EACR Conference Series

In addition to the biennial EACR Congress we organise a series of excellent cancer research conferences where education and interaction for participants are the very highest priorities.

Upcoming meetings in the EACR Conference Series

4th EACR-OECI Joint Training Course
Molecular Pathology Approach to Cancer
5 - 7 May 2014
De Rode Hoed, Amsterdam, the Netherlands

EACR Conference Series 2014
Goodbye Flat Biology
3D Models & the Tumour Microenvironment
2 - 5 November 2014 • Berlin, Germany

EACR Conference Series 2015
 Radiation Biology and Cancer
From Molecular Responses to the Clinic
5 - 7 February 2015 • Essen, Germany

EACR-AAICR-SIC Special Conference
Anticancer Drug Action and Drug Resistance
from Cancer Biology to the Clinic
20 - 23 June 2015 • Florence, Italy
Recent meetings in the EACR Conference Series

2nd EACR Conference on Cell Death in Cancer
30 January - 1 February 2014, Amsterdam, the Netherlands

The conference was held at De Rode Hoed, the oldest remaining hidden church in the Netherlands located in the historic centre of Amsterdam, and was designed to bring together basic researchers and clinical scientists from various disciplines with interest in the role of cell death in tumourigenesis, malignant progression and therapy resistance as well as in the exploitation of cell death pathways for therapeutic targeting.

The exciting scientific programme attracted 111 participants from 24 countries all over the world. The format of the conference provided an excellent platform for the informal interaction of young researchers and leading scientists engaged in basic, translational and clinical cancer research and provided an inspiring and exciting forum to share research findings, to establish or strengthen collaborations and to discuss the latest discoveries in the field.

The programme included 16 plenary lectures, and 11 proffered papers that were intensely discussed after each talk. The programme was completed by three keynote lectures and two poster sessions covering a total of 56 posters. The vivid poster sessions were very well attended and highly interactive. The generous support of EACR enabled us to award poster prizes to two young scientists, Chloe Falvey (Ireland) and Rémy Montagne (France), during the closing ceremony. The feedback received from speakers as well as delegates was outstanding, strongly supporting the continuation of this series of EACR conferences in the future.

For a full report of the scientific proceedings of the meeting and a summary of the findings of each speaker, see pp. 14-15.

Some comments from the delegate feedback surveys for other recent EACR conferences:

**EACR Special Conference:**
**Cancer Genomics**
**25 - 28 June 2013, Cambridge, UK**

“The scientific line-up was very impressive; the talks were excellent.”

“High quality speakers, and the small setting facilitated interactions.”

“Excellent range of top speakers in a relatively intimate setting. Small enough and focussed conference.”

**3rd EACR-OECI Joint Training Course:**
**Molecular Pathology Approach to Cancer**
**6 - 8 May 2013, Amsterdam, Netherlands**

“Excellent course with world-class speakers.”

“I was inspired by this meeting and found it extremely useful. The speakers were all excellent and there was plenty of time for discussion. I can’t wait for next year and I have already recommended it to my colleagues.”
The 2nd EACR Conference on Cell Death in Cancer was held in January 2014 at De Rode Hoed, the oldest remaining hidden church in the Netherlands located in the historic center of Amsterdam. It was organised as part of the Series of EACR Special Conferences designed to bring together basic researchers and clinical scientists from various disciplines with interest in the role of cell death in tumorigenesis, malignant progression and therapy resistance as well as in the exploitation of cell death pathways for therapeutic targeting. The exciting scientific programme attracted 111 participants from 24 countries all over the world, including 30 students.

The format of the conference provided an excellent platform for the informal interaction of young researchers and leading scientists engaged in basic, translational and clinical cancer research. The programme included 16 plenary lectures, and 11 proffered papers that were intensely discussed after each talk. The programme was completed by three keynote lectures and two poster sessions covering a total of 56 posters. The vivid poster sessions were very well attended and highly interactive. The generous support of EACR enabled us to award poster prizes to two young scientists during the closing ceremony. The feedback received from speakers as well as delegates was outstanding.

Programmed cell death pathways constitute a natural barrier against cancer. Vice-versa death resistance allows tumor cells to deal with environmental stress and to escape the cytotoxic action of chemotherapy, radiotherapy or targeted therapy. However, there is increasing evidence that under certain conditions cell death can have tumour promoting potential. Research about the diverse modes of programmed cell death and their dual role in tumorigenesis and therapy resistance is an exciting and rapidly evolving field which has enormous impact on the development and implementation of novel therapeutic strategies.

Pascal Meier (London, UK) discussed caspase regulation in apoptotic and non-apoptotic signalling. Activation of initiator caspases is regulated via the assembly of multi-protein platforms that integrate cellular signals and recruit initiator caspases via their death-fold domain. To gain novel insights into the regulatory mechanisms that govern activation of initiator caspases, his lab used a proteomics-based approach. This strategy resulted in the identification of an evolutionarily conserved regulator of caspases that controls caspases in their apoptotic and non-apoptotic roles.

Martin Leverkus (Mannheim, Germany) reported on the importance of cFLIP for maintaining the integrity of the epidermis. The clinical relevance of his findings was underscored by data showing that cFLIP protein was lost in the epidermis of patients with severe drug reactions associated with epidermal apoptosis. This was followed by Douglas Green (Memphis, USA) who discussed how caspases and receptor-interacting protein kinases (RIPK) control cell death and development and introduced another level of complexity. He proposed a model in which two signals function to regulate RIPK1 activation.

Peter Vandenabeele (Ghent, Belgium) reported on molecular mechanisms involved in the regulation and execution of necroptosis with a specific focus on mixed lineage kinase domain-like protein (MLKL). According to structure-function analysis, the first four alpha helices at the N-terminus of MLKL are critically required for its cytotoxic activity. This N-terminal domain of MLKL was also necessary for the assembly of higher order structures as well as for the recruitment of MLKL to the plasma membrane.

Jannie Borst (Amsterdam, The Netherlands) highlighted the importance of ubiquitin-dependent degradation for the function of Bcl-2 proteins. She was then followed by Patrick Mehlen (Lyon, France) who introduced the concept that dependence receptors are tumor suppressors that limit tumor progression by inducing apoptosis of tumor cells under conditions when their ligands are not available or not accessible. Many aggressive cancers escape this form of programmed cell death by loss of dependence receptors or, alternatively, by autocrine expression of ligands such as netrin-1. The first phase I clinical trial in humans using an agent interfering between netrin-1 and its receptors is planned to start in mid 2015.

Marja Jäättelä (Copenhagen, Denmark) discussed the control of cancer cell survival and autophagy by sphingomyelin metabolism. She showed that acid sphingomyelinase (ASM) activity is required for maintaining lysosomal stability, for autophagosome formation and the development of multidrug resistance of cancer cells. Simone Fulda (Frankfurt, Germany) then reported on recent discoveries showing that Obatoclax, a small-molecule inhibitor of antiapoptotic Bcl-2 proteins, triggers cell death via autophagy by stimulating the assembly of the necrosome on autophagosomal membranes, thereby connecting Obatoclax-stimulated autophagy to necroptosis. Ruggero de Maria (Rome, Italy) introduced the use of a locked nucleic acid (LNA)-based anti-miR library to functionally...
screen cancer cells for putative oncogenic micro RNAs (miR) that may be suited as selective therapeutic targets. He reported that his group identified miR-197 as pro-survival signalling molecule in non-small cell lung cancer (NSCLC) and showed that downregulation of miR-197 triggered p53-dependent apoptosis and prevented tumor growth in immunodeficient mice.

Verena Jendrossek (Essen, Germany) reported about the consequences of radiation-induced cell death for the adverse side effects of ionising radiation in the lung. Using a murine model, she showed that radiation-induced local lung damage is associated with vascular dysfunction and increased seeding and growth of lung metastases from circulating tumor cells. Jochen Prehn (Dublin, Ireland) then presented data on new patient stratification tools for apoptosis sensitisers based on systems level analysis of apoptosis deficiency in cancer. The group developed a computational tool named DR_MOMP that incorporates the network knowledge on processes controlling mitochondrial outer membrane permeabilisation (MOMP), leading to caspase-dependent and caspase-independent cell death.

Scott Lowe (New York, USA) highlighted the importance of combining cancer genomics, murine cancer models and RNA interference screening to identify and validate candidate cancer driver and maintenance genes in their specific genetic context. He showed that targeted disruption of the histone methyltransferase MLL3 only promotes tumor formation in the context of specific genetic changes, such as a p53-deficient background or loss of the transcription factor NF1. Jan Paul Medema (Amsterdam, Netherlands) later discussed the crucial role of the morphogenetic pathways Notch and Wnt in stem cells of normal colon tissue and colon cancer. By using matrigel-based intestinal organoid cultures from normal and cancerous tissue, he demonstrated that Notch signalling regulates self-renewal and lineage determination in both, normal and transformed tissues and that the Wnt-pathway – despite activating mutations – displays heterogeneous activity patterns in all disease stages.

To gain insight into the contribution of lymphangiogenesis to metastatic spread and drug response the group of Marisol Soengas (Madrid, Spain) developed a lymphoreporter knock-in mouse expressing enhanced green fluorescent protein (EGFP) luciferase in cells with activated VEGFR3, a classical marker of lymphangiogenesis. She showed that imaging of systemic VEGFR3-activation in lymph nodes shortly after tumor cell injection allows the identification of genes involved in metastasis and evaluation of the therapeutic potential of drugs interfering with the metastatic process.

Sharon Tooze (London, UK) introduced the basic mechanisms of autophagy signalling and provided new insights into the molecular machinery driving autophagosome formation. Nathalie Mazure (Nice, France) then reported on novel mechanisms of hypoxia-mediated resistance of tumor cells to anticancer drugs involving the hypoxia-inducible factor (HIF)1-dependent generation of enlarged mitochondria and of a C-terminal truncated variant of the mitochondrial voltage-dependent anion channel-1 (VDAC1), VDAC1-ΔC. VDAC1-ΔC retained the ability to bind to antiapoptotic hexokinase, thereby allowing cancer cells to maintain adenosine triphosphate (ATP) levels and survival in hypoxia. Inhibition of mitochondrial fusion or silencing of VDAC1-ΔC restored sensitivity of hypoxic cancer cells to chemotherapy-induced apoptosis. Importantly, VDAC1-ΔC was detected in tumor tissues of lung cancer patients and was found to be associated with tumor progression, suggesting the use of VDAC1-ΔC as a potential biomarker.

Gerry Melino (Rome, Italy & Leicester, UK) reported on the involvement of p73, a p53-family member, in senescence and metabolism, and provided insight into several newly identified transcriptional p73 targets. Tak Mak (Toronto, Canada) then delivered the closing lecture introducing the concept of targeting the consequences of oncogenic signalling in cancer such as alterations in cell metabolism and cellular redox state to improve treatment outcome. He discussed the dual role of ROS in cancer development and in response to cancer therapy and highlighted several molecular mechanisms that allow cancer cells to detoxify high levels of ROS, to adapt to chronic oxidative stress or both.

We would like to thank EACR for substantial financial and administrative support, including five Meeting Bursaries of €500 each for young researchers without their own funding. Two EACR Poster Prizes were also awarded.

In particular, we are grateful to Kathryn Wass and Tabitha Chetwynd for the excellent organisation of all administrative aspects of the meeting in Amsterdam. Furthermore, we are indebted to Pascal Meier, Nathalie Mazure, Patrick Mehlen, Marisol Soengas and Jannie Borst for their help with the review of the abstracts and in the award committee. Finally, we thank all speakers, poster presenters and delegates for their excellent contributions and discussions that built the success of the meeting.

Verena Jendrossek and Simone Fulda, Scientific Organising Committee