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Deciphering HIV infection into mucosal tissues

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The very early events leading to HIV-1 infection at mucosal sites are controversial. In particular, whether DCs are restricted to HIV infection or participate to early infection and dissemination is still a matter of debate. Therefore, our aim is to identify the first cells infected by HIV within the human mucosa. Methods: 1) The phenotype and distribution of T cell, DC and macrophage (Mf) subsets was characterized by multicolor flow cytometry and confocal microscopy in the mucosa of the colon and the female reproductive tract. 2) Cells isolated from human cervico-vaginal tissues were incubated with HIV-1 and infected cells were characterized by flow cytometry. 3) Polarized human cervico-vaginal and colon tissue explant cultures were incubated apically with virus and the distribution of immune cells determined by confocal microscopy. In the colonic mucosa, we observed that R5 HIV attracts CD11c+ CD64+ Mf and CD11c+ CD64+ DCs to the apical level of the mucosa. These cells expressed the migratory marker CX3CR1. In cervico-vaginal tissues, we observed that CD3+ cells represent the majority (about 60%) of the CD45+ cells while CD11c+CD64- DCs account for about 2%. Among these 4% express the CX3CR1 molecule. After 48h of incubation with a transmitted founder virus we identified about 6% of infected CD4+ lymphocytes in culture. Interestingly, about 7% of DCs were also infected, although this cell population was 15-fold less represented than CD4+ lymphocytes. Preliminary results showed that CX3CR1+ DCs were infected as well. Overall, our results demonstrate that DCs are strategic cells, infected during the first events of HIV transmission. HIV prophylactic vaccine design should take into account the role of DCs during transmission and include new strategies to prevent their infection.

Biography

Christiane Moog, PhD, is the Research Director at INSERM U1109, HDR, University of Strasbourg, France. She is also the Team Leader for "Neutralizing and enhancing activities of antibodies on primary HIV-1 isolates", responsible for the National Neutralization Laboratory developed under the aegis of ANRS since 1991. Dr. Moog is a pioneer in identifying the role of Fc-mediated antibody inhibitory function in protection against HIV to uncover novel strategies for prevention and treatment of HIV infection and virus-associated diseases. She has been actively participating in HIV vaccine projects, the Vaccine Research Institute (VRI), and European networks; aiming to define immunogens that induce an efficient protective humoral immune response. Her current research focuses on the inhibitory role of Abs during the early stage of HIV transmission at the mucosal site i.e. Ab inhibition in antigen presenting cells, inhibition of HIV cell to cell transmission and lysis of infected cells (ADCC), inhibition by Abs on ex-vivo tissue explants. Dr. Moog has published more than 80 papers in international indexed journals.

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