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Generation of HTS suitable cellular models to identify small molecules inhibitors of the anti-interferon proteins belonging to human pathogenic RNA viruses

The majority of emerging and re-emerging RNA viruses, responsible for life threatening diseases, have in common the ability to evade the innate immune responses mediated by type I interferon (IFN). This is mostly achieved through the expression of viral structural and non-structural proteins whose anti-IFN function is essential for virus replication. Such viral proteins have the ability to inhibit both the production and the ability of cells to respond to IFNs. Examples include the influenza viruses NS1 protein, West Nile virus NS2A, NS1 and NS4B proteins, Dengue virus NS5, NS2A, NS4A and NS4B proteins plus the NS2B/NS3 complex and Ebola virus VP35 and VP24 proteins.

Therefore, the above mentioned viral proteins represent ideal targets for the development of antiviral compounds aimed at allowing innate immune responses to efficiently contain the initial viral replication and thus promoting the development of an effective adaptive immune response.

This lecture will provide an overview on the RNA virus strategies to overcome the IFN system through the employment of viral gene products and will present data from our lab, describing the identification of two anti-influenza virus NS1 compounds through a multidisciplinary approach involving a diverse library of small molecule and a reporter assay able to measure the inhibition of the anti-IFN activity of the NS1 protein.

Moreover, the talk will discuss the generation of a myeloid cell model, that can be employed as a versatile module suitable for an high throughput screening of compounds potentially able to inhibit the function of RNA virus anti-IFN gene products, with a particular focus on the Ebola VP35 and VP24 proteins from the on-going epidemic in West Africa.

Biography

Marco Sgarbanti has studied molecular virus-host interaction for 15 years as deducible by his peer-reviewed publications. As researcher and principal investigator (PI), he has been studying the role of cellular transcription factors in HIV-1 LTR expression focusing on strategies aimed at eliminating viral reservoirs. Recently he has focused in the development of cellular assays suitable for high throughput screening (HTS) of small molecules, to find inhibitors of RNA viral proteins belonging to important human threatening virus diseases. Awards: winner of a Grand Challenges Exploration Grant in Global Health, Phase I, of the Bill & Melinda Gates Foundation.

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