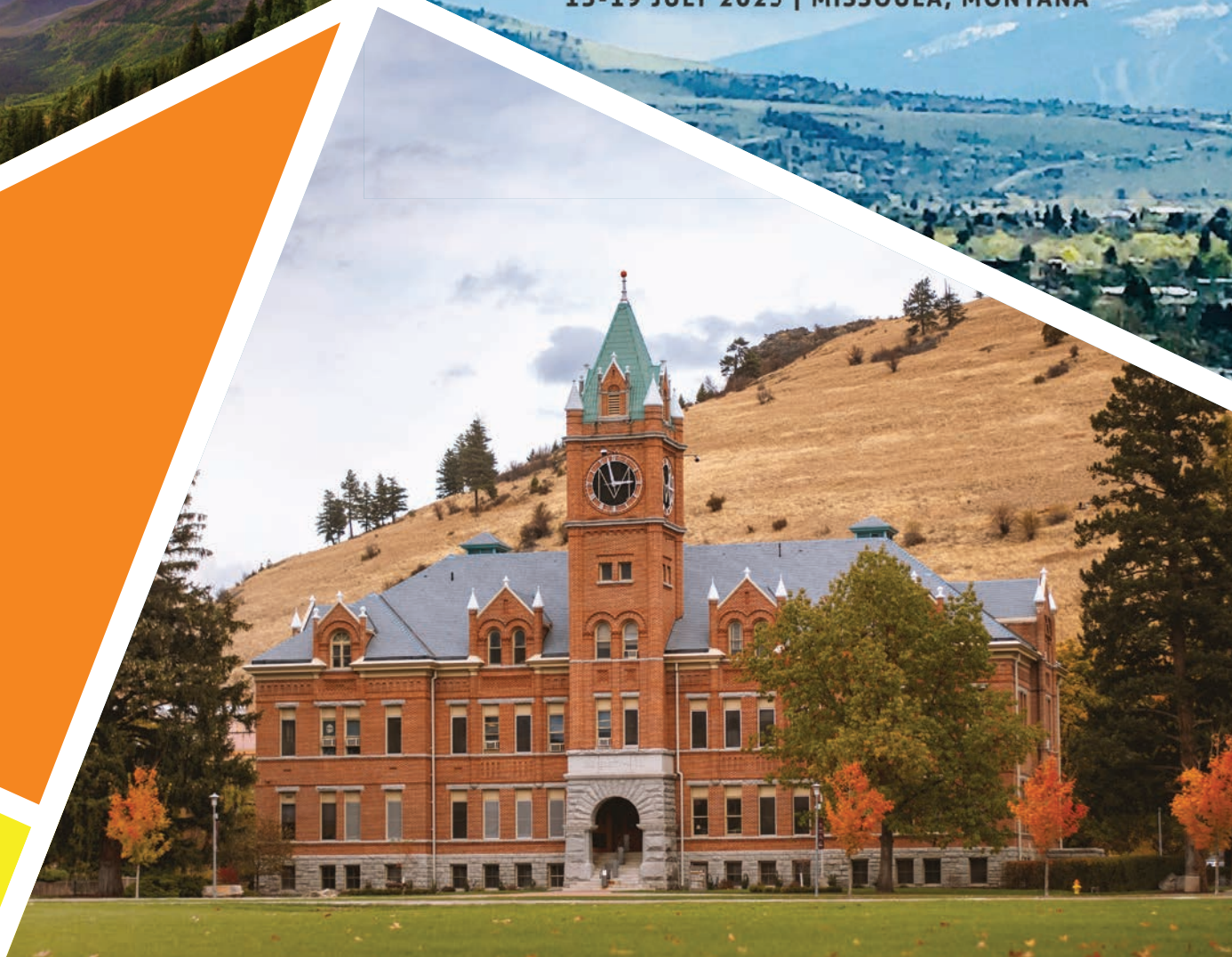
IHW 2023

INTERNATIONAL HERPESVIRUS WORKSHOP

15-19 JULY 2023 | MISSOULA, MONTANA



Saturday, 15 July

11:45	**Biologically Active Small Peptide Derived from KSHV LANA Protein Induces CHD4 Degradation to Promote Cell Differentiation and Inhibits Leukemic Cell Growth** Hiroki Miura*, Ashish Kumar, Tomoki Inagaki, Somayeh Komaki, Kenichi Nakajima and Yoshihiro Izumiya	**8.75**
12:00–13:00	**LUNCH**	UC Commons

08:30–12:00 Herpes Simplex Virus Satellite Workshop — UC Ballroom

Session Chairs: Roger Lippé and Kristen Conn

08:30	**IFI16 Phase Separation via Multi-phosphorylation Drives Innate Immune Signaling** Dawei Liu*, Krystal Lum, Nicholas Treen, Corazón Núñez, Michael Levine and Ileana Cristea	**6.34**
08:45	**c-Jun Acts at Multiple Stages to Promote HSV-1 Reactivation but does not Function During c-Jun N-terminal Kinase (JNK)-Mediated Exit from Latent Infection** Sara Dochnal, Patryk Krakowiak, Sean Cuddy, Abigail Whitford and Anna Cliffe*	**7.07**
09:00	**Chromatin Conformation of the Latent HSV-1 Genome in Human Neurons** Seth Frietze*, David Bloom, Donna Neumann, Princess Rodriguez and Terri Edwards	**3.05**
09:15	**Slug, a Stress-Induced Transcription Factor, Stimulates HSV-1 Replication and Transactivates a Cis-Regulatory Module Within the VP16 Promoter** Vanessa Claire Santos*, Jeffery Ostler, Kelly Harrison and Clinton Jones	**7.42**
09:30	**RVx201 Vaccine Suppresses HSV-1 Replication and Spread and Reduces Inflammation in the Vaginal Tissue and Spinal Cord Following Genital Infection** Daniel Carr* and Ed Gershburg	**6.06**
09:45	**HSV-1-induced PAD-mediated Citrullination as a New Target for Antiviral Therapy** Camilla Albano*, Selina Pasquero, Francesca Gugliesi, Gloria Griffante, Qiao Yang, Valentina Dell'Oste, Matteo Biolatti, Greta Bajetto, Linda Trifirò, Bianca Brugo, Paul Thompson, Sen Sudeshna, Santo Landolfo and Marco De Andrea	**8.01**
10:00–10:30	**REFRESHMENT BREAK**	UC Commons
10:30	**PRO-Seq Analysis of Herpes Simplex Virus Type 1 Infection in Lytic and Latency Models** Adam Whisnant*, Elena Weiß, Thomas Hennig, Caroline Friedel, David Price and Lars Dölken	**5.25**
10:45	**The Identification of Proteins in Proximity to Tegument-Associated HSV-2 pUL21 Following Viral Entry** Safara Holder*, Maike Bossert and Bruce Banfield	**8.52**
11:00	**Identification of a cryptic HSV-1 protein, UL31.6, as a novel neurovirulence factor** Akihisa Kato*, Ryoji Iwasaki, Kosuke Takeshima, Yuhei Maruzuru, Naoto Koyanagi and Yasushi Kawaguchi	**7.22**
11:15	**HSV-1 reduces expression of SLC19A1 Folate Receptor to promote viral replication** Zsuzsa Szemere* and Eain Murphy	**8.110**
11:30	**Neuronal miR-9 promotes herpes simplex virus 1 latency by repressing host Oct-1 and Onecut family genes** Yue Deng, Yuqi Lin, Siyu Chen, Hongjia Chen, Gloria Komazin-Meredith, Donald Coen and Dongli Pan*	**7.39**
11:45	**HSV-1 miRNAs are posttranscriptionaly edited in latently infected human ganglia** Andreja Zubković, Adwait Parchure, Mia Cesarec, Antun Ferenčić, Filip Rokić, Hrvoje Jakovac, Cristina Gómez, Dražen Cuculić, Angela Gallo, Oliver Vugrek, Michael Hackenberg and Igor Jurak*	**7.21**
12:00–13:00	**LUNCH**	UC Commons

8.01 **HSV-1-induced PAD-mediated Citrullination as a New Target for Antiviral Therapy**
Camilla Albano, Selina Pasquero, Francesca Gugliesi, Gloria Griffante, Qiao Yang, Valentina Dell'Oste, Matteo Biolatti, Greta Bajetto, Linda Trifirò, Bianca Brugo, Paul Thompson, Sen Sudeshna, Santo Landolfo and Marco De Andrea*

8.02 **Inhibition of Intracellular Peroxynitrite Production Alleviates CMV Replication**
Pragati Amratia, Lauren Kerr-Jones, Morgan Marsden, Mathew Clement, Richard Stanton and Ian Humphreys*

8.03 **Broadly-neutralizing anti-HCMV monoclonal antibodies represent novel therapeutics to limit virus infection and dissemination**
Kristina Atanasoff, Andrea Parsons, J. Duty and Domenico Tortorella*

8.04 **Identification of thymus tropism and dysregulation after neonatal murine roseolovirus infection**
Tarin Bigley, Michale Paley, Eden Xue, Andrei Belean and Wayne Yokoyama*

8.05 **Exploiting Lipid Metabolism by HSV-1: a Challenge to Rethink New Therapies for Alzheimer's Disease**
*Camilla Albano, Selina Pasquero, Linda Trifirò, Gloria Griffante, Francesca Gugliesi, Greta Bajetto, Weronika Hewelt-Belka, Erica Mina, Paolo Porporato, Adam Mullis, Dana Cairns, David Kaplan, Santo Landolfo, Marco De Andrea, Valentina Dell'Oste and Matteo Biolatti**

8.06 **Comparison of HEp-2 and Vero cell responses reveal unique proapoptotic activities of the herpes simplex virus type 1 alpha0 gene transcript and product**
John Blaho and Marie Nguyen*

8.07 **Identification of a binding pocket of Letermovir in the small terminase subunit pUL56 of HCMV**
*Lukas Kmetsch, Marie Knoblauch and Elke Bogner**

8.08 **Characterization of murine cytomegalovirus M72 interaction with the carbon catabolite repression 4-negative on TATA-less complex**
Olivia Brahms and Jason Upton*

8.09 **Modeling Epstein-Barr Virus Infection in the Rabbit**
Cole Burgess, Karla Balogh, Neil Christensen, Jeffery Sample and Clare Sample*

8.10 **Bringing Productive Infection into the Light: How a Dual-Fluorescent Reporter Epstein-Barr Virus Illuminates Host Shutoff**
Alejandro Casco, Makoto Ohashi and Eric Johannsen*

8.11 **KSHV PAN RNA Influences Paraspeckle Formation During Lytic Replication Through the Exclusion of Cellular Long Noncoding RNA NEAT1 and Interactions with NONO/SFPQ**
Evelyn Tara, Shannon Harger Payen and Cyprian Rossetto*

8.12 **Role of the Canonical Immediate Early 3 Protein in Murine Cytomegalovirus-Induced Necroptosis**
Jason Upton and Shawn Yates*

8.13 **Nonsense-Mediated Decay Controls Reactivation of the Oncogenic Human Herpesviruses EBV and KSHV**
Michiel van Gent, Adrian Reich, Fatiha Zaaraoui - Boutahar, Sadanandan Velu, George Verjans and Michaela Gack*

8.14 **Abemaciclib Restricts HCMV Replication by Suppressing pUL97-Mediated Phosphorylation of SAMHD1**
Georgios Vavouras Syrigos, Maximilian Feige, Alicia Dirlam, Ramona Businger, Lüder Wiebusch and Michael Schindler*

8.15 **Characterizing Donor Susceptibility to Epstein-Barr Virus Infection in the Nasopharynx using Organotypic Rafts**
Shweta Kitchloo, Joshua Walston, Eric Wang and Kathy Shair*

8.16 **Viral Gene Drive Spread during HSV-1 Infection in Mice**
Marius Walter and Keith Jerome*

8.01

HSV-1-induced PAD-mediated Citrullination as a New Target for Antiviral Therapy

Camilla Albano[1] (camilla.albano@unito.it), Selina Pasquero[2], Francesca Gugliesi[2], Gloria Griffante[3], Qiao Yang[1], Valentina Dell'Oste[2], Matteo Biolatti[2], Greta Bajetto[4], Linda Trifirò[2], Bianca Brugo[1], Paul R. Thompson[5], Sen Sudeshna[5], Santo Landolfo[2], Marco De Andrea[2]

[1]University of Turin, Turin, Torino, Italy, [2]University of Turin, Turin, Italy, [3]University of Eastern Piedmont, Novara, Italy, [4]University of Piemonte Orientale, Center for Translational Research on Autoimmune and Allergic Disease-CAAD, Novara, Italy, Novara, Italy, [5]UMass Chan Medical School, Worcester

Herpes simplex virus 1 (HSV-1) is a neuroinvasive and neurotoxic virus capable of entering the brain via peripheral nerves. Like other members of the Herpesvirus family, HSV-1 has developed different strategies, such as the exploitation of post-translational modification (PTM) of proteins, to ensure efficient viral replication and persistent infection. Citrullination is a PTM catalyzed by peptidyl-arginine deiminases (PADs), that convert peptidyl-arginine into peptidyl-citrulline. Here we show that HSV-1 infection triggers PAD-mediated citrullination through transcriptional activation of three PAD isoforms: PAD2, PAD3, and PAD4. Interestingly, the pan-PAD inhibitors, Cl-amidine and BB-Cl-amidine, and the PAD3-specific inhibitor, HF4, dramatically suppress HSV-1 replication. Finally, citrullinome analysis reveals significant changes in several host and viral proteins, with interferon (IFN)-inducible proteins IFIT1 and IFIT2 being among the most heavily deiminated ones. As genetic depletion of IFIT1 and IFIT2 strongly enhances HSV-1 growth, we propose the viral-induced IFIT1-2 citrullination as an HSV-1 evasion mechanism from host antiviral resistance. Altogether, these findings highlight the pivotal role of citrullination in subverting cellular responses to viral infection and demonstrate that PAD inhibitors efficiently suppress HSV-1 replication, suggesting their potential repurposing as HSV-1 antiviral drugs.

8.02

Inhibition of Intracellular Peroxynitrite Production Alleviates CMV Replication

Pragati S. Amratia[1] (SabberwalP@cardiff.ac.uk), Lauren E. Kerr-Jones[1], Morgan Marsden[1], Mathew Clement[1], Richard J. Stanton[1], Ian Humphreys[1]

[1]Cardiff University, Cardiff, South Glamorgan, United Kingdom

There is no licensed vaccine against HCMV, and current therapeutic approaches that target key viral proteins are toxic and/or prone to antiviral drug resistance. Targeting host pathways essential for virus replication provides an alternate strategy for the development of antivirals, which may reduce opportunities for resistance to evolve. Here we show that CMV exploits host oxidative/nitrosative stress responses for efficient viral replication. Oxidative/nitrosative stress is caused by the accumulation of intracellular reactive oxygen/nitrogen species (ROS/RNS). Using a range of ROS/RNS scavengers, we identified that peroxynitrite, a powerful oxidising/nitrating agent, promoted virus replication in both *in vitro* and *in vivo* models of CMV infection. HCMV rapidly induced the generation of intracellular peroxynitrite upon infection, and inhibiting peroxynitrite within the first 24 hours of infection prevented CMV replication in both cell-free and cell-associated infection systems. Thus, peroxynitrite production may impact virus entry and/or the initiation of replication. Interestingly, serotonin, a naturally occurring antagonist of peroxynitrite, also impinged on HCMV-induced production of peroxynitrite and exhibited anti-viral activity. Overall, our study highlights a novel role for intracellular peroxynitrite in CMV pathogenesis and implies that oxidative/nitrosative stress signalling pathways could be targeted as a novel strategy for inhibiting CMV infection.