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EDITORIAL

Amino acids special issue 'Protein interactions in the virus–host relationship'

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Viruses can be conceived as very active laboratories of genetic and biochemical strategies optimized for the hostile take over of the infected cell. The infection of a cell by a virus is a complex series of events that start at the cell surface, where the virus must gain access into the cell, proceeds through the establishment of a replication and transcription complex, and ends when the infectious virus leaves the cell to infect other targets. During this process, viruses must overcome several host factors' restriction points and the immune response.

Host protein interaction networks and biochemical pathways are altered by the invading viral proteins. An example of a biochemical pathway that is altered by virus infection is exemplified by viruses like the human herpes virus type 1 (HSV-1) that encodes for enzymes, such as thymidine kinase (TK) and ribonucleotide reductase (RR) that free the virus from normal cellular controls and allow nucleotide metabolism in cells that have shut down their DNA synthesis (Boehmer et al. 1997). On the other hand, the human immunodeficiency virus type 1 (HIV-1) Tat transactivator controls transcription from the integrated provirus through multiple protein–protein interactions (Marcello et al. 2001). The resulting new network topology favors excessive amounts of virus production at the expense of the host cell. Hence, understanding viral protein functions and their interactions with host proteins is a prerequisite for the rational development of antiviral compounds. Current antivirals are mostly targeted to virus-encoded enzymes (De Clercq 2004). For example nucleoside analogs like acyclovir or zidovudine inhibit HSV TK and HIV-1 reverse transcriptase (RT), respectively. But other strategies are directed toward different targets including membrane fusion, like the recently developed enfuvirtide capable of inhibiting HIV entry (Kilby et al. 1998), or the disruption of specific protein–protein interactions, including the heterodimeric HSV RR (Liuzzi et al. 1994; Marcello et al. 1994; Marcello and Palu 1995). Indeed, a wide armamentarium of antiviral targets is required to avoid the emergence of resistant viruses that would impair the effectiveness of a single-target therapy.

In this special issue, contributions from several groups address protein interactions that are established during viral infection. Both review-type and original articles are present allowing for an up-to-date grasp of the topic as well as for the several new experimental approaches that are being used in this field.

The contribution of Manjula Kalia and Shahid Jemeel discuss virus entry and provide an overview of the recent developments of this rapidly evolving field (Kalia and Jameel 2009). The entry topic is completed by the review of Karin Stiasny about the mechanism of Flavivirus membrane fusion during entry (Stiasny et al. 2009). Flaviviruses are a family of very important human pathogens that include yellow fever, Dengue virus, West Nile, Japanese encephalitis and tick-borne encephalitis viruses.

Gianni Cesareni and his group developed a database, VirusMINT, that stores in a structured format most of the published interactions between viral and host proteome (Carducci et al. 2010). The characterization of the host protein sub-networks disturbed by invading viruses is a critical step for the rational definition of the most appropriate targets/hubs that can be targeted by antiviral therapy.

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The review of Elisa Vicenzi provides an in-depth analysis of the Tripartite Motif (TRIM) proteins as anti-retroviral restriction factors (Kajaste-Rudnitski et al. 2010). This is an example of a post-entry block to virus replication that determines species barriers that has been particularly important also for the pathogenic history of HIV-1.

Alina Baum and Adolfo García-Sastre provide a detailed analysis of the recognition of viral RNA by pattern recognition receptors of the innate immune system (Baum and Garcia-Sastre 2010). Containment of incoming viruses by the interferon response is the first line of defense to viral infection and our understanding of the molecular determinants of this critical step are being heavily investigated.

Matias Machado and Sergio Pantano apply the method of molecular simulation to the study of protein–protein interactions that are involved in HIV-1 post-integrative latency (Machado et al. 2010). These methods are increasingly used as docking platforms for the virtual screens of novel antiviral compounds.

Awatef Allouch and Anna Cereseto conducted an innovative two-hybrid screen using constitutively acetylated HIV-1 integrase as a bait to find novel cellular partners of this important viral enzyme (Allouch and Cereseto 2009).

Finally, we exploited the technique of fluorescence resonant energy transfer (FRET) to study the subcellular localization of the interaction between the viral Tat protein and the host nucleosome assembly protein (hNAP-1) (De Marco et al. 2010).

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