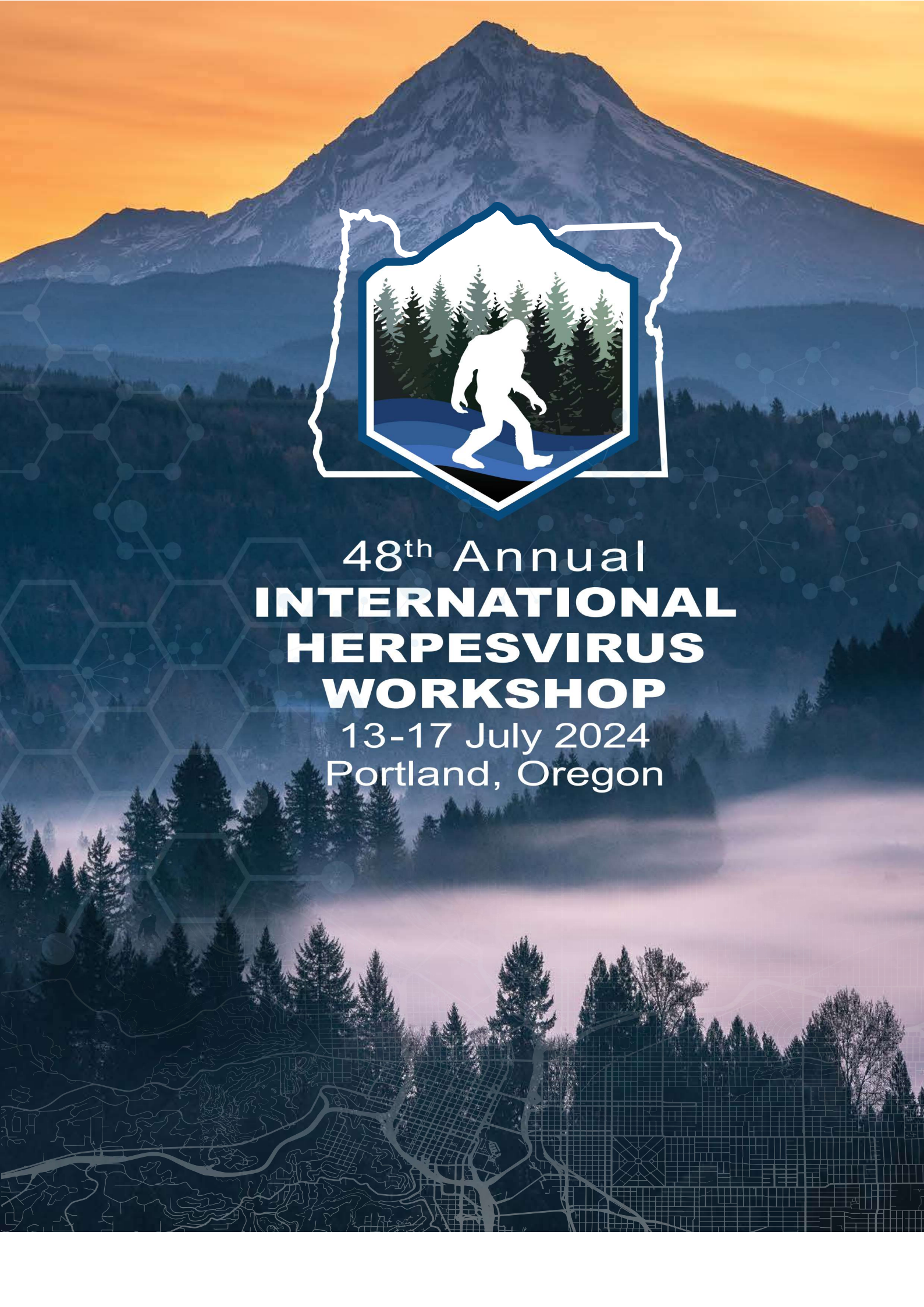
48th Annual
INTERNATIONAL
HERPESVIRUS
WORKSHOP
13-17 July 2024
Portland, Oregon

8.95

The Impact of Fatty Acid Synthase on HSV-1 Infectivity Unveils the Key Interconnection with Alzheimer's Disease

Matteo Biolatti[1] (matteo.biolatti@unito.it), Camilla Albano[2], Linda Trifirò[1], Weronika Hewelt-Belka[3], Dana Cairns[4], Selina Pasquero[1], Gloria Griffante[5], Francesca Gugliesi[1], Greta Bajetto[6], Dorota Garwolińska[7], Marika Rossi[8], Marta Vallino[8], Marco De Andrea[1], David Kaplan[4], Valentina Dell'Oste[1]

[1]University of Turin, Turin, Italy, [2]University of Turin, Turin, Torino, Italy, [3]Gdańsk, Poland, Gdańsk, Poland, [4]Tufts University, Medford, [5]Candiolo Cancer Institute, Turin, Italy, [6]University of Piemonte Orientale, Novara, Novara, Italy, [7]Gdańsk University of Technology, Gdańsk, Poland, [8]CNR, Turin, Italy

Herpes simplex virus type-1 (HSV-1) is a widespread human pathogen that relies on host metabolism to favor its replication. Here, we demonstrated that *de novo* lipogenesis is essential for HSV-1 infectivity. Particularly, HSV-1 infection upregulates fatty acid synthase (FASN) expression, 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, we show that a source of lipid-rich external factors provided by fetal bovine serum significantly increases HSV-1 infectivity. Lastly, in a 3D tissue culture model of herpesvirus-induced Alzheimer's disease (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 association with AD and highlighting potential therapeutic targets.

8.96

Investigate the cell specific responses to Herpes Simplex Virus 1 (HSV-1) on Keratinocytes

Zhousiyu Yang[1] (2491317Y@student.gla.ac.uk)

[1]University of Glasgow, Centre for Virus Research, Glasgow, United Kingdom

Herpes Simplex Virus 1 (HSV-1) is a double-strand DNA virus targeting on human skin. Keratinocytes, the predominant cell type in the epidermis of skin, serve as the initial site of HSV-1 infection, playing a crucial role in the pathogenesis and subsequent immune response. Currently, there are four keratinocytes established in our lab, include HaCaT, TIGK, NOK, and N-TERT. This study aims to investigate the cell-specific response of keratinocytes to HSV-1 infection, highlighting the importance of these cells in understanding the virus's pathogenic mechanisms. In this research, we use both wild-type HSV-1 (WT HSV-1) and dl1403 HSV-1 (ICP0 null-mutant HSV-1 strain). By employing a plaque assay, we observed a differential response among keratinocytes to HSV-1 infection, as evidenced by the variability in the number of viral plaques especially for dl1403 HSV-1 infection. This variance indicates the heterogeneity in keratinocyte susceptibility and response to HSV-1, suggesting that individual cellular factors may influence the outcome of the infection. To delve deeper into the molecular underpinnings of this differential response, we utilized RNA sequencing (RNA-seq) to analyze the transcriptomic changes in keratinocytes upon HSV-1 infection. Our analysis focused on identifying both conserved and unique pathways that are upregulated or downregulated in response to the virus. Our data showed that these keratinocytes have conserved response to HSV-1 infection. The antiviral responses, including cytokine signalling in immune system pathway are upregulate in all these keratinocytes. However, they also have differential responses to HSV-1 infections, as the enrichment of upregulated genes involved in antiviral response are different. On the other hands, we also found the viral infection pathway is differently regulated in these keratinocytes. These finding suggest that keratinocytes have a conserved but unique level of antiviral response during HSV-1 infection. For the future study, we will focus on pathways that may related to tissue specific responses