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Cell death: physiopathological and therapeutic implications

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Annual Meeting of the Associazione Italiana di Colture Cellulari (ONLUS-AICC: Italian branch of the European Tissue Culture Society) in collaboration with Phoenix-ONLUS Stem Cell Foundation for Human Life, 2–4 December 2009, Florence (Italy)

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The Annual Meeting of the Associazione Italiana di Colture Cellulari (ONLUS-AICC) in collaboration with Phoenix Stem Cell Foundation for Human Life (Phoenix-ONLUS) was held during 2–4 December 2009, in Florence (Italy).

AICC has been known for more than 20 years for its promoting initiatives regarding cell cultures. The Phoenix Foundation was born in March 2009 with the main aims of promoting research in the field of stem cells, guaranteeing ethical principles and transferring the results of stem cell research to clinics, in view of their possible impact on human health.

The Meeting brought together top Italian scientists to share their current knowledge and views on the cellular and molecular aspects of cell death (from programmed cell deaths, such as apoptosis, anoikis and autophagy, to necrosis), on the role of programmed cell death in maintaining an organism's homeostasis, on the impact of deregulation of death mechanisms in human diseases, and on the design of candidate apoptosis targeting therapeutics in Regenerative Medicine

The Meeting was also an occasion for stimulating interactions and for the exchange of points of view among senior and young scientists and undergraduate students.

The Opening Ceremony included the presentation of the Meeting topics by the President of AICC, Augusto Pessina, and the President of the Phoenix Foundation, Sergio Capaccioli, and was followed by the tributes of the local authorities, that is, Gianfranco Gensini and Sergio Pinzauti, Deans of the Faculties of Medicine and of Pharmacy of the University of Florence, respectively, and Antonio Panti, President of the Order of Physicians of the Province of Florence.

The Meeting consisted of four main sessions, the synthetic digests of which are reported below. The details can be found at http://www1.unifi.it/plrna/index.html.

Apoptosis, Autophagy and Necrosis: Physiology and Pathology

This session began with the lecture of Angelo Manfredi (University Vita-Salute San Raffaele, Milan, Italy) on the role of cell death in the maintenance of tissue homeostasis. Sandra Zecchi (University of Florence), Francesca Scarlatti (University of Turin) and Rosanna Supino (Tumour Institute, Milan) reviewed the main alternative forms of cell death, focusing on aponecrosis, autophagy and anoikis, respectively. Noteworthily, aponecrosis, an intermediate form of cell death sharing the morphological and molecular aspects of apoptosis and necrosis, was shown to abolish any antithesis between these two forms of cell demise. The physiological roles of cell death within the response to cellular stresses, such as microgravity, radiation and electromagnetic fields, were then examined by Monica Monici (University of Florence), Aldo Becciolini (University of Florence) and Lina Ghibelli (University of Tor Vergata, Rome). Seven young researchers were selected to present their results, which focused on cellular apoptotic response to the natural metabolites of lichen (Silvia Caggia, University of Catany), algae (Gian Luca Sala, University of Modena and Reggio Emilia), and to the alkaloid voacamine (Stefania Meschini, Superior Institute of Health, Rome); to the synthetic chemotherapeutics, including cisplatinum (Barbara Del Bello, University of Siena) and doxorubicin (Francesco Fabbri, IRST, Forlí-Cesena); and to the immunotherapeutic anti-CD99 monoclonal antibody (Clara Guerzoni, Rizzoli Orthopaedic Institute, Bologna). The role of the Ikaros gene in the apoptotic response was discussed by Daria Capece (University of L'Aquila).

Defective or Excessive Apoptosis in Pathology

The impact of cell death deregulation on a wide variety of severe human pathologies was discussed. While Gianluigi





Forloni (Mario Negri Institute, Milan) reviewed the role of apoptosis in the neurodegenerative diseases, Francesco Annunziato (University of Florence) focused on the effects of TGF-B in the development of human Th-17 lymphocytes and Giorgio Parmiani (University, Hospital San Raffaele, Milan) described the involvement of T-lymphocyte apoptosis in the immune response to cancer. The lectures of Davide Lauro (University of Tor Vergata, Rome) and Carlo Nucci (University of Tor Vergata, Rome) on the consequences of excessive apoptosis in diabetes and ophthalmologic pathologies, respectively, were followed by a discussion on the relationship between apoptosis and Herpes Simplex virus (Antonio Mastino, University of Messina) and on the contribution of apoptosis to the pathogenesis of muscle atrophy and cachexy (Paola Costelli, University of Turin). Three selected young researchers discussed the involvement of AMPK and mll gene in apoptosis (Benedetta Accordi, University of Padua), the role of NK cells in HIV infection (Domenico Mavilio, Humanitas Clinical Institute, Milan), and the involvement of lipoic acid in endoplasmic reticulum stress (Tania Camboni, University of Cagliari).

Modulators of Apoptosis as Therapeutic Tools

Novel paradigmatic modulators of apoptosis as candidate therapeutic tools were the protagonists of this session. In particular, the apoptotic effects of the acetyltransferase inhibitor CPTH6 (Donatella Del Bufalo, National Cancer Institute 'Regina Elena', Rome), the efficacy of the SWCNT nanoparticles as potential vehicles for antiangiogenetic drugs (Adriana Albini, Multimedica Group, Milan), the downregulators of AKT kinase in reactivation of apoptosis in drugresistant cells (Angelo Nicolin, University of Milan), and the new synthetic molecules in overcoming chemoresistance (Enrico Mini, University of Florence) were discussed. The overview of the emerging hypoxic cell targeting CA IX inhibitors (Claudiu Supuran, University of Florence), imatinib (Tiziana Negri, Tumour National Institute, Milan), and the oncosuppressive properties of MET oncogene in the enhancement of tumour apoptotic cell death (Maria Flavia Di Renzo, University of Turin) completed the presentations. The three selected communications of young researchers were focused on partenolide (Daniela Carlisi, University of Palermo), new CXCR4 cycle-peptide inhibitors (Luigi Portella, CNR, Naples), and ZnO nanoparticles (Maria Condello, Superior Institute of Health, Rome) as potential anticancer therapies.

Apoptosis and Regenerative Medicine: Future Perspectives

This session reflected the main purposes of the Phoenix Stem Cell Foundation for Human Life, which are 'to promote translational research in the field of stem cell science, to guarantee the ethical principles and to transfer to clinics the results of stem cells research, in view of their impact on human health'. Paolo Di Nardo (University of Tor Vergata, Rome) introduced the session with a lecture on tissue engineering as a new perspective in organ repair, which was followed by Franco Bambi (University of Florence), who

presented an exhaustive analysis of the risks occurring in the development of cellular therapeutics according to GMP (Good Manufacturing Practice, Florence, Italy). Paradigms of stem cell studies or pivotal application were reported by Maurilio Sampaolesi (University of Pavia), who discussed endogenous and exogenous stem cell administration as antiapoptotic tools in muscular dystrophies, and by Elisabetta Cerbai (University of Florence), who described the use of embryonic stem cells as a model of cardiomyocyte differentiation, as well as by Benedetta Mazzanti (University of Florence), who presented studies of the therapeutic potential of mesenchymal stem cells in autoimmune diseases. The four selected young researchers' presentations were dedicated to the role of sphingosine 1-phosphate as a differentiation inductor of mesangioblasts toward smooth muscle cells (Chiara Donati, University of Florence), the apoptotic role of rexinod in osteosarcoma and mesenchymal stem cells (Barbara Dozza, Rizzoli Orthopaedic Institute, Bologna), the bone tissue regenerative capacity of autologous stromal bone marrow cells in tibia inborn pseudoarthrosis (Valentina Devescovi, Rizzoli Orthopaedic Institute) and the potential regenerative role of mesenchymal stem cells in invertebrate disk degeneration therapy (Elisa Leonardi, Rizzoli Orthopaedic Institute).

The poster session provided an interesting opportunity for discussion, especially among young scientists. Particular curiosity and perplexity were aroused by Marco Ruggiero's (University of Florence) 'HIV and apoptosis of cancer cells: the killer's promises' poster, in which, based on welldocumented literature, he raised the possibility that HIV might be endowed with anti-tumour activity, which could be responsible for its symbiotic relationship with humans. Three prizes for the best posters were awarded to Daria Capece (University of l'Aquila), for her studies on the characterization of a novel antiapoptotic Ikaros splice variant, to Clara Guerzoni (Rizzoli Orthopaedic Institute), for demonstrating the involvement of the CD99 antigen in apoptosis induction in Ewing's sarcoma cells, and to Silvia Zappavigna (Second University of Naples), for shedding light on the synergic effects of interferon-beta and troglitazone in the treatment of pancreatic adenocarcinoma.

The oral presentations were followed by the plenary lecture of Gerry Melino (University of Tor Vergata, Rome) entitled 'The determinants of apoptosis as therapeutic targets', an interesting overview of cell death mechanisms as targets for therapeutic drugs, focusing on degradation of P73 as a novel therapeutic approach to enhance the chemosensitivity of tumour cells, which fit in perfectly with the translational spirit of the Meeting.

Honouring its spirit and commitment to promoting biomedical research and supporting outstanding researchers, AICC awarded four scientists: Monica Marra (Second University of Naples) and Domenico Mavilio (Humanitas Clinical Institute, Milan) with the Senior AICC Prize; Elisa Bianchi (University of Modena and Reggio Emilia) and Lavinia Nardinocchi (National Cancer Institute 'Regina Elena', Rome) with the Junior AICC Prize.

The Meeting closed with the concluding remarks of Sergio Capaccioli and Augusto Pessina and was followed by a visit to the Renaissance church of San Lorenzo, the first cathedral of Florence, with Costanza Capaccioli, art historian, as guide.



Conflict of interest

The authors declare no conflict of interest.

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