**IDENTIFICATION OF HIV TRANSMITTING CD11C$^{HI}$ HUMAN EPIDERMAL DENDRITIC CELLS**

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Langerhans cells (LC) represent one of the first lines of contact between the immune system and sexually transmitted pathogens, and in the human epidermis LCs have been thought to represent the only mononuclear phagocyte (MNP) population. Here show that it contains two additional MNP subsets that can be distinguished from LCs phenotypically as (i) CD11c$^{hi}$, CD1c$^{+}$ MR$^{+}$ (epidermal CD11c$^{+}$ DCs), and (ii) langerin$^{+}$CD1a$^{+}$CD33$^{lo}$ HLA-DR$^{lo}$ (epithelial CD33$^{low}$ MNPs). Epithelial CD33$^{low}$ MNPs express negligible amounts of costimulatory molecules and are very weak inducers of T cell proliferation. In contrast, CD11c$^{+}$ epithelial DCs express the highest levels of costimulatory markers and are efficient at T cell stimulation. Importantly, epithelial CD11c$^{+}$ DCs are i) enriched in the epithelium of anogenital tissues, ii) express the highest amounts of the HIV entry receptor CCR5, iii) can be visualised extending out processes at the epithelial surface to capture HIV virions, iv) support the highest levels of HIV replication among epithelial MNPs, and v) are highly efficient at transferring virus to CD4$^{+}$ T cells. Our findings reveal a new subset of epithelial DCs in skin and anogenital tissues with a potential key role in sexual transmission of HIV.