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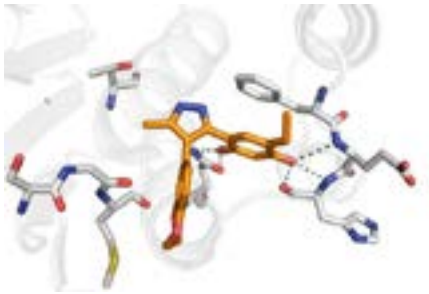
Adrian Whitehouse

University of Leeds, UK

Targeting herpesvirus ribonucleoprotein particle assembly: A novel antiviral strategy

Human herpesviruses are responsible for a range of debilitating acute and recurrent diseases, including a number of malignancies. Current treatments are limited to targeting the herpesvirus DNA polymerases, but with emerging viral resistance and little efficacy against the oncogenic herpesviruses, there is an urgent need for new antiviral strategies. Here, I will describe a mechanism to inhibit the replication of the oncogenic herpesvirus Kaposi's sarcoma associated herpesvirus (KSHV), by targeting the ATP-dependent formation of viral ribonucleoprotein particles (vRNPs). I will demonstrate that small-molecule inhibitors that selectively inhibit the ATPase activity of the cellular human transcription/export complex (hTREX) protein UAP56 result in effective inhibition of vRNP formation, viral lytic replication and infectious virion production. Strikingly, as all human herpesviruses use conserved mRNA processing pathways involving hTREX components, we demonstrate the feasibility of this approach for pan-herpesvirus inhibition.



Recent Publications

1. Schumann S, Jackson B R, Yule I, Whitehead S K, Foster R and Whitehouse A (2016) Targeting the ATP-dependent formation of herpesvirus ribonucleoprotein particle assembly as an antiviral approach. Nature Microbiology 2:16201.
2. Wood J J, Boyne J R, Paulus C, Jackson B R, Nevels M M, Whitehouse A and Hughes D J (2016) ARID3B : A novel regulator of the KSHV lytic cycle. Journal of Virology 90:9543-9555.
3. Baquero Perez B and Whitehouse A (2015) Hsp70 isoforms are essential for the formation of KSHV replication and transcription compartments. PLOS Pathogens 11(11):e1005274.
4. Hughes D J, Wood J J, Jackson, B R, Baquero Perez B and Whitehouse A (2015) NED Dylation is essential for KSHV latency and lytic reactivation and represents a novel anti-KSHV target. PLoS Pathogens 11(3):e1004771.

Biography

Adrian Whitehouse obtained a BSc in Microbiology from the University of Sheffield in 1991 and DPhil in Molecular Virology from the University of Oxford in 1994. Following Postdoctoral work at the Molecular Medicine Unit, St James's Hospital in Leeds, he was awarded a Medical Research Council Non-clinical Fellowship in 1998, and joined the School of Molecular & Cellular Biology, University of Leeds, as a Lecturer in 2002, and subsequently appointed to Reader in 2005 and Professor of Molecular Virology in 2010. His research focuses on investigating the virus-host cell interactions which regulate the replication and transformation of human tumour viruses.

a.whitehouse@leeds.ac.uk