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## Intestinal dendritic cells and macrophages differentially affect HIV-1 transmission across the intestinal mucosa

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HIV infection frequently occurs through colorectal mucosa where mononuclear phagocytes (MP), comprising dendritic cells (DC) and macrophages (Mf) are among the first target cells. We showed that colonic lamina propria CD11c+DCSIGN+CD68-cells sample luminal R5 HIV through an env-CCR5 interaction, a mechanism exploited by HIV to bypass the intact epithelial barrier. These data raise the question on which MP subset is mediating infection and thus, which may be the definitive fate of the virus. We used multicolor flow cytometry, immunofluorescence and *ex vivo* explant culture of colorectal mucosa to define MP distribution and their susceptibility to HIV/SIV infection and tissue samples from healthy human donors and *Cynomolgus macaques*. CD64 allowed to differentiating colonic DC (CD11c+CD64-) and Mf (CD11c+CD64+). Three subset of DC were identified on the basis of CD103 and CX3CR1 expression. The totality of colonic Mf was CX3CR1+ while about 50% expressed the CD163. Interestingly, CCR5 was preferentially expressed by the CD11c+CX3CR1+ cells, which support their involvement in active sampling of HIV and in transmission of infection *in situ*. In support of this, CD11c+CX3CR1+ but not CD103+ cells penetrated the intestinal epithelium following *ex vivo* R5 HIV-1 stimulation. Furthermore, only SIVmac but not SIVagm strains attract LP CD11c+ cells at intra-epithelial level, suggesting a role in the pathogenesis of the infection. In conclusion we outlined new findings concerning the phenotype and function of intestinal MP and discuss the relative contribution of different subsets of DC and Mf in the early events of HIV transmission at mucosal sites.

### Biography

Mariangela Cavarelli has completed her PhD in 2007 from University of Milan and Postdoctoral studies from San Raffaele Scientific Institute. She is a Researcher at the Commissariat à l'énergie atomique et aux énergies alternatives (CEA), France, where she is conducting studies that aim to understand the cellular and molecular mechanisms of HIV transmission through the intestinal mucosa in human and non human primates model. She has published 17 papers in reputed journals and is serving as an Editorial Board Member for *Frontiers in Immunology*.

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