

Proceeding of the 8th annual meeting of the Italian Society of Virology

In September 2008, the 8th National Congress of Italian Society of Virology was held in the beautiful historic city of Orvieto (TR), Italy. The meeting had an attendance of about 160 scientists with invited and selected lecturers covering the following topics: General virology and viral genetics; Viral oncology, Virus-Host interaction and pathogenesis; Emerging viruses and zoonotic, foodborne and environmental pathways of transmission; Viral immunology and vaccines; Viral biotechnologies and gene therapy; Medical virology and antiviral therapy. The final programme and the abstract book can be found at the web site <http://www.siv-virologia.it> or <http://www.infectagentscancer.com>. A summary of plenary lectures are reported.

J. Burgyan (Godollo, Hungary) described the mechanisms of RNA silencing evolved by plants as a defense against viruses. Replication intermediate or folded viral RNAs are able to activate the antiviral RNA silencing mechanism inducing small interfering (si)-RNAs, which represent key players in the antiviral response. To escape this mechanism of defense, viruses encode for suppressor proteins that target the antiviral silencing pathways, and in particular these si-RNAs which are the most conserved elements of RNA silencing.

For the Pioneer in Virology lecture, B. Roizman (Chicago, USA) reviewed the strategy used by HSV-1 to infect the host cell. HSV-1 encodes for several non-coding RNAs and 84 multifunctional proteins, of which 46 can be deleted without abrogating the capacity of the virus to replicate. Large part of these “dispensable” proteins are able of taking full control of the cell in order to block every way in which the host cell could respond to viral infection. Therefore, HSV-1 is able of i) blocking viral DNA silencing by host proteins; ii) inducing the degradation of cellular proteins that may interfere with viral replication; iii) encoding an RNase that selectively degrades mRNAs and a protein that blocks their splicing; iv) blocking the interferon defense pathways and the presentation of antigenic peptides to the immune system; v) disrupting cytoskeleton, nuclear lamina, nuclear pores and Golgi apparatus; and vii) blocking pro-apoptotic pathways activated by viral gene products or exogenous agents to insure uninterrupted viral replication.

In a special lecture dedicated to G.B. Rossi, N. Muller-Lantzsch (Homburg, Germany) revisited the potential role of endogenous retroviruses in human tumorigenesis. Approximately, 8% of the human genome consists of sequences of retroviral origin with 2,000 proviruses and more than 30,000 sequences related to the viral regulatory long terminal repeats, of which the vast majority have accumulated multiple nonsense mutations. Among the human endogenous retroviruses (HERV), Muller-Lantzsch focused on the HERV-K family, that contains intact open reading frames for the structural and enzymatic viral proteins. Noteworthy, patients with germ cell tumors frequently produce antibodies directed against HERV-K proteins, that are selectively expressed in

germ line tumors biopsies, thus suggesting that the HERV-K gene expression may participate in this type of cancer development.

G. Gerna (Pavia, Italy) focused on HCMV infection/disease, characterized either by systemic syndrome or organ localization, that represents the most important viral complication in transplant recipients. HCMV disease can be prevented by two strategies: i) prophylaxis, whose disadvantages are represented by toxic effects and costs related to long-term drug administration, emergence of late disease, possible selection of drug-resistant HCMV strains, and delayed HCMV-specific immune reconstitution; ii) pre-emptive therapy, raising concerns about the need of a strict virologic monitoring, the possibility of HCMV organ localization in the absence of virus in blood and the claimed indirect effects of subclinical HCMV infection, such as graft failure and increased susceptibility to bacterial and fungal infections. In particular, Gerna suggested to monitor weekly HCMV viral load in blood in the first three months after transplantation and proposes a cutoff of 100,000 HCMV-DNA copies/ml broncho-alveolar lavage fluid as criteria to start the pre-emptive therapy in lung transplant recipients.

L. Nicoletti (Rome, Italy) reported the Italian experience in the management of a Chikungunya virus (CHIKV) outbreak. Following several reports of cases of febrile illness of unknown origin cases in two contiguous villages in north-eastern Italy, an outbreak investigation was done to identify the primary source of infection and the modes of transmission. The disease was fairly mild in nearly all cases, with only one reported death. Analysis by PCR and serological assays of samples from patients showed that the outbreak was caused by CHIKV. The virus was detected also at the levels of the *Aedes spp* mosquitoes that play a role as the vector of infection. The presumed index case was a man from India. Phylogenetic analysis showed a high similarity between the strains found in Italy and those identified during an earlier outbreak on islands in the Indian Ocean, thus emphasising the need for vigilance and response to emerging infectious threats in the era of globalisation.

R. Manservigi (Ferrara, Italy) described the possible employment of oncolytic viruses in cancer therapy, since these replication-competent viruses display the unique property of selectively killing cancer cells via their normal replication pathways. One of the most important advantages, is their capability to replicate their genome and spread efficiently within the tumor mass, allowing them to amplify the oncolytic effect of an initial low dose of virus. Moreover, some of these viruses can be used as viral vectors to deliver transgenes whose expression will enhance their innate anti-tumor activity, through either the expression of potentially cytotoxic enzymes, or the induction/enhancement of tumor-specific immune responses, or specifically modifying the tumor microenvironment (i.e. angiogenesis inhibition).

M. Stevenson (Worcester, USA) focalised his presentation on the role of cellular restrictions in the biology of primate lentiviruses. Several reports have clearly demonstrated the presence of cellular “restrictions” that potently antagonize viral replication. In particular, Stevenson described the function of cytidine deaminases Apobec3 proteins, that compromise the formation and integrity of viral cDNA, and Bst2/tetherin, that prevents detachment of budding viruses from the surface of the infected cell. To counteract these restrictions, primate lentiviruses have evolved accessory proteins, such as the Vif protein, that targets Apobec3 for proteasomal destruction, and Vpu, that mislocalizes Bst2/tetherin away from the site of virus budding. Stevenson has recently identified a new restriction factor expressed in macrophages, that can potently antagonize the replication of retroviruses. Noteworthy, this restriction is counteracted by the viral accessory protein Vpx/Vpr. In addition, Stevenson indicated in the accessory proteins a potential target for new drug development. In this contest, he reported the use of small molecules to block the protein Vif in Apobec3-expressing cells, thus exhibiting anti-HIV activity.

E. Affabris (Rome, Italy) overviewed the HIV accessory protein functions in the context of virus-cell interactions. Among them, Affabris focused on Nef, which do not have any enzymatic activity, but functions by establishing connections between its targets and effectors, which are usually part of trafficking or signalling pathways. In particular, Affabris demonstrated that, in monocyte-derived macrophages (MDM), the presence of Nef regulates the expression of many transcripts, leading to the synthesis and the release of a set of pro-inflammatory cytokines/chemokines, that in turn activate several STAT proteins. Progress in understanding the biological phenomena underlying the complex role of Nef in HIV infection and pathogenesis could be relevant for future design of inhibitors to be employed along with conventional antiviral therapy.

In addition, to the plenary lectures, 40 selected oral presentations and 81 posters were discussed. During the congress 3 young scientists were awarded for the best posters. The next SIV meeting is scheduled to take place again in Orvieto, Italy, from 7 to 9 September 2009. The preliminary programme of the Congress will be available on the SIV website.