

# alumni

## DEUTSCHES KREBSFORSCHUNGSZENTRUM



*Heike Langlotz, Ilia Toshkov and Yun Niu take the chance for an informal chat during the alumni meeting.*

*Dear DKFZ Alumni,*

The development of the DKFZ Alumni Association made considerable progress in 2004. The 1<sup>st</sup> international Alumni Meeting took place in Heidelberg in June, and was attended by about 150 participants from all over the world. The abstracts of the stimulating scientific presentations and a report on the cheerful social events of the meeting are presented in this newsletter. In addition, the formal foundation of Alumni Deutsches Krebsforschungszentrum Heidelberg e. V. is briefly described. We received considerable feedback from many participants during and after the meeting, and two of the founding Alumni even made spontaneous generous donations to support the activities of the Association in the future. We are now expecting your favourable response to the foundation of the Association, especially your joining as a member of the Alumni Association. During the forthcoming Annual Meeting of the American Association for Cancer Research in California, attending DKFZ Alumni from

all over the world, particularly those from the USA, and Scientists currently working in the DKFZ are cordially invited to get together on April 18, 2005. The next meeting of the Alumni Association abroad will be devoted to our Chinese Colleagues, and has been scheduled for June 5, 2005, in Beijing, closely connected with a Sino-German Workshop of the Helmholtz Association on Cancer and Infectious Diseases. Our Colleagues in the USA and China may use these occasions to establish local DKFZ Alumni Clubs.

An additional outstanding event of the DKFZ in 2004 was the 40<sup>th</sup> anniversary of this institution. The appealing program of the birthday celebration attracted many participants from outside and inside of the DKFZ, including governmental officials from Berlin and Stuttgart, representatives of the large German Science Organisations, and leading colleagues from different Universities, particularly the University of Heidelberg. As an example of an exceptionally fruitful international collaboration in cancer research the newsletter contains

a report on the longstanding scientific cooperation between Israel and Germany. The great success of this program is documented by many joint publications. The excellence of other research programs of the DKFZ was once again reflected by a large number of national and international awards over the past year, the most outstanding of which are listed in this Newsletter.

Continuing its activities, the Alumni Association organized in 2004 a visit to one of the global industrial players, the BASF (which has traditionally had its headquarters in the region) for Guest Research Scientists presently working in the DKFZ. A lively comment on this very informative visit is given in the present newsletter by one of the participants. Recently, DKFZ Alumni living in the Heidelberg region have taken an initiative to meet more regularly in an informal way to maintain personal contact and exchange information on matters of mutual interest. The next general Alumni Meeting in Heidelberg has been scheduled for 2006. Details about the exact timing and the program will be communicated in forthcoming newsletters. In any case, we hope to be able to inform you early enough to avoid interference with other events possibly occupying your timetable. With this notice as a precaution I would like to extend the best wishes from all of us at the DKFZ.

*Peter Bannasch*

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# event

## An Appealing Birthday Celebration

*On November 5<sup>th</sup>, the DKFZ commemorated its 40<sup>th</sup> anniversary in an official ceremony. In his welcome speech to over 300 guests, Prof. Otmar D. Wiestler, Chairman and Scientific Director of the DKFZ Management Board, acknowledged the achievements of the past four decades, which have led to international recognition of the DKFZ as a center of excellence for fundamental research.*



*left: Paul Kirchhof and Otmar D. Wiestler answer intriguing questions on the ethical frontiers of research by Julia Rautenstrauch and Josef Puchta*

*right: Ursula Klingmüller – together with Adelheid Cerwenka and Walter Kröll – addressed the question whether junior researchers still get a chance.*

ior researchers still get a chance?” was one of the questions addressed to Prof. Walter Kröll, President of the Helmholtz Association. Prof. Wiestler and Prof. Paul Kirchhof, Director of the Institute of Finance Law and Tax Law at Heidelberg University and former Judge of the Federal Constitutional Court, concentrated on the subject “When research meets ethical frontiers”. Furthermore Dagmar



He congratulated his predecessors and the almost 2000 employees and staff members for their efforts and extended thanks to DKFZ's partners and sponsors. Now, Wiestler appealed, we should not rest on the laurels of these achievements, but rather use the results of excellent basic research in order to develop DKFZ into a driving force for translating research findings into clinical applications.

The Federal Minister of Education and Research, Edelgard Bulmahn, accentuated the importance of the projected National Center of Tumor Diseases Heidelberg (NCT) as a prime example of interdisciplinary cooperation, which she considers essential in the fight against cancer as a “challenge to us all”.

During four informal panel discussions moderated by Dr. Julia Rautenstrauch, Head of the Division of Press and Public Relations, and Dr. Josef Puchta, Administrative-Commercial Director of the DKFZ Management Board, scientists of the DKFZ as well as external experts had a critical look at the interactions between science, the clinic, and society. “Do jun-

Schipanski, President of the Deutsche Krebshilfe (German Cancer Aid), Prof. Markus Büchler, Director of the Surgical Hospital at Heidelberg University, and Dr. Frank Schirmacher, Editor of the daily newspaper Frankfurter Allgemeine Zeitung, stated their points of view on biomedical progress and its influence on society. Reflecting on each dialogue the Fastfood Theatre, Munich, gave impressive examples of their performing skills. A reception in the foyer of the Communication Center provided the chance for personal conversations between many former and present members of the DKFZ as well as official guests and friends from outside.

*Christopher Briele/Dagmar Anders*

# report

## DKFZ and Israeli Cancer Researchers

Three Decades of Fruitful Cooperation *by Wolfhard Semmler and Elfriede Mang*

*Israel has about 6,700,000 inhabitants and its area covers 21,000 km<sup>2</sup>. In spite of its small size the scientific output of this country is enormous, and the present cancer cooperation program not only resulted in much fruitful scientific exchange of knowledge but also yielded many friendly contacts between Israeli and German scientists.*



*Meeting of the Program Committee*

The cooperation in cancer research between the Israeli Ministry of Science (MOS, formerly National Council for Research and Development) and the DKFZ was launched in 1976. Usually 14 joint projects are in operation. Each consists of one Israeli and one DKFZ subproject, running for three years. Presently the Israeli subprojects are funded at a total financial level of about 600,000 Euro p.a.; for the corresponding DKFZ subprojects funding amounts to about Euro 500,000 p.a., originating from Germany's Federal Ministry of Education and Research (Bundesministerium für Bildung und Forschung, BMBF) and distributed by the DKFZ via its annual budget. From its onset up to end of 2003 11.7 million Euros have been allocated to the Israeli subprojects in total and an estimated sum of 8 million Euros to the DKFZ (German) subprojects. The scientific program committee, consisting of six experts in different fields of cancer agrees on new projects, evaluates ongoing projects every year during the meeting of the program committee and handles current problems with the cooperation program. Every third year a workshop with Israeli and German

principal investigators is held. Up to the end of December 2003, 98 projects were concluded successfully on the following areas of cancer research: mechanisms of action of chemical and viral cancerogenic and anticancerogenic agents in target organs and cells; tumor immunology; preclinical and clinical oncology. The results were documented in more than 800 publications in renowned journals. An era was concluded in 2003 when the coordinators Dr. Yair Degani (MOS) and Prof. Erich Hecker (DKFZ) both retired. In April 2003 they were honoured by a festive symposium and a reception arranged by the Israeli Embassy in Berlin. The two scientists had developed the program and were essential in creating its spirit of active cooperation.

From its very beginning, the program saw many renowned scientists taking part as principal investigators. One of them, Aaron Ciechanover, received last year's Nobel Prize for Chemistry, together with Avram Hershko and Irwin Rose. In the early 1980s, these scientists discovered how the human body disposes of proteins that are no longer needed. From 1998 to 2000, Aaron Ciechanover and Martin Scheffner from the German Cancer Research Center conducted a joint project entitled: Regulation of cell regulatory proteins by the ubiquitin-dependent proteolytic pathway. This project, among others, was considered of outstanding merit. **For more information on the cooperation program, especially on documentation, please have a look at our homepage: [www.dkfz.de/israel/](http://www.dkfz.de/israel/)**

*Coordinators of the Israeli-German cooperation for many years: Yair Degani and Erich Hecker*



### 27<sup>th</sup> Meeting of the Program Committee on March 22/23, 2004, in Tel Aviv

One of the major topics was the total of 13 oral reports by the principal investigators of the running Israeli subprojects. The Program Committee evaluated the cooperation projects and fixed the financial support. Furthermore new Priority Topics for the call in summer 2004 had to be agreed upon. Prof. Otmar D. Wiestler suggested some important guidelines for the future of the cooperation program:

- More young scientists should be encouraged to apply for new projects.
- The principal investigators of both subprojects should report on their project every year to strengthen the cooperation.
- More exchange of PhD students between Israeli and DKFZ laboratories should be promoted.
- More emphasis should be put on translational research.

### Perspectives of the German Coordinator Prof. Wolfhard Semmler:

In the future this program should be continued with the present funding by the BMBF or even increased, if possible. It is planned to put more emphasis on clinical aspects of research, i. e. diagnostic and therapeutical approaches. Realization of those goals can be supported by the planned Comprehensive Cancer Center in Heidelberg.

### Perspectives of the Israeli Coordinator Dr. Shlomo Sarig:

It is particularly gratifying to note that results of DKFZ-MOS projects have already found expression in cancer public health measures and clinical practice in Israel, Germany and elsewhere. In coming years, the Program should focus its resources on topics which are likely to lead the way in the investigation of the causes of cancer, its prevention and cure. Among the priority areas particularly appropriate for inclusion in the DKFZ-MOS program are control and regulation of gene expression, tumor vaccines and cytokine-mediated cancer therapy.

*The first Alumni Meeting, held at the DKFZ from June 25 to June 26, 2004, brought together about 150 former Guest Scientists and Alumni from Germany, Austria, China, Greece, India, Israel, the Netherlands, Poland, the U.S., and current staff of the DKFZ. It was a scientifically stimulating and socially most pleasant event. The DKFZ Management Board deserves the gratitude of all participants for the consistent support of all activities to develop the Alumni Association and to organize this first meeting.*

## Topics Presented by DKFZ Alumni:

### Abstract of the Abstracts selected by Peter Bannasch

On the first day, internationally renowned DKFZ alumni from the U.S., Germany and several other European countries presented the most recent results of their research on two main topics, both of which have a strong impact on our understanding of cancer as a biologic phenomenon and a life-threatening disease.

#### Pathobiology of cancer cells

**Allain Balmain** (San Francisco, USA) discussed genetic determinants of cancer susceptibility. In contrast to “high penetrance” genetic factors that confer very high risk such as the tumor suppressor genes RB and BRCA1, “low penetrance genes” interacting with environmental factors, which are responsible for the majority of sporadic cancers (>95 of all human cancers) are almost completely unknown and are extremely difficult to find using conventional methods. However, mapping of the location of multiple cancer modifier genes in inbred mouse strains resistant or sensitive to chemical carcinogens has shown that dozens of common “low penetrance” genetic variants act synergistically to confer increased risk of cancer. In order to further investigate the germline determinants of cancer susceptibility, and the nature of somatic events in tumor progression, multiple mouse models of cancer of the skin, lung, prostate, and lymphoma are presently being developed. Comprehensive analysis of the complex gene networks that control cell growth and behavior will require the integration of multiple experimental approaches from both mouse and human systems.

**Klaus H. Kaestner** (Philadelphia, USA) studied the role of Foxl1 as a mesenchymal modifier of APC gastrointestinal carcinogenesis. Constitutive activation of the Wnt/APC/beta-catenin pathway is observed in most sporadic and hereditary colorectal cancers as well as in sporadic gastric cancers. Mutations in the Adenomatous Polyposis Coli (APC) gene upregulate Wnt signalling by stabilizing beta-catenin and causing activation of downstream targets important in proliferation control. Kaestner demonstrated that loss of the mesenchymal transcription factor Foxl1 leads to a marked increase in tumor multiplicity in the colon of mice with a mutation of the APC gene (ApcMin). ApcMin/+; Foxl1-/- mice also develop gastric tumors not observed in ApcMin mice. Kaestner concluded that these effects are caused by earlier tumor initiation due to accelerated loss of heterozygosity at the Apc locus, suggesting that Foxl1 is the first

mesenchymal modifier of Min and plays a key role in gastrointestinal tumorigenesis.

The role of a cytokine of the interleukin (IL)-6 family, the IL-6 receptor (R) subunit glycoprotein (gp) 130 in stem cell biology and cancer was investigated by **Stefan Rose-John** (Kiel, Germany). In vivo, the IL-6/soluble IL-6R complex stimulates several types of target cells such as endothelial cells, smooth muscle cells and various stem cell populations, which are not stimulated by IL-6 alone since they do not express the membrane bound IL-6 receptor. This process has been named trans-signalling. Designer proteins specifically inducing or blocking trans-signalling were constructed. The superagonistic designer cytokine Hyper-IL-6 has been used for the cultivation and expansion of hematopoietic and other stem cells. Furthermore, in animal models of acute liver failure this protein has been shown to accelerate liver regeneration. The soluble gp 130Fc fusion protein is currently evaluated for its therapeutic potential in the treatment of several chronic inflammatory diseases, some of which are associated with a high risk of cancer development.



*Time for exchange on scientific and personal matters: Roland Moll, Frank Rösl, Allain Balmain and Angel Alonso*

Using epithelial mesenchymal transition (EMT) as an in vitro correlate of tumor progression and metastasis, **Hartmut Beug** and colleagues (Vienna, Austria) studied expression profiles of mammary epithelial cells showing different epithelial plasticity phenotypes

in response to various oncogenes and/or cytokines, and observed changes in six genes of the PDGF-signalling pathway to be specific for EMT. Autocrine PDGF secretion by mammary epithelial cells was found to be a consequence of TGFβ-induced EMT, cooperating with oncogenic Ras to hyperactivate the PI3K pathway. PI3K hyperactivation by autocrine PDGFR signalling appears to be essential for viability during EMT, while other PDGFR signals maintain invasive phenotypes. The cancer drug ST571 interferes with PDGFR signalling during EMT and metastasis, abolishes survival and EMT/invasion in cellular models, and prevents metastasis *in vitro*.

**Roland Moll** (Marburg, Germany) emphasized the usefulness of immunohistochemical demonstration of epithelial marker proteins in the diagnosis of primary neoplasms and metastases. Architectural proteins serving as valuable epithelial cell type and tumor markers include several cytokeratins (CKs), desmosomal proteins and structure-associated membrane proteins. CK5, CK6 and stratification-related desmosomal cadherins are sensitive markers for squamous cell carcinomas. In the frequent metastases of adenocarcinomas, the CK7/CK20 pattern is particularly useful in the differential diagnosis of tumor origin. In addition to a typical CK profile which includes CKs 7, 13 and 20, urothelial carcinomas often express the specific urothelial membrane marker uroplakin-III.

## Self versus non-self discrimination in health and disease

**Jacque Neefjes** (Amsterdam, The Netherlands) studied the principles of antigen presentation by MHC class I and II molecules by “single cell biochemistry” and exemplified his findings for the MHC class II microdomain. As demonstrated by confocal FRET technology in living cells, these molecules are transported to late endocytotic structures where peptide loading occurs supported by the editor HLA-DM (a specialized chaperone) – a mechanism which may be used by bacteria to prevent antigen presentation. Subsequently, MHC class II is transported to the plasma membrane. This process is controlled by interleukin IL-10 in human monocytes. Micromanipulation and visualization of processes in living cells reveals details of these chemical processes that cannot be recognized in tube experiments.

A strategy for the identification of peptides for individualized vaccination of tumor patients was presented by **Hans-Georg Rammensee** (Tübingen, Germany), basing his view on the notion that neoplastic cells differ from normal cells with respect to the genes expressed and to posttranslational modification of gene products. T-cells are able to recognize HLA-presented peptides from such differently expressed or modified gene products. How can the power of molecular analysis of the antigen expression in an individual tumor be combined with



*Hans-Georg Rammensee, Thomas Böhm and Günter Hämmerling in a lively discussion on recent research results*

the design of a tailored vaccine containing defined antigens? Five steps have been proposed: Step 1 is the differential gene expression analysis of neoplastic and corresponding normal cells; Step 2 is the differential analysis of human leukocyte antigen (HLA) ligands on neoplastic versus normal cells, including posttranslational modifications; Step 3 is data mining with the aim to select those antigens that might be suitable for tumor attack by the adaptive immune system; Step 4 is the on-the-spot clinical grade production of the constituents of the patient tailored vaccine, e.g. peptides; and Step 5 is then vaccination and monitoring. Application of these procedures in a pilot study on patients suffering from renal cell carcinomas has proven that this approach is technically and logistically feasible.

**Percy A. Knolle** (Bonn, Germany) demonstrated that a number of hepatic cell subpopulations contribute to the induction of immune tolerance in the liver sinusoidal endothelial cells (LSEC) being especially efficient in mediating T-cell tolerance towards exogenous antigens. As a function of their anatomical location and their extraordinary scavenger activity LSEC are well suited to act as antigen presenting cells for T-cells passing through the narrow hepatic sinusoids. Uptake of exogenous antigens and presentation of endocytosed antigens by LSEC on both MHC II and MHCI molecules leads to priming of naïve CD4+ and CD8+ T-cells. Although LSEC bear resemblance to immature dendritic cells, naïve T-cells primed by antigen-presenting LSEC fail to develop into effector cells but rather become anergic. The mechanisms underlying tolerance induction by LSEC remain elusive but appear to involve intensive cross-talk with CD8+ T-cells. Induction of T-cell tolerance by LSEC plays a role in two important situations: induction of tolerance towards oral antigens and mediation of immune escape of tumor cells travelling via the hematogenous route into the liver.



*Immunologist Bruno Kyewski is interested in the research findings of his colleague C. Garrison Fathman*

**C. Garrison Fathman** (Stanford, USA) presented the results of his extensive studies on GRAIL, a gene related to anergy in lymphocytes. In order to prevent autoimmune diseases, the immune system has developed mechanisms by which self-reactive lymphocytes are rendered unresponsive or anergic. So far, the molecular mechanisms of induction of anergy and cell surface markers for anergic T-lymphocytes are largely unknown. Fathman has discovered that during induction of anergy in CD4+ T-cells a novel protein, called GRAIL protein (gene related to anergy in lymphocytes) is induced, which contributes to the anergic status of the cell. Thus, constitutive expression of GRAIL by gene transfer into CD4+ T-cells was sufficient for induction of anergy in vivo. GRAIL was found to belong to the E3 ubiquitin ligases, components of the major protein degradation pathway of a cell. E3 ubiquitin ligase activity and subsequent targeting of specific molecules for proteolytic destruction has, therefore, emerged as a novel key molecular regulator mechanism of immune cell function.

**Thomas Boehm** (Freiburg, Germany) discussed the evolution of lymphoid organs and the origin of the adaptive immune system. He explained that antigen receptors which are generated by random gene rearrangements are subject to quality control on an ontogenetic time-scale. Lymphoid organs probably evolved in order to effectively orchestrate these processes during formation of a self-tolerant repertoire. The formation of the highly specialized microenvironment of primary lymphoid organs requires the action of particular transcription factors. Since most of these transcription factors are evolutionarily conserved, Boehm and colleagues investigated the function of evolutionarily diverged versions of certain transcription factors in the specification of the microenvironment of lymphoid organs, and found, for instance, that the microenvironment of the thymus can be converted into a developmental niche that accommodates the development of all lymphoid cells.

The scientific program of the first day was complemented by poster presentations of six alumni and two young scientists working at DKFZ: **Mihály Bak** (Budapest, Hungary); **Robert Eibl** (Miami, USA); **Marta Enderlin** (Heidelberg, Germany); **Zheng Lea** (Heidelberg, Germany); **Yun Niu** (Tiangin, China); **Sabine Rohrmann** (Baltimore, USA); **Renate Siebenhaar** (Mainz, Germany); **Ilia Toshkov** (Ithaca, USA).

## Some Representative Topics of the DKFZ Research Programs

On the second day of the meeting highlights from the six research programs (RP) of the DKFZ were presented, particularly achievements in cell and tumor biology, genome research, epidemiology, infectious agents and antibodies in cancer evolution and treatment, and innovative cancer treatment by ionizing radiation.

**Christoph Niehrs** presented highlights in RP Cell Biology and Tumor Biology. The focus of the Research Program is on extracellular cues and their receptors as well as on intracellular cascades and transcriptional regulation. Major aims are to characterize extra- and intracellular regulatory networks, to identify target genes of transcription factors and to find ways of molecular interference with these processes. Recent highlights include the analysis of a new family of Wnt antagonists, the dickkopf (dkk) genes. Dkk1 plays an important role in embryogenesis and adult bone physiology (Niehrs). Another highlight is an in vitro skin organ culture system, which has been used to analyze the role of AP-1 family members in paracrine signalling during epithelial-mesenchymal interactions (Angel, Fusenig).

**Stefan Wiemann** from the RP Structural and Functional Genomics discussed the application of large-scale genome analysis and bioinformatics towards a better understanding of the genetic basis of cancer. The program connects the development of technologies with their application for analysis of changes in genomes, transcriptomes, and proteomes. Gene identification, expression profiling, functional analyses, statistics, and data integration are focal points of the Division of Molecular Genome Analysis. The genome-wide screening for DNA copy number, protein annotation with automated task systems, candidate oncogene identification with animal model RNAi screens, automated image analysis of cell arrays, and central mass spectrometry are further complementary approaches within the research program towards the analysis of promising targets for disease prevention and improvement of therapy.

The RP Cancer Risk Factors and Prevention was represented by **Gabriele Nagel** from the Division of Clinical Epidemiology, who introduced the European Prospective Investigation into Cancer and

Nutrition (EPIC). EPIC is a prospective multicentre study that has been implemented to further the understanding of the association between diet and chronic diseases with emphasis on cancer. In Heidelberg, about 25,500 subjects aged 35 to 65 years in women and 40 to 65 years in men were recruited from June 1994 until October 1998. Apart from extensive questions about food intake, the participants were also asked to provide detailed information on lifestyle and medical history. Additionally, the participants also gave blood samples, and anthropometric measures and blood pressure was taken in standardized manner.

**Gerhard Moldenhauer** from the RP Tumor Immunology described the successful use of antibodies in cancer therapy. The main objective of Moldenhauer and colleagues has been to develop novel therapeutic strategies for the treatment of both carcinomas and malignant lymphomas. Several bispecific monoclonal antibodies and recombinant single-chain Fv constructs were produced in order to focus and redirect cytotoxic T-cells against various tumor targets. In collaboration with colleagues at the Heidelberg University Hospital, a clinical trial for patients with advanced ovarian carcinoma and malignant ascites refractory to standard therapy was conducted. Ten women were treated by paracentesis of the ascites and subsequent intraperitoneal instillation of 1 mg of bsAb HEA125xOKT3 at weekly intervals. All patients responded clinically well to the treatment: eight women experienced a complete and sustained remission of ascites production whereas a significant reduction of ascites volume was noted in two of them. In addition, a decrease of the CA125 tumor marker level was observed in the serum of several patients. Thus, intraperitoneal therapy using bispecific antibodies appears to be a promising, easy and cost effective palliative approach for the treatment of recurrent ascites arising from ovarian carcinoma.

**Wolfgang Schlegel** from the RP Innovative Cancer Diagnostics and Therapy presented exciting new developments in cancer treatment with ionizing radiation. Besides surgery, radiotherapy is the most important modality in cancer treatment. At DKFZ, research in radiotherapy concentrates on new methods of conformal irradiation of localized tumours. In this context, special patient positioning and immobilization techniques for stereotactic treatment have been developed, together with 3D treatment planning systems and beam shaping devices (multi leaf collimators). A new and very efficient method based on 3D inverse treatment planning is Intensity Modulated Radiotherapy (IMRT), which was developed at DKFZ starting in 1988 and has been applied for patient treatment since 1997. IMRT is suitable for all complex shaped tumors or lesions growing in the vicinity of critical organs such as brain tumors, head and neck tumors, paraspinal tumours, prostate and breast cancer. In the near future, research in medical physics will focus on image guided radiotherapy and radiotherapy with protons and heavier charged particles (e.g. C-12 and O-16-ions).

**Michael Pawlita** from the RP Infection and Cancer focused on seroepidemiological studies to link Human Papillomavirus (HPV) infections to human cancer. Certain types of HPV are recognized as carcinogens. Antibodies to HPV structural and regulatory (onco-) proteins are epidemiological and potentially diagnostic and prognostic markers of infection and of HPV-associated malignant diseases. Serological analysis is complex due to over 100 serologically distinct HPV types that can infect humans. With Multiplex Serology a new technique has been developed using in situ affinity-purified complete viral proteins and fluorescence-labeled beads as antigen carriers that allows the simultaneous analysis of antibodies to up to



*Should auld acquaintance be forgot?  
Emmanuel Fragoulis, Constantino  
Sekeris (with Elena Sekeris) meet their  
former colleague Günther Schütz.*

100 different antigens. Examples of HPV antibody patterns associated with cancer of the cervix uteri and other anogenital neoplasias, with a subgroup of head-and-neck squamous cell carcinomas and possibly with non-melanoma skin cancers are discussed.

# review

## Perspectives of the DKFZ, Poster Awards and a Symphony

In addition to the scientific sessions, a memorable social event of the Alumni Meeting was the reception of all participants by the DKFZ Management Board in the evening of the first day. In a vivid speech the Chairman and Scientific Director of the Management Board, **Otmar D. Wiestler**, reflected on “Perspectives of cancer research at the DKFZ”. He gave an overview of the current situation and intermediate and future goals of the research program, and particularly announced the establishment of an interdisciplinary Comprehensive Cancer Center (NCT: Nationales Centrum für Tumorerkrankungen Heidelberg), which should be completed in December 2005.

Three scientists were honoured with awards for their scientific poster presentations, each endowed with a travel grant of 500 Euros:

**Mihály Bak** (Budapest, Hungary): “Expression and prognostic value of the lung resistance-related protein (LRP) in germ cell testicular tumors.”

**Robert Eibl** (Miami, USA): “Single-molecule adhesion forces on living metastatic cells.”

**Yun Niu** (Tiangin, China): “Expression of cell cycle regulators in ductal carcinoma in situ and papillomatosis of the breast.”

A pleasant setting was provided by the Heidelberg MD Orchestra conducted by Professor Michael Steinhausen. Together with the two soloists, Almut Nikolayczik (Violin) and Jutta Rübenacker (Viola), a symphony by Wolfgang Amadeus Mozart was performed. During a buffet dinner the participants discussed scientific and personal matters of mutual interest in a friendly atmosphere.



## Relaxing on a Neckar Boat Trip

After all tasks had been fulfilled, a boat trip on a warm and brilliant sunny afternoon gave not only an excellent opportunity for relaxation but also for admiration of unique views of Heidelberg with its neighboring villages embedded in the beautiful wooded hills along the Neckar valley. Some scientific discussions continued on this occasion, but the exchange of many other personal experiences during the times at the DKFZ and thereafter predominated. It was obvious that all participants enjoyed this concluding social event and are looking forward to the next alumni meeting in Heidelberg.



*Mihály Bak and Robert Eibl received awards for their poster presentation*



*The Heidelberg MD Orchestra contributed a musical highlight: a symphony by Mozart*

# perspectives



## The Alumni Association is born and needs support to grow

An important part of the meeting was the assembly of about 30 participants in order to found an alumni association, named the Alumni Deutsches Krebsforschungszentrum Heidelberg e.V. The assembly passed a constitution, the electronic version of which is available in German and English languages via the home page of the DKFZ ([www.dkfz.de/alumni](http://www.dkfz.de/alumni)), in which the

*above: Dedicated to the Alumni Association: Ilana Lowi, Konrad Buschbeck and Mieczyslaw Choranzyc*

*Peter Bannasch and the poster prize winner Yun Niu*

aims of the non-profit association are detailed. This was formally signed by 20 participants. Under the chairmanship of Professor Harald zur Hausen, the Founding Members elected the Members of the Board: Professor Peter Bannasch, Dr. Konrad Buschbeck (Treasurer), and Elfriede Mang (Secretary). The Chairman and Scientific Member of the DKFZ Management Board, Professor Otmar D. Wiestler, is a Member of the Board of the Association by virtue of his office (ex officio). The Board elected Peter Bannasch as Chairman. The assembly decided not to request membership fees at present, but to ask for donations from members and any other person or institution supporting the aims of the association. We are obliged to two founding members from the U.S., namely Dr. Gunter Rütter, Washington, and Dr. Ilia Toshkov, Ithaca, who spontaneously offered generous donations to the association during the general assembly. *Peter Bannasch*

## How to become a Member of Alumni DKFZ Heidelberg e.V.

We are primarily interested to bring together all former guest scientists as well as former and present co-workers of the DKFZ from all over the world who would like to keep their links and continue to further the important aims of this institution. We invite you to become a member of Alumni Deutsches Krebsforschungszentrum Heidelberg e. V. We kindly ask you to complete a membership application form which is available in electronic version or can be provided by the Alumni Secretariat.

**No membership fees, but donations are welcome!**

Our intention is to avoid any fixed membership fee for the association in the foreseeable future. It goes without saying, however, that we will only be able to accomplish our aims, particularly the development of an international net-

work of DKFZ Alumni and the sustained support of the international exchange of young scientists devoted to cancer research, if we raise appropriate funds. The board appeals to all present and potential future members of the association to support the activities of the association, some of which are described in this newsletter, by personal donations and/or the stimulation of donations by institutions. However, we would like to emphasize that donations are not a prerequisite for membership.

### Bank account

Germany  
Sparkasse Heidelberg  
(Bank code number 672 500 20),  
Account-Nr.: 1000597810  
Abroad  
Sparkasse Heidelberg, IBAN:  
DE31672500201000597810,  
BIC/SWIFT: Solade S1 HDB

*Renowned for her organizational skills: Elfriede Mang*



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## Get-together of Alumni and current Scientists of DKFZ during AACR Meeting 2005

During the forthcoming 96<sup>th</sup> Annual Meeting of the American Association for Cancer Research (AACR) in Anaheim, Orange County, California, attending Alumni and current Scientists of the DKFZ are cordially invited to a reception, taking place in the Anaheim Hilton on Monday, April 18, between 6:00 pm and 8:00 pm. The Chairman and Scientific Director of the DKFZ Management Board, Prof. Otmar D. Wiestler, will give an overview on the present research programs of the DKFZ at this occasion. The Chairman of the Board of Alumni DKFZ, Prof. Peter Bannasch, will present the development of this Association. There should be sufficient time to discuss and, perhaps, also realize the establishment of a DKFZ Alumni Club in the USA.

*Please inform the Alumni Secretariat (E.Mang@dkfz.de) at your earliest convenience whether you intend to participate in the reception.*

## First Chinese DKFZ Alumni Meeting in Beijing 2005

During the past two decades Chinese colleagues represented the largest group among Guest Research Scientists from abroad in the German Cancer Research Center. Many of these colleagues made considerable contributions to cancer research in this period. Hence, it was suggested at the foundation assembly of Alumni DKFZ in 2004 that one of the first Alumni meeting abroad be conducted in China. When we considered an appropriate time point, place and schedule for this meeting, we were glad to learn that there was already the intention of two institutions of the Helmholtz Association, namely the DKFZ in Heidelberg and the Gesellschaft für Biologische Forschung (GBF) in Braunschweig, to organize a joint Sino-German Workshop on Cancer and Infectious Diseases in Beijing in 2005. In view of this coincidence the Board of Alumni DKFZ decided to organize the Alumni Meeting in close contact with the Sino-German Workshop which will immediately follow this meeting (see below). All Chinese DKFZ Alumni are cordially invited to participate in both the Alumni Meeting and the following workshop.

We would highly appreciate the presentation of ongoing scientific work in posters by all Chinese Alumni in the afternoon of Sunday, June 5. After the poster presentations some time for the foundation of a Chinese DKFZ Alumni Club has been provided in the program. Chinese DKFZ Alumni may ask for reimbursement of a first-class sleeping wagon return train ticket, and accommodation in the Sino-German Center for Research Promotion. Please contact the Chief Representative of the Helmholtz Association in Beijing, Dr. Hong He (Landmark Tower 2-1723, 8 Dongsanhuan North Road, Chaoyang District, 100004, Beijing; e-mail: hong.he@helmholtz.cn) for further details. The authors of the three most outstanding posters will receive awards (300 Euro each). The Reception for the DKFZ Alumni on Sunday evening will at the same time serve as a Welcome Reception for the participants of the following workshop. We sincerely hope that both the Chinese and the German participants will have an excellent chance to exchange ideas of mutual interest on this occasion. I look forward to seeing you in Beijing!

*Peter Bannasch*



## Sunday, June 5, Sino-German Center for Research Promotion

### 12.00 h Welcome Lunch

### 13.00 h Poster Presentation and Discussion with Tea and Coffee

### 16.30 h Foundation of a Chinese DKFZ Alumni Club

*Peter Bannasch*, Chairman of the Board Alumni DKFZ  
Introduction: Activities and Aims of Alumni DKFZ

### 17.00 h Reception

#### Welcome and Introduction

*He Hong*, Helmholtz Association Beijing  
*Peter Bannasch*, Alumni DKFZ

#### Research Programs of DKFZ and GBF

*Otmar D. Wiestler*, Chairman of the DKFZ Management Board:  
Perspectives of Cancer Research at the DKFZ  
*Rudi Balling*, Scientific Managing Director of the GBF:  
Perspectives of Biotechnological Research at the GBF

**Buffet Dinner** with traditional Chinese music



*Sino-German  
Center for Research  
Promotion in Beijing*

## Sino-German Workshop on Cancer and Infectious Diseases June 6 – 8, 2005, Sino-German Center for Research Promotion

### Monday 6<sup>th</sup> June

#### Global Health Research:

##### What are the new challenges?

(chair: *Depai Liu*, President CAMS)

Speakers: *Depai Liu*, CAMS; *Otmar D. Wiestler*, DKFZ; *Rudi Balling*, GBF; *Chinese Scientist*.

#### Molecular Mechanisms of Pathogenesis

(chair: *Otmar D. Wiestler*, DKFZ)

Speakers: *Chen Jie*, CAMS; *Singh Chhatwal*, GBF; *Jürgen Wehland*, GBF; *Peter Lichter*, DKFZ.

#### Animal models: From Mice to Men

(chair: *Rudi Balling*, GBF)

Speakers: *Christof Niehrs*, DKFZ; *Qin Chuan*, CAMS; *Andreas Lengeling*, GBF; *Jan Buer*, GBF.

#### Parallel topic discussions and laboratory visits

Topics: Pathogenesis, Animal Models, Immunity, Chemical Biology, Systems Biology

Evening meal and informal discussions

### Tuesday 7<sup>th</sup> June

#### Infection and Immunity

(chair: *Scientist of GBF*)

Speakers: *Zihe Rao*, CAS; *Dirk Heinz*, GBF; *Peter Krammer*, DKFZ; *Matthias Gunzer*, GBF; *Jean Rommelaere*, DKFZ.

#### Cancer and Immunity

(chair: *Peter Krammer*, DKFZ)

Speakers: *Lutz Gissmann*, DKFZ; *Adelheid Cerwenka*, DKFZ; *Margareta Müller*, DKFZ; *Chinese Scientists*.

#### Epidemiology

(chair: *Chinese Scientist*)

Speakers: *Xue Zhang*, CAMS; *Kari Hemminki*, DKFZ; *Helmut Bartsch*, DKFZ.

#### Parallel topic discussions and laboratory visits

Topics: Pathogenesis, Animal Models, Immunity, Chemical Biology, Systems Biology

Evening meal and informal discussions

### Wednesday 8<sup>th</sup> June

#### Chemical Biology:

##### The need for small molecules

(chair: *Chinese Scientist*)

Speakers: *Ronald Frank*, GBF; *Gang Liu*, CAMS; *Wen Han Lin*, Peking University; *Dieter Keppler*, DKFZ.

#### Systems biology – from experiment to prediction

(chair: *Peter Lichter*, DKFZ)

Speakers: *Ursula Klingmüller*, DKFZ; *An-Ping Zeng*, GBF; *Chinese Scientists*.

#### Two Parallel Round-table discussions on Cancer

(Chairmen: *Xue Zhang* and *Otmar D. Wiestler*)

#### and Infectious Diseases

(Chairmen: *Mifang Liang* and *Rudi Balling*)

After the meeting small delegations travel to Shanghai, Wuhan and Xi'an.

# people

## Appointments

**Dr. Dirk Bossemeyer**, formerly member of the Division of Pathochemistry, is now in charge of the Research Group Structural Biochemistry.

**Dr. Roland Eils** has accepted a C4-professorship at the Faculty of Biosciences at Heidelberg University. Thereby he is now in charge of the Division of Bioinformatics and Functional Genomics at the Institute of Molecular Biotechnology of Heidelberg University and at the same time heads the Division of Theoretical Bioinformatics at the DKFZ.

In June 2004 **Prof. Michael Eisenhut** was appointed head of the Division of Radiopharmaceutical Chemistry, of which he had provisionally been in charge since September 2002.

**Prof. Stefan Hell** is head of the new Research Group High Resolution Optical Microscopy, a unit established in cooperation with the Max Planck Society.

Since January 2005 **Dr. Dr. Peter Huber** is head of the Clinical Cooperation Unit Radiation Oncology, a position to which he had previously been provisionally appointed.

Since the end of June 2004 **Prof. Bruno Kyewski**, formerly a member of the Division of Cellular Immunology, has been head of the newly established Division of Developmental Immunology.

**Dr. Frank Lyko** is now provisional head of the recently appointed Division of Epigenetics.

**Dr. Margareta Müller**, formerly member of the Division of Differentiation and Carcinogenesis, heads the Research Group Tumor and Microenvironment.

**Dr. Martin Müller**, formerly member of the Division of Genome Modifications and Carcinogenesis, is in charge of the Research Group Tumorvirus-specific Vaccination Strategies.

In May 2004 the Research Group Molecular Neuro-Oncology headed by **Dr. Wilfried Roth** started its work at the DKFZ.

Since December 2004 **Dr. Matthias Weiss** is in charge of the Research Group Cellular Biophysics. The DKFZ group is one out of three junior research groups of the Center for Modelling and Simulation in the Biosciences (BIOMS) in Heidelberg.

## Retirements

**Prof. Norbert Fusenig**, Head of the Division of Differentiation and Carcinogenesis, retired on 1<sup>st</sup> April 2004.

**Prof. Herwig Ponstingl**, Head of the Division of Molecular Biology of the Mitosis, retired on 1<sup>st</sup> October 2004.

## Awards



**Hassan Adwan** of the Toxicology and Chemotherapy Group received the Bon-dronat Scientific Award (10,000 Euro) for his work on bone metastases.

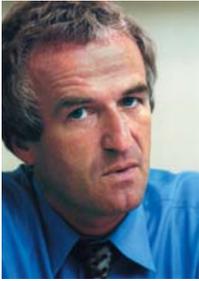


**Dr. Annette Bornhäuser**, Member of the Staff Position Prevention of Cancer, received the Pfizer Scientific Award "Living Smokefree" (3,000 Euros) for her publishing recommendations for an effective tobacco control policy in Germany.



For their fundamental findings in the field of immune defense, **Dr. Philipp Beckhove** and **Dr. Markus Feuerer**, Division of Cellular Immunology, were awarded the Walther and Christine Richtzenhain prize of 10,000 Euros.

# people



**Prof. Peter Lichter**, Head of the Division of Molecular Genetics, received the prestigious Deutsche Krebshilfe Preis by the German Cancer Aid for the development of a novel technique in genome analysis and its establishment for clinical use.



**Dr. Frank Lyko**, provisional head of the Division of Epigenetics, has been selected for the "TR100 list" by the U. S. magazine "Technology Review". The journal has lauded him as one of the 100 top young innovators of the world.



**Prof. Otmar D. Wiestler**, Chairman and Scientific Director of the DKFZ Management Board, and **Prof. Jürgen Becker** (Würzburg University), have been honoured with the translational part of the German Cancer Award, endowed with 7,500 Euros. Wiestler received the prize for establishing the reference center for brain tumors in Bonn and for his contribution to quality management in the diagnosis of brain tumors.



The German Verdienstkreuz am Bande des Verdienstordens der Bundesrepublik Deutschland was awarded to **Prof. Werner Franke**, Head of the Division of Cell Biology and his wife **Brigitte Franke-Berendonk** for their continuous efforts against doping in sports on a national and international level.



**Dr. Stephan Herzig** and his Research Group Molecular Metabolic Control is one of four scientific teams being awarded grants from the Novartis Foundation for Therapeutic Research. The molecular biologists will receive funds of 150,000 Euros for a planned project on arteriosclerosis research.



For his pioneer work in tumor virology and his outstanding achievements as the Chairman of the DKFZ Management Board for two decades, **Prof. Harald zur Hausen** received the Große Verdienstkreuz des Verdienstordens der Bundesrepublik Deutschland.



**Dr. Bernhard Radlwimmer** of the Division of Molecular Genetics at the DKFZ and **Dr. Christel Herold-Mende** (Neurosurgical Clinic of the Heidelberg University) received the Sibylle Assmus Award (10,000 Euros) for the identification of tumor markers in brain tumors.



**Dr. Angela Risch**, Division of Toxicology and Cancer Risk Factors, obtained one of the two Emil Salzer Awards 2004, endowed with 5,000 Euros, for her research on the impact of genetic factors on the risk of lung cancer.

# report

## Visit to a Global Industrial Player: the BASF

by Marina Edelson-Averbukh

*On one of these rare sunny March mornings our bus departed from the main building of DKFZ heading to the Ludwigshafen BASF (Badische Anilin & Soda Fabrik) complex. The way to Ludwigshafen took only about twenty minutes, but the trip seemed to us even shorter as everybody was busy talking to each other, asking about the country that he or she had come from and about their research in the DKFZ. There was an atmosphere of general excitement and anticipation of an interesting tour.*

Upon arrival at the BASF site, we were warmly invited by our guide, Dr. Frank Höfer into a seminar room of one of the research buildings of the plant to hear a couple of lectures. The presentations by Dr. Barbara Jessel (university relationship coordinator of BASF) and by Dr. Corinna Klopprogge (head of a biotechnology laboratory) were gripping indeed. Dr. Jessel told us about the BASF history which started from production of synthetic colours in 1865 and continues nowadays with manufacturing of more than 8,000 various products. The broad product range of BASF today includes chemicals, plastics, performance products (additives to paper, textile, colors, etc.), agricultural and nutrition products. One of the most remarkable recent developments in the technology giant is establishment of the BASF verbund (cooperation). The production verbund on BASF means that the manufacturing plants are linked into a network where a by-product of one of them becomes a raw material for another one. This amazing structure of the BASF verbund not only saves money (500 million Euros per year in Ludwigshafen alone), but also protects the environment by helping to reduce waste and emissions. The scientific lecture of Dr. Klopprogge unveiled the captivating world of biotechnology research carried out in BASF. Dr. Klopprogge lucidly explained the role of biotechnology in the mass production of BASF chemicals, such as vitamin B2 and lysine. The use of the microorganisms for these syntheses allows biochemists to replace complex and multistage conventional chemical approaches by fast and cost-effective processes. And still more interestingly, BASF scientists use techniques of metabolic engineering to modify the microorganism strains making them optimal for biocatalysis.

After the lectures we were anxious to have a look inside the BASF plants in order to see by our own eyes how this incredibly huge complex functions. At this point everybody of us got a helmet and safety goggles with which we didn't part until the end of the visit. The first stop was the Bio Pilot plant in which the testing of the biotechnological research is carried out. Our excursion was guided by Dr. Bryan Cooper (head of this Biotechnicum) who arrived in BASF from USA at the beginning of eighties and was one of the founding scientists of the plant. He showed us the fermentation laboratory where we had a possibility to see the laboratory fermenter (special stirrer vessel in which the fermentation processes take place) and learn about its structure and the principle of its function. Then we visited one of the workshops of the Bio Pilot and continued to a short excursion to the historical part of BASF guided by Dr. Höfer.

Our next destination was the Steamcracker, one of the first and most important plants of BASF, which is busy with breaking down (by steam and strong heating) the petroleum fraction naphtha into ethylene, propylene, dienes and aromatics. It is "the heart" of the BASF verbund network supplying a wide variety of chemical substances (some of



*Equipped with helmets a group of guest scientists of DKFZ had a look inside BASF plants, among them the steamcracker, the "heart" of the BASF verbund*

them are obtained in a rapidly branching series of upgrading chain reactions of the main cracker compounds) to other BASF plants. For example, ethylene and benzene, produced during the cracking, react to give ethylbenzene which after dehydrogenation gives rise to a styrene monomer – the base product for BASF styrenics. The Steamcracker produces 400,000 tons of ethylene per year and only 20 percent of this is destined for the external market. The extremely interesting and detailed explanation of the cracker process was presented by Dr. Helmut Wörz (former head of the steamcracker plant) in a big hall housing the model of the Steamcracker plant. After the end of the lecture, accompanied by the demonstration of the samples of the materials and compounds being used and produced in the cracker process, we had an opportunity to walk in the area of the plant and to gaze at the giant-size constructions surrounding us. Interestingly, in spite of the huge amounts of the chemicals involved in the processes going on inside the towering reservoirs and wiggling tubes, the air in the terri-

tory of the steamcracker plant is relatively clean. Dr. Wörz told us that, for example, the concentration of gasoline (one of the cracker products) in the territory of Steamcracker is 0.3 ppm (parts per million) while the concentration of the material on the city roads can reach 30 to 50 ppm.

After leaving the Steamcracker, we had a 45-minute bus tour through the territory of the BASF complex which extends for no less than 7.11 km along the Rhein. Among the sites we passed by were the acrylic acid plant (acrylic acid is a basic material for superabsorbents used in baby diapers, for example), the plant for production of polytetrahydrofurane which is used for manufacture of elastic textile fibers, the chemical pilot plant (for 1-100 kg-scale chemical reactions), the chlorine plant and many others. We also had a chance to approach the safety torches of BASF reaching 130 meters in height.

At the end of the day, on our way to Heidelberg there was a feeling that everybody in the group is well familiar with each other. We were eager to share the impressions from the delightful excursion. We are thankful to Alumni DKFZ Heidelberg for the opportunity to visit one of the World's leading chemical companies and at the same time to meet many fellow guest scientists staying at the DKFZ.

## Recreation in the Botanical Gardens

The Botanical Gardens of the University were founded in 1593; the area in the Neuenheimer Feld has been used for this purpose since 1915. For further details like ongoing research activities, visitor information, public lectures and a photo gallery please see [www.botgart.uni-hd.de](http://www.botgart.uni-hd.de).

The Botanical Gardens lie in the vicinity of the German Cancer Research Center. Therefore, in my lunch break I like to make a stroll admiring the plants from



throughout this world, especially America, Asia and Africa. In the exceptional hot summer of 2003, it was so comfortable to sit beyond one of its huge old trees, enjoying an ice cream. Several birds find their food in this natural spot. Frogs exist in the pond, and water lilies grow in different significant colours. The air is much better than in the crowded city of Heidelberg, and the calm atmosphere makes it a good place for recreation. Different parts of the Botanical Garden show various types of vegetation like ferns, succulents or orchids. In ten minutes you can pass a variety of plants where you otherwise would need to travel many kilometers. In "Golden October" the wind makes the coloured leaves dance. Throughout the whole year the garden shows exciting views and abundant blossoms. Unfortunately, in the past few years controversial discussions were held to remove this Garden from the Neuenheimer Feld due to other needs. Recently the local press reported that excavators will soon dig in the botanical gardens. In spring 2005, the botanical gardens will undergo a fundamental reconstruction supported by sponsors. *Elfriede Mang*

## Obituary

On September 14, **Professor Otto Westphal**, former Scientific Chairman of the DKFZ Management Board, passed away at the age of 91. He became the first president of the German Society of Immunology and thereby he helped to establish this subject as a field of study at German universities. His work on the tumor-destroying effect of endotoxins, molecular chains in the bacterial cell wall, contributed to the development of

important cancer drugs. From March 1982 to April 1983 Professor Westphal held the position of the Scientific Director of the DKFZ. During this time he intensively supported scientific research, and later on as a Member of the Board of Trustees (until 1986) he continued to do so. Staff and employees continue to hold his memory in honour.

## Impressum

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in der Helmholtz-Gemeinschaft

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### Editing:

Dagmar Anders, Dr. Malcolm Moore

Images: p. 1: Philipp Rothe, p. 2: Yan de Andres, p. 3: Israeli Ministry of Science and Technology (top), Axel Kull (bottom); p. 4: Heide Zerban; p. 5–8: Philipp Rothe; p. 8: Elfriede Mang (top); p. 9: Philipp Rothe; p. 11: Sino-German Center for Research Promotion; p. 12: private (top), Brigitte Engelhardt (middle), Dagmar Welker (bottom); p. 13: Josef Wiegand, Yan de Andres, Brigitte Engelhardt, Dagmar Welker, privat; p. 15: Jianhong Li; p. 16: Botanical Gardens of Heidelberg University, Dr. Peter Sack