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ABSTRACT BOOK

9.06

Human epidermal dendritic cells and their role in Herpes Simplex Virus and HIV infection

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Human epidermis is thought to contain a single dendritic cell (DC) population called a Langerhans cell (LC). We have recently described a second DC population, found in human epidermis that are transcriptionally and phenotypically related to dermal cDC2s. They are more abundant in genital tissues including foreskin, labia, glans penis, vagina, and fossa navicularis. They support high levels of HIV infection and transfer HIV to T cells. Prior Herpes Simplex Virus (HSV) type 2 infection as well as inflammation enhance HIV acquisition > 3-fold.
Previously we have shown HSV2 infection of monocyte-derived DCs and LCs enhances expression of the HIV co-receptor CCR5 through production of TNFα by infected cells. Here we have examined the role LCs and epidermal cDC2s play in enhancing HIV acquisition. We have found epidermal cDC2s are highly susceptible to infection by HSV1 and HSV2 and produce TNFα after infection by HSV2. We are currently dissecting which chemokines produced by HSV2 infected keratinocytes and genital tissue epidermal explants recruit cDC2s to the epidermis. Further understanding of the mechanisms underlying HSV infection of human skin DCs should lead to better preventions for preventing HIV-acquisition and lead to more informed vaccine design for both HSV and HIV.

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9.07 ORAL

IFI16 is a Negative Regulator of Glucose and Cellular Lipid Metabolism during Human Cytomegalovirus Infection

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Cellular lipid metabolism plays a pivotal role in human cytomegalovirus (HCMV) infection. Increased lipogenesis occurs upon HCMV infection most likely to favor the envelopment of newly synthesized particles. Here, we demonstrate that IFN-γ-inducible protein 16 (IFI16), previously characterized as a restriction factor of HCMV replication, interferes with metabolic pathways during infection. Specifically, we report that IFI16 hampers glucose uptake after HCMV infection by inhibiting the expression of the glucose transporter (GLUT) 4, resulting in decreased glucose consumption. GLUT4 downregulation is induced by a cooperation between IFI16 and the carbohydrate-response element-binding protein (ChREBP) on the GLUT4 promoter. Consequently, IFI16 reduces the transcription of the genes encoding lipogenic enzymes, leading to a decreased lipid synthesis and a reduced amount of enveloped viral particles in the infected cells. Finally, an untargeted lipidomic approach highlights the differences in lipid composition between WT and IFI16 KO cells particularly significantly increased cholesteryl esters content in IFI16 KO cells in comparison to WT cells. Overall, our data unravel a new role for IFI16 in the regulation of glucose and lipid metabolism upon HCMV replication and shed light for new promising targets in antiviral therapy.

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