Internship Proposal

Project's title: Impact of the Microbiota on Sexually Transmitted Infections in the Female Reproductive Tract

Supervisor's name: **Elisabeth MENU-MISTIC team**

Welcoming institution and team (short presentation in 10 lines maximum) :

The research center, ImVA, (directed by Dr Roger Le Grand) brings together more than 100 scientists working on common scientific challenges related to innate and adaptive immunity in the context of viral infections and regulation of autoimmune disorders. ImVA is a mixed research unit (UMR1184) involving CEA, INSERM, Université Paris-Sud and a strong partnership with the Institut Pasteur.
Research programs are supported by outstanding technological platforms (*in vivo* imaging, cytometry, bio-informatics, non human primate models, pharmacology, biobanks…).
http://www.idmitcenter.fr
The ImVA is located at the CEA at Fontenay-aux-Roses, closed to Paris (15 mn by public transportation).
The MISTIC team is working on the role of the local environment on mucosal immunity and sexually transmitted infections in the female reproductive tract.

IDOH co-supervisor : (if you have already identified someone, please indicate the name of the IDOH co-supervisor. If not, please let it empty and we (the IDOH Coordinating office) will identify someone) :

Summary of the project (1page max):

Heterosexual transmission from male to female is the major route of sexually transmitted infections (STI) and occurs mainly via the female reproductive tract (FRT) mucosae. Mucosal immunity in the FRT is affected by different physiological events, such as the microbiota. Among healthy women, the microbiota is predominantly colonized by *Lactobacilli*. These bacteriae can maintain an acidic pH, a weak inflammatory environment and modulate the local immune responses against pathogens. Imbalance in the microbial community (dysbiosis), from *Lactobacilli* dominant to anaerobic bacteria dominant (*Gardnerella*, *Prevotella*, *Sneathia*…), can lead to bacterial vaginosis and inflammatory environment. Such alterations of the

FRT microbiota are associated with a higher risk of STI including HIV-1. This situation is similar in the majority of the female macaques who do not have detectable *Lactobacilli* and such reproduces a situation known to increase the risk of viral transmission.

Coinfections induce an inflammatory response that could be associated with an increased risk of HIV-1 acquisition in the FRT.

The aim of this project is to study the role of coinfection on the susceptibility of the FRT to HIV-1 infection and to ascertain the impact of the vaginal microbiota on coinfection. We will study the mechanisms involved and the local immune responses (innate and specific). We will focus especially on the role of the inflammation. We will test the hypothesis that the maintenance of a low inflammatory environment by the manipulation of the microbiota protect from sexually transmitted coinfection.

The master student will participate to this project by developing *in vitro* (cell lines), *ex vivo* (FRT explants) or *in vivo* (non human primate model) approaches. These experiments will allow to 1) determine the mechanisms involved in the impact of the microbiota on the susceptibility to coinfection; 2) have a better understanding of the role of the inflammation and the pathways involved, thanks to cytokines profiles and cell population characterization (recruitment, activation markers). It will inform about the nature and extension of the humoral and cell associated immune responses, at systemic and mucosal level, induced during a coinfection according to the local environment.

Supervisor's Significant publications (5 maximum)