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Nucleocytoplasmic trafficking of gene products from RNA viruses: Targets for anti-virals

Protein movement into and out of the nucleus through the importin superfamily of transporters is central to the replication of viruses in infected mammalian cells and, thereby, pathogenesis in host organisms. Although RNA virus replication is generally cytoplasmic, we have shown that a number of RNA viruses of importance to human health express gene products that traffic into the host cell nucleus. In particular, we have delineated the importins and targeting signals responsible for the nuclear import/export of specific proteins from Dengue virus [DENV], Respiratory Syncytial Virus (RSV), Rabies virus and HIV-1. Importantly, using reverse genetics, culture selection and animal infection models, we have shown that signal-dependent nucleocytoplasmic transport of specific viral proteins including DENV non-structural protein 5, RSV matrix protein and Rabies Virus phosphoprotein is integral to viral infectivity/pathogenesis. Intriguingly, the role of these viral proteins in the nucleus appears to relate to inhibition of specific or general host cell transcription to dampen the cellular anti-viral response/host innate immune response. Our results have important application in developing strategies to combat viral infection by generating specific inhibitors of viral protein nuclear trafficking, as well as for vaccine development using live attenuated viruses impaired in nuclear trafficking of critical gene products.

Biography

Prof. Jans completed his Ph.D at the age of 25 years at the Australian National University (Canberra) and postdoctoral studies at the Friedrich Miescher Institut (Basel, Switzerland) and Max Planck Institut fuer Biophysik (Frankfurt am Main, Germany). He is presently an NHMRC Senior Principal Research Fellow (SPRF1) and Head of the Nuclear Signalling Lab. at Monash University (Melbourne, Australia). His research over the last 15 years has focused on the regulation of transport into and out of the eukaryotic cell nucleus, and how this relates to viral disease, cancer and development, and how it may be exploited for drug delivery. He has >240 peer-reviewed publications in eminent journals (> 7000 citations; H-factor of 50) and currently serves as an editorial board member of Biochemical Journal (since 2006) and committee member of the International Photodynamic Association (2005-2011).