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DISSECTING THE EARLY EVENTS OF HIV MUCOSAL TRANSMISSION

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Sexual transmission of HIV is the main route for HIV acquisition. Infection frequently occurs through colorectal mucosa where mononuclear phagocytes (MP), comprising dendritic cells (DC) and macrophages (Mf), are among the first target cells of the virus. We showed that human colonic lamina propria CD11c+DCSIGN+CD68- cells sample luminal R5 HIV in an ex vivo model, a mechanism exploited by HIV to bypass the intact epithelial barrier. However, little to nothing is known about resident DC and Mf in the lower intestinal tract, the extent to which different subsets exist, and their role in HIV acquisition.

We used multicolor flow cytometry, immunofluorescence and *ex vivo* explant culture of colorectal mucosa obtained from healthy human donors and *Cynomolgus macaques*, to define MP distribution and their susceptibility to HIV/SIV infection.

CD64 allowed to differentiating colonic DC (CD11c+CD64-) and Mf (CD11c+CD64+). Three major DC subsets were identified on the basis of CD103 and the fractalkine receptor (CX3CR1) expression. The totality of colonic Mf was CX3CR1+ while about 50% expressed the M2 marker CD163. Cells were further characterized for the expression of the CD172a and CD11b. At steady state, CD11c+CD103+ DC were detected underneath the luminal epithelium and at cript level. Following ex vivo R5 HIV-1 stimulation, both CD11c+CD64+ and CDtransmission at mucosal sites.

11c+CX3CR1+ cells penetrated the intestinal epithelium, whereas an increase in CD11c+CD103+ cells migration was not observed. Interestingly, CCR5, that we showed to drive CD11c+ cells migration toward the intestinal lumen, was preferentially expressed by the CD11c+CD64+CX3CR1+ cells, which support their involvement in active sampling of HIV and in transmission of infection in situ.

In conclusion we have unravel a previously underestimated complexity in the phenotype and function of the intestinal MP in human and NHP and discuss the relative contribution of different subsets of DC and Mf in the early events of HIV

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