Topic: Virus-host interactions

Title: HERPES SIMPLEX VIRUS TYPE 1 EXPLOITS LIPID METABOLISM: IMPLICATIONS FOR VIRAL INFECTIVITY AND ALZHEIMER'S DISEASE

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ABSTRACT

Herpes simplex virus type 1 (HSV-1) is a widespread human pathogen that relies on host metabolism to favor its replication. Several studies have revealed that an increase in fatty acid biosynthesis leads to the accumulation of lipids that are used for the formation of the viral envelope. Here, we show that HSV-1 infection upregulates fatty acid synthase (FASN) expression, a key enzyme regulating the final stage of de novo lipid synthesis, and is increased in patients affected by Alzheimer's disease. Notably, this is accompanied by a marked increase in lipids concentration and a differential lipid species distribution. Conversely, silencing FASN or using FASN inhibitors CMS121 and C75 reduces viral infectivity, affecting virion structure and entry into host cells. Additionally, FASN inhibition prompts compensatory fatty acids uptake via upregulated CD36. Lastly, in a 3D tissue culture model of herpesvirus-induced AD, both CMS121 and C75 display a potent inhibitory effect on Aß-like plaque formation, linking HSV-1-mediated lipid metabolism dysregulation to AD etiopathogenesis. Altogether, our findings reveal how HSV-1 manipulates lipid metabolism, offering insights into its link with AD and highlighting potential therapeutic targets.