European Journal of Cancer

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Donations to Support Cancer Research

The EACR is a charitable organization, active in promoting research into the best treatment and care of cancer patients. Donations in support of its work may be made directly to the EACR treasurer, Dr Klaus Schlaefer at k.schlaefer@dkfz-heidelberg.de


In the last EACR Newsletter I wrote that ‘EACR is growing rapidly, both in numbers of members and in its range of activities’. I am delighted to report that this rate of growth has increased still further over the last year with one new member joining every two days. The EACR staff have worked hard to meet high targets, particularly at ECCO13 where we signed up 100 new members in 5 days – a considerable achievement. I see the building up of our membership as a means of building our influence and strength. Although I am very pleased by this tremendous growth in membership, I want to see it continue and expand still further, so I encourage you to ask your colleagues who are not members to visit www.eacr.org and join EACR today.

Our drive to make EACR more attractive to young researchers has also been extremely successful. Student numbers have doubled over the last two years and young investigators now play a very active part in the EACR. We have two young members on the Executive Committee and the EACR-19 Scientific Programme Committee has a strong Young Researchers’ Section chaired by Bob White who have made a considerable contribution to what is an excellent scientific programme. We also organized a Special Young Speakers’ Session at ECCO13 in Paris consisting of six young members (who were selected and invited by EACR) and Dr Heike Allgayer, the winner of our prestigious annual EACR Young Cancer Researcher Award. You can read more detail of Heike Allgayer’s exceptional award winning lecture on page 4 and we hope some of you will apply for this award in 2007.

We enjoyed a new format at our Council Meeting at ECCO13 in Paris. Bill Gullick, mindful of the increased responsibilities of the Council as our advisory body, initiated a more interactive meeting, with presentations from four eminent council members on cancer research in their countries. Their presentations stimulated excellent discussion and will provide a forum for future discussions and increased involvement and influence of our Council Members.

This year EACR has sponsored a record number of meetings and reports of six of these appear in the following pages. This increase is seen as a very healthy development. A key aim of ours is to enhance scientific communication and by facilitating this we not only fulfill our aspirations, but it gives us the opportunity to recruit new members and enhance our visibility. I would like to encourage all members to apply for these grants to assist them with meetings they may be organizing.

The EACR Fellowship Programme continues to thrive and again you will read several interesting and informative reports from young members who won these awards. We are indebted to the Association for International Cancer Research (AICR) who co-fund these awards. The awards are designed to allow members to attend technical workshops and courses, rather than to finance their attendance at meetings. They are also intended to support collaborative research by allowing people to visit other laboratories to learn new techniques or approaches. We welcome new applications and again please visit our website for application information and forms.

The new website is very successful with members using it to access information and apply for fellowships, awards and bursaries. We will add a ‘Members’ Page’ shortly and plan to have a continuously rolling programme of information and interaction. We invite you to visit the site and welcome your suggestions and ideas.

Now we are looking forward to EACR-19, to an excellent scientific meeting and to welcoming as many members as possible to Budapest making this a really memorable event. I look forward to meeting many of you there.

Richard Marais
Welcome to this, the second edition of the EACR Newsletter produced during my Presidency. When I read the first new style Newsletter, before I took office, I was most impressed by the vibrancy not only of the pages themselves, but also of the activities of our Association which they portrayed. As you will see this has been another eventful year and one of real growth and achievement and I feel privileged to have been part of it. The Communications Committee piloted, I understand, by the staff in the EACR office, are to be congratulated once again - and not only on this publication. They have been a very busy team as our splendid new website has been launched this year, and here I must offer particular thanks to Charlie Laughton who has managed this project enthusiastically and successfully. Please visit www.eacr.org

We have also seen the launch of a very successful membership drive spearheaded by our Secretary General Richard Marais, which you will have read about on the previous page. Many new members joined us at ECCO13 where the EACR desk was a hive of activity, as our staff welcomed well known colleagues and new members from around the world and provided a focal and friendly point throughout a very busy meeting for us all to gather, regroup and set the scientific world to rights!

Two awards have given me particular pleasure this year, the EACR Young Researcher Award presented to Dr Heike Allgayer who gave her lecture at the ECCO13 meeting in Paris and the Mike Price Fellowship which has gone this year to Dr Annette Affolter for her work on signal transduction in cancer cells. This latter award is also funded by the British Association for Cancer Research and the Federation of European Cancer Societies.

The EACR has been widening its horizons somewhat with a joint session to be held in Istanbul with the European Society for Medical Oncology and with a booth for the first time at the AACR meeting. We have agreed that they will also have a stand at our future meetings in a reciprocal arrangement so please don’t think they are invading Europe it is actually us invading the USA!

With all the above as well as our normal activities the EACR office has been exceptionally busy but they assure me that they look forward to welcoming myself, Marco Pierotti and Suzanne Eccles to Nottingham for the now well established one day EACR/BACR annual symposium on July 21st.

There has been a good deal of to-ing and fro-ing at the Federation of European Cancer Societies with uncountable and occasionally unbearable meetings. I am grateful to the various members of the EACR Executive Committee for their help and support in these negotiations. At the end of the day I believe the outcome is quite favourable for the EACR in that it retains its independence but stays a member of a growing umbrella organisation now to welcome “organ orientated” societies for the first time as full members. Hopefully this will allow more interdisciplinary interactions between the EACR and these important groupings.

I must on behalf of the Executive Committee and the EACR Office express our thanks to our out-going (and I mean that in more than one sense of the word!) Treasurer, Klaus Schlaefer, who has guided our finances through thick and (very) thin for the last twelve years. I am pleased to say he leaves this role with the EACR in the best financial shape we have ever been in. In his personal life he is the President of the German Horological Society so I have always known who to turn to if I wanted to know the time. Best wishes Klaus.

This is my last address as EACR President. It has been an interesting and challenging experience (interpret that as you will!) but overall I have enjoyed my time. I now hand over to Dr Marco Pierotti in whose safe and effective hands I am certain the EACR will grow and prosper.

Bill Gullick
**EACR Young Cancer Researcher Award**

The European Association for Cancer Research confers the EACR Young Cancer Researcher Award in recognition of an outstanding contribution in the field of fundamental research in cancer. This award is presented on an annual basis to a young member of the Association. On the occasion of ECCO'13 the award was presented to Heike Allgayer, Department of Experimental Surgery, and Joint Unit Molecular Oncology of Solid Tumors--DKFZ (German Cancer Research Center) Heidelberg.Klinikum Mannheim, Ruprecht Karls University Heidelberg, 68135 Mannheim/Germany.

Heike Allgayer summarized her lecture Molecular Regulation of an Invasion-Related Molecule – Options for Tumor Staging and Clinical Strategies

U-PAR overexpression in malignant cells is largely regulated at the transcriptional level. During the recent years we and others identified some of the most relevant u-PAR-promoter elements and transcription factors driving u-PAR gene expression and u-PAR-mediated invasion. In colon cancer, constitutive and PMA-inducible expression of the gene required u-PAR promoter region -190/-171 containing an AP-1 consensus motif bound with Jun-D, c-Jun, c-Fos and Fra-1, this motif mediating u-PAR gene induction via the MAPK- and the JNK-pathway. Furthermore, this AP-1 motif was also required for the induction of u-PAR gene expression brought about by mutated K-ras. Another region (-152/-135) bound with an AP-2-like protein, Sp1 and Sp3, is a multifunctional transcriptional regulator of u-PAR, the AP-2-like factor mediating a high constitutive and PMA-inducible gene expression, and Sp1 mediating inducible u-PAR gene expression and invasion brought about by c-Src. Both motifs had been shown by us to act synergistically, especially via JunD and the AP-2-like protein. An inhibition at the transcriptional level using dominant-negative AP-2, and also u-PAR- and Src-inhibition led to a significant reduction of invasion of cultured colon cancer cells, and suggested a potential therapeutic relevance of these u-PAR-regulatory mechanisms. However, these were in vitro studies which can only give limited information about the situation in patient tumors.

To investigate the in vivo-relevance of such transcriptional regulators, and first to differentiate patient subpopulations in whom such transcriptional mechanisms might be used as targeting mediators, we investigated a large series of patients for differential transcription factor binding in tumor and normal tissues. In a first translational study on 145 patients with resected colorectal or gastric cancers, we found an almost tumor-specific binding of the AP-2-like transcription factor and Sp1 to u-PAR promoter motif -152/-135 in almost 60% of cases, which correlated with high endogenous u-PAR protein amounts in tumor tissue, but not in normal tissues, suggesting that, in a subpopulation of as high as 60% of patients, a rather tumor-specific transactivation of u-PAR gene expression by this combined AP-2/Sp1/Sp3 promoter motif could be speculated. Tumor-specific AP-1 binding to region -190/-171 of the u-PAR promoter was found in 40% of patients, which is less than for the AP-2/Sp1/Sp3 motif. AP-1-binding correlated significantly...
The cellular proto-oncogene her-2/neu is amplified in ~20% of breast cancers and this is a marker of poor prognosis in some, but not all patients. One group of patients with the amplification dies in 2-3 years, whereas another group survives for over 10 years without developing metastatic disease (A. Zetterberg, unpublished data). Thus, it appears that her-2/neu amplification alone is not the only risk factor in breast cancer and that additional aberrations combine with the amplification to produce the high risk of metastases.

The aim of this study, which I performed in Anders Zetterberg’s laboratory, was to define a genetic pattern to distinguish the patients with good prognosis from those with poor prognosis. Importantly, the host institution possesses a unique collection of fresh frozen tumour samples and associated clinical follow-up data. I used the funding provided by the Mike Price Fellowship to study 42 tumours in which her-2/neu is amplified, applying a powerful combination of two newly developed techniques that allow high-resolution analysis of the human genome. These are ROMA (representational oligonucleotide microarray analysis) and QM-FISH (quantitative multigene fluorescence in situ hybridization). I collected ROMA and QM-FISH data from these tumours and this is currently being analyzed for abnormalities to determine if we can separate the long-term and short-term survivors from each other. If successful, we will validate the study with a larger data set.

Furthermore, I adapted QM-FISH for use with paraffin embedded material, thereby opening the enormous potential for retrospective studies within the host institution. This also has the additional advantage that it is now possible to isolate and analyze single nuclei from defined regions of the tumour.

I would like to sincerely thank the European Association for Cancer Research (EACR) for this prestigious fellowship, which gave me the opportunity to work with exceptional collaborators and made it possible to initiate this fascinating project. I am pleased to report that I am fortunate to have been able to extend my period of study at the Cancer Center Karolinska into a long-term fellowship.

Rita Narath
Cancer Center Karolinska
Stockholm, Sweden
April to September 2005

I was a PhD student at The Children’s Cancer Research Institute (CCRI, St. Anna Kinderspital) in Vienna, Austria, where I studied paediatric cancers (Neuroblastoma), specifically focussing on MYCN gene amplification. This established my interest in the role of gene amplification in cancer and the opportunities for using fluorescence microscopy and single cell analyses to study this problem.

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Highly Commended Awards

were presented to six young researchers whose applications were of a very high quality and who were also invited to speak in the EACR Special Session in Paris

Adrian Whitehouse
Oncogenic herpesviruses: understanding the latent-lytic switch

Leonard Gimirita
IGF-1 receptor in cancer: the perfect target, searching the perfect bullet

Gustavo Baldassarre
Role of p27kip1/stathmin interaction in the regulation of cell motility

Ronit Satchi-Fainaro
HPMA copolymer-TNP-470 (caplostatin) and Avastin show synergistic inhibition of human tumor growth in mice

Margaret Ashcroft
Regulation and targeting of the hypoxia-inducible factor pathway

Carla Boccaccio
The MET oncogene drives a genetic program linking cancer to haemostasis

Heike Allgayer
The MET oncogene drives a genetic program linking cancer to haemostasis

The EACR President and Award Winners at ECCO 13: from left Margaret Ashcroft, Gustavo Baldassarre, Ronit Satchi-Fainaro, Heike Allgayer, Bill Guilick, Carla Boccaccio, Leonard Gimirita, Adrian Whitehouse
Fragilome – Chromosomal Instability, Fragile Sites and Cancer
17–19 February 2005, Heidelberg, Germany

Genetic instability is a hallmark of most cancer cells. Normal cells have repair pathways that ensure the fidelity of DNA replication and checkpoints to maintain chromosomal stability during cell division. However, cancer cells often lose these checks and consequently they often have widespread genomic instability, which in advanced cancers is seen as chromosomal deletions, translocations or amplifications. Independent genomic damage at different genetic loci among individual tumour cells in the same patient results in generation of genetic heterogeneity in the tumour cells. These genetically and consequently biochemically and metabolically different cells have different sensitivity to therapeutic drugs and thus genetic heterogeneity is the major roadblock that inhibits success in cancer therapy.

One molecular pathway to chromosomal rearrangements starts from “common fragile sites”. There are at least 100 of these non-random predetermined chromosomal breakage regions in the human genome and in recent years, exciting progress has been made in this field. Molecular pathways that activate these fragile sites appear to exist, leading to generation of chromosomal damage that stimulates tumour progression and leads to therapeutic drug resistance. Understanding the biological and clinical consequences of individual or global genomic changes is essential to understanding tumour development and predicting the clinical course of a tumour. Furthermore, the availability of new diagnostic tools will allow us to predict tumour growth and therapy sensitivity and the Fragilome may play an important role in this.

However, scientific activities in the Fragilome field are dispersed throughout the world and networks to allow discussion of this important topic do not exist. The Heidelberg meeting, was arranged within the framework of the European Activity COST B19 “Molecular Cytogenetics of Solid Tumours” (http://www.costb19.net/) with the specific aim of bringing together prominent European scientists and American experts, to provide and opportunity for networking and consequently biochemically and metabolically different cells have different sensitivity to therapeutic drugs and thus genetic heterogeneity is the major roadblock that inhibits success in cancer therapy.

The meeting opened with an excellent overview of the Fragilome by Dr Tom Glover (Ann Arbor, USA) and additional brilliant “Expert Lectures” from David Smith (Rochester, USA), Marcelo Aldaz (Smithville, USA), Kay Huebner (Columbus, USA), and Yuh-Hwa Wang (Piscataway, USA) covered all of the important issues in Fragilome research. Scientific Sessions on selected topics presented by prominent European scientists invited and funded through COST covered topics from the evolutionary aspects of fragile sites, to cloning and molecular characterization of these sites and analysis of molecular pathways of chromosomal instability and DNA repair. Translational studies on the role of genetic instability for particular human diseases were also discussed. Two “Contributed Abstract Sessions” featured 12 selected short oral presentations and participants had the opportunity to discuss Fragilome research during two well-attended Abstract Sessions. A particular highlight of the meeting was the EACR-sponsored Special Lecture by Jan Hoeijmakers (Rotterdam, The Netherlands) who currently is doubtless one of the world leaders in the field of DNA repair.

This meeting brought together, probably for the first time, international leaders in this field and the participants expressed their great satisfaction at this achievement. The meeting has provided a platform for further activities in this field and allowed Fragilome research to explore new research directions, such as studies on the biological function of fragile sites, the characterization of genes damaged at fragile sites, studies of DNA-repair pathways, the role of chromatin structure in genomic stability and the role of chromosome instability in human disease. All are now integrated under the Fragilome roof. A major development from the meeting is the recognition that common fragile sites may play a role in human neuropsychiatric diseases. The excellent scientific discussions during formal and informal sessions established new professional contacts that will provide an excellent basis from which further activities into Fragilome research can develop.

Manfred Schwab, Meeting President

Mini Reviews on selected topics of this meeting are published as a Special Issue of the international journal Cancer Letters http://intl.elsevierhealth.com/journals/cale/

Reports of Sponsored Meetings

We performed a bioinformatic search and predicted multiple potential sites of post translational modification in the Ruk sequence. There appeared to be only one tyrosine residue available for phosphorylation, but 15 threonine and 48 serine available residues. Recently, the possibility of Ruk/CIN85/SETA/CD2BP3 self-regulation through intramolecular interactions, mediated by SH3 domains and proline-rich sequences as well as C-terminal coiled-coil region was demonstrated. We have discovered that in transiently transfected HEK293 cells Ruk, Glu-tagged associated with unknown protein kinase(s) in vivo, which determine its phosphorylation. Stimulation of HEK293 cells with serum or insulin led to a significant increase of 32P incorporation into Ruk, Glu-tagged Ruk, Glu-tagged isoform was phosphorylated to a lesser extent and this level of modification was decreased in protein purified from serum- and insulin-treated cells. Phosphorylation of Ruk, Flag-tagged on tyrosine residue in position 10 was observed both in EGF- and NGF-treated PC12 cells with inducible expression of recombinant protein. Phosphorylation of Ruk, Flag-tagged on serine and threonine residues is observed NGF-treated but not EGF-treated PC12 cells. Phosphorylation of Ruk, Flag-tagged on serine/ threonine residues was revealed in NGF-treated PC12 cells with inducible expression of recombinant protein. Differences in EGF- and NGF-induced signalling mechanisms may thus result in different types of Ser/Thr modification of Ruk, adaptor protein and consequently in different outputs.
Families showing no abnormalities in EXT1 or EXT2 by DHPLC analysis underwent further analysis by Multiplex Ligation-dependent Probe Amplification (MLPA).

Point mutations can be detected by SSCP and DHPLC but the MLPA technique can detect large rearrangements or deletions/duplications in the exons of genes with highly and sensitive accuracy. Our screening revealed 2 families with deletions of exon 1 of EXT1. A deletion of exon 1 of EXT1 was detected as a decrease in relative peak area of the amplification product. Subsequently, we obtained a normal MLPA profile from the DNA of related unaffected parents, according to the presence of exon 1 in EXT1 gene.

Our results underline the importance of a complete screening of EXT mutations by a synergy of at least two different techniques. In fact, by these techniques it is possible to identify not only mutations known in the literature, but also several new mutations in EXT genes. These results will be discussed in a paper in preparation.

Volodymyr Svinchuck
Home Institution: Lviv State University, Institute of Cell Biology, National Academy of Sciences of Ukraine
Host Institution: Cardiff School of Biosciences, Biomedical Sciences Building, Cardiff University
“Phosphorylation of adaptor protein Ruk/CIN85/SETA/CD2BP3 isoforms under the influence of growth factors and apoptosis-inducing agents”

I worked at the Cardiff School of Biosciences for over two months on the EACR Fellowship. My project was to study the role of phosphorylation of isoforms of the adaptor/scaffold protein Ruk/CIN85/SETA/CD2BP3 in the control of their biological activity.

The widely expressed Ruk/CIN85/SETA protein is composed of three SH3 domains, Pro- and Ser-rich sequences, and C-terminal coiled-coil region. Multiple binding sites in the Ruk/CIN85 structure have a potential to create various combinations of multiprotein complexes which determine its ability to organize and regulate signalling networks involved in control of important intracellular processes.

The 2005 International Workshop on Ataxia-Telangiectasia, ATM and DNA Damage Response
8 – 11 June 2005 Hotel Villa Carlotta, Belgrate, Italy

193 clinicians, researchers and representatives of Ataxia-Telangiectasia (A-T) family associations met at Belgrate, Italy, for the 2005 International workshop on Ataxia-Telangiectasia, ATM and the DNA damage response. The ATM gene was cloned only ten years ago and this meeting included eight sessions ranging from clinical reports on A-T patients to basic studies on DNA damage sensing proteins, signalling and DNA repair, and the links to cancer, ageing and neurodegeneration. We started by discussing how to strengthen links from laboratory to clinical studies, emphasizing the importance of understanding the phenotypic diversity of A-T patient disease progression and severity. This will facilitate identification of genetic modifiers and to allow translational research programmes to develop. Patient registries, clinical research networks and standardisation of assessment protocols are required if correct evaluation of clinical trials (for example involving the antioxidant α-lipoic acid and the PARP inhibitor nicotinamide) is to be achieved. Approaches to express full-length ATM in patients with point mutations should be investigated because even low-level expression can slow neurological progression and Dr Richard Gatti (UCLA, USA) reported that aminoglycosides can stimulate read-through expression of full-length ATM in cell lines with PTC mutations. Thus less-toxic drugs and further animal studies should be pursued.

To help researchers integrate and interpret new information on ATM networks, Dr Yossi Shiloh (Tel Aviv University, Israel) developed SHARP-showcase, a bioinformatic tool that analyses data and suggests new networks (http://www.cs.tau.ac.il/~shiloh). Dr Keith Caldecott (University of Sussex, UK) discussed single-strand break repair (SSBR) in several neurodegenerative diseases/syndromes such as A-T, ATLD, SCAN1 and AOA1. DNA damage repair was discussed in three other sessions, providing insight into recent findings on damage sensing and signalling, ATM activation and the role of the MRN complex, 53BP1, Mdc1/NFBD1, H2AX, Artemis, hM0F, other PI3 kinases and many other factors. The role of these factors in nonhomologous end-joining, homologous recombination repair and cell cycle control was covered and six new ATM substrates (ATF2, HDMX, DRP1, BIX, CMP, Che-1) were described. A session on NBS1/nibrin focussed on its role in homologous recombination and elegant mice studies revealed its essential and non-essential functions in ATM activation and development. These sessions brought together outstanding scientists (too many to mention individually) from Australia, Japan, the US, Canada and Europe, whose thought-provoking presentations were excellent.

Sequence alterations in damage response genes and links to cancer was also discussed. Dr Thilo Dörk (Hanover Medical School, Germany) reviewed the diversity of ATM mutations and their impact on diagnosis, counselling and therapeutic approaches. Dr Nadine Andrieu (INSERM, Paris, France) provided preliminary evidence that breast cancer risk does not vary with type of ATM mutation and Dr Jonine Bernstein (Memorial Sloan-Kettering Cancer Center, USA) presented preliminary results from WECARE (Women’s Environmental Cancer and Radiation Exposure), a study that examines the relationship between ATM mutation, radiation and breast cancer. WECARE reveals an increased risk of a second primary breast cancer in women receiving radiation therapy for a first breast cancer, especially in younger patients. Dr Tatjana Stankovic (National Research UK, UK) spoke elegantly on inactivation of ATM damage responses in sporadic leukaemia and its implications for treatment and Dr Shuki Mizutani (Tokyo Medical and Dental University, Japan) spoke on the key role played by ATM in preventing childhood leukaemia caused by MLL gene rearrangements.

The meeting ended with a round-table discussion lead by Dr Danilo Tagle (National Institute of Neurological Disorders and Stroke, USA) on future directions for A-T research. A-T family associations representatives from many countries described the day-to-day problems encountered by patients and emphasized the urgent need for translational research and new therapeutic approaches.

Finally, 95 posters reported studies in the main topic areas of the meeting and provided young researchers with a forum to present their work. The meeting organisers greatly appreciate the financial support of the EACR and the next meeting will be in Canada in September 2006.

Janet Hall, Scientific Committee Member
3rd International Symposium on the Molecular Biology of Breast Cancer
22 - 26 June 2005, Molde, Norway

This EACR-sponsored meeting was the third of its kind in Norway. The first symposium was held in Lillehammer in 1995 and was organized by Anne-Lise Barresen-Dale in collaboration with late Ruth Sager of the Dana-Farber Cancer Institute. Ruth Sager died in 1997, and the two following meetings have been held in honour of her strong personality and brilliant science. The meeting gathered 358 scientists from all over the world with 45 speakers and 111 poster presentations. The quality of the science presented was at a very high level with many exciting talks and discussions.

Molde Natives Come Home to Their City of Roses

The following days were filled with exciting talks covering topics from genetic susceptibility, hormonal influence, preventing strategies, and the role of stroma in tumor initiation and treatment, to the influence of stem cells, growth factor receptor signaling on progression recurrence and metastasis. Ruth Sager's husband Arthur Pardee (84) gave an astonishing lecture about new strategies for apoptotic chemotherapies that impressed the younger ones in the audience of the 'Recurrence and metastasis' session. Throughout the meeting it became clear that with the various large scale molecular technologies now at hand we have come one step closer in understanding the complexity of breast cancer but it has also presented us with new challenges in treating the individual patient. The meeting ended with highlights of new frontiers in breast cancer research. Georg Klein (80) Karolinska Institute, Sweden brilliantly summed up the meeting during his 40 minutes closing remarks, taking the audience also through a lifetime of cancer research.

The participants also appreciated and enjoyed the social and cultural activities in the "Town of roses with the panorama of the 87 mountain peaks, the midsummer cruise on the fjord, and the discussions late at night but still in daylight.

It started out with Nancy Davidson from Johns Hopkins, setting the stage for the symposium discussing the challenges in translating present knowledge of the molecular biology into clinical use. She was followed by Norway's Prime Minister Kjell Magne Bondevik who officially opened the symposium and welcomed all the scientists to his and the organizer Anne-Lise Barresen-Dale’s hometown.

Magne Bondevik emphasized the importance of cancer research and the involvement of the government as crucial for the field to move forward. He was unexpectedly open and told about how hard his own family had been hit by cancer and breast cancer in particular. After entertainment from young and brilliant local jazz musicians that set the spirit of the rest of the meeting, Harald Moses gave Ruth Sager's Honorary Lecture about the role of stroma and epithelial signaling in breast tumorigenesis.

The abstracts of the talks and posters were published in Breast Cancer Research and can be found at http://breast-cancer-research.com/supplements/7/S2

from the Organising Committee

In conclusion, this exciting stay in New York proved to be highly useful, not only for me but also for my home department (Institute of Pathophysiology at the Medical University of Vienna). Therefore, I would like to express my sincere gratitude to the EACR which generously supported this visit.

Carla Oliveira
Home Institution: Institute of Molecular Pathology and Immunology of University of Porto (IPATIMUP), Porto, Portugal
Host Institution: Vancouver Cancer Centre, Vancouver, Canada
February - July 2005

"Alternative genes/mechanisms to E-cadherin mutations in Familial Gastric Cancer"

Background: Familial gastric cancer (FGC) is an uncommon disease and Hereditary Diffuse Gastric Cancer (HDGC) is even less common, yet the severity of this disease justifies a major research effort. Despite all efforts to determine the genetic basis of familial gastric cancer, a single gene, E-Cadherin/CDH1, has been identified and is specifically associated with HDGC. Approximately 30-40% of HDGC families harbour germline CDH1 deleterious mutations. Two thirds of HDGC families and the majority of FGC families screened worldwide, remain genetically unexplained. Thus the objectives of this project are to: 1) identify new mechanisms inactivating the CDH1 gene, such as large germline deletions in FGC/HDGC; and 2) identify germline defects in alternative genes in FGC/HDGC.

Results and discussion: Together with point mutations and small deletions/insertions, large germline deletions have also been recently described as germline alterations in hereditary cancer syndromes. Germline deletions involving one or more exons of cancer susceptibility genes are easily missed by classical PCR based mutation detection methodologies. We have used a specific CDH1 MLPA kit to screen for large germline deletions, that is currently restricted to be used in the lab of Dr. David Huntsman in Vancouver. We have studied 100 FGC families, negative for CDH1 point mutations, from different geographic origins, but no deletions have been identified, strongly suggesting that these alterations are not involved as a mechanism in germline CDH1 inactivation in families with aggregation of gastric carcinoma (manuscript in preparation).

To address the second objective we have chosen the C-MET gene. This tyrosine kinase receptor transduces motility, proliferation, and morphogenic signals of hepatocyte growth factor/scatter factor (HGF/SF) in epithelial cells. C-MET germline mutations have been reported in patients with hereditary papillary renal carcinoma (HPRC), somatic overexpression of this gene has been reported in gastric carcinomas and germline MET mutations have been described in a few patients with gastric cancer. In the present study we have studied 40 well characterized Canadian/USA gastric cancer families for C-MET germline mutations by DHPLC.

To date, 15 out of the 21 exons of the gene have been screened and several aberrant patterns have been found, in comparison to normal controls. Sequencing is underway and this will reveal whether these probands carry polymorphic sequence variants or deleterious germline defects.
DNA fluorescent in situ hybridization to human chromosomes on metaphase spreads and RNA fluorescent in situ hybridization to drosophila embryos and fixed cells. I had an opportunity to become skilled at operating several confocal microscopes and gained extensive knowledge in deconvolution microscopy.

In the last section of the course I was exposed to advanced techniques of live cell imaging which gave an invaluable insight into the powers and limitations of each technique. The experimental section provided several basic and advanced protocols such as live cell imaging of yeasts cell cycle, high resolution fluorescence imaging of actin and chromatin dynamics during mitosis, fluorescence resonance energy transfer (FRET) analysis of fixed and living HeLa cells, fluorescence recovery after photobleaching (FRAP) of FP protein fusions and photoactivation analysis of GFP fusion proteins.

In addition to practical experience gained at the course, I have profited enormously from daily morning discussions and afternoon lecture series, which introduced participants to successful application of various optical microscopy based techniques.

Daniel Lechner
Home Institution: Institute of Pathophysiology, Vienna, Austria
Host Institution: Rockefeller University in New York City, Strang Cancer Prevention Research Center
January to April 2005
“Colorectal cancer prevention – from basic research to clinical trials”

Being an MD who had been working solely in basic research, it was a great privilege to me to receive an invitation to visit the Strang Cancer Prevention Center from Dr. Martin Likpin and Dr. Peter Holt, who are highly renowned scientists in the field of colorectal cancer prevention with great expertise in clinical research as well as in basic science. I joined Dr. Petr Protva and learned about recruitment of suitable patients, how to design a proper “experimental” diet plan for the inpatients, the technique for colonoscopy combined with the extraction of biopsies from the colonic mucosa, and finally how to perform the appropriate statistical evaluation. One recently completed human study had been performed to determine the impact of estrogens on the colonic mucosa under special consideration of the local vitamin D metabolizing machinery. In collaboration with the groups of Dr. Breslow and Dr. Augenlicht the specimens were evaluated by microarrays and results confirmed by quantitative real time-PCR, e.g. of the 25-vitamin D$_{3}$-1α-hydroxylase-encoding gene CYP27B1. I was able find an interesting increase of CYP27B1 after administration of both estrogen and genistin in cancer cell lines derived from breast and colon (not published yet).

Our group is also interested in epigenetic events involved in gene regulation. It was therefore highly valuable to learn from Dr. Protva how histones from colonic cell lines can be isolated. We evaluated histone deacetylase-inhibiting activities of certain mammae compounds which earlier had been purified by the group of Dr. Connelly (Lehman College, City University of New York). Unfortunately, no conclusive data could be generated during my stay.

At Strang Cancer Research Center I also gained insight into the highly professional work of the group headed by Dr. Yang who has compiled an impressive amount of in vivo data (mostly immunohistochemistry evaluation of the local colonic vitamin D system) over the last decade.

The translation of recent advances in cell and molecular biology into targeted cancer therapeutics is a key challenge in current cancer research. With the theme “Cancer Drug Discovery, Development and Evaluation”, leading international academic and industry experts assembled on Friday 15th July to discuss recent developments. Over 90 UK and overseas delegates attended this event, which was co-sponsored by EACR and BACR.

The morning session, chaired by Richard Marais (Institute of Cancer Research, London and EACR Secretary General) covered basic cell signalling alongside targeted therapy development. Richard described the importance of B-RAF in human cancer, discussing the frequency of B-RAF mutations and how B-RAF regulates cell growth, work that underscores many B-RAF drug discovery programs. Neal Rosen (Memorial Sloan-Kettering Cancer Center, New York) gave a thought-provoking talk on the limited successes of mechanism-based therapies. Highlighting past mistakes, he argued that many good cancer targets and drugs exist, but have limited clinical success because of the failure to incorporate biological knowledge or appropriate animal models into drug development or when attempting to determine optimal dosing or combination schedules. Heidi Lane (Novartis, Basel, Switzerland) described the rationale for targeting the mTOR (mammalian Target of Rapamycin) pathway in cancer, providing compelling preclinical data on the orally available inhibitor RAD001 (everolimus), in single agent and combination strategies. Finally, Caroline Springer (Institute of Cancer Research, Sutton, UK) described gene-directed enzyme prodrug therapy (GDEPT). Oncolytic adenoviruses are used to deliver the bacterial enzyme cytosine deaminase to tumours and CPG2 then converts a prodrug to a potent cytotoxic at the site of the tumour. Caroline presented some very promising preclinical data.

In the afternoon session, chaired by Bill Gullick (University of Kent, UK, and EACR President), Ian Stratford (University of Manchester, UK) described the importance of hypoxia to human cancer. The role of HIF-1 as a key regulator of cell adaptation to low oxygen environments was discussed, as were hypoxia-activated drugs (eg tirapazamine, Phase III) and the potential of using hypoxia for tumour-selective drug delivery. Malcolm Stevens (University of Nottingham) provided an entertaining insight into “chemistry-driven” drug discovery, exemplified by the development of novel small molecule inhibitors of telomerase that function by stabilising high order DNA structures known as G-quadruplexes. Criteria for successful clinical candidate selection of quinoxacinilum salts were discussed. Finally, Garth Powis (Arizona Cancer Center, Tucson, US) discussed drugs that target tumour “stress responses”. Compounds that target enzymes (PX-12, Phase III), the p38-α pathway (PX-316 and PX-866, preclinical), and HIF-1α (PX-478, preclinical) were described. The recurrent themes of target validation and biomarker development were again stressed in this illustration of contemporary cancer drug development.

The day provided a fascinating insight into drug discovery and development and the speakers are congratulated for the quality of their presentations. This symposium should inspire more effective translation of basic research findings into therapeutic products.

Richard Marais and Andrew Westwell
Agents that prevent cancer, delay its onset, or reverse premalignant conditions could have a dramatic beneficial impact on the health of citizens in Europe and elsewhere. Although there is an urgent need for such novel agents preventing malignancies, researchers in the field suspect that this area of scientific endeavor in Europe leads a Cinderella existence, both in terms of perception of importance, research funding and investment.

In order to review current activities in this prevention field and to seek a consensus evaluation, an exploratory workshop was held in September 2005 at the German Cancer Research Center (DKFZ) in Heidelberg, Germany, sponsored mainly by the European Science Foundation (ESF), and also supported by the European Association for Cancer Research (EACR) and the German Cancer Society.

The 35 experts from European countries and the United States of America assessed the state-of-the-art of cancer chemoprevention research in Europe. Presentations during the workshop summarized impressive and high quality work currently conducted in Europe in the area of experimental and clinical cancer chemoprevention research. A considerable array of novel, diet-derived agents discovered in laboratories across Europe awaits further testing in rodents and/or in human trials. However, in contrast to the US, where the NCI fosters and coordinates many chemoprevention research and clinical activities in this prevention field and to seek a consensus evaluation, an exploratory workshop was held in September 2005 at the German Cancer Research Center (DKFZ) in Heidelberg, Germany, sponsored mainly by the European Science Foundation (ESF), and also supported by the European Association for Cancer Research (EACR) and the German Cancer Society.

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In this training period, I visited two different centres in Europe in order to learn new surgical approaches for the management of gynaecological cancers. First I visited the Gynaecology Clinic of Leipzig University in Germany. At this clinic, I observed the surgical operations of Prof. M. Hockel such as total mesomeral resections, laterally extended endopelvic resection and vulvo-vaginal reconstructions with different kind of flaps. I was also able to observe the laparoscopic operations of Prof. H. Alexander for benign gynaecological diseases as well as having the opportunity to work with Prof. K. Kuhndel in order to learn the principles of colposcopic evaluations of patients with HPV infections and preinvasive cervical intraepithelial neoplasias. Then I visited the Center Oscar Lambret in Lille, France in order to learn the principles of laparoscopic oncological surgery from Dr. Eric Leblanc. At this clinic I learned the principles of laparoscopic hysterectomy and extraperitoneal lumbo-aortic laparoscopic lymadenectomy and assisted at operations.

During my visits, I was also able to discuss various surgical and medical problems with my hosts and other academic staff. Furthermore, maybe more importantly, I have gained the friendship of many colleagues from different countries.

There is no doubt, EACR fellowship gave me an excellent opportunity to obtain advanced surgical oncology training from the European pioneers of gynaecological oncological surgery. I would like to thank EACR for its generous support of my advanced surgical training for the management of the patients with gynaecological cancers.

Sergii Ivakhno
Home Institution: Institute of Molecular Biology and Genetics, Kiev, Ukraine
Host Institution: Cold Spring Harbor Laboratory, NY, USA
20 October - 3 November 2005
“Immunocytochemistry, In Situ Hybridization & Live Cell Imaging advanced laboratory course”

I would like to begin this report by acknowledging support from European Association of Cancer Research in the form of a travel fellowship that allowed me to attend an advanced practical course in Immunocytochemistry, in situ hybridization and live cell imaging at the Cold Spring Harbor Laboratory, CSHL (NY, USA). My interest in the course was largely spawned by our research into cytokine properties of tyrosyl-tRNA synthetase (TyrRS), which gave evidence about its involvement in apoptotic and/or post-apoptotic events. The next step is to ascertain which pathways TyrRS utilizes to exert its cytokine activities. In addition, my second project on Bayesian network modeling of cancer protein networks from biochemical and cell biological data will require practical understanding of many cell biological assays.

Each section of the course began with a set of basic protocols that served as an introduction into the fields after which participants were able to choose more specialized methods that suited their interests. I started with non-immunological staining of live cells, followed by use of fluorescently labeled antibodies to detect cytoskeleton proteins in fixed cells. Apart from learning techniques themselves I was given excellent advice on the overall design of immunochemical experiments.

In the in situ hybridization section I performed
that TSC1-TSC2 complex does this by inhibiting mTOR/S6 kinase pathway, while PI3-K/Akt signalling relieves this inhibition. At the Institute at Ukraine, I have created two "bait" vectors, expressing full-length and C-terminus domain of TSC2. Extensive screening of two cDNA libraries from Mouse Embryo and HEa cells with TSC2 baits led to the isolation of 102 positives clones. During my visit to the University College London I have identified isolated clones. We are particularly interested in further analysis of TSC2-BP1 and TSC2-BP5 clones, which have the potential to regulate the phosphorylation status and the stability of TSC1-2 complex. We are currently investigating the specificity of their interaction with TSC1-2 by co-immunoprecipitating transiently expressed and endogenous proteins.

I would like to thank EACR for the financial support, which gave me an excellent opportunity to gain further experience in modern techniques at University College London and to discuss the draft of a paper on our findings. The manuscript has recently been submitted for publication. Also I am very grateful to Prof. Ivan Gout for his time and support.

**Dimitri Pchejetski**

Home Institution: INSERM U466, Toulouse, France
Host Institution: McGill University, Montreal, Canada
27 July 2005 - 28 October 2005
“The role of prosaposin expression and sphingolipid metabolism in prostate cancer cells sensitivity to chemotherapy”

The goal of this project was to investigate the relationship between the lysosomal protein prosaposin which can potentially regulate the so-called “sphingolipid biostat”, which in turn is implicated in chemoresistance of prostate cancer cells.

Prosaposin has a prosurvival function in various types of cells and in prostate cancer cells was associated with cell mobility, chemoresistance and independence to androgens. Recently it was found that besides its main function as a lysosomal protein which regulates the sphingolipid metabolism, prosaposin can also be “exogenised” and induce paracrine signalling via yet unidentified G-coupled receptors, implicating ERK and PKC signalling pathways. A short peptide derived from the prosaposin sequence (prosapptide) induces similar effects in PC12 cells prosaposin treatment induced ERK activation, DNA synthesis and rescued cells from ceramide-induced apoptosis by activating sphingosine kinase (SK).

During my stay I obtained results suggesting that SK mediates prosaposin expression. In contrast to serum withdrawal, chemotherapeutic treatment altered neither the endogenous prosaposin expression nor SK activity. These initial results will be followed by more profound studies using cells overexpressing siRNA to SK and prosaposin, which are currently being generated. An ex vivo studies will be performed using prosaposin KO mice.

I would like to thank EACR for the travel fellowship, which allowed me to commence this challenging and exciting project that has already led to quite unexpected and interesting results.

**Polat Dursun**

Department of Obstetrics and Gynecology, Hacettepe University Faculty of Medicine, Ankara, Turkey
Host Institution : Gynecology Clinic of Leipzig University in Germany and Department of Gynecologic Oncology, Center Oscar Lambret in Lille, France
September, October, November 2005
“Advanced Surgical Training for the Management of Gynecologic Malignancies”

The incidence of gynaecological malignancies is increasing in the Turkey due to the increasing percentage of the aging women in the population. Although there are different treatment modalities available for the management of gynaecological malignancies today, surgery represents the cornerstone for treatment.

**Responses to DNA Damage: Insights from Chemical, Biochemical, Structural Biology and Cellular Studies**

Cells are constantly subjected to DNA damage from intra- and extra-cellular sources. Mounting an efficient and appropriate response to DNA damage is vital to the maintenance of genomic stability and the avoidance of carcinogenesis. Responses to DNA damage include mechanisms of DNA repair, cell cycle checkpoint arrest and the onset of apoptosis. Our understanding of these mechanisms is rapidly advancing and studies now encompass interdisciplinary approaches ranging from chemical studies that provide insight into the nature of the lesions induced, biochemical, structural biology and cellular approaches that reveal information about the individual proteins and their interaction in pathways. The aim of this conference was to bring together scientists working in the field of DNA damage responses with expertise in these different disciplines with a focus on the chemistry and biochemistry. The meeting was jointly organised by the Biochemical Society and the Nucleic Acids Group of the Royal Society of Chemistry’s Chemical Forum. The organisers were Penny Jeggo, Keith Caldecott, Alan Lehmann and Aidan Doherty.

The meeting commenced with a lecture entitled “Surveillance, recognition and repair of oxidative lesions in DNA” from Greg Verdine, who was then presented with the 2005 Nucleic Acids Award. The focus was on how the DNA N-glycosylase, Ogg1, removes 8-oxo-7,8-dihydroguanine (8-oxoG) from DNA, 8-oxoGua represents an important mutagenic lesion since it mispairs during replication. Elegant models were presented showing how 8-oxoG enters the Ogg1 active site in contrast to G, which is excluded by steric hindrance. MutM, the E.coli Ogg1 homologue, was used to examine the early stages of the reaction prior to exclusion. 8-oxoG enters the MutM active site by simple bond rotation about the DNA backbone. MutM diffusion is fast with base sampling occurring a thousand times per 0.1 of a second. The remainder of the first session focused on studies on oxidative DNA lesions, spanning from chemical to structural studies and then from biochemical to biological studies. Jean Cadet discussed the spectrum and frequency of oxidative damage. Barbara Sedgwick discussed how siRNA suppression of 3-alkyladenine-

DNA glycosylase sensitised carcinoma cells to alkylating agents. Peter Karran described the basis underlying the mutagenic potential of thiopurines, which are used as immunosuppressants in transplant patients. Patients receiving thiopurine derivatives frequently derive secondary skin carcinomas. Thiopurines within DNA absorb UVA generating reactive oxygen species, which cause further mutagenic DNA damage.

A further session was devoted to double strand break repair. Steve West reviewed the process of homologous recombination and presented evidence that the process is cell cycle regulated via cyclin-dependent kinase (CDK) phosphorylation of the C-terminus of Brca2 which inhibits its interaction with Rad51. Laurence Pearl described the process of non homologous end-joining focusing on the three dimensional structure of the DNA-PKcs, Ku70/Ku80 complex. Translesion synthesis was the subject of the next session with Robert Fuchs describing how DNA polymerases trade places during the process. Advances in understanding the process of DNA cross-link repair were considered. Kevin Hiom described the identification of Brca1-interacting protein (BRIP1) as the protein defective in Fanconi’s anaemia group J. A further highlight of the meeting was the British Biophysical Society Award Lecture presented by Mark Szczelukin who described how type I restriction enzymes use motors to translocate DNA and introduce double strand breaks.

In summary, this meeting revealed how studies exploiting different disciplines can coalesce to reveal important insights. Interdisciplinary meetings of this nature are important in providing the opportunity for cross-disciplinary collaborations and interactions. In addition to presentations by internationally recognised scientists, several younger European scientists gave excellent short presentations. The meeting provided the opportunity for these younger European scientists to hear excellent speakers and to learn about different disciplines impacting upon their field of research.

Penny Jeggo
**EACR’s Tribute to Hans Grunicke**

As well as being an outstanding scientist, Hans became an outstanding leader in many fields. He combined his position as Dean of the Medical School here with that of being the first Chair of ACOE, the Accreditation Council for Oncology in Europe, and in year 2000 took on the position of President Elect, to the delight of the EACR Executive Committee. But it is particularly his years as EACR President which I should like to celebrate here, because from 2002 to 2004 he was indeed a tower of strength to the Association and it was under his presidency that EACR achieved one of the highlights of its existence, the most successful conference ever held – EACR-18 in Innsbruck in the summer of 2004. Our current President, Bill Gullick wrote of that occasion in the EACR Newsletter:

"...we also had the best yet, mainly as a result of our Past-President's hard work and creative thinking. One of our American speakers said to me "if this meeting was held in the USA you would have seven thousand delegates not seven hundred"."

As a deeply modest man Hans would rate his own contribution as small, but as a leader of 5000 EACR members, he achieved much. In a period of radical and sometimes daunting change in the world of oncology, he never lost the importance of the individual researcher or cancer patient. And his work goes on, here in Innsbruck and in the European Association for Cancer Research. He is now a valued Past President, who may have left the limelight of presidency behind, but whose calm and steadfast advice is deeply valued.

The ceremony then ended with two special events. The first was a speech by the EACR President Elect, Dr. Marco Pierotti who recognized and paid tribute to the huge contribution which Hans made to the European cancer community when EACR President and presented him with a commemorative plate. The second was a very intriguing one, an address by a highly regarded American anthropologist, Prof Helen E. Fisher, who delighted the audience with a very stimulating talk entitled "The nature and chemistry of romantic love".

The rest of the evening - cocktails and dinner - were in keeping with the conference theme.

**EACR’s Tribute to Hans Grunicke**

On Friday October 7th 2005 the Academic body, the relatives, colleagues and friends of Prof Hans Grunicke, gathered at the magnificent Kaiser-Leopold-Saal of the Medical Faculty of Innsbruck University to celebrate his 70th birthday. It was a spectacular ceremony where, in between several speeches, the audience enjoyed masterpieces of Baroque music. Hans’ accomplishments and his importance for Innsbruck communities were the themes of speeches delivered by Officials of the Faculty, including the Rector, the Chairman of the Academy Senate, significant political representatives of the Region and the City of Innsbruck, the Sud-Tyrol Governor, the Deputy Mayor. Some of Hans’ colleagues recalled lively and amusing episodes which highlighted not only the scientific excellence of his career but also revealed the delightful aspects of his character and emphasized his deep humanity.

The ceremony then ended with two special events. The first was a speech by the EACR President Elect, Dr. Marco Pierotti who recognized and paid tribute to the huge contribution which Hans made to the European cancer community when EACR President and presented him with a commemorative plate. The second was a very intriguing one, an address by a highly regarded American anthropologist, Prof Helen E. Fisher, who delighted the audience with a very stimulating talk entitled "The nature and chemistry of romantic love".

The rest of the evening - cocktails and dinner - were in keeping with the conference theme.
dependent gene reporter lacZ. Moreover, I was able to demonstrate an interaction between the p53 protein and the sensitizer using fluorescence correlation spectroscopy measurements. To understand the role of the sensitizer itself in the response of cancer cells to porphyrin-mediated photodynamic therapy further studies should be carried out on cellular mechanisms leading to cell death. I will now continue these studies in my lab in Poland.

The insulin-like growth factor-1 receptor (IGF-1R) plays several crucial roles in cancer, yet the precise molecular mechanisms involved in expression and function of IGF-1R are still poorly understood. Phosphorylation is known to be the central process governing IGF-1R signalling, however, we have recently described the involvement of ubiquitination on IGF-1R function in a process involving the ubiquitine ligase MDM-2 and an adaptor protein - β-arrestin. The major aim of the present project was to determine the effect of IGF-1R stimulation on receptor trafficking, with particular emphasis on interactions with the β-arrestin adaptor protein.

Using the confocal microscopy facilities available at the Lefkowitz lab and under the expert guidance of Dr Sudha Shenoy, I analyzed the pattern of β-arrestin/IGF-1R association. The effects of siRNA-induced reduction of β-arrestin 1, 2, or both, on ERK activation by the IGF-1R were also tested. Using this model it was found that ERK activation correlates with the pattern of β-arrestin recruitment to the IGF-1R, demonstrating a new role of β-arrestins in IGF-1R signalling. β-arrestins are involved in MDM2 recruitment to the IGF-1R and represent a nodal point of the IGF-1R/MDM2/p53 axis.

It was a great support for the project to carry it out under Galina Selivanova’s supervision. She is an expert on p53 regulation in the cell and her research group has all the relevant methodological expertise. I am also very grateful to the EACR for granting a travel fellowship for my stay in Karolinska Institutet.

Leonard Girnita
Home Institution: Department of Oncology-Pathology, Cellular and Molecular Tumor Pathology, Cancer Center Karolinska, Karolinska University Hospital, Stockholm, Sweden
Host Institution: Prof. Robert J. Lefkowitz, Duke University Medical Center, Howard Hughes Medical Institute, Department of Medicine, Duke University Medical Center, Durham, USA
February-March 2005
“IGF-1R ubiquitination: A new dimension in IGF-1 signalling pathways”

Over the last few years our laboratory has been in collaboration with Dr. Lefkowitz’s lab in the investigation of the regulation and signalling cascades of the insulin growth factor-1 receptor (IGF-1R), where we demonstrated the important role of an adaptor protein (β-arrestin) for IGF-1R function.

During my short stay I accomplished numerous aims including the strengthening of existing collaborations and improved practical knowledge of various aspects of cell signalling. Even more importantly I made new friends within the members of the Lefkowitz lab and scientific community at Duke University. I should like to say a big thank you to the EACR for making this possible.

Forthcoming EACR Sponsored Meetings

Molecular Staging of Cancer - 2nd International Conference
June 22 - 26, 2006, German Cancer Research Center (DKFZ Heidelberg) joint meeting with Klinikum Mannheim, University of Heidelberg

There is a most important development in the field of molecular characterization of tumor diseases, especially considering powerful high-throughput screening methods for molecular tumor characterization, attempts at molecular targeting strategies, innovative bioinformatic approaches to analyze large amounts of molecular data in tumor diseases, and translational research aiming at a highly efficient transfer of basic molecular research into clinical and therapeutic applications. Interdisciplinary and international interactions are increasingly necessary for a concerted approach to develop new concepts of cancer diagnosis, staging and therapy. Therefore, the 2nd International Conference on Molecular Staging of Cancer will offer a discussion platform, focusing on aforementioned topics, for internationally well-known experts out of different fields in basic cancer research, clinical and surgical oncologists, prominent representatives of industry, and institutions trying to strengthen networks between universities and companies. In addition, we will have a special session on the topic of Comprehensive Cancer Centers and their decisive importance for a state-of-the-art cancer research, diagnosis and innovative therapy. This will be an open meeting allowing participation of everybody interested in the topic.

As key-note speakers, we are happy to report that highly ranked international experts, such as John Mendelsohn, President of the MD Anderson Cancer Center, Houston, Keichi Maruyama, President Emeritus of the National Cancer Center, Tokyo, Joseph Schlessinger, Yale University, Douglas Boyd, Gary Gallick and Menashe Bar-Eli, MD Anderson Cancer Center, Houston, Francesco Blasi and Marco Pierotti, Instituto dei Tumori/IFOM, Milano, Italy, Keld Dano, Director, Finsen Laboratory, University of Copenhagen, as well as local experts, such as Otmar Wiestler, Annemarie Pouska, Peter Lichter and Roland Eils, among others have confirmed their participation in this meeting.

This meeting will be continued as a conference series in 4-5 year intervals. Heike Allgayer

BRECOSM Breast Cancer and Metastasis Meeting
22 – 24 June 2006, Institut Curie, Paris, France

Within the European Union 6th Framework Programme, the European Commission has established the BRECOSM research network “Identification of molecular pathways that regulate the organ-specific metastasis of breast cancer”

As part of its activities, BRECOSM will host this international meeting “Breast cancer and metastasis” which will cover a number of hot topics in cancer research, including gene expression profiling analysis, mammary and tumor stem cells, mechanisms of tumor cell dissemination and organ-specific metastasis. We have already attracted many internationally renowned scientists to take part in the conference.

Confirmed speakers include:-
Non-BRECOSM - Kari Alitalo, Carlos Arteaga, Hartmut Beug, Michael Clarke, Peter Friedl, Marina Glukhova, Nancy Hynes, Jos Jonkers, Dan Medina, Klaus Pantel, Pier Guiseppe Pellici, Jeffrey Rosen, Dennis Slamon, Pat Steeg, Laura van’t Veer, Ashok Venkitaraman, Danny Welch, Zena Werb.

Members of the BRECOSM consortium - Geert Berx, Gerhard Christofori, John Collard, Eugene Lukandin, Agnes Noël, Jonathan Sleeman, Roland Stauber, Peter ten Dijke, Jean Paul Thiery, Frans van Roy, Massimo Zollo.

Through the talks and posters we aim to provide a platform for the establishment of new scientific contacts and alliances in the field of cancer research, particularly between academia and industry.

Jonathan P. Sleeman
The 19th biennial meeting of the European Association for Cancer Research will be held in the beautiful city of Budapest, providing the perfect setting for the stimulating and fascinating presentation of the best of basic and translational cancer research in Europe. The scientific programme will cover all aspects of current molecular biology, cell biology, immunology and genetics. In addition, there are a number of key-note speakers who will discuss the success of transferring basic research into effective, low toxicity targeted therapies.

EACR have always put young cancer researchers at the forefront of their meetings. Each year, EACR selects outstanding young cancer researchers to receive numerous awards; including the prestigious EACR Young Cancer Researcher Award. There are also Educational lectures, special Young Cancer Researcher Workshops focussing on career development and additional emphasis on poster sessions. Awards generously sponsored by the Pezcoller Foundation will be presented to the best poster presentations and Merck Sharp & Dohme are generously sponsoring awards for the best abstracts submitted by young investigators.

There is a joint EACR workshop with WICR (Women in Cancer Research) and AACR on "Networking, communication and negotiation: an open forum on effective strategies in career and leadership development" for women who want to advance their careers in research.

The Presidential sessions will be particularly exciting, highlighting the very best ongoing research of the moment and presenting late breaking data. This conference gives participants the opportunity to discuss their research with leading scientists from all over the world and it is hoped all those who attend EACR-19 will find it a truly memorable and valuable experience.

For more updated information about the programme, registration and other aspects of this conference, please go to www.fecs.be and click through EACR19.
Saturday July 1

Opening Ceremony 13.00 – 13.30

Mühlbock Lecture 13.30 – 14.30
The control of DNA replication and its exploitation for cancer diagnosis or treatment
Chair W Gullick (UK)
Speaker R Laskey (UK)

Symposium 15.00 – 17.00
Cancer Cell Growth
Chair R J White (UK)

The role of RNA polymerase III transcription in cell growth and cancer
Speaker R J White (UK)

How TOR signalling controls cell growth
Speaker M N Hall (CH)

Does the ribosome translate cancer?
Speaker S Volarevic (HR)

The role of RNA polymerase I transcription in cell growth and cancer
Speaker R D Hannan (AU)

Symposium 15.00 – 17.00
Genetics and the Environment
Chair P Boffetta (FR)

Whole genome scans: lessons from the analysis of breast cancer susceptibility
Speaker A L Børresen-Dale (NO)

What linkage analysis can still tell us?
Speaker D Goldgar (US)

The search for gene-environment interactions: association studies in Central Europe
Speaker P J Brennan (FR)

The importance of non-genetic causes of cancer
Speaker P Boffetta (FR)

Welcome Reception 17.00 – 19.00

Sunday July 2

Educational Lecture 08.00 – 09.00
Signal Transduction Network
Speaker Y Yarden (IL)

Gene Expression Profiling
Speaker T Sörlie (NO)

Plenary Lecture 09.00 – 09.45
Europe Against Cancer
Chair E Olah (HU)
Speaker P Boyle (FR)

Symposium 10.15 – 12.15
Molecular Determinants of Site Specific metastasis
Chair S A Eccles (UK)
Speaker A J Minn (US)

Bone metastasis
Speaker A M Teti (IT)

HDACS and angiogenesis
Speaker V Castronovo (BE)

Lymphatic metastasis
Speaker K Alitalo (FI)

Symposium 10.15 – 12.15
Canceromics
Chair T Sörlie (NO)

The cancer kinome and phosphatome
Speaker A Bardelli (IT)

Cancer cell genome
Speaker M Stratton (UK)

Proteomic analysis for early detection of cancer
Speaker G Whiteley (US)

High-throughput technologies for molecular oncology research
Speaker O Kallioniemi (FI)

Young Cancer Researchers’ Workshop
12.45 – 13.45
How to be effective in applying for fellowships
Co-ordinator R J White (UK)

How to apply for fellowships at Cancer Research UK
Speaker R J White (UK)

How to apply for EMBO fellowships
Speaker J Celis (DK)
How to apply for fellowships  
Speaker O Wiestler (DE)

Award Lecture 13.45 – 14.30  
The Anthony Dipple Carcinogenesis Award  
Molecular Targets for Prevention & Treatment of Colorectal Cancer: PGE2, WNT, & EGFR  
Speaker R DuBois (US)

Presidential Session 14.35 – 16.05  
Top eight abstracts will be presented

Poster session 16.05 – 18.00

Plenary Lecture 18.00 - 18.45  
Angiogenesis  
Chair H Grunicke (AT)  
Speaker W G Kaelin, Jr (US)

Monday July 3

Educational Lecture 08.00 – 09.00  
Proteomics and Mass Spectrometry  
Speaker G Whiteley (US)

Educational Lecture 08.00 – 09.00  
Radiation Oncology  
Chair C Belka (DE)

Plenary Lecture 09.00 – 09.45  
p53 and Cancer  
Chair R Marais (UK)  
Speaker K Vousden (UK)

Symposium 10.15 - 12.15  
Experimental Therapeutics  
Chair J C Lacal (ES)  
Speaker R Marais (UK)

Therapeutic approaches to target Raf signalling in cancer  
Speaker R Marais (UK)

PI3K/mTOR pathway as therapeutic targets  
Speaker G B Mills (US)

Preclinical and clinical studies of Hsp90 molecular chaperone inhibitors  
Speaker P Workman (UK)

Choline kinase in human carcinogenesis  
Speaker J C Lacal (ES)

Symposium 10.15 – 12.15  
Cancer Stem Cells  
Chair H Clevers (NL)

Cancer stem cells  
Speaker M F Clarke (US)

Breast cancer stem cells  
Speaker M Smalley (UK)

Wnt signalling, intestinal stem cells and cancer  
Speaker H Clevers (NL)

Title to be confirmed  
Speaker R Fodde (NL)

Young Cancer Researchers’ Workshop  
12.45 – 13.45  
EACR Young Cancer Researcher’s Award  
Speaker I Dikic (DE)

Symposium 14.35 – 16.05  
Inflammation and Cancer  
Chair M P Colombo (IT)

Pathogens induced chronic inflammation and cancer  
Speaker M Naumann (DE)

NF-kappaB in inflammation-associated cancer  
Speaker E Pikarsky (IL)

Immune cells promoting cancer development  
Speaker L M Cossens (US)

Macrophage produced extracellular matrix in cancer development  
Speaker M P Colombo (IT)

Symposium 14.35 – 16.35  
Cancer Epigenetics  
Chair R J White (UK)

Nucleotide excision repair and genomic instability  
Speaker R Waters (UK)

Epigenetic regulation by DNA methylation of tumour suppressor genes  
Speaker P A Jones (US)

Chromatin regulation during proliferation and differentiation  
Speaker A Brehm (DE)

Epigenetic marks in chromatin/identification of chromatin modifying enzymes by bioinformatics  
Speaker R Aasland (NO)

Plenary Session 16.35 – 18.00  
Plenary Lecture 18.00 – 18.45  
Identification of cancer-relevant genes using functional genetic approaches  
Chair J Cells (UK)  
Speaker R Bernards (NL)

Conference Dinner 20.00 – 23.00

Tuesday July 4

Educational Lecture 08.00 – 09.00  
Dynamic imaging of cancer cell invasion in vitro and in vivo  
Speaker P Friedl (DE)

Educational Lecture 08.00 – 09.00  
Bioinformatics  
Speaker A Brazma (UK)

Plenary Lecture 09.00 – 09.45  
Systems Biology  
Chair V Jendrossek (DE)  
Speaker J W Gray (US)

Presidential Session 10.15 – 11.45  
Top eight abstracts will be presented

Poster Session 11.45 – 13.45

EACR/WICR/AACR Workshop 12.45 – 13.45  
Networking, communication and negotiation: an open forum on effective strategies in career and leadership development  
Chair M Foti (US)  
Speaker S A Eccles (UK)

Symposium 15.00 – 17.30  
Cancer Cell Biology, Therapy & Epigenetic Markers  
Chair J C Lacal (ES)  
Speaker R Waters (UK)

Dalmau Lecture 15.00 – 16.00  
Understanding cancer cell migration  
Speaker A Hamburger (US)

Closing Ceremony 15.30 – 15.45

Acknowledgements

The European Association for Cancer Research would like to thank the following companies for their generous sponsorship to the 19th EACR Meeting:

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This list reflects commitments as of 1 May 2006
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Co-ordinator G R P Blackledge (UK)

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Chair M Pierotti (IT)
Speaker S A Eccles (UK)
Speaker A Hamburger (US)
Speaker D Groo (HU)
Speaker A Albini (IT)

Award Lecture 13.45 – 14.30
Carcinogenesis Young Investigator’s Award
Speaker M F Clarke (US)

Cancer epigenetics: from basic knowledge to translational applications
Speaker M Esteller (ES)

Mike Price Lecture 14.30 – 15.30
Targeted Therapy
Chair M Pierotti (IT)
Speaker J Baselga (ES)

Closing Ceremony 15.30 – 15.45
EACR/BACR Joint Symposium

The European Association for Cancer Research and the British Association for Cancer Research join
Cancer Research at Nottingham for the

3rd Annual Translational Cancer Research Nottingham Meeting
Venue: Arts Centre Lecture Theatre, University of Nottingham

Friday 21 July 2006
Cancer Drug Discovery, Development and Evaluation

Morning session: Chair: Sue Eccles (ICR, London)

10.00 - 10.40 Gene Expression Profiling
Marco Pierotti (European Institute of Oncology, Milan)

10.40 - 11.20 Individualised cancer treatment utilising genomic and proteomic profiling
Brian Leyland-Jones (McGill University, Montreal, Canada)

11.20 – 11.40 Tea and Coffee

11.40 - 12.20 Title to be confirmed
Angelika Burger (Greenebaum Cancer Center, University of Maryland School of Medicine, Baltimore, MD)

12.20 – 13.00 Cell cycle inhibitors in cancer therapy
Peter Fischer (University of Nottingham)

13.00 – 14.00 Lunch

Afternoon session: Chair: Bill Gullick (University of Kent)

14.00 – 14.40 Mechanisms of drug resistance – epigenetic silencing
Robert Brown (Beatson Institute for Cancer Research, Glasgow)

Nicola Curtin (Northern Institute of Cancer Research, Newcastle)

15.20 – 16.00 Repair of DNA interstrand crosslinks as a mechanism of chemotherapy resistance (Nucleotide excision repair)
John Hartley (UCL)

Further information from:
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Nottingham NG5 1PB UK
International Fax Number: +44 115 8231849
E-mail julie.stanley@nottingham.ac.uk
The 19th biennial meeting of the European Association for Cancer Research will be held in the beautiful city of Budapest, providing the perfect setting for the stimulating and fascinating presentation of the best of basic and translational cancer research in Europe. The scientific programme will cover all aspects of current molecular biology, cell biology, immunology and genetics. In addition, there are a number of key-note speakers who will discuss the success of transferring basic research into effective, low toxicity targeted therapies.

EACR have always put young cancer researchers at the forefront of their meetings. Each year, EACR selects outstanding young cancer researchers to receive numerous awards; including the prestigious EACR Young Cancer Researcher Award. There are also Educational lectures, special Young Cancer Researcher Workshops focussing on career development and additional emphasis on poster sessions. Awards generously sponsored by the Pezcoller Foundation will be presented to the best poster presentations and Merck Sharp & Dohme are generously sponsoring awards for the best abstracts submitted by young investigators.

There is a joint EACR workshop with WICR (Women in Cancer Research) and AACR on “Networking, communication and negotiation: an open forum on effective strategies in career and leadership development” for women who want to advance their careers in research. The Presidential sessions will be particularly exciting, highlighting the very best ongoing research of the moment and presenting late breaking data. This conference gives participants the opportunity to discuss their research with leading scientists from all over the world and it is hoped all those who attend EACR-19 will find it a truly memorable and valuable experience.

For more updated information about the programme, registration and other aspects of this conference, please go to www.fecs.be and click through EACR19.

EACR Travel Fellowship Reports

The EACR Travel Fellowship programme is generously sponsored by the Association for International Cancer Research (AICR)

Ásta Björk Jónsdóttir
Home Institution: The Icelandic Cancer Society, Reykjavik, Iceland and the Faculty of Medicine, University of Iceland
Host Institution: Department of Molecular Cell Biology, Leiden University Medical Center, Leiden, The Netherlands
September 2004- February 2005
“Chromosomal Instability in BRCA2 Mutated Cell Lines”

The EACR travel fellowship enabled me to visit the Department of Molecular Cell Biology, Leiden University Medical Center, and gave me the opportunity to use the Multicolor FISH method developed there for molecular karyotyping. The objective of the research was to examine the influence of BRCA2 on chromosome stability in BRCA2-mutant and wild-type human mammary epithelial cell lines. Inherited germ-line mutations in the breast cancer susceptibility genes BRCA1 and BRCA2 greatly increase the risk of breast cancer. The BRCA pathways have been shown to be involved in maintenance of genomic stability. BRCA2 is known to be involved e.g. in homologous recombination repair of double-strand DNA breaks, suppression of cell proliferation, centrosome duplication and recently it was suggested that it plays a role in cytokinesis. Combined Binary FISH labelling-fluorescence in situ hybridization (COBRA-FISH) is a multicolour FISH technique where 4 fluorophores are used to achieve colour discrimination of the human chromosomes. COBRA-FISH can be used to detect chromosomal aberrations, e.g. translocations and complex chromosomal rearrangements. The studied cell lines showed several genomic rearrangements including numerical and structural rearrangements such as gains and losses of whole chromosomes (monosomy and trisomy), translocations deletions and telomeric associations. Several of these aberrations were not clonal and in some cell lines both rearranged and normal cells were seen.

At the time when I was starting my project, an article was published where it was shown that BRCA2 inactivation delays and prevents cytokinesis. At the host institution there are facilities for doing live-cell imaging and therefore the project was expanded and I prolonged my stay. I was then able to use this method to examine cell division in primary human fibroblasts from BRCA2 mutation carriers and non-carriers.

Joanna Zawacka-Pankau
Home Institution: Department of Biotechnology, Intercollegiate Faculty of Biotechnology, University of Gdansk and, Medical University of Gdansk, Kladki 24, 80-822 Gdansk, Poland
Host Institution: Microbiology and Tumor Biology Center, Galina Selivanova Research Group, Karolinska Institutet, Nobelsväg 16 SE-17177 Stockholm, Sweden
February - March 2005
“Investigating the interactions between tumor suppressor protein p53 and protoporphyrin IX”

My project was mainly focused on investigating the impact of a porphyrin sensitizer on cancer cells with different p53 status. Cell proliferation was affected by the sensitizer at concentrations of 5 – 10 µg/ml. I did not observe a p53-dependence of the growth suppression effect of the sensitizer. Induction of cell death by porphyrin was also analyzed. Significant accumulation of cells in sub-G phase, indicative of cell death and also G2/M arrest was observed for p53+/− whereas for p53− the cell cycle arrest was not so pronounced. Western blot analysis did not show a p53-dependent induction of apoptotic factors. However, I observed marked phosphorylation of Ser-15 of the p53 protein in human fibroblasts which may lead to induction of cell cycle-regulating proteins and finally to cell cycle arrest. I did not observe any induction of p53-transactivation function in cells treated with porphyrin sensitizer using p53-
dependent gene reporter lacZ. Moreover, I was able to demonstrate an interaction between the p53 protein and the sensitizer using fluorescence correlation spectroscopy measurements. To understand the role of the sensitizer itself in the response of cancer cells to porphyrin-mediated photodynamic therapy further studies should be carried out on cellular mechanisms leading to cell death. I will now continue these studies in my lab in Poland.

It was a great support for the project to carry it out under Galina Selivanova’s supervision. She is an expert on p53 regulation in the cell and her research group has all the relevant methodological expertise. I am also very grateful to the EACR for granting a travel fellowship for my stay in Karolinska Institutet.

Leonard Girnita
Home Institution: Department of Oncology-Pathology, Cellular and Molecular Tumor Pathology, Cancer Center Karolinska, Karolinska University Hospital, Stockholm, Sweden
Host Institution: Prof. Robert J. Lefkowitz, Duke University Medical Center, Howard Hughes Medical Institute, Department of Medicine, Duke University Medical Center, Durham, USA
February-March 2005
“IGF-1R ubiquitination: A new dimension in IGF-1 signalling pathways”
Over the last few years our laboratory has been in collaboration with Dr. Lefkowitz’s lab in the investigation of the regulation and signalling cascades of the insulin growth factor-1 receptor (IGF-1R), where we demonstrated the important role of an adaptor protein (β-arrestin) for IGF-1R function.

The insulin-like growth factor-1 receptor (IGF-1R) plays several crucial roles in cancer, yet the precise molecular mechanisms involved in expression and function of IGF-1R are still poorly understood. Phosphorylation is known to be the central process governing IGF-1R signalling, however, we have recently described the involvement of ubiquitination on IGF-1R function in a process involving the ubiquitine ligase MDM-2 and an adaptor protein - β-arrestin. The major aim of the present project was to determine the effect of IGF-1R stimulation on receptor trafficking, with particular emphasis on interactions with the β-arrestin adaptor protein.

Using the confocal microscopy facilities available at the Lefkowitz lab and under the expert guidance of Dr Sudha Shenoy, I analyzed the pattern of β-arrestin/IGF-1R association. The effects of siRNA-induced reduction of β-arrestin 1, 2, or both, on ERK activation by the IGF-1R were also tested. Using this model it was found that ERK activation correlates with the pattern of β-arrestin recruitment to the IGF-1R, demonstrating a new role of β-arrestins in IGF-1R signalling. β-arrestins are involved in MDM2 recruitment to the IGF-1R and represent a nodal point of the IGF-1R/MDM2/p53 axis.

During my short stay I accomplished numerous aims including the strengthening of existing collaborations and improved practical knowledge of various aspects of cell signalling. Even more importantly I made new friends within the members of the Lefkowitz lab and scientific community at Duke University. I should like to say a big thank you to the EACR for making this possible.
A Birthday Celebration for Hans Grunicke, EACR’s Past President

On Friday October 7th 2005 the Academic body, the relatives, colleagues and friends of Prof Hans Grunicke, gathered at the magnificent Kaiser-Leopold-Saal of the Medical Faculty of Innsbruck University to celebrate his 70th birthday. It was a spectacular ceremony where, in between several speeches, the audience enjoyed masterpieces of Baroque music. Hans’ accomplishments and his importance for Innsbruck communities were the themes of speeches delivered by Officials of the Faculty, including the Rector, the Chairman of the Academy Senate, significant political representatives of the Region and the City of Innsbruck, the Sud-Tyrol Governor, the Deputy Mayor. Some of Hans’ colleagues recalled lively and amusing episodes which highlighted not only the scientific excellence of his career but also revealed the delightful aspects of his character and emphasized his deep humanity.

The ceremony then ended with two special events. The first was a speech by the EACR President Elect, Dr. Marco Pierotti who recognized and paid tribute to the huge contribution which Hans made to the European cancer community when EACR President and presented him with a commemorative plate. The second was a very intriguing one, an address by a highly regarded American anthropologist, Prof Helen E. Fisher, who delighted the audience with a very stimulating talk entitled “The nature and chemistry of romantic love”.

The rest of the evening - cocktails and dinner - were in keeping with the conference theme.

EACR’s Tribute to Hans Grunicke

As well as being an outstanding scientist, Hans became an outstanding leader in many fields. He combined his position as Dean of the Medical School here with that of being the first Chair of ACOE, the Accreditation Council for Oncology in Europe, and in year 2000 took on the position of President Elect, to the delight of the EACR Executive Committee. But it is particularly his years as EACR President which I should like to celebrate here, because from 2002 to 2004 he was indeed a tower of strength to the Association and it was under his presidency that EACR achieved one of the highlights of its existence, the most successful conference ever held – EACR-18 in Innsbruck in the summer of 2004. Our current President, Bill Gullick wrote of that occasion in the EACR Newsletter

As well as being held in a spectacular setting and an excellent conference centre the scientific programme was the best yet, mainly as a result of our Past-President’s hard work and creative thinking. One of our American speakers said to me “If this meeting was held in the USA you would have seven thousand delegates not seven hundred”.

As a deeply modest man Hans would rate his own contribution as small, but as a leader of 5000 EACR members, he achieved much. In a period of radical and sometimes daunting change in the world of oncology, he never lost the importance of the individual researcher or cancer patient. And his work goes on, here in Innsbruck and in the European Association for Cancer Research. He is now a valued Past President, who may have left the limelight of presidency behind, but whose calm and steadfast advice is deeply valued.

Martin Barr

Home Institution: Thoracic Oncology, Institute of Molecular Medicine, St. James’ Hospital, Dublin, Ireland
Host Institution: Hamon Center for Therapeutic Oncology Research, UT Southwestern Medical Center, Dallas, Texas
April 2005

“Establishment of primary cultures and immortalized cell lines from lung cancer”

Lung cancer is the leading cause of cancer mortality in Ireland. Non-small cell lung cancer (NSCLC) accounts for approximately 80% of all lung cancers. Despite advances in surgery, radiotherapy and chemotherapy, and the recent introduction of effective targeted therapies such as selective epidermal growth factor receptor tyrosine kinase inhibitors, Gefitinib and Erlotinib, the overall 5-year survival is poor, being less than 15% of all treated cases.

As a new Thoracic Oncology Research Group, our main interests include lung cancer carcinogenesis and chemoprevention, focusing on the roles of inflammation and hypoxia in tumorigenesis, in addition to translational research studies linked to clinical trials at St. James’ Hospital, Dublin. An important component of our research will involve the culturing of primary NSCLC and bronchial epithelial cells, a crucial technique to our studies.

An EACR Travel Fellowship permitted my travel to the laboratory of Prof John Minna in the Hamon Centre for Therapeutic Oncology Research at the University of Texas Southwestern Medical Centre, Dallas in April 2005. Primary culture techniques for the isolation, immortalisation and in vitro maintenance of primary NSCLC and human bronchial epithelial cells were established during this time and are currently being implemented within our research group at St. James’ Hospital in Dublin as a valuable tool in our lung cancer research programme. The immortalised primary cultures will allow us to examine a range of molecular markers and signalling pathways/events in response to established and novel anti-cancer therapies and to correlate these in vitro findings with observed tumour responses in vivo. I am most grateful to the EACR for this travel award and to Prof John Minna and his laboratory personnel for their help and kindness during my time there.

Oksana Malanchuk

Home Institution: Institute of Molecular Biology and Genetics, National Academy of Sciences of Ukraine
Host Institution: University College London, London, UK
2 July to 1 August 2005

“Identification and characterization of TSC2 binding proteins by yeast two-hybrid screening”

I am a first year PhD student at the Institute of Molecular Biology and Genetics, National Academy of Sciences of Ukraine. The main objective of my PhD project is to identify novel TSC2-binding molecules by the yeast two-hybrid approach and to characterize the functional importance of these interactions in mammalian cells in context of PI3K signalling pathway.
that TSC1-TSC2 complex does this by inhibiting mTOR/S6 kinase pathway, while PI3-K/Akt signalling relieves this inhibition. At the Institute at Ukraine, I have created two “bait” vectors, expressing full-length and C-terminus domain of TSC2. Extensive screening of two cDNA libraries from Mouse Embryo and HeLa cells with TSC2 baits led to the isolation of 102 positives clones. During my visit to the University College London I have identified isolated clones. We are particularly interested in further analysis of TSC2-BP1 and TSC2-BP5 clones, which have the potential to regulate the phosphorylation status and the stability of TSC1-2 complex. We are currently investigating the specificity of their interaction with TSC1-2 by co-immunoprecipitating transiently expressed and endogenous proteins.

I would like to thank EACR for the financial support, which gave me an excellent opportunity to gain further experience in modern techniques at University College London and to discuss the draft of a paper on our findings. The manuscript has recently been submitted for publication. Also I am very grateful to Prof. Ivan Gout for his time and support.

Dimitri Pchejetski
Home Institution: INSERM U466, Toulouse, France
Host Institution: McGill University, Montreal, Canada
27 July 2005 - 28 October 2005
"The role of prosaposin expression and sphingolipid metabolism in prostate cancer cells sensitivity to chemotherapy"

The goal of this project was to investigate the relationship between the lysosomal protein prosaposin which can potentially regulate the so-called “sphingolipid biostat”, which in turn is implicated in chemoresistance of prostate cancer cells.

Prosaposin has a prosurvival function in various types of cells and in prostate cancer cells was associated with cell mobility, chemoresistance and independence to androgens. Recently it was found that besides its main function as a lysosomal protein which regulates the sphingolipid metabolism, prosaposin can also be “exogenised” and induce paracrine signalling via yet unidentified G-coupled receptors, implicating ERK and PI3K signalling pathways. A short peptide derived from the prosaposin sequence (prosaptide) induces similar effects in PC12 cells prosaposin treatment induced ERK activation, DNA synthesis and rescued cells from ceramide-induced apoptosis by activating sphingosine kinase (SK).

During my stay I obtained results suggesting that SK mediates prosaposin expression. In contrast to serum withdrawal, chemotherapeutic treatment altered neither the endogenous prosaposin expression nor SK activity. These initial results will be followed by more profound studies using cells overexpressing siRNA to SK and prosaposin, which are currently being generated. An ex vivo studies will be performed using prosaposin KO mice.

I would like to thank EACR for the travel fellowship, which allowed me to commence this challenging and exciting project that has already led to quite unexpected and interesting results.

Polat Dursun
Home: Department of Obstetrics and Gynecology, Hacettepe University Faculty of Medicine, Ankara, Turkiye
Host Institution: Gynecology Clinic of Leipzig University in Germany and Department of Gynecologic Oncology, Center Oscar Lambret in Lille, France
September, October, November 2005
"Advanced Surgical Training for the Management of Gynecologic Malignancies"

The incidence of gynaecological malignancies is increasing in the Turkey due to the increasing percentage of the aging women in the population. Although there are different treatment modalities available for the management of gynaecological malignancies today, surgery represents the cornerstone for treatment.
ESF Workshop on Cancer Chemoprevention
“Development of Novel Cancer Chemopreventive Agents in Europe—Neglected Cinderella Rising Phoenix?”
18 - 20 September 2005, DKFZ, Heidelberg, Germany

Agents that prevent cancer, delay its onset, or reverse premalignant conditions could have a dramatic beneficial impact on the health of citizens in Europe and elsewhere. Although there is an urgent need for such novel agents preventing malignancies, researchers in the field suspect that this area of scientific endeavor in Europe leads a Cinderella existence, both in terms of perception of importance, research funding and investment.

In order to review current activities in this prevention field and to seek a consensus evaluation, an exploratory workshop was held in September 2005 at the German Cancer Research Center (DKFZ) in Heidelberg, Germany, sponsored mainly by the European Science Foundation (ESF), and also supported by the European Association for Cancer Research (EACR) and the German Cancer Society.

The 35 experts from European countries and the United States of America assessed the state-of-the-art of cancer chemoprevention research in Europe. Presentations during the workshop summarized impressive and high quality work currently conducted in Europe in the area of experimental and clinical cancer chemoprevention research. A considerable array of novel, diet-derived agents discovered in laboratories across Europe awaits further testing in rodents and/or in human trials. However, in contrast to the US, where the NCI fosters and coordinates many chemoprevention research and clinical activities, Europe lacks an appropriate coordinating and supporting infrastructure for such activities.

This situation seems to be particularly apparent with respect to large clinical trials, of which the outcome could offer great potential health benefits and lower costs for health care of increasingly aging populations. Therefore also in Europe financial support must be earmarked to enlarge the further development of chemopreventive agents, and most importantly their clinical efficacy and safety evaluation. The workshop recommends that participants should persuade key persons in each member state to influence policy makers and to society at large. Establishing an organization or institutional focal point for cancer prevention research in Europe would greatly facilitate the continued development of this area, and for instance EORTC should be one of the organizations that should be approached. Such action could help to boost the area of chemoprevention agent development and its applications in Europe, shifting emphasis from the cure of end-stage disease to early reversal of carcinogenesis.

In this training period, I visited two different centres in Europe in order to learn new surgical approaches for the management of gynaecological cancers. First I visited the Gynaecology Clinic of Leipzig University in Germany. At this clinic, I observed the surgical operations of Prof. M. Hockel such as total mesometrial resections, laterally extended endopelvic resection and vulvo-vaginal reconstructions with different kind of flaps. I was also able to observe the laparoscopic operations of Prof. H. Alexander for benign gynaecological diseases as well as having the opportunity to work with Prof. K. Kuhnel in order to learn the principles of colposcopic evaluations of patients with HPV infections and preinvasive cervical intraepithelial neoplasias. Then I visited the Center Oscar Lambret in Lille, France in order to learn the principles of laparoscopic oncological surgery from Dr. Eric Leblanc. At this clinic I learned the principles of laparoscopic hysterectomy and extraperitoneal lumbo-aortic laparoscopic lymphadenectomy and assisted at operations.

During my visits, I was also able to discuss various surgical and medical problems with my hosts and other academic staff. Furthermore, maybe more importantly, I have gained the friendship of many colleagues from different countries.

There is no doubt, EACR fellowship gave me an excellent opportunity to obtain advanced surgical oncology training from the European pioneers of gynaecological oncological surgery. I would like to thank EACR for its generous support of my advanced surgical training for the management of the patients with gynaecological cancers.

Sergii Ivakhno
Home Institution: Institute of Molecular Biology and Genetics, Kiev, Ukraine
Host Institution: Cold Spring Harbor Laboratory, NY, USA
20 October - 3 November 2005
“Immunocytochemistry, In Situ Hybridization & Live Cell Imaging advanced laboratory course”

I would like to begin this report by acknowledging support from European Association of Cancer Research in the form of a travel fellowship that allowed me to attend an advanced practical course in Immunochemistry, in situ hybridization and live cell imaging at the Cold Spring Harbor Laboratory, CSHL (NY, USA). My interest in the course was largely spawned by our research into cytokine properties of tyrosyl-RNA synthetase (TyrRS), which gave evidence about its involvement in apoptotic and/or post-apoptotic events. The next step is to ascertain which pathways TyrRS utilizes to exert its cytokine activities. In addition, my second project on Bayesian network modeling of cancer protein networks from biochemical and cell biological data will require practical understanding of many cell biological assays.

Each section of the course began with a set of basic protocols that served as an introduction into the fields after which participants were able to choose more specialized methods that suited their interests. I started with non-immunological staining of live cells, followed by use of fluorescently labeled antibodies to detect cytoskeleton proteins in fixed cells. Apart from learning techniques themselves I was given excellent advice on the overall design of immunohistochemical experiments.

In the in situ hybridization section I performed...
DNA fluorescent in situ hybridization to human chromosomes on metaphase spreads and RNA fluorescent in situ hybridization to drosophila embryos and fixed cells. I had an opportunity to become skilled at operating several confocal microscopes and gained extensive knowledge in deconvolution microscopy.

In the last section of the course I was exposed to advanced techniques of live cell imaging which gave an invaluable insight into the powers and limitations of each technique. The experimental section provided several basic and advanced protocols such as live cell imaging of yeasts cell cycle, high resolution fluorescence imaging of actin and chromatin dynamics during mitosis, fluorescence resonance energy transfer (FRET) analysis of fixed and living HeLa cells, fluorescence recovery after photobleaching (FRAP) of FP protein fusions and phototactivation analysis of GFP fusion proteins.

In addition to practical experience gained at the course, I have profited enormously from daily morning discussions and afternoon lecture series, which introduced participants to successful application of various optical microscopy based techniques.

Daniel Lechner

Home Institution: Institute of Pathophysiology, Vienna, Austria
Host Institution: Rockefeller University in New York City, Strang Cancer Prevention Research Center

January to April 2005
“Colorectal cancer prevention – from basic research to clinical trials”

Being an MD who had been working solely in basic research, it was a great privilege to me to receive an invitation to visit the Strang Cancer Prevention Center from Dr. Martin Likpin and Dr. Peter Holt, who are highly renowned scientists in the field of colorectal cancer prevention with great expertise in clinical research as well as in basic science.

I joined Dr. Petr Protiva and learned about recruitment of suitable patients, how to design a proper “experimental” diet plan for the inpatients, the technique for colonoscopy combined with the extraction of biopsies from the colonic mucosa, and finally how to perform the appropriate statistical evaluation. One recently completed human study had been performed to determine the impact of estrogens on the colonic mucosa under special consideration of the local vitamin D metabolizing machinery. In collaboration with the groups of Dr. Breslow and Dr. Augenlicht the specimens were evaluated by microarrays and results confirmed by quantitative real time-PCR, e.g. of the 25-vitamin D$_3$-1α-hydroxylase–encoding gene CYP27B1. I was able find an interesting increase of CYP27B1 after administration of both estrogen and genistein in cancer cell lines derived from breast and colon (not published yet).

Our group is also interested in epigenetic events involved in gene regulation. It was therefore highly valuable to learn from Dr. Protiva how histones from colonic cell lines can be isolated. We evaluated histone deacetylase-inhibiting activities of certain mammeea compounds which earlier had been purified by the group of Dr. Connelly (Lehman College, City University of New York). Unfortunately, no conclusive data could be generated during my stay.

At Strang Cancer Research Center I also gained insight into the highly professional work of the group headed by Dr. Yang who has compiled an impressive amount of in vivo data (mostly immunohistochemistry evaluation of the local colonic vitamin D system) over the last decade.
The following days were filled with exciting talks covering topics from genetic susceptibility, hormonal influence, preventing strategies, and the role of stroma in tumor formation and treatment, to the influence of stem cells, growth factor receptor signaling on progression recurrence and metastasis. Ruth Sager’s husband Arthur Pardee (84) gave an astonishing lecture in treating new strategies for apoptotic chemotherapies that impressed the younger ones in the audience of the “Recurrence and metastasis” session. Throughout the meeting it became clear that with the various large scale molecular technologies now at hand we have come one step closer in understanding the complexity of breast cancer but it has also presented us with new challenges in treating the individual patient. The meeting ended with highlights of new frontiers in breast cancer research. Georg Klein (80) Karolinska Institute, Sweden brilliantly summed up the meeting during his 40 minutes closing remarks, taking the audience also through a lifetime of cancer research.

The participants also appreciated and enjoyed the social and cultural activities in the ‘Town of roses’ with the panorama of the 87 mountain peaks, the midsummer cruise on the fjord, and the discussions late at night but still in daylight.

It started out with Nancy Davidson from Johns Hopkins, setting the stage for the symposium discussing the challenges in translating present knowledge of the molecular biology into clinical use. She was followed by Norway’s Prime Minister Kjell Magne Bondevik who officially opened the symposium and welcomed all the scientists to his and the organizer Anne-Lise Børresen-Dale’s hometown.

Magne Bondevik emphasized the importance of cancer research and the involvement of the government as crucial for the field to move forward. He was unexpectedly open and told about how hard his own family had been hit by cancer and breast cancer in particular. After entertainment from young and brilliant local jazz musicians that set the spirit for the rest of the meeting, Harald Moses gave Ruth Sager’s Honorary Lecture about the role of stroma and epithelial signaling in breast tumorigenesis.

The abstracts of the talks and posters were published in Breast Cancer Research and can be found at http://breast-cancer-research.com/supplements/7/S2 from the Organising Committee

In conclusion, this exciting stay in New York proved to be highly useful, not only for me but also for my home department (Institute of Pathophysiology at the Medical University of Vienna). Therefore, I would like to express my sincere gratitude to the EACR which generously supported this visit.

Carla Oliveira
Home Institution: Institute of Molecular Pathology and Immunology of University of Porto (IPATIMUP), Porto, Portugal
Host Institution: Vancouver Cancer Centre, Vancouver, Canada
February - July 2005
“Alternative genes/mechanisms to E-cadherin mutations in Familial Gastric Cancer”

Background: Familial gastric cancer (FGC) is an uncommon disease and Hereditary Diffuse Gastric Cancer (HDGC) is even less common, yet the severity of this disease justifies a major research effort. Despite all efforts to determine the genetic basis of familial gastric cancer, a single gene, E-Cadherin/CDH1, has been identified and is specifically associated with HDGC. Approximately 30-40% of HDGC families harbour germline CDH1 deleterious mutations. Two thirds of HDGC families and the majority of FGC families screened worldwide, remain genetically unexplained. Thus the objectives of this project are to: 1) identify new mechanisms inactivating the CDH1 gene, such as large germline deletions in FGC/HDGC; and 2) identify germline defects in alternative genes in FGC/HDGC.

Results and discussion: Together with point mutations and small deletions/insertions, large germline deletions have also been recently described as germline alterations in hereditary cancer syndromes. Germline deletions involving one or more exons of cancer susceptibility genes are easily missed by classical PCR based mutation detection methodologies. We have used a specific CDH1 MLPA kit to screen for large germline deletions, that is currently restricted to be used in the lab of Dr. David Huntsman in Vancouver. We have studied 100 FGC families, negative for CDH1 point mutations, from different geographic origins, but no deletions have been identified, strongly suggesting that these alterations are not involved as a mechanism in germline CDH1 inactivation in families with aggregation of gastric carcinoma (manuscript in preparation).

To address the second objective we have chosen the C-MET gene. This tyrosine kinase receptor transduces motility, proliferation, and morphogenic signals of hepatocyte growth factor/scatter factor (HGF/SF) in epithelial cells. C-MET germline mutations have been reported in patients with hereditary papillary renal carcinoma (HPRC), somatic overexpression of this gene has been reported in gastric carcinomas and germline MET mutations have been described in a few patients with gastric cancer. In the present study we have studied 40 well characterized Canadian/USA gastric cancer families for C-MET germline mutations by DHPLC.

To date, 15 out of the 21 exons of the gene have been screened and several aberrant patterns have been found, in comparison to normal controls. Sequencing is underway and this will reveal whether these probands carry polymorphic sequence variants or deleterious germline defects.
Emanuela Massi
Home Institution: Campus Bio-Medico, Facoltà Medica Area Patologia Generale, Sezione Medicina Molecolare E Biotecnologie, Via E Longoni 47, 00155, Roma, Italy
Host Institution: Department of Medical Genetics, University and University Hospital of Antwerp, Universiteitsplein 1 Building T, 6th floor 2610 Wilrijk, Belgium
26 June 2005 - 22 July 2005
“Mutational analysis of EXT genes by DHPLC in HME (hereditary multiple exostoses) Italian patients”

The EACR travel fellowship gave me the opportunity to visit the Department of Medical Genetics at the University of Antwerp and perform a mutational analysis on 9 HME Italian families (16 patients) by DHPLC technology (Denaturing High Performance Liquid Chromatography) to identify point mutations not detected by preliminary single-strand conformation polymorphism analysis (SSCP).

All EXT1 and EXT2 exons were amplified using specific primers. Amplicons showing an abnormal profile were sequenced. After direct sequencing six abnormal profiles were revealed as non-pathogenic known polymorphisms. In particular, we detected four different polymorphisms in EXT1 and three different polymorphisms in EXT2.

Families showing no abnormalities in EXT1 or EXT2 by DHPLC analysis underwent further analysis by Multiplex Ligation-dependent Probe Amplification (MLPA).

Point mutations can be detected by SSCP and DHPLC but the MLPA technique can detect large rearrangements or deletions/duplications in the exons of genes with highly and sensitive accuracy. Our screening revealed 2 families with deletions of exon 1 of EXT1. A deletion of exon 1 of EXT1 was detected as a decrease in relative peak area of the amplification product. Subsequently, we obtained a normal MLPA profile from the DNA of related unaffected parents, according to the presence of exon 1 in EXT1 gene.

Our results underline the importance of a complete screening of EXT mutations by a synergy of at least two different techniques. In fact, by these techniques it is possible to identify not only mutations known in the literature, but also several new mutations in EXT genes. These results will be discussed in a paper in preparation.

Volodymyr Svinchuck
Home Institution: Lviv State University, Institute of Cell Biology, National Academy of Sciences of Ukraine
Host Institution: Cardiff School of Biosciences, Biomedical Sciences Building, Cardiff University
“Phosphorylation of adaptor protein Ruk/CIN85/SETA/CD2BP3 isoforms under the influence of growth factors and apoptosis-inducing agents”

I worked at the Cardiff School of Biosciences for over two months on the EACR Fellowship. My project was to study the role of phosphorylation of isoforms of the adaptor/scaffold protein Ruk/CIN85/SETA/CD2BP3 in the control of their biological activity.

The widely expressed Ruk/CIN85/SETA protein is composed of three SH3 domains, Pro- and Ser-rich sequences, and C-terminal coiled-coil region. Multiple binding sites in the Ruk/CIN85 structure have a potential to create various combinations of multiprotein complexes which determine its ability to organize and regulate signalling networks involved in control of important intracellular processes.
Fragilome – Chromosomal Instability, Fragile Sites and Cancer
17–19 February 2005, Heidelberg, Germany

Genetic instability is a hallmark of most cancer cells. Normal cells have repair pathways that ensure the fidelity of DNA replication and checkpoints to maintain chromosomal stability during cell division. However, cancer cells often lose these checks and consequently they often have widespread genomic instability, which in advanced cancers is seen as chromosomal deletions, translocations or amplifications. Independent genomic damage at different genetic loci among individual tumour cells in the same patient results in generation of genetic heterogeneity in the tumour cells. These genetically and consequently biochemically and metabolically different cells have different sensitivity to therapeutic drugs and thus genetic heterogeneity is the major roadblock that inhibits success in cancer therapy.

One molecular pathway to chromosomal rearrangements starts from “common fragile sites”. There are at least 100 of these non-random predetermined chromosomal breakage regions in the human genome and in recent years, exciting progress has been made in this field. Molecular pathways that activate these fragile sites appear to exist, leading to generation of chromosomal damage that stimulates tumour progression and leads to therapeutic drug resistance. Understanding the biological and clinical consequences of individual or global genomic changes is essential to understanding tumour development and predicting the clinical course of a tumour. Furthermore, the availability of new diagnostic tools will allow us to predict tumour growth and therapy sensitivity and the Fragilome may play an important role in this.

However, scientific activities in the Fragilome field are dispersed throughout the world and networks to allow discussion of this important topic do not exist. The Heidelberg meeting, was arranged within the framework of the European Activity COST B19 “Molecular Cyogenetics of Solid Tumours” (http://www.costb19.net/) with the specific aim of bringing together prominent European scientists and American experts, to provide up-to-date information on the status of international Fragilome research. In addition, it provided and opportunity for networking to further develop this exciting area.

The meeting opened with an excellent overview of the Fragilome by Dr Tom Glover (Ann Arbor, USA) and additional brilliant “Expert Lectures” from David Smith (Rochester, USA), Marcelo Aldaz (Smithville, USA), Kay Huebner (Columbus, USA), and Yuh-Hwa Wang (Piscataway,USA) covered all of the important issues in Fragilome research. Scientific Sessions on selected topics presented by prominent European scientists invited and funded through COST covered topics from the evolutionary aspects of fragile sites, to cloning and molecular characterization of these sites and analysis of molecular pathways of chromosomal instability and DNA repair. Translational studies on the role of genetic instability for particular human diseases were also discussed. Two “Contributed Abstract Sessions” featured 12 selected short oral presentations and participants had the opportunity to discuss Fragilome research during two well-attended Abstract Sessions. A particular highlight of the meeting was the EACR-sponsored Special Lecture by Jan Hoeijmakers (Rotterdam, The Netherlands) who currently is doubtless one of the world leaders in the field of DNA repair.

This meeting brought together, probably for the first time, international leaders in this field and the participants expressed great satisfaction and this achievement. The meeting has provided a platform for further activities in this field and allowed Fragilome research to explore new research directions, such as studies on the biological function of fragile sites, the characterization of genes damaged at fragile sites, studies of DNA-repair pathways, the role of chromatin structure in genomic stability and the role of chromosomal instability in human disease. All are now integrated under the Fragilome roof. A major development from the meeting is the recognition that common fragile sites may play a role in human neuropsychiatric diseases. The excellent scientific discussions during formal and informal sessions established new professional contacts that will provide an excellent basis from which further activities into Fragilome research can develop.

Manfred Schwab, Meeting President

Mini Reviews on selected topics of this meeting are published as a Special Issue of the international journal Cancer Letters http://intl.elsevierhealth.com/journals/cale/

We performed a bioinformatic search and predicted multiple potential sites of post translational modification in the Ruk sequence. There appeared to be only one tyrosine residue available for phosphorylation, but 15 threonine and 48 serine available residues. Recently, the possibility of Ruk/CIN85/SETA/CD2BP3 self-regulation through intramolecular interactions, mediated by SH3 domains and proline-rich sequences as well as C-terminal coiled-coil region was demonstrated. We have discovered that in transiently transfected HEK293 cells Ruk, Glu-tagged associated with unknown protein kinase(s) in vivo, which determine its phosphorylation. Stimulation of HEK293 cells with serum or insulin led to a significant increase of 32P incorporation into Ruk, Glu-tagged isoform was phosphorylated to a lesser extent and this level of modification was decreased in protein purified from serum- and insulin-treated cells. Phosphorylation of Ruk, Flag-tagged on tyrosine residue in position 10 was observed both in EGFr- and NGF-treated PC12 cells with inducible expression of recombinant protein. Phosphorylation of Ruk, Flag-tagged on serine and threonine residues is observed NGF-treated but not EGF-treated PC12 cells. Phosphorylation of Ruk, Flag-tagged on serine/threonine residues was revealed in NGF-treated PC12 cells with inducible expression of recombinant protein. Differences in EGFr- and NGF-induced signalling mechanisms may thus result in different types of Ser/Thr modification of Ruk, adaptor protein and consequently in different outputs.
Rita Narath
Cancer Center Karolinska
Stockholm, Sweden
April to September 2005

I was a PhD student at The Children’s Cancer Research Institute (CCRI, St. Anna Kinderspital) in Vienna, Austria, where I studied paediatric cancers (Neuroblastoma), specifically focusing on MYCN gene amplification. This established my interest in the role of gene amplification in cancer and the opportunities for using fluorescence microscopy and single cell analyses to study this problem.

The cellular proto-oncogene her-2/neu is amplified in ~20% of breast cancers and this is a marker of poor prognosis in some, but not all patients. One group of patients with the amplification dies in 2-3 years, whereas another group survives for over 10 years without developing metastatic disease (A. Zetterberg, unpublished data). Thus, it appears that her-2/neu amplification alone is not the only risk factor in breast cancer and that additional aberrations combine with the amplification to produce the high risk of metastases.

The aim of this study, which I performed in Anders Zetterberg’s laboratory, was to define a genetic pattern to distinguish the patients with good prognosis from those with poor prognosis. Importantly, the host institution possesses a unique collection of fresh frozen tumour samples and associated clinical follow-up data. I used the funding provided by the Mike Price Fellowship to study 42 tumours in which her-2/neu is amplified, applying a powerful combination of two newly developed techniques that allow high-resolution analysis of the human genome. These are ROMA (representational oligonucleotide microarray analysis) and QM-FISH (quantitative multigene fluorescence in situ hybridization). I collected ROMA and QM-FISH data from these tumours and this is currently being analyzed for abnormalities to determine if we can separate the long-term and short-term survivors from each other. If successful, we will validate the study with a larger data set.

Furthermore, I adapted QM-FISH for use with paraffin embedded material, thereby opening the enormous potential for retrospective studies within the host institution. This also has the additional advantage that it is now possible to isolate and analyze single nuclei from defined regions of the tumour.

I would like to sincerely thank the European Association for Cancer Research (EACR) for this prestigious fellowship, which gave me the opportunity to work with exceptional collaborators and made it possible to initiate this fascinating project. I am pleased to report that I am fortunate to have been able to extend my period of study at the Cancer Center Karolinska into a long-term fellowship.

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Announcement of the Winner of the 2006 Mike Price Fellowship

Annette Affolter has been awarded the 2006 Mike Price Fellowship

Home Institution: Mannheim University Hospital, Department for Otolaryngology, Head and Neck Surgery, D-68135 Mannheim, Germany

Host Institution: The Institute of Cancer Research, Signal Transduction Team, Section for Cell and Molecular Biology, 237 Fulham Road, London SW3 6JB

Supervisor: Richard Marais, PhD

The project will be conducted from April 1 to August 31, 2006

The title of the planned research project is:

The clinical significance of B-RAF mutations in melanoma

B-RAF is mutated in approximately 70% of human melanomas, where it stimulates proliferation and survival. However, the B-RAF inhibitory drug sorafenib is ineffective at curing this disease. In order to obtain greater insight into the mechanism of action of sorafenib, I will develop sorafenib-resistant versions of oncogenic B-RAF and study their biological properties. These studies will allow us to better understand why sorafenib is not effective at treating melanoma. They will also allow us to develop better drugs to target B-RAF in melanoma and will begin to address the important issue of whether resistance to B-RAF-targeted therapies is likely to develop in the clinical setting. The host institution was selected for these studies because Richard Marais is a leader in the field of B-RAF signalling in cancer. I have been working in his team for the past 12 months, which already gave me a strong background understanding of this field and I anticipate that this experience will be a great benefit to my academic career.

Applications are invited for the 2007 Mike Price Fellowship

To enable young cancer researchers to visit a European Institution in order to undertake a specific project related to cancer research, from basic science to treatment or care.

Application forms are available from the EACR Secretariat and on www.eacr.org

Guidelines

* Applications will be accepted from European oncologists aged under 40.
* Applicants should have worked actively in oncology for at least two years and they should possess a doctorate degree or the equivalent medical qualification.
* Proposed projects may be related to any aspect of cancer research, from basic science to treatment or care.
* The duration of the Fellowships will be from 3 to 6 months.
* Applicants must arrange for a letter of invitation and approval of the project from the host institution to be included with their application.

Further information is available from:

EACR Secretariat
Tel: +44 115 9515114 Fax: +44 115 9515115
E-mail: eacr@nottingham.ac.uk
In Memoriam - Arnold Graffi

Honorary Member of EACR since 1981

Arnold Graffi died in Berlin on January 30, 2006, at the age of 95. It was the end of a full and eventful life in which he had received numerous honours as an outstanding pioneer in experimental cancer research in the post war period, and in which his great scientific achievements easily surmounted the almost completely closed borders of the German Democratic Republic (DDR) to be recognized all over the world.

His main interest was the elucidation of the mechanism of neoplastic cell transformation. To this end he initially studied the effects of various chemical carcinogens in animal models, and proposed a mutation hypothesis of carcinogenesis as early as 1940. Since the 1950s the predominant investigations of Arnold Graffi and his internationally renowned research team were directed towards the elucidation of the role of viruses in neoplastic development. Graffi and his co-workers discovered several oncogenic animal viruses, one of which was later named after Graffi. Based on the broad scientific horizon of Arnold Graffi many additional innovative ideas in cell and molecular biology were considered in his team, including the possibility of gene therapy of cancer in the early 60s.

Born in Transylvania (Romania), Arnold Graffi studied medicine in Marburg, Leipzig and Tübingen, and graduated from the Charité in Berlin, where he also started his academic career as an assistant of the famous surgeon Ferdinand Sauerbruch. After positions in Frankfurt, Prague, and Budapest he returned to Berlin working for some time in a research laboratory of Schering AG, and at the Kaiser Wilhelm Institute for Cell Physiology with the Nobel Prize laureate Otto Warburg. In 1949 Graffi earned his venia legendi from the Humboldt University in Berlin, and became Department Head at the Institute of Biology and Medicine of the Academy of Sciences in Berlin-Buch. He later became Director of the Institute of Cancer Research of the Academy (which is now part of the Max Delbrück Center for Molecular Medicine of the Helmholtz Association of National Research Centers). He was active in research until his retirement in 1975, and even several years beyond. In addition to his election as an Honorary Member of EACR, Professor Graffi received numerous awards, among which his membership of the Academy of Natural Scientists Leopoldina (1964), the Paul Ehrlich Prize in Frankfurt/Main (1979), the Helmholtz Medal of the Academy of Sciences in Berlin (1984), an honorary doctorate of the University of Leipzig (1990), and the Cross of the Order of Merit of the Federal Republic of Germany (1995) are the most remarkable.

Arnold Graffi was not only an excellent scientist but also a warm hearted, versatile and gifted person, painting and playing the piano in his spare time. Together with his highly esteemed wife and scientific co-worker, who became his devoted nurse during his last years, he provided a most positive and supportive environment for all his scientific team.

The closed borders between East and West Germany created many problems for the advancement of science during this period and Graffi and his team were sadly not able to contribute to the early development of the German Cancer Research Centre in Heidelberg. However great science surmounts all obstacles and all those who had the privilege of meeting Arnold Graffi cannot fail to have been influenced by him and will remember him as an exemplary scientist and delightful colleague.

Peter Bannasch
EACR President 1987-1993
In the last EACR Newsletter I wrote that ‘EACR is growing rapidly, both in numbers of members and in its range of activities’. I am delighted to report that this rate of growth has increased still further over the last year with one new member joining every two days. The EACR staff have worked hard to meet high targets, particularly at ECCO13 where we signed up 100 new members in 5 days – a considerable achievement. I see the building up of our membership as a means of building our influence and strength. Although I am very pleased by this tremendous growth in membership, I want to see it continue and expand still further, so I encourage you to ask your colleagues who are not members to visit www.eacr.org and join EACR today.

Our drive to make EACR more attractive to young researchers has also been extremely successful. Student numbers have doubled over the last two years and young investigators now play a very active part in the EACR. We have two young members on the Executive Committee and the EACR-19 Scientific Programme Committee has a strong Young Researchers’ Section chaired by Bob White who have made a considerable contribution to what is an excellent scientific programme. We also organized a Special Young Speakers’ Session at ECCO13 in Paris consisting of six young members (who were selected and invited by EACR) and Dr Heike Allgayer, the winner of our prestigious annual EACR Young Cancer Researcher Award. You can read more detail of Heike Allgayer’s exceptional award winning lecture on page 4 and we hope some of you will apply for this award in 2007.

We enjoyed a new format at our Council Meeting at ECCO13 in Paris. Bill Gullick, mindful of the increased responsibilities of the Council as our advisory body, initiated a more interactive meeting, with presentations from four eminent council members on cancer research in their countries. Their presentations stimulated excellent discussion and will provide a forum for future discussions and increased involvement and influence of our Council Members.

This year EACR has sponsored a record number of meetings and reports of six of these appear in the following pages. This increase is seen as a very healthy development. A key aim of ours is to enhance scientific communication and by facilitating this we not only fulfill our aspirations, but it gives us the opportunity to recruit new members and enhance our visibility. I would like to encourage all members to apply for these grants to assist them with meetings they may be organizing.

The EACR Fellowship Programme continues to thrive and again you will read several interesting and informative reports from young members who won these awards. We are indebted to the Association for International Cancer Research (AICR) who co-fund these awards. The awards are designed to allow members to attend technical workshops and courses, rather than to finance their attendance at meetings. They are also intended to support collaborative research by allowing people to visit other laboratories to learn new techniques or approaches. We welcome new applications and again please visit our website for application information and forms.

The new website is very successful with members using it to access information and apply for fellowships, awards and bursaries. We will add a ‘Members’ Page’ shortly and plan to have a continuously rolling programme of information and interaction. We invite you to visit the site and welcome your suggestions and ideas.

Now we are looking forward to EACR-19, to an excellent scientific meeting and to welcoming as many members as possible to Budapest making this a really memorable event. I look forward to meeting many of you there.

Richard Marais  

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