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Broad spectrum anti-virals: Viral protein nuclear import as a target?

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Viral disease is one of the greatest burdens of human health, with an urgent need for new anti-viral strategies. Our work examining a number of DNA and RNA viruses indicates that regulated protein movement into and out of the nucleus through the importin (IMP) superfamily of transporters is central to viral infection (see [1]). This is particularly striking in the case of RNA viruses where although viral replication generally occurs in the cytoplasm, gene products important in virus replication/assembly traffic into the host cell nucleus generally to dampen the host cell anti-viral response. Using a variety of in vitro and in vivo approaches, we have delineated the IMPs and targeting signals responsible for the nuclear import/export of specific viral proteins from DNA tumor viruses such as cytomegalovirus/Herpes Simplex Virus, as well as the RNA viruses Dengue (DENV), Respiratory Syncytial Virus (RSV), and Human Immunodeficiency Virus (HIV)-1. Intriguingly, many of the different viral gene products utilize either IMPβ1 or IMPα/β for nuclear import, and IMPβ homologue EXP1/CRM1 for nuclear export, implying that agents targeting their cellular nuclear transport proteins could represent crude broad spectrum anti-viral agents. Our recent results [2,3] support this idea, with 3 different novel inhibitors of IMPα/β -dependent nuclear import reducing infection by DENV as well as HIV-1, by reducing nuclear import of the non-structural protein 5 and integrase proteins, respectively. Nucleocytoplasmic transport thus appears to be a viable target of great significance in the fight against pathogenic viruses.

Biography

Dr. Wagstaff completed her Ph.D in 2007 at Monash University (Melbourne) where she has remained for her post-doctoral studies. She is presently an ARC Australian Post-Doctoral Research Fellow and manages a small group as part of the Nuclear Signalling Laboratory (Monash). Her research focusses on the transport of proteins into and out of the eukaryotic cell nucleus and its therapeutic applications, including the development of inhibitors of theis process as anti-viral agents and how the nuclear transport machinery may be exploited for drug delivery. She has 18 peer-reviewed publications in eminent journals (H-factor of 11) and numerous prestigious awards/prizes.

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