EUROPEAN JOURNAL OF CANCER 42 (2006) 3084–3094

available at www.sciencedirect.com

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journal homepage: www.ejconline.com

Position Paper

EACR-19: The best of European cancer research

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ARTICLE INFO

Article history:
Received 23 August 2006
Accepted 25 August 2006
Available online 11 October 2006

Keyword:
EACR

ABSTRACT

The 19th biennial meeting of the European Association of Cancer Research, EACR-19, was held in Budapest, the splendid capital of Hungary, in June 2006. It proved an exciting forum for researchers engaged in basic, translational and clinical cancer research to discuss key areas of major current interest. This review presents a meeting report and attempts to provide an impression of the scientific excellence of EACR-19.

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1. Introduction

From Saturday 30th June to Tuesday 4th July EACR-19 welcomed 761 researchers, including 191 students, to the friendly and inspiring atmosphere of the Hungarian capital, Budapest. W. Gullick, Conference and Scientific Chairman, together with the Co-Chairman R. J. White, the Scientific Programme Committee and the Young Cancer Researchers' Committee designed a strong scientific programme with keynote lectures, plenary lectures, scientific symposia and educational lectures given by leading scientists in the field, covering key areas of current interest and the latest discoveries.

A successful novel initiative at EACR-19 was the organisation by the Young Researchers' Scientific Committee of two workshops dedicated specifically to cancer researchers at the beginning of their scientific careers. These workshops discussed effective strategies for fellowship applications as well as scientific research in pharmaceutical drug development. Another event attracting a large audience was the second joint forum of EACR together with the American Association for Cancer Research (AACR) and Women in Cancer Research (WICR) on 'Networking, communication and negotiation: an open forum on effective strategies in career and leadership development'.

The programme was completed by three prestigious award lectures, three poster sessions covering a total of 421 posters and two satellite symposia. From submitted abstracts, the Scientific Committee selected twelve especially interesting contributions for oral presentation at two symposia entitled 'Presidential Sessions' reflecting the high quality of the free communications to EACR-19.

The friendliness and hospitality of our hosts in Budapest, the Hungarian lifestyle and the Art Nouveau cityscape gave a special atmosphere to the social events. In this regard, the conference dinner, held in the stunning Hungarian Agricultural Museum, provided a memorable highlight of the meeting. The success of this meeting would not have been possible without the tremendous work of the local organising committee with its Chairman E. Olah together with the organising team of FECS and the EACR Secretariat in Nottingham, to whom we express our sincere thanks and appreciation.

2. Mühlbock lecture

The opening lecture, named after one of the founding members of EACR, Professor Otto Mühlbock, was delivered by R. Laskey (Cambridge, UK) focusing on 'The control of DNA replication and its exploitation for cancer diagnosis or treat-

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doi:10.1016/j.ejca.2006.08.018

ment'. An important question in the study of DNA replication is why there can be multiple origins of replication but little danger of copying DNA twice. In the first part of his lecture, Professor Laskey discussed the concept of a 'DNA replication licence' achieved by the sequential binding of the components of a pre-replication complex. One protein involved is Geminin, which has been found to be down regulated by proteolysis in trophoblast cells undergoing the unusual process of multiple DNA replication cycles without division.

A hypothesis arising from this work is that loss of Geminin might allow genomic instability and multiple DNA replication cycles. In a knock-out mouse model, embryos arrest at the eight cell stage but all the cells showed over-replication of their DNA, thus behaving like trophoblast cells. Surprisingly, in some cases of primary breast cancer, immunohistochemical staining showed overexpression of Geminin and this was associated with poor prognosis. Similarly, antibodies to another component of this complex, the MCM proteins, can be used to identify malignant cells in cervical smears as these, but not the normal exfoliated superficial epithelial cells, remain in the cell cycle and thus express the protein.

DNA replication proteins may also be useful targets for new forms of anti-cancer drugs. One example Professor Laskey discussed was his work on the enzyme MCM3 acetylase. This is a product of a gene which also encodes the Germinal Centre Associated Nuclear Protein due to the use of a cryptic promoter. In normal cells induction of MCM acetylase caused a minor stimulation of cell growth but it caused cell death in a number of malignant cell lines suggesting that this system could indeed represent a good target for drug development and emphasising the potential of this and other novel pathways in anti-cancer drug research.

3. Symposium: Cancer cell growth

The first scientific symposium of the meeting focused on cancer cell growth, defined as an increase in the size or mass of cells. It is essential for sustained proliferation, because otherwise each cell division would produce progressively smaller progeny. Indeed, cell cycle checkpoints operate to ensure that division cannot proceed until adequate growth has been achieved. Doubling time is usually limited, not by the time required to duplicate and divide the genome, but rather by the time required to double cell mass. Despite these facts, which have been known for over 30 years, cell growth has received relatively little attention from cancer biologists, who have traditionally focused on the cell cycle. That situation is beginning to change, as an increasing number of prescient researchers are focusing on the crucial issue of growth.

Since 80–90% of a cell's dry mass is protein, the rate of protein accumulation is the primary determinant of how fast a cell can grow. S. Volarevic (Zagreb, Croatia) described evidence from mouse models for a p53-dependent checkpoint that responds to changes in the level of ribosomal protein S6. Growing cells expend ~80% of their energy on manufacturing components of the protein synthetic apparatus. A sizeable proportion of this energy is spent in the synthesis of rRNA and tRNA, which together account for ~95% of total cellular RNA. RNA polymerase I (pol I) is responsible for producing three of the four rRNA molecules found in each ribosome. RNA polymerase III (pol III) makes the fourth and smallest rRNA, as well as tRNA and a variety of other short untranslated RNAs.

Talks by R. White (Glasgow, UK) and R. Hannan (Melbourne, Australia) described how the output of pols I and III is directly regulated by the retinoblastoma tumour suppressor RB, which thereby can restrain production of rRNA and tRNA. This provides a mechanism for growth control by RB, which will complement its well-characterised ability to elicit cell cycle arrest by targeting the transcription factor E2F. Transcription by pols I and III can also be inhibited by p53, providing the potential for growth restraint in response to a variety of stresses. Conversely, a number of oncogenic factors stimulate production of rRNA and tRNA, providing increased capacity for cell growth. An example of this is provided by c-Myc, which directly binds and activates the transcription apparatus that is used by pols I and III. In addition, c-Myc induces synthesis of this transcription apparatus itself. Ribosomal proteins and translation factors are also induced by c-Myc. As such, c-Myc can increase production of much of the protein synthetic machinery, which may explain its potent ability to drive cell growth.

R. Hannan also described how rRNA synthesis can be stimulated by the target of rapamycin (TOR) kinase pathway, which plays a key role in coordinating cell growth with the availability of nutrients and growth factors. This pathway is abnormally active in hamartoma syndromes and a large proportion of malignancies, due to mutations in components such as the tuberous sclerosis and PTEN tumour suppressors or the oncogenic phosphoinositide-3-kinase PIK3CA. Indeed, the TOR inhibitor rapamycin and its derivatives are currently being evaluated in clinical trials as cancer treatments.

M. Hall (Basel, Switzerland) described how TOR is found in two distinct complexes, which regulate different aspects of cell growth and may respond to different signals. It was a surprise to discover that one of these complexes does not respond to rapamycin. This insensitive complex controls cytoskeletal organisation and spatial aspects of cell growth; it might present a valuable target for therapeutic intervention.

4. Symposium: Genetics and the environment

The symposium 'Genetics and the Environment' at EACR-19 consisted of four presentations. A.L. Børresen-Dale (Oslo, Norway) provided a summary of important results produced in her laboratory on the use of microarrays to classify breast cancers according to gene expression profiles. This new approach has important potential applications in the clinical management of the patients, and contributes to the understanding of breast carcinogenesis. It also has a potential in aetiological research.

D. Goldgar (Utah, USA) discussed the contribution of linkage analysis in the discovery of high-risk cancer genes. Although very successful in the past (e.g. identification of BRCA1 and BRCA2), this approach has not resulted in major discoveries in the recent years, possibly because most high-risk cancer genes have already been identified. The remaining genetic predisposition to cancer is probably linked to a constellation of intermediate- and low-risk genes, which are less amenable to classic genetic methods.

P. Brennan (Lyon, France) followed Dr. Goldgar's reasoning by discussing the complementary approach of genetic

association studies in the search for low-penetrance variants in cancer susceptibility genes. He described recent results from case-control studies of cancers of the lung, head and neck and kidney, which stressed the need for replication of promising results and of large sample sizes in these investigations.

Finally, P. Boffetta (Lyon, France) described the results of an estimate of the proportion of cancers due to non-genetic factors in France, based on a systematic review of cancer risk factors and data on prevalence of exposure. Overall, only about 40% of cancers in men and 25% in women can be attributed to known modifiable risk factors, i.e. can be realistically prevented. Overall, the session provided an overview of complementary aspects of the causes and mechanisms of human cancer, including in particular the limitations of our current understanding of both genetic and environmental factors in carcinogenesis.

5. Plenary lecture: Europe against cancer

In the first plenary lecture of EACR-19, P. Boyle (Lyon, France) gave a comprehensive overview of cancer mortality trends in the EU. Cancer remains a major public health problem and the burden is set to increase as the population ages. The current cancer mortality data and the forecast for the coming decade in Central and Eastern Europe give reason for concern. The achievements of the EC 'Europe Against Cancer' programme and the new European initiatives against cancer were described. These include the European Code Against Cancer (Boyle *et al.*) and the EUROCAN PLUS for coordination of cancer research at the European level.

6. Symposium: Molecular determinants of site-specific metastasis

Ever since Stephen Paget's prescient observations on the non-random nature of breast cancer metastasis over 100 years ago, oncologists and basic scientists have been fascinated by the nature of the 'seed and soil' that determines cancer spread. While anatomical features account for some organ distribution patterns, others are less easy to explain unless there is some kind of 'tropism' at work. Recently, research has received new impetus from the recognition of 'poor prognosis' gene signatures in primary cancers – which challenges the classical hypothesis that metastatic progression is a late and rare event in subsets of cells – and the suggestion that there can also be superimposed specific gene expression patterns that predict organ tropism. In the case of lymphatic metastasis, it is not entirely clear whether this is an active process, or merely due to the relative ease of access of tumour cells to lymphatic vessels and passive transport to draining nodes. This session was designed to address the issue of molecular mechanisms of metastasis to bone, soft tissue and lymph nodes, and also to explore new possibilities for therapy.

A. Minn (University of Chicago Hospital, USA) began by discussing his work in seeking to define and interpret gene expression patterns in breast carcinoma metastasis to lung; studies which commenced in Joan Massagué's lab at the Memorial Sloan-Kettering Cancer Centre in New York. The work was initially based on an experimental xenograft model, MDA MB 231, in which the types of gene expression studies used in clinical material can be coupled to functional studies to determine which 'markers' of metastasis have functional significance. Single cell populations (SCPs) were cloned from MDA MB 231 which showed a predilection for metastasis to bone or lung and the latter property was enhanced by further *in vivo* selection to produce the LM2 line. A lung metastasis signature (LMS) was defined, and the functional contribution of the genes within it confirmed by their single or multiple transfection into parental cells. The LMS was then shown to be able to predict patients who specifically relapsed with lung metastases. Interestingly, the LMS signature gave the MDA MB 231 cells a growth advantage at the primary site, and therefore it was suggested that the genes are selected for during this phase; this was also shown in patients where cancers with the LMS signature were larger than others. The larger tumours also allow a greater probability of intravasation, and once in the lung, there is evidence that further gene changes occur which favour growth in this environment – termed 'metastatic virulence'.

A. Teti (University of L'Aquila, Italy), co-ordinator of an EC consortium concerned with site-specific determinants of breast cancer metastasis ('METABRE') then discussed bone metastases. She began by explaining just how frequent bone metastases are, (especially in breast and prostate cancers) and the fact that there are no effective therapies except bisphosphonates, which merely ameliorate the symptoms. Breast cancer bone metastases are mainly osteolytic and prostate cancers mainly osteotropic, but in a sense, both show 'osteomimicry' and a vicious cycle of bone degradation and remodelling. Several bone metastasis gene signatures have been published, and osteopontin, bone sialoprotein, IL-11 and CXCR4 have been implicated. SPARC and COX2 are also increased (as in the lung metastasis signature) whereas S100A4 is downregulated in bone metastases and upregulated in visceral metastases. Tumour cells may survive in the bone environment in a dormant state (perhaps in a stem cell type niche), but emerge when activated by stimuli such as inflammatory cytokines. Turning to possible therapeutic targets, Professor Teti showed that c-src plays a key role in osteoclast and osteoblast activity, and also in metastatic tumour cells. In preclinical studies a c-src inhibitor showed significant activity against bone (and soft tissue) metastases in the MDA MB 231 xenograft model.

V. Castronovo (University of Liège, Belgium) continued the theme of new targets for therapy, this time in relation to angiogenesis, a prerequisite for metastasis. Histone deacetylases (HDACs) are key regulators of gene transcription, and non-selective inhibitors such as SAHA have anti-tumour and anti-angiogenic effects and are in early clinical trials. The aim of the work he described was to identify the HDAC(s) implicated in angiogenesis in order that more effective/selective inhibitors could be designed in the future. Each of seven HDACs was selectively knocked down by siRNA and effects on endothelial cell (EC) activities including proliferation, adhesion, migration and tubular morphogenesis were measured. Only HDAC7 was able to affect EC function, and this was manifest primarily in haptotaxis and tubularisation. Transcriptome analysis on cells lacking HDAC7 showed significant upregulation of PDGF-B, suggesting that this particular HDAC normally functions to repress PDGF-B gene expression in activated endothelial cells.

Unfortunately K. Alitalo had to cancel his attendance at short notice and no abstract was received for his presentation on lymphatic metastasis.

The session provided much food for thought and stimulated many excellent questions. It opened the possibility not only of better prediction of metastatic probability (and even the likely sites of relapse) but also of new targeted therapies which may directly address this most devastating aspect of cancer.

7. Symposium: Canceromics

'Omics' approaches in cancer research show great potential to thoroughly characterise cancer cells at the genomic, transcriptomic and proteomic level. In this symposium, three presentations highlighted efforts to identify cancer specific alterations and contributions towards improved prognostics and more personalised therapy for cancer patients. Knowledge and information gained through this research needs to be studied in a systematic manner which joins forces across different disciplines and takes into account the heterogeneity of cancers as well as the inherent variability of the patients.

In the first talk, A. Bardelli (Torino, Italy) described his group's comprehensive sequencing of the kinome and the phosphatome in colorectal tumours in an effort to dissect key signalling pathways. Next, he showed the potential for isogenic models of tumour progression in which known oncogenic mutations were knocked in, to serve as better models for the *in vivo* situation. Finally, he reasoned how alterations in kinases could be exploited in therapeutic strategies, using the improved response to anti-EGFR agents in patients with increased copy number of the EGFR gene as an example.

M. Stratton (Cambridge, UK) gave an overview of the results from systematic searches for somatic mutations in human cancer genomes. He distinguished between pathogenic 'driver' mutations subject to selection and 'passenger' mutations that are not cancer-causing and where no selection is involved. Overall, of 200 individual cancers subjected to exon resequencing of 518 kinases, only about half had mutations, which means that a large proportion of tumours have no such mutations. The frequencies and patterns of mutations vary between different tumour types and give information about mutator phenotypes and risk factor exposures. Kinases often contain driver mutations and contribute substantially to oncogenesis as a whole.

G. Whitely (NCI, USA) presented technologies and approaches for proteomic analysis of sera from cancer patients and reflected on the prospects of proteomics for early detection. Mass spectrometry (MS) methods were used to identify proteomic patterns that discriminated cancer from non-cancer cases with high sensitivity and specificity. A specific aim was to identify marker peptides trapped by albumin in serum, which normally would be secreted, using high-resolution MS. A prospective trial is ongoing in which 2000 women are enrolled to examine the feasibility for proteomic-based tests for diagnostics, screening and monitoring purposes.

8. Anthony Dipple Award lecture: Molecular mechanisms for cancer prevention

For major contributions in the field of carcinogenesis, Professor Raymond DuBois, Vanderbilt University, USA, was presented with the Anthony Dipple Carcinogenesis Award. This award is sponsored by the journal 'Carcinogenesis' and Oxford University Press. Professor DuBois reviewed recent preclinical and clinical studies of COX-2 inhibitors in the prevention of colon carcinogenesis. He also identified novel molecular targets that are downstream in the COX-2 pathway and are less likely to have the toxic effects of current COX-2 inhibitors.

9. Plenary lecture: Functions of the VHL tumour suppressor protein

In his lecture, W.G. Kaelin from the Dana Farber Cancer Center (Boston, USA) focused on the functions of the von Hippel-Lindau (VHL) tumour suppressor protein. Mutations in the VHL tumour suppressor gene cause tissue-specific tumours including sporadic haemangioblastomas and clear cell renal carcinomas. The *VHL* encoded protein (pVHL) has been implicated in various cellular activities including hypoxia responses, cell cycle arrest, apoptosis and extracellular matrix remodelling. The best understood function of pVHL relates to its role as the substrate recognition unit of an E3 ligase that targets the heterodimeric transcription factor factor HIF (hypoxia inducible factor) for destruction in the presence of oxygen. Down-regulation of HIF2 is both necessary and sufficient for renal tumour suppression by pVHL in xenograft tumour models. Known inhibitors of VEGF or VEGF receptors have shown to be effective against renal cell carcinoma, emphasising the biological significance of HIF-induced up-regulation of VEGF in oncogenesis and tumour development.

Some VHL mutations associated with familial pheochromocytoma do not interfere with HIF regulation. Evidence was presented that in these cases mutated pVHL inhibits apoptosis of primitive neuronal cells by up-regulating JunB which, in turn, antagonises pro-apoptotic c-Jun. Other genes linked to familial pheochromocytoma such as mutations of NF1 and c-RET appear to act by a similar mechanism, i.e. enhanced survival of neuronal cells after growth factor (NGF) withdrawal. Evidence was presented that the prolyl hydroxylase EglN3 acts downstream of c-Jun and is specifically required among the three EglN family members for apoptosis in this system. EglN3 is inhibited by succinate. The proapoptotic activity of EglN3, therefore, requires succinate dehydrogenase (SDH) activity. It is not surprising, therefore, that mutations or deletions of SDH isozymes B, C, or D are also linked to familial pheochromocytoma.

10. Presidential session I

Presidential session I consisted of six proffered papers. Five of these six contributions dealt with various novel aspects of tumour progression, invasion and metastasis. Angiogenesis is an important parameter in tumour progression. M. Andre (Birmingham, UK) presented evidence for a role of 'roundabout' receptors in tumour angiogenesis. Roundabout receptors are molecular guidance molecules that function by interaction with Slit proteins to regulate axon guidance, neuronal migration and leukocyte chemotaxis. The group succeeded in isolating a novel roundabout gene, Robo4, which is restricted in expression to the endothelium. Expression of Robo4 was found to be particularly high in embryonic vasculature and

tumour endothelium. Although the molecular function of Robo4 is not yet clear, the data presented by Sheldon and co-workers suggest an additional role of roundabouts in angiogenesis. Robo4 may indeed represent an interesting new target for anti-angiogenic strategies.

By employing comparative global gene expression analysis, S. Alberti (Chieti, Italy) identified TROP2 as a major determinant of metastatic spread in human cancer. Indeed, TROP2 was the only gene they found to be up-regulated in metastasising cells across species. A large scale analysis of TROP2 expression in stomach, breast, and ovarian tumours similarly demonstrated TROP2 over-expression in metastatic cells. Deletion of the activating proteolytic domain of TROP2 abolished its pro-metastatic activity, emphasising a causal link between TROP2 expression and the metastatic phenotype.

New insights into the role of the MET proto-oncogene were presented by S. Giordano, (Candiolo, Italy). MET encodes the receptor for the hepatocyte growth factor (HGF). HGF controls a complex genetic program regulating cell growth, invasion and survival. Giordano and co-workers demonstrated that silencing the expression of endogenous MET by siRNA compromised the invasive phenotype and even resulted in tumour regression. Evidence was presented that the continuous expression of MET is required to drive metastatic growth even in cells transformed by other, unrelated oncogenes.

TGF-signalling via Smads is known to promote metastasis in late state tumours and to be correlated with poor prognosis. Signalling through Smads involves a large number of transcription factors (TF). The group represented by S. Sladecek (Vienna, Austria) focused on the role of the TF LEF-1 which has been shown to associate and cooperate with Smad2 in the induction of epithelial to mesenchymal transition (EMT), a well known *in vitro* marker for metastatic potential in some cell types. The group presented evidence that phosphorylation of a defined tyrosine in Smad2 is mandatory for Smad2-LEF-1 interaction. Phosphorylation of this tyrosine residue was found to be enhanced during EMT and also in highly metastatic breast cancers *in vivo*. Overexpression of Smad2 led to an increase in LEF-1 dependent transcription. The data suggest that activation of LEF-1 mediated transcription by Smad2 is essential for breast cancer metastasis.

W. Berger (Vienna, Austria) presented evidence that over-expression of the major vault protein (MVP) contributes to the malignant phenotype of human glioblastoma multiforme. MVP is the main component of vaults, large ribonucleoproteins implicated in the regulation of cellular signalling cascades, transport mechanisms and drug resistance, although the molecular function of vaults still remains to be defined. The group represented by Dr. Berger presented evidence that MVP is strikingly up-regulated in astrocytomas including glioblastoma multiforme. Ectopic expression of MVP in MVP-negative H7 glioma cells significantly increased cell proliferation and locomotion. Over-expression of MVP also protected cells against apoptosis following growth factor withdrawal. The effects induced by ectopic MVP expression could be reversed by down-modulation of MVP expression with shRNA. Thus, MVP appears to play an essential role in the development of glioblastoma and may be of interest as a target for therapeutic intervention.

Novel findings regarding cross-talk between the NF-κB and oestrogen receptor (ER)-signalling pathways were presented by S. van Laere (Antwerp, Belgium). Data were presented indicating that expression of all selected NF-κB target genes was significantly elevated in specimens derived from inflammatory breast cancers (IBC), compared to non-inflammatory breast cancer (nIBC). Furthermore, transcriptionally active NF-κB dimers were more frequently found in oestrogen receptor negative (ER-) breast tumours. To further investigate the negative interaction between NF-κB and ER signalling, the group studied the expression of ERα and ten ER target genes in IBC and nIBC employing RT-PCR. The data revealed that ERα gene expression anti-correlated significantly with gene expression for seven out of eight NF-κB target genes. This suggests that ER down-modulates NF-κB expression and that IBC results from a release of the ER-mediated NF-κB repression with a concomitant increase in expression of NF-κB target genes.

11. Plenary lecture: p53 and cancer

In a magnificent talk K. Vousden (Glasgow, UK) gave an overview on the function of p53 as a tumour suppressor protein and introduced novel fascinating aspects of p53 signalling. P53-mediated protection against cellular stress and suppression of malignant progression involves a whole plethora of mechanisms including cell cycle arrest, induction of cell death and preservation of genomic stability. Since loss of p53 is observed in many cancer types and reactivation of p53 is suggested to selectively induce cell death in cancer cells, there is a hope for p53 as an effective target in cancer therapy. However, for a rational use of p53 as a therapeutic target understanding the mechanisms of p53-mediated regulation of cell death in cancer cells as well as in normal tissue cells is mandatory. Although there is accumulated evidence that differential activation of p53 target genes determines the cellular outcome of p53 activation, the choice of the cellular response to p53 activation is still not completely understood. Professor Vousden introduced ASPP1 as a newly identified protein acting as a cofactor for p53-induced pro-apoptotic gene expression. ASPP1 constitutes a transcriptional target of E2F1 and may thus contribute to improved activation of p53 proapoptotic target genes in cells with up-regulated activity of E2F1.

Professor Vousden then switched to the regulation of p53-mediated cell cycle arrest and cell death upon application of genotoxic stress. In this regard, balance between pro-death and pro-survival p53 target genes will define the cellular response to p53 activation. She described a novel p53 target protein identified by her group, named TIGAR (TP53-induced glycolysis and apoptosis regulator), that alters the pathways for glucose utilisation in cells conferring resistance to oxidative stress and promoting cell survival. TIGAR, which shares sequence homology with the bisphosphatase domain of fructose-2,6-bisphosphatase was shown to decrease levels of fructose-2,6-bisphosphate thereby switching glucose utilisation from glycolysis to the pentose phosphate shunt. By this means, TIGAR increases the levels of cellular NADPH and glutathione and enables detoxification of reactive oxygen species. Consequently, TIGAR can protect cells

from oxidative-stress mediated DNA-damage. On the one hand this may allow p53-mediated preservation of genomic stability but on the other hand may contribute to drug resistance allowing protection against DNA-damage induced apoptosis.

12. Symposium: Cancer stem cells

Having been neglected and even dismissed for decades, the concept of cancer stem cells has now returned with a vengeance, fuelled by the recent advances in stem cell research in general. In the first of four talks given in the symposium M.F. Clarke (Stanford, USA) gave a general introduction to the principle of stem cells and cancer stem cells. He emphasised that cancer stem cells share the property of unlimited growth potential and self-renewal with normal stem cells. Like their normal counterparts they form a very small proportion of the cell population and divide only slowly, and, remarkably, they can regenerate tumours of the same phenotypic heterogeneity as the primary tumour from which they were derived, analogous to the capacity of normal stem cells for tissue renewal. This has been illustrated by the seminal work of Professor Clarke on serially transplantable human breast cancers in mice. Using surface-marker based cell sorting, he has identified small populations of CD24- cells within human tumours that can be defined as cancer stem cells. They can be serially transplanted and reconstitute the entire histology of the original tumour. Breast cancers showing a gene expression signature that includes stem cell-specific genes have an increased risk of relapse even if other markers would predict a favourable diagnosis. If a wound repair signature is added to this pattern the prognosis becomes worse still, indicating the involvement of a stem cell niche.

Breast cancer stem cells were also the theme of the next presentation by M. Smalley (London, UK). Working with a mouse model, he and his colleagues have demonstrated that the mouse luminal epithelium contains two distinct cell populations, prominin-1 positive and prominin-1 negative, characterised by expression of genes for either hormone receptors or milk proteins, respectively. They showed that a $CD24^{lo}$, ER- stem cell gives rise to progeny that form normal structures containing ER+ and ER- compartments. This raises questions about the origin of human breast cancers, the most common form consisting of a majority of ER+ proliferating cells. It can be envisaged that initial mutations occur in the stem cell compartment with further mutations being acquired in ER+ progeny within this field of mutated cells. The cellular context of oncogenic mutations is thus important and the clinical implication is that unless the field is eliminated the potential target for renewed growth will remain. In a field of mutated cells, one final mutation which will turn an apparently phenotypically normal cell into a cancer cell has a high likelihood of occurring in either the mutant stem cell or in a more differentiated luminal cell. Alternatively, if differentiated cells have life spans comparable to stem cell populations, they could accumulate enough mutations to cause transformation independently. Distinguishing between these possibilities is fundamental in understanding the origins and behaviour of different breast cancer types.

The APC gene is mutated in the majority of colorectal carcinomas and many of the remaining tumours contain mutations in the gene for β-catenin, another component of the Wnt signalling pathway. In his contribution H. Clevers (Utrecht, The Netherlands) asked why this pathway is always targeted in carcinogenesis in the colon and described how mutations in the Wnt pathway component APC cause colorectal cancer (CRC). Physiological Wnt target gene expression is restricted to the crypt, but target genes can be sub-classified based on expression patterns within the crypt. Analysis of the genes regulated by the Wnt pathway-activated transcription factor TCF has now led to the conclusion that Wnt is the single dominant pathway controlling crypt cell biology and maintenance of an undifferentiated phenotype. The group of Professor Clevers identified three target genes which are expressed uniquely in the crypt stem cells. However, the Wnt cascade is not the only signalling pathway controlling cell fate along the crypt-villus axis. Conditional removal of the common Notch pathway transcription factor CSL/RBP-J 2, induces conversion of proliferative crypt cells into post-mitotic goblet cells. A similar phenotype was obtained by blocking the Notch cascade using a gamma-secretase inhibitor. The inhibitor also induced goblet cell differentiation in intestinal adenomas. Thus, gamma-secretase inhibitors, developed for Alzheimer's disease, may be of benefit in colorectal neoplastic disease. He concluded that maintenance of undifferentiated, proliferative cells in crypts and adenomas requires the concerted activation of both the Notch and Wnt cascades.

In the final talk of the session R. Fodde (Rotterdam, The Netherlands) presented ongoing work on APC-mutant mouse models for cancer. To study how different dosages of Wnt signalling activation may influence multi-organ tumourigenesis, he generated several hypomorphic alleles of the Apc tumour suppressor gene by gene targeting. His group has shown that one of these strains of mice, the Apc+/1572T mutants, do not develop intestinal tumours but rather multi-focal and rapidly growing mammary tumours of two different histological types. Both types contain luminal and myoepithelial phenotypes, indicating stem cell origin, and thus are different from tumours developing in ErbB2-mutated mice that are derived from progenitor cells. Notably, Apc1572T mammary tumours also form lung metastases. Both the primary tumours and their metastases were classified as lobular carcinomas with different degrees of metaplastic squamous differentiation. As previously observed for intestinal cancers, intracellular *β-catenin* accumulation, the earmark of canonical Wnt signalling activation, was found to be heterogeneous within the tumour mass. However, when lung micrometastases (20–100 cells in size) were analysed by IHC and compared with the macrometastases and with the primary mammary lesions, differentiation was found to be significantly reduced whereas almost every cell showed cytoplasmatic and/or nuclear *β-catenin* accumulation. These results indicate that the specific Wnt signalling dosage encoded by the Apc1572T mutation differentially affects homeostasis of the mammary stem cell compartment. Experiments in a mouse with a KRAS mutation added to the APC1638N mutation indicate that phosphorylation of β-catenin may be required in addition to the increased intracellular pool mediated by APC for nuclear translocation.

These mice show rapid development of aggressive and metastatic tumours.

In sum, the biology of stem cells in self-renewing tissues and of cancer stem cells are closely related. New cancer therapies will exploit these insights to focus on development of treatment modalities for the eradication of cancer stem cells.

13. EACR young cancer researcher award lecture: Ubiquitin signalling and cancer pathogenesis

The EACR Young Cancer Researcher Award is conferred in recognition of an outstanding contribution in the field of fundamental research in cancer. On the occasion of EACR-19, the award was presented to I. Dikic, Frankfurt, Germany, for his work on ubiquitin signalling in cancer pathogenesis. You will find a summary of his contribution in this issue of the European Journal of Cancer.

14. Symposium: Inflammation and cancer

Tumours develop in the context of tissue stroma that includes cells of the immune system. The means by which B lymphocytes and macrophages, amongst others, influence tumour progression was discussed during this symposium.

L.M. Coussens (San Francisco, USA) reported on B cell involvement in a mouse model of epithelial carcinogenesis (K14-HPV16 mice). By depleting several leukocyte subsets through genetic crosses she obtained evidence that IgG deposition in tumour areas as a function of a B cell response also sustains granulocyte and mast cell infiltration. In the same vein, other cells of the immune system fulfil the paradox of immune cells promoting cancer.

Nuclear factor-κB (NF-κB) is the transcription factor most likely linking inflammation and cancer. In a model of hepatocellular carcinoma, it was found to activate a survival program in hepatocytes while triggering TNFα production in nearby inflammatory cells. This helps to explain why individuals with chronic inflammation are more susceptible to cancer development. Presenting this and other models of hepatocellular carcinomas, E. Pikarsky (Jerusalem, Israel) underlined how NF-κB can also reduce tumour formation depending on type, dose and schedule of the pathogenic agent.

The Janus face of macrophage activities was illustrated by A. Sica (Milan, Italy) in terms of M1 and M2 genetic signatures and functions. Particularly important is the finding of oncogenes activating an inflammatory programme through HIF1α and CXCR4 as a common signal recruiting macrophages to tumours.

M.P. Colombo (Milan, Italy) provided insight into novel aspects of tumour-immune cell interactions which occur in a complex interplay that involves matrix proteins. Indeed, elimination of SPARC, a matrix protein produced during wound healing, changes stromal architecture and composition. Such changes have been shown to exert profound effects on the immune response and metastatic progression of certain tumours. In keeping with these findings, SPARC is commonly found to be differentially expressed in tumours versus normal tissues as well as in primary tumours versus metastases.

15. Symposium: Cancer epigenetics

The heritable expression patterns of genes can be controlled without changes to their DNA sequences through epigenetic mechanisms that involve covalent modifications to DNA or its associated histones. This field was elegantly summarised by P. Jones (Los Angeles, USA). The best characterised example of epigenetic control is provided by the methylation of cytosines present in CpG sequences, which has long been known to have an inhibitory effect on gene transcription. Aberrant methylation of CpG sequences is responsible for silencing tumour suppressor genes in many types of cancer. Drugs that reverse this effect have been found to be beneficial in some contexts. The effects of CpG methylation are reinforced by covalent modifications to the histone proteins which wrap DNA into nucleosomes that are the building blocks of chromatin. For example, acetylation of histones is frequently found at active promoters. Drugs that inhibit histone deacetylases can often reactivate genes that have been silenced epigenetically, providing another avenue for therapeutic intervention. Dr. Jones finished by describing his most recent work concerning microRNAs, which are also subject to epigenetic regulation. Some microRNAs can influence the expression of oncogenes and may therefore have impact on tumour development.

The other speakers in this symposium described various approaches to study chromatin-associated proteins and how these can influence gene transcription. R. Aasland (Bergen, Norway) described how bioinformatic analysis can be used to identify polypeptide motifs that are responsible for recognising histones that carry specific covalent modifications. Two talks demonstrated how model organisms are used as tractable systems for analysing chromatin-mediated gene regulation.

A detailed mechanistic analysis of an individual example of epigenetic control was provided by R. Waters (Cardiff, UK). He uses budding yeast as a model and focuses on the MFA2 gene, which encodes a component of the DNA repair apparatus. Clear evidence was found that induction of this gene involves the histone acetyltransferase Gcn5 and is associated with acetylation of histone H3. A series of nucleosomes are positioned over the promoter when the MFA2 gene is silent; these nucleosomes are likely to hinder access of the transcription machinery. Induction of the MFA2 gene appears to require displacement of the positioned nucleosomes as well as acetylation of their component histones. A number of chromatin remodelling factors have been described that can displace histones in this way. Many of these are present in high molecular weight complexes that contain multiple subunits.

A. Brehm (Munich, Germany) described the purification and characterisation of one such complex from fruit flies. He named this complex dREAM and demonstrated that it is conserved in nematodes. One of its most intriguing features is that it contains homologues of the mammalian retinoblastoma tumour suppressor protein RB.

16. Plenary lecture: Deciphering cancer-relevant signalling networks through RNA-interference-based genetic screens

R. Bernards, Head of the Division of Molecular Carcinogenesis at the Netherlands Cancer Institute (Amsterdam, The Netherlands) gave a very stimulating and comprehensive lecture on the identification of cancer-relevant genes by using powerful new tools to perform functional genetic screenings.

Professor Bernards began by addressing the identification of biomarkers that predict response to drugs; in particular he addressed the role of histone deacetylase (HDAC) inhibitors as anti-cancer therapeutics and described experiments aimed at the identification of genes that confer resistance to HDACs as well as the pathways affected. To this end his group used Ras-transformed mouse fibroblasts, infected them with a retroviral cDNA library, and selected clones resistant to the HDAC inhibitor PXD101. Two genes that conferred resistance to the inhibitor were identified: the nuclear retinoic acid receptor (RAR) alpha and the human tumour antigen PRAME (preferentially expressed antigen in melanoma). The presence of seven putative nuclear receptor (NR) boxes in PRAME suggested that this protein could act as a transcriptional modulator of nuclear receptor signalling, and indeed further experiments showed that PRAME acts as a dominant repressor of RAR signalling. In addition, it was shown that PRAME binds to RAR in the presence of retinoic acid (RA), thus preventing ligand-inducer receptor activation and target gene transcription through recruitment of polycomb proteins. What was learned from these studies is that HDACs target RA signalling and that RA and HDAC inhibitors (HDACi) synergise to activate RAR, thus providing a rational for combining RA and HDACi in clinical trials.

In the second part of the talk, Professor Bernards described functional genetic approaches to identify cancer relevant genes, in particular the use of RNA interference libraries (loss of function genetic screen). He addressed the role of de-ubiquitinating enzymes (DUBs) and cancer, and presented their strategy for the functional screening of DUBs that regulate NF-κB activity. These studies revealed that loss of CYLD, which encodes a deubiquitinating enzyme that is mutated in familial cylindromatosis, activates NF-κB leading to inhibition of apoptosis. Loss of CYLD causes activation of the IKK-β kinase and this effect can be counteracted by aspirin. Since the oral aspirin dose required was too high to treat patients, they opted for topical applications of salicylic acid instead. Indeed, topical application of this substance to patients with familial cylindromas led to a substantial decrease in the size of the lesions.

The lecture ended with a description of the human RNAi library (NKi library) which contains 55,000 vectors targeting 23,000 genes. He introduced the concept of siRNA bar code screening and exemplified the potential of the new technology by describing the identification of SMAD 4 as a molecule required for TGF-β signalling, thus validating the approach. He also emphasised the use of screening RNA interference libraries to identify 'smart' drug targets. Moreover, he addressed the use of siRNA to identify synthetic lethal interactions.

17. Carcinogenesis young investigator award lecture: Cancer epigenetics: From basic knowledge to translational applications

M. Esteller (Madrid, Spain) received the Carcinogenesis Young Investigator Award for his outstanding work on epigenetic changes in human cancer. In his lecture he stressed that aberrant patterns of epigenetic changes in transformed cells including global genomic hypomethylation, promoter hypermethylation, histone deacetylation or methylation of tumour suppressor genes will not only provide novel means for cancer diagnosis and prognosis but also constitute promising targets for therapeutic intervention.

18. Mike Price lecture: Targeting ras signalling pathways in cancer: Past, present and future

J. Baselga (Barcelona, Spain) gave the third memorial Mike Price lecture to acknowledge the contributions of Professor Price to EACR over his 21 years as its Secretary General. In his remarkable lecture, Professor Baselga reviewed the concepts and the major accomplishments of 'targeted therapy'. He pointed out how one of the most relevant developments in cancer research in recent years has been the clinical validation of molecularly targeted drugs that inhibit the action of pathogenic tyrosine kinases. In this context, using the BCR–ABL example in CML as a paradigm, he analysed the main features of tyrosine kinases as molecular targets, including c-KIT, PDGFR, HER2 and EGFR. He showed how treatment of appropriately selected patients with drugs directed against these targets can alter the natural history of their disease and improve survival. These drugs include the proto-type Imatinib (STI-571 or Gleevec) which was initially shown to be active in CML (as reported above) through the target represented by the fusion oncogene BCR–ABL. It was then found also to be therapeutically active in a subset of gastrointestinal tumors (GIST) expressing mutated versions of c-KIT or of PDGFR, thus acting as a 'promiscuous' tyrosine kinase inhibitor.

An addition to this example of drugs designed to antagonise ATP-binding to tyrosine kinases, Professor Baselga discussed the role of trastuzumab (or Herceptin) in HER2 over-expressing breast cancer patients. Trastuzumab is a humanised monoclonal antibody that binds to the extracellular region of HER2 and inhibits the growth of HER2 over-expressing cells. In five large studies involving more than 14,000 women, the results showed that the post-operative administration of trastuzumab given either in combination with chemotherapy or sequentially after chemotherapy, reduces local and distant recurrences by about 50% and, as expected, improves patient survival by over one-third in those trials with sufficient follow-up.

Another outstanding example discussed in this context was the one of anti-EGFR therapies. Human tumours of epithelial origin express high levels of EGFR, therefore this tyrosine kinase receptor was first proposed for targeted therapy more than 20 years ago. Initially, monoclonal antibodies directed against the extracellular domain of the receptors were created. In addition small molecule inhibitors have been subsequently developed and recently, both types of compounds

have received regulatory approval for the treatment of cancer. Both result in a very similar functional effect by blocking the major signal transduction pathways downstream of EGFR, including the MAP kinases, the PI3K/Akt and the JAK/STAT pathways.

Anti-EGFR antibodies have shown clinical activity in a variety of tumours, and one of them, cetuximab, has recently been approved for the treatment of colon and head and neck cancers. Similar to trastuzumab, cetuximab was more effective when used early, in combination with chemotherapy. EGFR tyrosine kinase inhibitors are largely inactive in colon cancer but two of these compounds, gefitinib and erlotinib, have been approved for the treatment of non small cell lung cancer. In this latter case it was found that a subset of these tumours harbour somatic mutations in the EGFR gene and the presence of these mutations correlates with a positive clinical response.

After these convincing examples of the success of targeted therapy, Professor Baselga's lecture examined the problems related to acquired drug resistance and the development of second generation tyrosine kinase inhibitors. Resistance can be caused by amplification of the oncogenic protein kinase or other mechanisms, but more often, it is due to a selection of cancer cells with a secondary mutation in the gene encoding the targeted kinase. Agents active against new mutations that arise during therapy with first-generation tyrosine kinase inhibitors have been promptly developed. They include dasatinib capable of blocking ABL kinase which is active in patients with imatinib-resistant CML, and sutent which, in GIST with acquired resistance to imatinib, shows an activity most likely due to its multitarget (VEGF/PDGFR/c-KIT) inhibitory properties.

Finally he reviewed further tumour types with a kinase dependence such as melanoma where MEK inhibitors provided encouraging results, and outlined the potential clinical relevance of mTOR- and PI3K inhibitors which are under current development. Professor Baselga concluded his talk by predicting that future research on molecularly target therapy will mainly be focused on identification of new drugs and new targets and improved selection of tumours sensitive to the drug by developing more sophisticated tools for molecular diagnosis. In addition, a rational design and optimisation of combination therapies will play a pivotal role in this context. Finally he stated that these new concepts and discoveries will move oncology from the current state of empiric approaches to a more rational mechanistic management that will successfully integrate several areas of cancer research such as molecular biology and pathology, imaging techniques and clinical medicine.

19. EACR young cancer researcher's workshops

EACR is keen to promote her student and young scientist members. Therefore, at EACR-19 R.J. White together with the Young Researcher's Scientific Committee organised for the first time two workshops dedicated specifically to cancer researchers at the beginning of their scientific careers. There was a great interest in both workshops with a considerable number of students and young cancer researchers in the audiences.

In the well-attended session 'How to be efficient in applying for fellowships' R. J. White (Glasgow, UK), J. Celis (Kopenhague, Denmark) and T. Efferth (Heidelberg, Germany) introduced funding opportunities at a national (Great Britain and Germany) as well as at an European level. Moreover, they outlined the formal procedures, provided tips for successful applications and helpful indications of pitfalls to avoid. At the end of the session, there was plenty of time for specific questions from the audience.

The second Young Cancer Researchers' Workshop dealt with an 'Introduction to pharmaceutical research and development'. In the first talk, S. Cosulich (AstraZeneca, Cheshire, UK) gave an overview of the route from a given target identified by basic research to the preclinical selection of a candidate drug, meeting all criteria for further clinical development. G.R.P. Blackledge (AstraZeneca, Cheshire, UK) then introduced the complex, expensive and time consuming clinical development part that is required to 'make a drug a medicine'. He stressed the continued need of the pharmaceutical companies for excellent scientists with very different scientific skills in this process. The active discussion at the end of the session reflected the enthusiasm of the audience for this kind of workshop.

20. EACR/WICR/AACR workshop: Networking, communication and negotiation: An open forum on effective strategies in career and leadership development

EACR together with the American Association for Cancer Research (AACR) and Women in Cancer Research (WICR) organised a specialised forum dedicated to 'Networking, communication and negotiation: an open forum on effective strategies in career and leadership development'. This was the second such event, which was launched at ECCO in 2005, largely due to the initiative of A. Albini (IST, Genova, Italy) and M. Foti (CEO, AACR, USA). It was chaired on this occasion by M. Foti and M. Pierotti, incoming President of the EACR, and attracted a large audience.

M. Foti (CEO, AACR, USA) introduced the session and indicated that WICR, a membership body within the AACR, is enthusiastic about collaboration with EACR. Careers in science are difficult and competitive irrespective of gender, but women have particular problems in spite of some recent improvements. She stressed that there is still low female representation in key positions: plenary speakers, chairs, senior faculty etc. Although 50% of science graduates are women, there is a high drop-out rate at later career stages, which she ascribed partly to a lack of training in leadership and networking.

A. Hamburger (WICR Council Chair, University of Maryland, USA) gave some interesting statistics: success rates for women equal those of men in competing for project grants, but the amounts awarded are 40% lower for women – in fact women ask for less. In medicine, 50% of applicants are women, but only 12% make full professor, compared with 30% of men. She considered the major barriers to advancement were the lack of clear policies, persistence of entrenched attitudes, inadequate career information and the 'culture' of science. The solutions are: leadership (espe-

cially from women who have made it to the top) dialogue at all levels, staying power, resources and advocacy. In terms of networking, she emphasised the need for setting goals and making sure you meet the right people. It is also important to have both a career mentor and a scientific mentor, and to manage multiple (and sometimes conflicting) demands. Finally, she outlined some WICR programmes within AACR from which EACR could learn and perhaps begin to emulate.

S. Giordano's (IRCC, Italy) presentation drew attention to the Third European Report on Science and Technology Indicators released in 2003 which showed major inequalities in female career progression, and interestingly, wide disparities between countries. For example, Portugal and Ireland have the highest proportion of women higher education researchers in science (44–46%) and Belgium, The Netherlands and Germany the lowest (15–19%). The famous 'scissors' diagrams (which plot the proportion of males and females at different career stages) show that for all countries examined, the number of female science students is equal to or exceeds male numbers, but, for each succeeding career step, the proportion of women decreases and of men increases, although how 'wide' the scissors are varies. Dr. Giordano also gave some Italian statistics and indicated that there is now legislation encouraging equal opportunities, although this has yet to translate into real changes in career structures. Overall, the percentage of women in the highest positions was similar to (or slightly worse than) that reported for the US. Interestingly, there is some evidence that countries that have more recently become active in scientific research have less conservative attitudes to male and female roles. The equal opportunity initiatives that have been largely introduced seem to be largely for economic reasons (since a large proportion of women are not reaching their full potential) rather than to rebalance women's chances of success.

D. Gróó, (Director, Hungarian Science and Technology Foundation) a member of an Expert Committee set up by the EC for a survey on gender issues in scientific research in new member countries, gave a talk on 'The Career of Women Researchers in the European Union'. The statistics she quoted for the proportion of women professors and leaders was very similar to those in the US and Italy given by the previous speakers. She showed clear evidence that the new EU member states had the highest proportion of women research scientists, whereas the countries with the largest R&D expenditure had the lowest proportion, perhaps reflecting entrenched conservative gender role attitudes. The overall gender pay gap is also 27% in life science and health professions, which is higher than the overall average of 15%, again indicating a greater disparity in science. Dr. Gróó concluded that we have to acknowledge that there is a problem, which has to be analysed, discussed and addressed.

The EACR, under the Presidency of M. Pierotti, followed by A.-L. Børresen-Dale, will take on this challenge. Together with the help of our highly respected American colleagues, excellent progress towards ensuring better and more fulfilling careers for all of our young researchers, (women and men) will be made in the near future.

21. Educational lectures

The outstanding quality of scientific programme was completed by six excellent educational lectures scheduled for 8:00 a.m. each day. In the first educational lecture, Y. Yarden (Rehovot, Israel) gave a comprehensive overview on the complexity of the EGF-R signal transduction network and its involvement in human cancer. Based on several properties shared with robust engineered systems such as modularity, redundancy and control circuits he introduced novel ideas for multi-targeting EGF-R pathway in cancer from a systems biology approach.

T. Sorlie (Oslo, Norway) emphasised the implications of gene expression profiling in cancer research, and focused on two important discoveries: i) the possibility of gene-expression profile-based classification of tumours in distinct subgroups and ii) the prognostic relevance of this classification for prediction of overall- and disease-free survival in breast cancer and other malignancies. In addition she discussed challenges in how to use these technologies for the selection of treatment strategies.

C. Belka (Tübingen, Germany) gave an overview on hot topics in molecular radiation oncology research. He first highlighted the importance of radiation therapy in cancer treatment and then focused on combinations of radiation therapy with molecularly defined radiation response modifiers to increase the therapeutic gain and to overcome radiation resistance. In particular, approaches targeting cell death and survival pathways, hypoxia and angiogenesis as well as molecular approaches to increase normal tissue tolerance were discussed in detail.

G. Whiteley (Gaithersburg, USA) provided insight into recent developments in mass spectrometry for proteome research including innovative instruments, sample preparation techniques and bioinformatics. Moreover, he discussed further requirements for the use in clinical diagnosis and treatment selection.

A. Brazma (Cambridge, UK) reported on the application of bioinformatics as a major tool for the management and interpretation of data generated by genomics and other high throughput methods. Moreover he discussed the problems of modern high throughput bioinformatics.

In a visually stunning final educational lecture on 'Dynamic imaging of cancer cell invasion *in vitro* and *in vivo*' P. Friedl (Würzburg, Germany) pointed out that cancer cell interactions with the extracellular matrix and migration involve adhesion receptors of the integrin family, a dynamic cytoskeleton, as well as proteolytic mechanisms to overcome tissue barriers. He used mesenchymal HT-1080 fibrosarcoma cells as a model cell line which migrates in an integrin-dependent manner and proteolytically cleaves extracellular matrix structures, 3D collagen lattices. After interference with integrin and protease function, cancer cells can switch to amoeboid migration programs and thereby rescue migration by alternative mechanisms. In addition to single cell migration, tumour cells are able to perform collective cell invasion. These types of movements were demonstrated by applying intravital multiphoton microscopy of human tumour xenografts. The speaker outlined the principles and advantages of two-photon microscopy

and nicely demonstrated how spreading properties of melanoma tumour cells may explain migrational characteristics and dissemination into tissues to generate metastasis.

22. Poster presentations

Finally, 421 posters were presented at EACR-19 in three poster sessions. Each day the Pezcoller Foundation generously supported an award for the best poster presentation which were presented to A. Csiszar from Vienna, Austria, K. Müller-Decker from Heidelberg, Germany, and A. Gamez from Madrid, Spain. R. Zappacosta won the MSD-EACR Research Award at EACR-19 for the best proffered abstract in basic cancer research.

I hope that this meeting report provides a glimpse of the scientific excellence of EACR-19.

All are cordially invited to attend the 20th biennial meeting of EACR which will be held in Lyon, France 5st–8th July 2008 to celebrate the 40th anniversary of EACR. Please visit www.eacr.org **for further detail.**

Conflict of interest statement

None declared.

Acknowledgement

Because of the size and scope of EACR-19, it has not been possible to cover every aspect of the excellent sessions in this review, and I apologise for any omissions. I am extremely grateful to the chairpersons (W. Gullick, R.J. White, J. Celis, E. Olah, S. Eccles, T. Sorlie, H. Clevers, H. Ögmundsdottir, H. Grunicke, P. Boffetta, M.P. Colombo, A. Harris, K. Schläfer, M. Pierotti and J. Szollosi) who kindly contributed summaries of their sessions and to S. Eccles for her much appreciated help in the compilation of this report.