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MEETING REPORT

# Meeting Report on 3rd National Congress of the Italian Society of Virology (SIV)

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The 3rd National Congress of the Italian Society of Virology (SIV) was held on September 22–24, 2003 at the Centro Convegni S. Agostino, Cortona (Arezzo, Italy). Invited lectures and selected oral communications covered the following topics: general virology and viral genetics; innovative diagnostics; vaccines, cytokines and antiviral immunity; taxonomy and viral evolution; biological terrorism and emerging infections; antiviral therapy; viral biotechnologies; pathogenesis of viral infections. The final program and abstract book can be found at the web site http://www.siv-virologia.it/Congressi1.htm. In the opening lecture, C. Cogoni (Roma) presented an overview on RNA mediated gene silencing describing the first observation of this phenomenon in plants and the molecular bases of gene silencing characterized in several organisms. In the session, "General Virology and viral Genetics" P. Caposio (Torino) provided evidence on the essential role of IKK2 in productive replication of HCMV and emphasized the feasibility of blocking NF-κB activation as a mechanism to inhibit viral infection. A. Gallina (Milano) described UL131, UL130, and UL128 as the HCMV factors essential for the endothelial and leukocyte tropism, and M. Patrone (Milano) suggested a new approach for a rapid mutagenesis of HCMV with a single-nucleotide resolution. Anti-apoptotic mechanism of HSV-1, based on NF-κB-dependendent activation, were elucidated by M.T. Sciortino (Messina) while the ability of nef, a virulence factor of HIV-1, to activate an extracellular signaling in human monocyte-derived macrophages and in THP-1 monocytic cells was shown by Z.A. Percario (Roma). L. Rubino (Bari) proposed *Saccharomyces cerevisiae* as a means to study the replication of tombusviruses while L. Stavolone (Bari) described the interactions between the virion associated protein of cauliflower mosaic virus and the movement protein together with the role of these interactions in the virus cell-to-cell movement. M. Valentini (Siena) presented a study on nucleotide sequence analysis of NSm and G1 protein ORFs of Toscana bunyavirus for investigating the hypothetic presence of different neurotropic variants. Sequence analysis of cellular factors binding sites involved in viral transcription of human polyomavirus JC elucidated the hypothesis that particular variants might represent additional risk factors for the occurrence and the progression of Progressive Multifocal Leukoencephalopathy (M. Mischitelli, Roma). The study of N-myc-2 activation in a WHV/woodchuck model of HBV induced hepatocellular carcinoma (HCC) may also provide insights into further mechanisms of cellular gene activation, that may play a role in HBV integration, as described by R. Bruni (Roma). The cell cycle perturbation, in a human hepatoblastoma cell line, induced by a constitutive expression of hepatitis C virus core protein was discussed by A. Ruggieri (Roma) and A. Costantino (Roma) who described the endoplasmic reticulum stress-mediated apoptosis induced by expression of hepatitis C virus structural proteins. B. Roizman (Chicago), an honorary member of SIV, highlighted his views on how to reconciliate the phenotype of infected cells protein 0 (ICP0) of herpes simplex virus type 1 with the functions encoded in its gene. In particular, he described the role of ICP0 in blocking the interaction of viral DNA with cellular proteins that attempt to mute viral gene expression. This may be the major function responsible for the phenotype of ICP0. The session "Innovative diagnostics" was dedicated to a quantitative real-time PCR approach for the surveillance of herpes virus infection in bone marrow transplant recipients and in patients affected by encephalitis and/or meningitis (F. Bertolotti and O. Varnier-Genova). L. Tagliaferro (Lecce) described a real-time PCR approach that allows a rapid and accurate quantitation of different HCV genotypes. M.G. Padula (Siena) proposed the development of a new diagnostic and therapeutic tool based on the study of E2 glycoprotein. An improved diagnostic approach (Genescreen Plus HIV Ag-Ab) that enable to avoid the risk of missing HIV seroconversion in the window phase was elucidated by G. Spreafico (Milano).

In the "Vaccines, cytokines and antiviral immunity" session, F. Belardelli and L. Bracci (Roma) analyzed the effect of interferons as natural adjuvants in the induction of antiviral immunity and stressed the interferon roles in the development of vaccine strategies. In particular F. Belardelli showed the effect of interferon

The Italian Society of Virology annually promotes a meeting where young researchers present their work and get the opportunity to gain scientific experience. A summary of the last meeting is reported.

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type I in affording to mice a total protection against influenza infection. A.M. Iorio (Perugia) described a study demonstrating that repeated annual influenza immunizations of elderly high-risk subjects did not significantly impair their humoral immune response against vaccine components that were not changed in sequential years. The ability of interferon-inducible IFI16 gene to inhibit tube morphogenesis and proliferation of primary, but not of HPV16 E6/E7-immortalized human endothelial cells were described by R. Ravera (Torino). To treat the HPV16-associated tumors, C. Giorgi (Roma) proposed a vaccine, with improved anticancer activity, based on crude *Nicotiana benthamiana* extracts containing the HPV16 E7 protein. In addition, S. Vannucchi (Roma) elucidated the mechanism of INF-β induced apoptosis, by the trail/death receptor pathway, in cervical carcinoma cell lines. Protocols for hepatitis delta virus vaccination was presentated by E. D'Ugo (Roma). A. Radaelli (Milano) proposed a combined vaccine modality for anti-SIV immune reconstitution in long-term slow-progressor Rhesus macaques subjected to HAART, while M. Alfano (Milano) described that the HIV-1 inhibitory effect of urokinase plasminogen activator (uPA) interacting with its receptor is based on an INF-mediated-like mechanism. The evolution of T helper immune response in primary human cytomegalovirus infections was described by D. Lilleri (Pavia) while L. Lozza (Pavia) proposed an approach to simultaneous detection of HCMV-specific $CD4^+$ and $CD8^+$ effectors cells, by coculture of peripheral blood mononuclear cells with autologous HCMV-infected dendritic cells. The session on "Taxonomy and viral evolution" was opened by an overview on virus taxonomy by G.P. Martelli (Bari) while D. Galitelli (Bari) and A.M. Vaira (Torino) highlighted their studies on Pelargonium zonate spot virus and Ophiovirus respectively. The increased frequency of HIV-1 non-B strains in Italy was elucidated by the phylogenetic analysis of pol gene sequences presented by C. Riva (Milano).

The lecture of G. Ippolito on Bioterrorism debated the risk of the biological weapons most likely to be deployed in case of microbial warfare, i.e., poxvirus and *Bacillus anthracis*, and introduced the session on "Biological terrorism and emerging infections." In this section, C. Serra and G. Mameli (Sassari) discussed some aspects of pathogenesis of multiple sclerosis-associated retrovirus (MSRV) in patients with multiple sclerosis or monosymptomatic optic neuritis. The development of a mouse model for the study of Toscana virus (TOSV) neuropathogenesis was described by G. Gori Savellini (Siena). In this model, viral replication and apoptosis were restricted to the neuron of the cortical and hippocampal regions without any signs of inflammation in brain tissue. The possibility of developing prophylactic measures against TOSV infections was also discussed. E. Cancellotti (Padova-Edinburgh) described the molecular and intracellular characterization of gene-targeted transgenic mice with alterations of PrP glycosylation as a means to approach the study, under normally regulated gene function conditions, of familial fatal insomnia (FFI) and Creutzfeldt-Jakob Disease (CJD). In the "Roundtable on SARS: debate on Italian experiences," M. Rapicetta (Roma) overviewed some relevant aspects of diagnosis, epidemiology and pathogenesis of SARS. C. Balotta and E. Vicenzi (Milano) described the identification and molecular characterization of a coronavirus associated with SARS in an Italian patient. M.R. Capobianchi (Roma) discussed on the Spallanzani Institute experience in the SARS management.

The session on "Antiviral therapy" was introduced by a lecture of A. Alberti (Padova) that described the relationship between HCV and host cells, with the interplay of viral and cellular genes (NS3-NS5, PKR-IEF3-INF) relevant to pathogenesis and drug sensitivity. Oral communications were prevalently focused on HIV-1 infections. J.L. McDermott (Genova) described a study on HIV-1 replication. After 5 years of HAART, only integrated provirus and not 2LTR DNA (unintegrated DNA) was detectable in patients, probably for the complete suppression of viral replication. The problems related to the diffusion of non-B subtypes of HIV-1 and the clinical significance of the development of genotypic traits of drug resistance in the HIV-1 genome was discussed by M. Zazzi (Siena). A novel Peptide nucleic acid (PNA) hybrid molecule was reported to be able to inhibit HIV-1 replication *in vitro* (C.D. Pesce, Roma); M. Alfano (Milano) described the pertussis toxin B-oligomer (PTX-B) as a tool for inhibiting HIV-1 replication. PTX-B is a non-toxic molecule that inhibits HIV infection and replication in different *in vitro* models and in SCID mice reconstituted with human PBMC. I. Martini (Genova) proposed some *in vitro* and *in vivo* test models for identifying microbicides against mouse retroviruses. Applications of siRNA as antiviral agents to counteract poliovirus type 2 infections in human cell lines or geminivirus in plants were discussed by A.L. Salvati (Roma) and E. Noris (Torino), respectively. C. Cermelli (Modena) reported the antiviral activity of essential oils.

In the "Viral biotechnologies" session, L. Naldini (Milano) described the characteristics of lentiviral vectors as instruments for gene transfer in stem cells. He underlined the efficient delivery, robust long-term expression, cell targeting and exogenous regulation of transgenes that can be obtained *in vivo* with lentiviral vectors. The kinetics of FIV replication *in vivo* following adoptive transfer of autologous virus-specific-T cells was proposed as a model therapeutic approach against lentiviral infections by F. Bonci (Pisa) while C. Zanotto (Milano) described the ultrastructural, biological and molecular characterization of Simian-Human Immunodeficiency Virus-like particles produced by recombinant Fowlpox viruses. He suggested that these virus-like particles might represent a good booster candidate to elicit a long-lasting memory versus the lentiviral infection. Newer anticancer strategies relying upon the use of non-replicative HSV-1 based vectors expressing antiangiogenic factors and suicide genes, were reportated by E. Berto (Ferrara) while strategies based on the intracellular expression of anti HPV16-E7 antibodies in single-chain format were discussed by M.G. Donà (Roma). As on attempt to studying the neuropathogenesis of herpes viruses in mice, G. Donofrio (Parma) described the development of a recombinant bovine herpes virus 4 (BoHV-4) expressing enhanced green fluorescent protein. Last session, "Pathogenesis of viral

infections," was introduced by P. Lusso (Milano) who described the interactions between HIV and chemokines, particularly underlining the implications for pathogenesis, therapy and vaccine development. A. Garzino-Demo (Baltimore) highlighted the role of CCR5 ligands as potent and specific inhibitors of strain of HIV-1 that use CCR5 as co-receptor. In particular, some ligands may have a role in protecting $CD4^+$ memory T cells from infection. Some evidences that SCCA1, the HBV receptor, may be involved in hepatocellular carcinoma (HCC) were shown by S. Quarta (Padova) who described activation of proliferation mediated by SCCA1 in HepG2 cells. F. Maggi (Pisa) provided the first evidence that TT virus can be an immunomodulatory agent while S. Delbue (Milano) presented data on amplification, characterization and expression of JC virus in brain tumors. This data suggested a possible association of JCV with CNS tumors, especially with glioblastoma. Human herpesvirus-6 can infect the central nervous system and is probably associated to multiple sclerosis, D. Donati (Maryland) reported. He presented data on HHV-6 infections in patients with mesial temporal lobe epilepsy and the data suggested that viral reactivation in the CNS might trigger a cascade of biochemical events leading to focal neuronal damage and seizures. P.G. Conaldi (Varese) described the enterovirus infection of polarized monolayers of human intestinal epithelial cells; he demonstrated a vectorial release of progeny virions from the epithelial cells, associated to a tuning of the mucosal inflammatory response. The mechanism of action of a new anti-HIV-1 quinolones based on a specific recognition of the tar sequence was described by S. Richter (Padova). E. Caselli (Ferrara) described the reactivation of HIV-1 replication in cells of macrophage and endothelial lineages after *in vitro* infection with HHV-8. This data suggested a role of HHV-8 as a co-factor in the progression of HIV-1 disease. In the last oral presentation, M. Sgarbanti (Montreal) demonstrated that an HHV-8 lytic reactivation with productions of replicative competent virions can be induced by NF-κB in primary effusion lymphoma cells.

Abstract of poster presentations are available in the SIV web site.