public policies will be discussed.

These multidisciplinary research projects in HIV transmission were funded by the Pierre Bergé endowment fund in collaboration with Sidaction.

SPEAKERS:

Origin, nature and role in vaginal transmission of HIV/SIV infected cells in semen: from basic science to prevention strategies' proof of concept

Roger Le Grand, CEA iMETI/
Division of Immuno-Virology, CEA.
Nathalie Dejuq-Rainsford,
University of Rennes

Summary 1:

HIV-infected cells in genital secretions play an important role in the sexual transmission of HIV and an increasing number of broadly neutralizing antibodies (bnAbs) are considered leads for HIV-1 vaccine development and novel therapeutics. We performed a detail characterization of macaque semen leukocytes and developed in vitro assays in order to evaluate the impact of bnAbs against cell-free and cell-to-cell transmission. Our results demonstrate that cell-to-cell transmission is less sensitive to neutralizing antibodies compared to cell-free transmission and support the use of antibody combinations against cell-associated virus in future candidate therapeutic regimens.

Authors:

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S. Bernard-Stoecklin¹, C. Gomett¹,
M. Tolazzi², G.Scarlatti², **R. LeGrand¹**

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Summary 2:

Understanding the origin of HIV in semen is key to the design of novel prevention and eradication strategies. To this end, we performed phylogenetic comparisons of viral strains isolated from semen, blood and 6 different male genital organs from cynomolgus macaques chronically infected with SIVmac251. We identified for the first time specific male genital organs as sources of HIV/SIV in semen. These data provide a new basis for innovative targeted strategies to prevent and eradicate HIV in the male genital tract.

Authors:

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Defining the HIV keys target at the mucosa following HIV infection

Christiane Moog, Institut of virology, Strasbourg;

Summary:

Several routes of HIV-1 infection at the mucosa were proposed; however, the very early events leading to infection and protection are still controversial. We performed ex-vivo studies of HIV-1 infection of genital and intestinal mucosal explants from macaques and humans. GFP Fluorescent virus is tracked in the explants and the infected cells are characterized by fine phenotyping. We observed a high frequency of infected mucosa dendritic cells and HIV-1 specific antibodies were able to protect these cells from infection. These results suggest that dendritic cells play a key role as virus vehicle, infected cells and mediators of efficient local antibody responses. If induced locally by HIV prophylactic vaccine, such antibodies may protect from HIV sexual transmission.

Authors:

Camille Ducloy¹, Tilo Schorn², Delphine Beaulieu³, Bin Su⁴, Luzia Mayr¹, Stefania Dispinseri², Chiara Foglieni², Mariangela Cavarelli³, Ugo Elmore⁵, Olivier Garbin⁶, Michel Hummel⁶, Jeanine Ohl⁶, Catherine Chapon³, Gabriella Scarlatt², and **Christiane Moog**¹

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Biodegradable nanocarrier as a new tool to elicit HIV mucosal immunity

Bertran Verrier, Institut of Biology and Chemistry of Proteins, CNRS, Lyon;

Summary:

We have recently developed a new vaccine delivery system based on poly-lactic-acid (PLA) nanoparticles. Such particles could be coated by HIV vaccine antigens, such as p24, gp140 ou trimeric BG505, mimicking HIV virions. Furthermore, by incorporating specific PRR ligands, (Nod2 or TLR2-NOD2 chimeric molecules) in the particle core during their synthesis, we could specifically induce mucosal immunity, either after mucosal administration or even after sub-cutaneous administration.

Authors:

Verrier B.¹, Phelip C.¹, Pavot V.¹, Gutjahr A.¹, Le Grand R.², Moog C.³, **Paul S.**⁴

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Mitochondrial toxicity of LPV/r and 3TC used for infant pre-exposure prophylaxis (PreP) to prevent breastfeeding transmission of HIV-1

Philippe Van De Perre, INSERM, Montpellier

Summary:

In order to assess mitochondrial toxicity associated with extended use of antiretroviral drugs in infants, mitochondrial DNA (MDC) copy numbers were measured in infants receiving either oral LPV/r or 3TC for PreP during breastfeeding (max. 12 months) in the ANRS 12174 trial. Both drugs were associated with a reduction of 50% of MDC number at 12 months. The attrition of MDC number may represent a safety concern for these treatments.

Authors:

Audrey Anouilh¹, Jean-Pierre Molès¹, Marianne Peries¹, Nicolas Méda², James Tumwine³, Justus Hofmeyr⁴, Thorkild Tylleskär⁵, Nicolas Nagot¹, **Phillipe Van de Perre**¹, for the ANRS12174 consortium

¹Inserm, Montpellier France, ²Centre Muraz, Bobo Doulasso, Burkina Faso, ³University of Makerere, Kampala, Uganda, ⁴University of Western Cape, East London, Republic of South Africa, ⁵Centre for International Health, Bergen, Norway

Roll-out of voluntary medical male circumcision in Orange Farm (South Africa): Effect on HIV incidence among women

Bertran Auvert, Hôpital Ambroise Paré, Boulogne-Billancourt ;

Summary:

The objective was to assess the association between HIV levels among women with the MC status of their partners in Orange farm (South Africa), a setting where the roll-out was ongoing in the years 2008-2010. A total of 4909 women were involved in the study, of which 1443 (29.4%) reported having exclusively had circumcised partners since their sexual debut. HIV prevalence was higher among women who reported having had at least one uncircumcised partner (36.3%; 34.7% to 37.9%) in comparison with women who reported having had only circumcised partner (21.5%; 19.4% to 23.7), with an adjusted difference in HIV prevalence of 19.9% (7.6% to 33.6%) p=0.001. HIV incidence rate was higher by 20.5% (1.0% to 44.9%) among the former group in comparison with the latter group. These differences were higher among women aged 15-24. Conclusions: In term of HIV levels, women of Eastern and Southern Africa may benefit from having only circumcised partners.

Authors:

Barbara Maraux¹, Séverin Guy Mahiane², Pascale Lissouba³, Kévin Jean⁴, Reathe Rain-Taljaard⁵, Beverley Singh⁶, Julie Bouscaillou⁷, Gilles Peytavin⁸, Dirk Taljaard⁹, David Lewis¹⁰, ¹¹ Adrian Puren⁶, **12, Bertran Auvert**^{1, 13, 14}

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SPEAKERS' BIO

Dr. Roger Le Grand is Head of the Department of 'Immunology of viral infections and auto-immune diseases' of the Institute of Emerging Diseases and Innovative Therapies (iMETI) at the CEA (Commissariat à l'Énergie Atomique), in France. His research focuses on non-human primate (NHP) models of human viral infections including HIV, Ebola, HBV, Zika... He is particularly interested in host-pathogen interactions and the prevention of viral transmission and vaccines research. He is associated with many high level studies and work as an expert, providing consulting services to several French national research agencies and the French government.

Dr Nathalie Dejuqc-Rainsford is a research director at the French National Institute of Health and Medical Research (INSERM). She heads a team of 30, studying the physiology and physiopathology of the uro-genital tract within the IRSET-INSERM U1085 in Rennes (France) (www.irset.org). Her research interest is at the interface between the biology of reproduction and virology/immunology. One specific aim of her research is to better understand viruses' sexual transmission and the host local antiviral responses, with a focus on the male genital tract. In this respect,

she has demonstrated that several semen-producing organs are infected by HIV/SIV in both humans and macaques, shown that male genital organs can constitute viral reservoirs and characterized the testicular antiviral defense system. She serves as an expert in several national and international committees.

Dr. Christiane Moog developed her own group working on neutralizing antibodies at the University of Strasbourg and created the neutralizing antibody plate-form in which experiments are performed under GcLP (good clinical laboratory practices) conditions. She notably participated in the standardization of neutralization assays and is a member of various coordinated actions and partner of several HIV vaccine projects. She was pioneer in investigating the various Fc-mediated inhibitory functions of non-neutralizing HIV-1 specific antibodies to be induced in addition or as alternative to neutralizing antibodies with the aim to develop new vaccination strategies.

Trained as molecular virologist, **Dr. Bernard Verrier** has been working on HIV for more than 20 years, first on Tat and Rev regulatory proteins, before moving to HIV glycoprotein studies and designing HIV vaccine, based on viral vectors (rMVA) or synthetic particulate vaccine. He is currently head of a joint

lab between CNRS and University of Lyon, and his research group is elaborating biodegradable particulate HIV vaccines using innate immunity ligands as adjuvants, testing different routes and devices for immunization to induce HIV mucosal immunity.

Philippe Van de Perre is a Professor of medical virology (PUPH, classe Excep.) at the University of Montpellier. He is the head of the Department Bacteriology-Virology at the University Teaching Hospital (CHRU) of Montpellier, and Director INSERM Unit 1058 «Pathogenesis and Control of Chronic Infections». He has a great experience in multicentric research in sub-Saharan Africa, especially in PMTCT.

Bertran Auvert, MD, PhD is a Professor of Public Health at the medical school of the University of Versailles, France. He was the principal investigator for the first randomized control trial, in South Africa, to assess the impact of male circumcision on the transmission of HIV. He is currently working on designing and evaluating the roll-out of male circumcision in sub-Saharan Africa.



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