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dkfz. GERMAN CANCER RESEARCH CENTER IN THE HELMHOLTZ ASSOCIATION

alumni

DEUTSCHES KREBSFORSCHUNGSZENTRUM

Second General Alumni Meeting Heidelberg: Eiman Aleem, Ada and Donald Olins enjoy the lovely views during the Neckar boat trip .

Dear DKFZ Alumni,

The headline event of our Association in 2006 was the Second General Alumni Meeting in Heidelberg, which was considered a great success by all participants. A detailed report on this meeting, containing abstracts of the outstanding scientific contributions of internationally renowned Alumni constitutes the core of this Newsletter. Additional activities included poster presentations and awards, highlights from the DKFZ Research Programs, a Reception with authoritative speeches on perspectives of cancer research and research funding, the General Assembly of our Association, and last but not least a boat trip on the Neckar.

Alumni meetings abroad were held during the conferences of AACR 2006 in Washington, and EACR 2006 in Budapest. Colleagues attending the Alumni reception in Washington took the initiative to address all scientists in America in order to create an All American Alumni Club. For the future of both the DKFZ and our Alumni Association it is very promising that the Alumni of the Life-Science Lab have expressed great interest in a close cooperation (see page 14). We highly welcome this initiative, and sincerely hope that joint efforts between this fountain of youth and our somewhat older Alumni will be of mutual benefit.

The importance of international links in cancer research is emphasized in two contributions to this Newsletter, namely the further formalization of a longstanding French-German cooperation in tumor virology, and the report of a former Russian guest scientist on molecular changes in pediatric brain tumors. The increasing number of guest scientists is reflected by a lively description of a very informative visit to the pharmaceutical company Merck looking back over a history of 300 years. Although the main building of the DKFZ is only some 30 years old, there was an urgent need for a fundamental reconstruction permitting modern science in a modern building as outlined overleaf. In spite of this enormous effort, research is going on in the DKFZ without any serious interruption, as documented by many new appointments of leading scientists and by the large number of awards given to members of the DKFZ recently.

On behalf of the Board of Alumni DKFZ I would like to express my appreciation to all registered members who have supported our activities by voluntary contributions. It is only some weeks ago that we had asked for such donations and we are confident that additional contributions will be provided. In this context, we gratefully acknowledge the generous donations by the Dietmar-Hopp-Foundation and by Roche Diagnostics sponsoring the Second General Alumni Meeting. A recent sponsorship agreement with Merck Pharma opened particularly promising horizons for a long lasting cooperation of this company with Alumni DKFZ in the future, and we expect more companies to follow these encouraging examples.

Finally, I invite all former and current members of the DKFZ who take advantage of, or are ready to support, the activities of the Alumni Association, to formally register as members if they have not done so previously. With best wishes from the center of the growing cancer network extending from Heidelberg all over the world

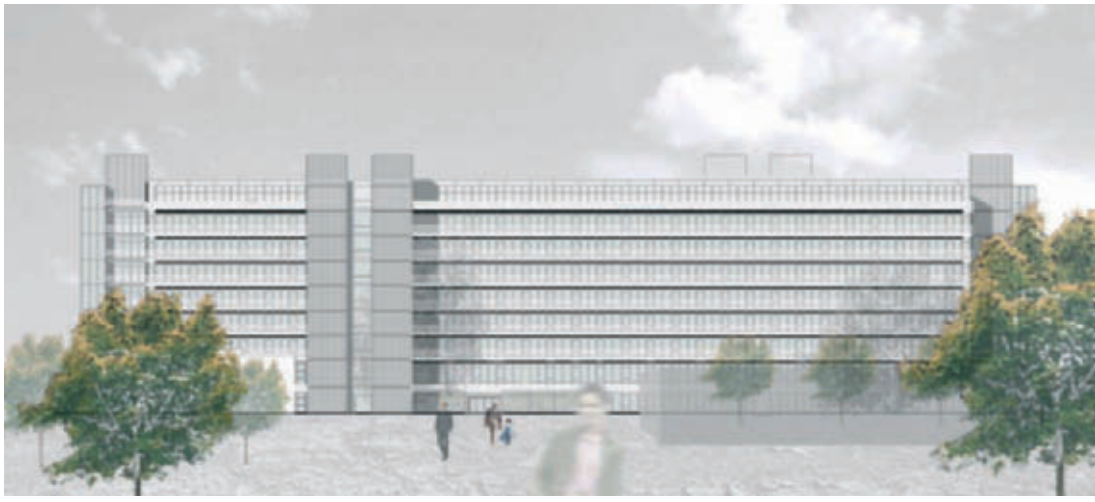
Peter Bannasch

perspectives

Modern Science in A Modern Building

by Josef Puchta

After more than 30 years of intense use it was high time to renovate the main building of DKFZ. The technical installations and the laboratories don't meet the modern standards required for our high quality of science. The renovation measures will take quite a while. However, when everything is finished, we will be able to carry out science in modern high standard laboratories.



Innovative architecture housing innovative research (right). However, it will take quite a while until the former building (above), established in 1972, will belong to the past.

Due to the large extent of the necessary renovation measures it was first considered to pull down the whole main building and build a new one. But this would have been the more expensive solution. Furthermore the necessity of moving out the whole staff without having the needed premises at our disposal argued against this option. So we decided to reconstruct the main building in two phases: At first the eastern part will be renovated from top to bottom while in the western part of the building work can be continued. After having finished the eastern part after 1.5 years, roles will be switched.

Our department for technical services developed an ingenious concept for the move of the affected departments. About 5000 sqm have been rented in the "Technologiepark" (technology park) close by and equipped with the necessary infrastructure for laboratories. Most of the departments from the eastern part of the main building have moved to those new premises in Technologiepark, and will stay there until they can move back into the reconstructed western part in the end of 2009. Staff working now in the western part will move to the newly renovated eastern part.

The renovation measures are resulting in an enormous burden for the whole staff of DKFZ. Nearly all colleagues are affected either by the troubles of moving or by annoyance due to noise and dust. But we believe the reconstruction is worth while. Afterwards we will be able to carry out science in modern high standard laboratories. Aside from the technical aspects, the main building will get a completely new design: The 2-corridor-system will be abandoned in favour of only one not centred hall way leading along the front on one side and along the back on the other side of the main building. In the middle of each floor an area for communication will be arranged with a kitchenette. The presently small laboratories will be substituted with open-plan workspaces.

In 2010, when the multi-storey building is finished, the part of the building called "Radiology" will be compltely rebuilt. The present annexe, including the former reactor building will be demolished to clear space for a new center for patients. It is planned to install all medical devices like PET, Linac or Magnetic Resonance Imaging closely together in order to improve the procedures for patients and scientific progress. This renovation measure will take another three years.

From now on we have to bear disturbances connected with the renovation measures for about six years to a greater or lesser extent. Our department for technical services and the side management are doing their best to keep the colleagues unmolested. We set great store by informing the staff about individual affectedness, but also about progress of construction work. To the latter end, our department for press and public relations provides information by intranet, our journal "dkfz intern" and by an advertising pillar in the entrance area of the main building.

French-German Alliance in Tumor Virology

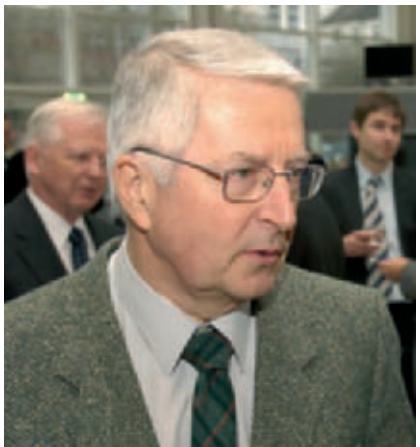
by Heide Zerban-Michelfelder and Jean Rommelaere

French-German cooperation has a long tradition at the DKFZ. An outstanding example of this is in the research co-operation programme, which was set up recently between the DKFZ and the Cancéropôle du Grand-Est (covering the eastern part of France) in order to unravel the advantages and disadvantages of viruses in oncology.

Signing the contract is the starting signal for virologists on both sides of the Rhine. The DKFZ Management Board together with the President of the Regional Council of Alsace and the Director of Cancéropôle; at the back: Germany's Federal Minister for Education and Research Dr. Annette Schavan and her French colleague François Goulard with the French ambassador Claude Martin.

In 1993 a joint research unit was established in the field of tumor virology between the French National Institute of Health and Medical Research (INSERM, Institut National de la Santé et de la Recherche Médicale) and DKFZ. Last year, this unit headed by Professor Jean Rommelaere was re-established for a new term.

In 2002 the President of France Jacques Chirac promulgated the Charter of Paris – an international plan of action against cancer to support the research and fight against cancer with a budget of 1.5 billion Euro until the year 2007. The central point of this ambitious action plan was the establishment of a virtual National Cancer Institute (INCa, Institut National du Cancer) which started in spring 2005 in Paris. One of the main tasks of INCa is the promotion of oncology networks.



Pierre Oudet, Scientific Coordinator of Cancéropôle du Grand-Est

Seven so called Cancéropôles were founded, each covering a distinct region of France. These regional multicentric networks of excellence are composed of teams located in cancer centers, university hospitals and research organizations. Among other missions, scientific exchange with institutions abroad is encouraged by the Cancéropôles. On February 23rd 2006, a convention on a research co-operation programme was signed at the DKFZ by representatives of both countries, in the presence of the Ministers of Research of Germany, Annette Schavan, and France, François Goulard.

Both partners decided to combine their research means and efforts to better understand the role of human papillomaviruses (HPV) in the development of cervical cancer and other malignant tumors (e. g. non-melanoma skin cancers). The virologists from both sides of the Rhine will join their efforts to unravel the contributions of HPV and cofactors in the initiation and progression of tumors. Besides basic research aspects, issues of direct relevance to clinical practice will be addressed. The main aim is to identify new prognostic markers and elaborate novel therapeutic protocols. More particularly the researchers want to develop new molecular HPV tests replacing the cellular tests presently in use to allow a more refined diagnosis and earlier recognition of HPV-related (pre)cancerous lesions.

Jean Rommelaere

This French-German cooperation is set for five years with a budget of 1.4 million Euro per year. An important component of this cooperative agreement strives for an intensive personnel exchange of scientists, clinicians, PhD students, and technicians. In addition, it is planned to establish technological platforms accessible to both partners, in particular in the field of genomics and proteomics. This commitment illustrates the willingness of DKFZ to become more internationalized. This is already achieved at the individual level through hosting scientists from abroad, as testified by the large number of DKFZ Alumni scattered all over the world. The joint programme of DKFZ and Cancéropôle du Grand-Est exemplifies another, complementary level of DKFZ opening through international agreements.

review

Second General Meeting of Alumni DKFZ Heidelberg

The second General Meeting of the Alumni Association took place in the Communication Center of the DKFZ from May 12 till 13. Beside current DKFZ Scientists, Alumni from China, Egypt, Finland, Germany, India, Italy, Luxembourg, Poland, Spain, Switzerland and the USA were among the 150 participants, providing an ideal basis to achieve one of the main aims of the Alumni Association, namely the worldwide promotion of personal contacts and the mutual exchange of scientific ideas between former and current members of the DKFZ.

Topics Presented by DKFZ Alumni: Invited Oral presentations

During the first day the demanding scientific program was exclusively covered by internationally renowned DKFZ-Alumni who presented important aspects of the regulation of gene expression and cell replication, of the differentiation of hematopoietic stem cells and their application to cancer therapy. The lectures reflected the state of the art in the respective research areas and stimulated a lively discussion. Short abstracts give an idea of the main topics.

Regulation of Gene Expression and Cell Replication

Peter B. Becker (Adolf-Butenandt-Institut, LMU, Munich)
ATP-dependent remodeling by ISWI- containing complexes

ATP-consuming nucleosome remodeling machines are indispensable for the functioning of eukaryotic genomes. They contribute to the assembly and maintenance of chromosomes, the detection and repair of DNA damage, the replication of the genomes, the recombination of chromosomal segments as well as faithful execution of gene expression programs. Nucleosome remodeling ATPases reside in large multiprotein complexes in association with regulators and targeting subunits. Their deregulation frequently correlates with malignant tumor phenotypes. One of the current models for nucleosome remodeling assumes that these machines act as 'anchored DNA translocases'. Bound to the histone moiety of the nucleosome they translocate on either the adjacent linker DNA or on internal DNA, or both. This leads to a displacement of a DNA segment from the histone surface, which may be propagated around the histone octamer for nucleosome movement, or remain trapped on the surface of the nucleosome to generate a state of increased accessibility of nucleosomal DNA. Given that remodeling complexes have several chromatin binding domains, one has to consider the possibility that these machines have non-catalytic, structural roles in certain chromatin environments.
ATP-dependent nucleosome remodelling synergises with covalent histone modifications to alter chromatin structure. The nucleosome remodeling ATPase ISWI catalyses the sliding of histone octamers on DNA. We now found a novel principle, by which these two activities may be integrated. ISWI is acetylated at lysine (K) 753 by the acetyltransferase GCN5 in vivo and in vitro. The sequence surrounding K753 resembles the N-terminus of histone H3, where the corresponding lysine, H3K14, is also a prominent substrate of GCN5. This finding raises the exciting possibility that properties of nucleosomes and remodelling enzymes may be regulated in concert by acetylation.
We found ISWIK753ac to be particularly abundant in the earliest developmental stages. Remarkably, this protein was found concentrated on mitotic chromosomes of synchronously dividing preblastoderm nuclei and on the prophase I-arrested meiotic karyomer of the germinal vesicle, in contrast to bulk ISWI, which is excluded from condensed chromatin. Thus, K753 acetylation marks an ISWI form with novel, unprecedented properties and functions.


Francis Stewart


Peter Becker

Stewart, Francis (University of Technology, Dresden)
Epigenetics of active chromatin

Until recently, epigenetic mechanisms have been equated with the inheritance of heterochromatin, exemplified by DNA methylation in mammals. Evidence that transcriptionally active states of chromatin can also be epigenetically maintained is now accumulating. This paradigm shift began with the realization that DNA methylation is secondary to a more universal mechanism for epigenetic silencing based on methylation of histone 3 lysine 9 (H3 K9) for constitutive heterochromatin and H3 K27 for facultative heterochromatin. Evidence that active chromatin states may also be epigenetically maintained came from the realization that other histone lysine methylations, mainly at H3 K4, characterize active chromatin and preclude H3 K9 methylation. The functional opposition of these two classes of histone lysine methylation was further supported by link-

age to the antagonism between Polycomb- and trithorax-Group (PcG and trxG) action. The association of trxG action with H3 K4 methylation and PcG action with H3 K27 methylation provides a molecular explanation for this antagonism.
The silencing methylations at both H3 K9 and H3 K27 are epigenetically maintained via positive feedback loops. Recent evidence indicates that epigenetic maintenance of active chromatin occurs in the same way, because a constituent protein of all H3 K4 methyltransferase complexes, WDR5/SWD3 binds to methylated H3 K4.
These observations support a polarization model of chromatin, which is based on opposing positive feedback loops. Both active and heterochromatic states involve several positive feedback loops that reinforce the local status quo. Hence, each state has an implicit epigenetic status that adds stability and reduces the chances of inadvertent transitions to the other state.
Epigenetic mechanisms are thought to play important roles in lineage commitment during development. The simplest model suggests that the epiblast is pluripotent because there are relatively few epigenetic marks in chromatin. Lineage commitment restricts pluripotency because epigenetic marks are imposed on chromatin. These marks are likely to include histone methylations, which can direct inheritable states of gene silencing or activation. This model also suggests that cellular identity in the adult is maintained, in part, by epigenetic mechanisms.


Walter Keller

Walter Keller (Department of Cell Biology, Biozentrum, Basel)
Quality control of RNA: new roles for new poly(A) polymerases

Until recently the prevailing belief has been that the polyadenylation of RNAs has completely different functions in prokaryotes compared to eukaryotes. Polyadenylation of RNAs in bacteria is a prelude to degradation whereas it protects RNAs against destruction in eukaryotic cells. We and several other groups have identified a new protein complex with poly (A) polymerase activity from Saccharomyces cerevisiae that contains the Trf4 protein as catalytic subunit. In accordance with earlier in vivo studies, we could show that aberrantly folded tRNAs are preferentially polyadenylated by the Trf4 complex in vitro. Moreover, the Trf4 complex stimulates the degradation of unmodified tRNAs by purified nuclear exosome fractions. Degradation is most efficient when coupled to the polyadenylation activity of the Trf4 complex, indicating that the poly(A) tails serve as signals for the recruitment of the exosome. This polyadenylation-mediated RNA surveillance resembles the role of polyadenylation in bacterial RNA turnover.

Eiman Aleem (National Cancer Institute, Frederick, Present Address: Faculty of Science, Alexandria University, Alexandria)
The cell cycle revisited: Cdk1/cyclin E complexes regulate the G1/S phase transition of the cell cycle in vivo

The transition between phases of the cell cycle is regulated by cyclin-dependent kinases (Cdks) and their cyclin regulatory subunits. In yeast, a single Cdk is able to regulate diverse cell cycle transitions by associating with multiple stage-specific cyclins. The evolution of multicellular organisms brought additional layers of cell cycle regulation in the form of numerous Cdks, cyclins and Cdk inhibitors to reflect the higher levels of organismal complexity, but how many of these cyclin-Cdk complexes are essential? According to the current model of mammalian cell cycle regulation, Cdk2/cyclin E was thought to be the only Cdk, which controls entry into S phase. Cdk2/cyclin A controls progression through S phase and transition into G2 phase. However, mice lacking Cdk2 develop normally and Cdk2-/- MEFs show minimal defects in proliferation and some delay in S phase entry.
The surprising fact that the in vivo loss of Cdk2 has no effect on mitosis raises two important questions: (1) which kinase compensates for the loss of Cdk2 and regulates S phase entry in vivo? (2) Considering that Cdk2 is the only known kinase, which binds cyclin E, what is the function of cyclin E in the absence of Cdk2? A major inhibitor of Cdk2 is p27, which is also a tumor suppressor. Overexpression of p27 results in G1 arrest in cell lines. p27-/- mice have enlarged body size, increased cell proliferation, pituitary gland tumors, and a 10-fold increase in Cdk2 activity in thymocytes. These findings support the role of Cdk2 as a major target of p27. In this study, we hypothesized that loss of Cdk2 should modify the p27-/- mouse phenotypes. We generated p27-/-Cdk2-/- double knockout (DKO) mice and found no functional complementation in these mice. One hundred percent of the female DKO mice develop ovary tumors, which are not found in p27-/- mice. Interestingly, we observed elevated levels of S phase and mitosis in tissues of DKO mice similar to those observed in p27-/- tissues. Cdc2 activity was significantly elevated in DKO extracts and p27 binds to Cdc2, cyclin B1, cyclin A2, or suc1 complexes in wild-type (WT) and Cdk2-/- extracts. We also observed that cyclin E binds and activates Cdc2 and cyclin B1 binds Cdk2. Therefore, both cyclin E and p27 regulate Cdc2 in vivo.
Cdc2 was silenced using shRNA in Cdk2-/- and WT MEFs, then proliferation and S phase entry after quiescence were measured. We

found Cdk2-/- MEFs expressing shCdc2 to proliferate at a lower rate and enter into S phase with delayed kinetics, compared to the WT MEFs with shCdc2. Our results uncover a critical role for Cdc2 in the regulation of G1/S transition and provide evidence that Cdc2 compensates the loss of Cdk2 function. We suggest a new cell cycle model with high levels of redundancy among the molecular players.

Martin Vingron (Max Planck Institute for Molecular Genetics, Berlin)
Computational methods in gene expression and gene regulation

The availability of complete genome sequences as well as functional genomics data, e.g, large scale gene-expression data has revived interest in computational prediction of cis-regulatory elements. This talk introduced computational methods for visualizing associations between genes and conditions in DNA-microarray data. These techniques will also be applied for establishing associations between gene expression data and transcription factor binding sites. While for yeast this can be done based on published transcription factor binding data, for human data the researchers draw on comparative analysis with mouse data in search for binding sites.

Hematopoietic Stem Cell Differentiation and Cancer Therapy

Thomas Graf (Albert Einstein College of Medicine, New York, and Center for Genomic Regulation, Barcelona)
Cell fate decisions of blood cells

How do hematopoietic stem cells in the bone marrow differentiate into either macrophages or lymphocytes? These specialized cells have very different functions in the body: while macrophages provide a first barrier of protection against infecting viruses and bacteria and remove dead cells, lymphocytes attack invaders through the production of antibodies and direct cell killing. Lineage decisions are mediated by transcription factors that govern cell type specific gene expression programs, and that give macrophages and lymphocytes their unique properties. To study how this works at the molecular level we use a gain of function approach, consisting of the enforced expression of macrophage associated transcription factors in committed lymphoid precursors. Our results show that it is possible to reprogram fully committed B and T cell progenitors into functional macrophages by the expression of C/EBP alpha. The induced up-regulation of macrophage genes and the extinction of lymphoid genes are separable processes, the first one, but not the latter, requiring endogenous PU.1. The extinction of lymphoid genes is mediated by direct antagonisms between C/EBP alpha on the one hand, and Pax5, Notch1 and GATA-3 on the other. We also found out that over-expression of PU.1 in T cell precursor reprograms them to acquire a dendritic cell fate. Our experiments re-establish in differentiated cells, to some extent, the transcription factors expression pattern of early progenitors and thus restore plasticity lost during lineage commitment. Understanding the transcription factor antagonisms and synergisms that are operative in this process allows to model cell fate decisions in the blood cell system.

Thomas Graf

Thomas Boehm (Max-Planck Institute of Immunobiology, Freiburg)
Lymphoid development in mouse and zebrafish

T cell differentiation has so far been primarily studied in mammalian species. Although these studies have yielded a fairly detailed picture of these processes, many questions remain. To address these problems, we have recently begun to study T cell differentiation in a non-mammalian model through the use of genetic screens after ENU mutagenesis. After a discussion of the design of the screen and its overall results some initial findings on the role of the Ikaros transcription factor on hematopoietic development in the zebrafish were presented. The presentation highlighted similarities and differences between mouse and zebrafish lymphocyte development.

Achim Leutz (Max-Delbrück-Center for Molecular Medicine, Berlin)
Molecular Genetics of an Onco-Developmental Gene Switch

CCAAT/enhancer binding proteins (C/EBP) and the c-Myb protein are transcription factors that synergistically control cell fate in the hematopoietic system. On the molecular level, C/EBP plus c-Myb interact

with each other, with multiple transcription co-factors, and with chromatin remodeling machines. How these interactions are spatiotemporally coordinated has to be revealed in detail, yet, C/EBPs were found to be involved in the remodeling of chromatin and in the recruitment of large, so called "Mediator" complexes that activate or that silence genes. Disruption of discrete C/EBP functions is associated with the development of acute leukemia.
Distinct mutations in the solvent exposed surface of the Myb DNA binding domain turn Myb into a leukemia protein. Wild type Myb but not its leukemic counterpart bind to the N-terminal tail of Histone H3 and catalyze its modification. The Myb–H3 interaction and the subsequent histone modification are essential for cell differentiation while abrogation of the H3 interaction is correlated with leukemogenicity. Thus, the Myb–C/EBP team acts as a molecular switchboard to orchestrate enzymatic conversion of chromatin and cell differentiation. Abrogation of several of its functions is tumorigenic.

Achim Leutz

Anthony D. Ho

Radek C. Skoda (University Hospital, Basel)
JAK2 mutation in the pathogenesis of myeloproliferative disorders

Radek Skoda and Rainer Haas

Myeloproliferative disorders (MPD) are a group of blood diseases characterized by aberrant proliferation of the myeloid lineages. They represent clonal stem cell disorders with an inherent tendency towards leukemic transformation. A mutation in the Janus kinase 2 (JAK2) gene that substitutes a valine to phenylalanine at position 617 of the Jak2 protein (JAK2-V617F) has been found in the majority of MPD patients. This mutation results in a constitutively active JAK2 protein and represents a potential drug target for developing a specific inhibitor. Remarkably, the mutation occurrs in the same codon in all MPD patients studied to date. The implications for the diagnosis, prognosis and treatment of MPD were discussed.

Rainer Haas (University Hospital, Düsseldorf)
Molecular characterization of circulating hematopoietic stem cells

CD34+ hematopoietic stem cells are used to support cytotoxic therapy. During the steady-state, small amounts of these cells are present in the peripheral blood. Reconstitution after chemotherapy or administration of hematopoietic growth factors such as G-CSF facilitates the mobilization of CD34+ cells into the peripheral blood. However, the exact molecular mechanisms of stem cell mobilization are not yet clear. In order to identify the molecular basis for the functional differences between sedentary and circulating hematopoietic stem and progenitor cells we compared CD34+ cells from bone marrow with those from peripheral blood during G-CSF-induced mobilization using cDNA arrays. We found a specific gene expression profile of CD34+ cells from both compartments. Circulating CD34+ cells showed a higher expression of proapoptotic genes and genes involved in transcription, whereas genes involved in the cell cycle demonstrated low expression in peripheral blood CD34+ cells. This supports the view that circulating CD34+ cells consist of a higher number of quiescent and early stem and progenitor cells as well as a higher proportion of apoptotic cells.
Recent studies suggest that hematopoietic stem cells might be able to transdifferentiate into non-hematopoietic cells and might therefore serve as a cellular source for non-hematopoietic tissue. Moreover, the presence of sensory and autonomic nerves in the bone marrow could be morphologic correlates of a neural regulation of hematopoiesis. This is supported by a recent study showing that G-CSF-induced mobilization of hematopoietic stem cells in mice is mediated by the sympathic nerve system. We examined human

CD34+ cells for expression of genes involved in neurobiologic functions using specialized cDNA arrays and flow cytometry. We found expression of ligand- and voltage-gated ion channnels as well as of G protein-coupled receptors of neuromediators such as for example GABA, CRH and orexin receptors in CD34+ cells. Expression was higher in more immature CD38 negative CD34+ cells suggesting that these receptors play a role in developmentally early progenitor cells. Alterations of intracellular cAMP concentrations following stimulation of CRH and orexin receptors showed that these receptors are functionally active. Our findings suggest a molecular interrelation of neuronal and hematopoietic signaling mechanisms and might be the molecular basis for a neural regulation of hematopoiesis and mobilization.

Thorsten Heinzel (Institute of Biochemistry and Biophysics, University of Jena,)
Histone deacetylase inhibitors in cancer therapy

The modulation of signaling events by histone deacetylase inhibitors can induce apoptosis or differentiation of carcinoma cells. Thus, HDAC inhibitors are candidate drugs for the treatment of cancer. We discovered that the drug valproic acid (VPA) is a powerful inhibitor of HDAC enzymatic activity which also induces proteasomal degradation of one specific isoenzyme, HDAC2. Our functional studies on the molecular mechanisms of HDAC inhibitor therapy showed that Stat1 and NF-kB, two key regulators of signal transduction, gene expression and apoptosis are linked via lysine acetylation of Stat1. Stat1 acetylation is a prerequisite for the interaction with NF-kB p65. As a consequence, p65 DNA-binding, nuclear localization and expression of anti-apoptotic NF-kB target genes are decreased. Alterations of the crosstalk between signaling pathways are likely to play an important role in the response of tumor cells to HDAC inhibitor therapy.

All of these excellent presentations stimulated lively discussion which was continued during the poster presentation.

Poster Presentations

Right after the symposium the attention of researchers and Alumni was drawn to 12 posters reflecting most recent research results. The first authors of the three most outstanding posters, which were selected in the late afternoon by a small committee consisting of Dietrich Keppler, Manfred Schwab, and Michael Schwarz, were awarded a prize of 300 Euro each:

Daniel Mertens (Divisions of Molecular Genetics and of Epigenetics, DKFZ, Heidelberg):
Allelic silencing at 13q14.3: a novel oncogenic mechanism

E. A. Moskalyov (Division of Functional Genome Analysis, DKFZ, Heidelberg, and Department of Biochemistry, Voronezh State University, Voronezh, Russia):
Development of array-based assay for high-resolution DNA-methylation profiling of B-cell chronic lymphocytic leukemia

Alexander Hermani (Research Group Hormones and Signal Transduction, DKFZ, Heidelberg):
The calcium binding proteins S100A8 and S100A9 as novel markers for human prostate cancer

Manfred Schwab, Akshish Shukla (middle) and Alexander Hermani (right)

The awards were handed over to the laureates during a reception by the Chairman of Alumni DKFZ, Professor Peter Bannasch.

Highlights of DKFZ Research

In the morning of May 13, representatives of the research programs (RP) of the DKFZ introduced outstanding research results. This session was co-chaired by Clarissa Gerhäuser and Dietrich Keppler who elegantly monitored the lively discussion elicited by the following talks, all of which were at a high scientific level and gave a most informative insight into the current research activities of the DKFZ.

Christof Niehrs (RP Cell Biology and Tumor Biology)
Highlights in tumor and cell biology at the DKFZ

Jörg Hoheisel (RP Structural and Functional Genomics)
Functional genomics and proteomics in cancer research

Clarissa Gerhäuser (RP Cancer Risk Factors and Prevention)
Cancer without disease? Highlights from cancer chemoprevention research

Bruno Kyewski (RP Tumor Immunology)
Tumor tolerance: obstacle and chance

Jürgen Biederer (RP Innovative Diagnostics and Therapy)
MRI of lung cancer

Christof Niehrs, Thomas Böhm

Jörg Schlehofer (RP Infection and Cancer)
Virotherapy of cancer

Reception

Highlights of the reception were an overview on research perspectives of the DKFZ by the Chairman and Scientific Member of the DKFZ Management Board, Professor Otmar Wiestler, and a presentation of perspectives, challenges and solutions of international research

After the scientific talks Alumni took the chance for a private chat.

funding by the Secretary General of the German Research Foundation (Deutsche Forschungsgemeinschaft), Dr. Reinhard Grunwald – former Administrative Member of the DKFZ Management Board for many years.

This most recent information on science policy was framed by beautiful pieces of music performed by the Heidelberg Doctor´s Orchestra under the direction

Reinhard Grunwald meets Elfriede Egenlauf and Gabriele Hundsdörfer

of its founder and longstanding conductor, Professor Michael Steinhausen, with Michael Veit as solo cellist. The musicians left a permanent impression on all audience, particularly with the wonderful adagio "Kol Nidre" by Max Bruch.

In the afternoon, the remaining hardcore of the meeting made a wonderful boat trip on the Neckar. All participants will remmber the lovely spring panorama of the Neckar valley, and the lively personal exchange of ideas during this trip.

It is very encouraging that we did not only receive many positive responses from participants of the Second General Alumni Meeting during the past few

Claus H. Schröder and Konrad Buschbeck

months, but also a number of proposals for possible improvements of our meetings which the Board of Alumni DKFZ will carefully consider.

Peter Bannasch

Peter Bannasch and Elfriede Mang (right): Already discussing new ideas for the next Alumni Meeting?

General Assembly

The morning of May 13 was concluded by the General Assembly of DKFZ Alumni. In addition to the Chairman, the Treasurer, Dr. Konrad Buschbeck, and the Secretary of Alumni DKFZ, Elfriede Mang, were predominantly responsible for the preparation and smooth running of the general assembly. Elfriede Egenlauf and Dr. Fritz Klimek were elected unanimously as future auditors of the Association.

We highly appreciate that representatives from the Alumni Association of the Life-Science Laboratory participated in our assembly and expressed their interest in a close cooperation with the DKFZ-Alumni (see also the report by Christian Stoy and Malte Gersch on page 14 of this Newsletter).

The Treasurer gratefully acknowledged the general, and particularly the financial, support of almost all activities of our Association by the DKFZ Management Board. In addition, he could make the most enjoyable announcement that the Dietmar-Hopp-Stiftung has sponsored the meeting with a generous donation of 5,000.00 Euro. In the meantime, we were pleased to receive a further donation of 1.000,00 Euro by Roche Diagnostics. We are most grateful for this substantial financial support of our ever increasing activities, and sincerely hope that this can not only be maintained but increased in the future. The participants of the general assembly realized, however, that this will only be possible if the members of our Association contribute to the financial basis of our organization. This prompted us to ask all of you for voluntary contributions as detailed in a special letter which should have reached you recently. See our web site for minutes of our assembly.

PBa

membership

A Letter to All Alumni in America

Dear Colleagues,

With this letter we would like to inform you about a meeting of former and current scientists of the DKFZ during the AACR meeting in 2006. At the same time we invite you to become a member of an All American Alumni Club, which will convene during the next meeting of AACR, April 16, 2007 in Los Angeles, CA.

The usual hectic pace of Washington, D.C., the capital of the United States, was turned up a notch with the presence of thousands of attendees at the 97th Annual AACR Meeting at the Washington D.C Convention Center. This year's theme of new and promising therapeutic approaches, was reflected in the Opening Plenary Session, "Looking into the Future of Cancer Therapy." This session featured Bert Vogelstein, Todd R. Golub, Gregory L. Verdine, Ralph Weissleder, Susan D. Desmond-Hellmann, and Irving L. Weissman, world leaders in the fields of cancer genetics, molecular diagnostics, chemistry, imaging, clinical research, and stem cell biology, respectively. In addition there were a large number of Forums and Special Sessions, Symposia, Minisymposia, Meet-the-Expert Sunrise Sessions, New Concepts in Organ Site Research Sessions, Poster Sessions featuring nearly 6,000 abstracts, and a wide array of Educational Sessions and Methods Workshops. The AACR Annual Meeting is the most important cancer research meeting in the world thus giving the some 17,000 attendees the opportunity to increase their knowledge and broaden their perspectives.

The DKFZ took advantage of this large meeting to gather members of the DKFZ Alumni Association for their second annual meeting in the United States, held on April 3, 2006 in the McPherson Square Room of the Grand Hyatt Hotel. From 6:00 until 8:00 pm there was a wonderful opportunity for former and present DKFZ members to stop, relax, and enjoy some food and drink. In attendance were scientists currently at the DKFZ, other Universities in Germany or at Universities all over the United States. Some were beginning their training. Others were established scientists. Some had spent time as a post-doctoral trainee or visiting scientist at the DKFZ. Thus, it was an ideal opportunity for prospective trainees to meet potential mentors and for scientists to share their insights on cancer research.

Professor Peter Bannasch welcomed the participants and described the progress with the various Research Programs of the DKFZ, and particularly with the newly organized National Center for Tumor Diseases (NCT) Heidelberg. This new organization offers comprehensive services and care for cancer patients as well as an interface between basic research and clinical practice at the DKFZ, the Heidelberg University Hospitals, and the associated Thorax Clinic in Heidelberg-Rohrbach. Professor Bannasch also emphasized the importance of supporting young scientists and the efforts of the DKFZ to establish young scientist programs. Furthermore, he discussed the possibility of forming an All American Alumni Club that could strengthen the ties between the DKFZ and its graduates and former visiting scientists.

There already are regional Alumni Clubs in China and in the Heidelberg area. The first meeting of the Chinese Alumni Club took place in connection with a Sino-German Workshop on Cancer and Infectious Diseases (attended by approximately 120 scientists from both sides) in the Sino-German Center for Research Promotion in Beijing in June 2005. About 20 Chinese Alumni and young scientists interested in visiting the DKFZ presented their most recent research results as posters. The Heidelberg Alumni Club meets once or twice a year. At its next meeting (October 26) Professor von Kalle, Director of the NCT, will speak on aims and projects of translational cancer research in Heidelberg. Following these successes we propose the formation of a regional Alumni Club for America. At present about 80 DKFZ Alumni living in the US and Canada, and some 15 Alumni in South America, particularly in Brazil, are listed in the Alumni Secretariat, but it is likely that contact with many others has been lost. The Alumni Club would provide a perfect setting to meet with old friends and to organize activities and networks, serving as a platform for scientific or social exchange and meetings. Members also could provide a network for newcomers to the area. A local Alumni webpage could include valuable resources, such as information on regional activities, organizations and job opportunities, as well as other helpful tips. The American Alumni Club should be headed by a DKFZ Alumnus (or Alumna) who is willing to volunteer in coordinating activities.

The Secretariat of the Alumni Association in Heidelberg is prepared to support the activities of the regional Alumni Clubs. Anybody who is interested in joining should contact Frank Diehl (address below) and visit the website of the Alumni Association (www.dkfz.de/alumni) in order to get more detailed information, and, especially, to register as a member.

We would highly appreciate your participation in this initiative.
With best wishes,

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cooperation

Cooperative Fishing for Molecular Changes in Pediatric Brain Tumors

by Andrey Korshunov

Medulloblastomas and ependymomas are frequent entities among pediatric brain tumors. Both neoplasms require combined treatment including radio- and chemotherapy, however their clinical outcomes are not promising so far. Trying to find out about the molecular base of genetic alterations associated with these diseases, I obtained the excellent opportunity to develop a cooperative research project together with Peter Lichter, Head of the Division of Molecular Genetics at the DKFZ.

For a long period of time I have been working as a diagnostic neuropathologist at a neurosurgical institute in Russia. Although primary tumors of the central nervous system (CNS) are encountered in approximately one percent of all human malignancies, the frequency of pediatric CNS malignanices is increasing and its rate amounts to approximately twenty percent of all neoplasms in childhood.

Andrey Korshunov graduated from 3-rd Moscow Medical University in Russia, and obtained his degree "doctor of medicine" in 1984. His career was continued in Moscow Neurosurgical NN Burdenko Institute where he consequently obtained degrees of PhD (1986), Doctor of Medical Sciences (1993) and Professor of Pathology (1998). At present, Professor Andrey Korshunov is Chairman of the Department of Neuropathology and Molecular Neuro-oncology in the Burdenko Institute. He worked as a visiting scientist at the DKFZ (Heidelberg, Germany) from 2002 to 2003.

To optimize treatment strategies for patients with medulloblastomas and ependymomas, a more precise understanding of the molecular basis of these diseases is clearly necessary. Unfortunately, our opportunities in this field of research were limited here in Moscow, because our "molecular armament" was scanty at that time.

In the course of investigating the world's research literature, I became aware of the work developed in the Division of Molecular Genetics at the DKFZ that was based on the application of the modern microarray (gene chip) technology. I wrote to Professor Harald zur Hausen enquiring about the possibilities to carry out molecular genetic studies on pediatric CNS tumors under supervision of Professor Lichter and his colleagues. After their agreement, we developed a cooperative research project, which was funded from April 2002. I obtained the excellent opportunity to investigate more than 100 tumor specimens from my personal collection by means of microarray technology and other molecular methods.

The project was initiated in summer 2002 by studying gene expression profiles of ependymomas and medulloblastomas with cDNA microarrays generated at the DKFZ. During this study we found novel data concerning aberrant expression of a few genes in ependymomas (CLU, RAF1, AK1, FOXJ1, MSX1: most of these genes were found to be involved in embryogenesis and carcinogenesis) and confirmed the results obtained by QRT-PCR (quantitative reverse transcriptase polymerase-chain reaction). Furthermore, we discovered genetic signatures specific for ependymomas with various locations, different grades of malignancy and age. Microarray-based screening of 35 medulloblastomas allowed us to reveal a set of 54 genes associated with unfavorable clinical outcomes. Among them there are MYCC, NRAS, STMN, STK15 and other genes, mostly encoding cell cycle activators and viral oncogene homologs.

My second visit started in summer 2003 and was dedicated to a project with wide-screening analyses with respect to the prognostic value of multiple markers previously detected by the gene expression profiling. To this end we used tissue microarrays constructed from 170 medulloblastomas with clinical follow-up. Various immunohistochemical markers and DNA probes for FISH (Fluorescence in-situ Hybridization) analysis were applied. As a result independent prognostic significance for STK15 overexpression (a gene responsible for duplication-distribution abnormalities in chromosomes) and copy number gains was found.

Also, we have begun projects based on matrix CGH (Comparative Genomic Hybridization) analysis of ependymomas and medulloblastomas. We found novel chromosomal imbalances and candidate genes involved in carcinogenesis of these neoplasms. Also, prognostic significance of CDK6 overexpression (the gene controls proliferation and differentiation) for medulloblastomas and 1q gains for ependymomas was established during this project.

In summary, being an absolute beginner in molecular oncology, I received an excellent training in this field of medico-biological research. At present, we have introduced new molecular techniques for everyday work in our department, such as FISH and array-based CGH. I would like to express a sincere gratitude to all my former colleagues from DKFZ. I spent an excellent time working with them and I hope that our collaboration will be maintained with ongoing projects.

people

New Scientific Council

The Council is composed of the speakers of the seven Research Programs and one elected scientist from each.

Cell and Tumor Biology:
Prof. Christof Niehrs, Prof. Ingrid Grummt
Functional and Structural Genomics:
Prof. Annemarie Poustka, Dr. Jörg Hoheisel
Cancer Risk Factors and Prevention:
Prof. Kari Hemminki, Dr. Peter Schmezer
Tumor Immunology:
Prof. Peter Krammer, PD Dr. Frank Momburg
Innovative Cancer Diagnostics and Therapy:
Prof. Wolfgang Schlegel, Prof. Hans-Ulrich Kauczor
Infection and Cancer:
Prof. Henri-Jacques Delecluse, PD Dr. Ingrid Hoffmann
Translational Cancer Research:
Prof. Christof von Kalle, Prof. Dirk Schadendorf

In its constituent assembly on September 25th **Prof. Christof Niehrs** and **Prof. Christof von Kalle** were elected as Chairperson and Vice-Chairperson, respectively.

Appointments

Prof. Hellmut Augustin is Head of the newly established Division of Vascular Medicine. He investigates molecular mechanisms of angiogenesis and the interaction of tumors with blood and lymphatic vessels during metastasis.

Prof. Alwin Krämer took up the position as Head of the Clinical Co-operation Unit Molecular Hematology/Oncology on January 1, 2006. His research focuses on mechanisms leading to chromosomal instability in malignant tumors. Krämer investigates disorders in cell cycle regulation as well as the role of structural and functional characteristics of centrosomes for the development of leukaemia and lymphomas.

Prof. Hermann Brenner and his team from the German Center for Research on Aging (DZFA) moved to the DKFZ. The researcher took up the position as Head of the Division of Clinical Epidemiology and Aging Research. His work focuses on clinical epidemiology of cancer, chronic diseases acquired due to aging,and epidemiological methodology.

Dr. Frank Lyko, Head of the Division of Epigenetics, was appointed full Professor of the Medical Faculty of Heidelberg University.

Dr. Dirk Nettelbeck is in charge of the Helmholtz-University Young Investigators Group "Oncolytic Adenoviruses". The biologist is working on targeted therapies using viruses selectively destroying tumor cells.

Dr. Georg Stöcklin took up the position as Head of the Helmholtz-Young Investigators Group "Posttranscriptional Gene Regulation". His work focuses on the regulation of mRNA half life in normal and tumor cells.

Awards

Prof. Christof von Kalle, Head of the Division of Translational Oncology and Director of the National Center of Tumor Diseases Heidelberg, was honoured by the Paul-Ehrlich-Institute for his research on the safety of gene therapy. He shares the Langener Wissenschaftspreis 2005 of 10,000 Euros with colleagues from Hannover Medical University, the University Hospital Hamburg-Eppendorf, and Freiburg University.

Prof. Heike Allgayer, Head of the Clinical Co-operation Unit Molecular Oncology of Solid Tumors, received the „Dr. Hella Bühler-Preis 2005". The prize endowed with 50,000 Euros acknowledges her research on stomach and colon cancer.

Prof. Hermann Brenner recently received one half of the Felix Burda Award 2006 in the field of "Medical Prevention". The prize endowed with 10,000 Euros acknowledges evaluation studies on prevention measures against colorectal cancer.

Prof. Thomas Efferth, Division of Toxicology and Cancer Risk Factors and Head of the International PhD-Programme, was awarded the Willmar Schwabe Preis of 10,000 Euros by the Society for Medicinal Plant Research for findings on medicinal plants and natural products. He also received 66,000 Euros from the Deutsch-Französische Hochschule in order to establish a German-French College for graduate students.

people

Dr. Jens-Peter Knemeyer, Division of Functional Genome Analysis, is one of the prize-holders honoured with the Klaus-Georg und Sigrid Hengstberger-Award endowed with 15,000 Euro. The grant allows for the organization of this year's Ruperto-Carola-Symposium.

Dr. Marc-André Weber, Division of Radiology, was awarded with the Felix-Jerusalem-Prize 2006. The Deutsche Gesellschaft für Muskelkranke acknowledged his work on the use of magnetic resonance imaging for muscle diseases. The award is endowed with 7,500 Euros.

Dr. Selma Ugurel, Clinical Co-operation Unit Dermato-Oncology, received the Oncology Research Award 2006 funded by the Hector Stiftung. The prize of 20,000 Euros acknowledges the fingerprinting method for serum proteomes allowing the identification of stage-specific tumor markers.

Prof. Gerhard van Kaick, former Speaker of the Research Programme Diagnostics and Therapy in Radiology and former Head of the Division of Oncological Diagnostics and Therapy, is one of two awardees honoured with the Boris Rajewsky Medal 2006 by the European Association of Radiology.

Dr. Beate Straub, Division of Cell Biology, is one of two prize-holders awarded with the Joachim Siebeneicher Promotionspreis 2005 of 5,000 Euros. The Medical Faculty of Heidelberg University honoured her outstanding doctoral thesis on a new kind of cell junction in the cortex adhaerens.

Dr. Ana Martin-Villalba, Division of Immunogenetics, was the first to receive the Paul Ehrlich- and Ludwig Darmstaedter Award for junior researchers. The prize of 60,000 Euros acknowledges her internationally recognized findings on the role of the CD95-signalling system for physiological and patho-physiological processes in the neuronal system. Martin-Villalba showed that blocking this signalling system in mice enhances the regeneration of the spinal cord after a transverse lesion. Due to these results Martin-Villalba was also one of the six awardees honoured with this year's Heinz Maier-Leibnitz-Prize by the German Research Foundation, an award of 16,000 Euros.

Prof. Harald zur Hausen, former Chairman of the DKFZ, received the Medal for Merit of the Federal State Baden-Württemberg. He was also honoured with the 13th Raymond Bourgine Award for his findings on the viral origin of cervical cancer and his merits on the reputation of the DKFZ. The New York Cancer Research Institute dedicated the William B. Coley Award 2006 to zur Hausen for his contributions to immunology.

Dr. Stephan Herzig, Head of the Emmy-Noether-Junior-Group Molecular Metabolic Control, and his collaborator **Ulrike Lemke** obtained the Schoeller-Junkmann-Prize 2006 funded by the German Society of Endocrinology. The award of 10,000 Euros acknowledges the finding that "Glucocorticoids promote fatty liver development through dual track inhibition of transcriptional repressor Hes-1".

Science Talents Welcome the Next Generation

by Christian Stoy and Malte Gersch

Roughly six years ago the Heidelberg Life-Science Lab was founded with the aim to offer a special support to gifted girls and boys at the age of 13 to 19. Ever since, young talents sharing a great passion for science in all its different shades can take advantage of this opportunity to improve their knowledge about life sciences and to develop communication and management skills. Since 2002, DKFZ and the Technologiepark Heidelberg GmbH jointly foster the activities of the Lab.
With thriving efforts the idea to establish an Alumni network has been pursued since the first students graduated. Finally, this led to the foundation of an Alumni Association in the fall of 2005.

The club chiefly aims at bringing together the former members of the Life-Science Lab in order to make their resources and knowledge available to the Alumni themselves as well as to the current members of the Lab. The willingness to give something back to the organization that influenced their lives for several years is highly present among the Lab's Alumni. Many of those who are studying nearby have consequently stayed in touch as student mentors for the Lab's scientific work groups.
Many other Alumni, however, have joined universities throughout Germany with one small hot spot at Munich. Hence, these Alumni cannot be active as mentors anymore though they are seeking for cooperate experiences, too.
On the occasion of this year's farewell of graduate students, the association organized for the first time a celebration to bring participants and Alumni together. Especially when those students are about to decide on their study subject and the most suitable university, the Alumni's first-hand information can be of great help. Whenever Lab participants are planning an internship at a university or a research institute, it is of mutual benefit if Alumni serve as persons of contacts or give useful guidance. The positive outcome of further advice on scientific issues or career planning must not be underestimated.
Additionally, Alumni can get involved in Lab projects such as the Science Academies Munich, San Francisco and Estonia in 2007. Furthermore, Alumni can report about their master's or PhD thesis and the Lab's influence on their scientific career during one of the Lab's weekly Friday lectures.
Beside these aspects of supporting the Life-Science Lab the Alumni are also eager to broaden their own horizons. Since the Life-Science Lab is part of DKFZ it is obvious to search for various forms of cooperation with the DKFZ Alumni. Many Lab Alumni studying life sciences would greatly appreciate current and former scientists of the DKFZ offering their support. This could reach from simple questions about cancer research up to providing lab internships or giving talks at seminars, lectures or academies organized by the Lab Alumni themselves.
By combining the resources of both Alumni networks a fruitful cooperation might be achieved. The Lab Alumni could profit from the knowledge and experience of renowned scientists and build contacts all over the world. On the other hand DKFZ Alumni will have the opportunity to get in touch with young motivated upcoming scientists who might eventually become an enrichment to their own research group. At the same time this will strengthen the efforts to counter the deficiencies of Germany's educational systems.
We are really looking forward to getting in touch with you at info@lab-alumni.com.

Time to take over and enter the realm of high-class research

Gifts for gifted pupils

Facing new tasks: Alumni of Life-Science Lab stand close together to support young talents.

excursion

Merck: A Glimpse into 300 Years of Growth of A Pharmaceutical Company

by Urmila Nair

It was on January 24, 2006, when the bus set out for Darmstadt. Even before it left, our group of 42 DKFZ guest scientists from all over the world took the chance to get to know each other. And there were still a lot more interesting things to learn on this day...

After about an hour's drive we reached the plant of Merck for a guided visit. Driving through the company's huge complex, our guide pointed out the various departments, some of which we would get an opportunity to visit later. Our first stop was at the visitors' center, where a beautiful blue glass pyramid (picture below) stood at the entrance. We were given a conducted tour of a small museum, where pictures and relics covering its 300 years history from the humble beginning were on display. It all began in Darmstadt, where Friedrich Jacob Merck acquired the Engel-Apotheke (pharmacy) in 1668.

A last glimpse into the winter sun after a stimulating day at Merck.

Then, in 1827, Heinrich Emmanuel Merck started industrial-scale production of alkaloids, plant extracts and other chemicals. This has now expanded to today's large sprawling enterprise. It is supposed to be the oldest pharmaceutical and chemical company in the world which is still operating in both sectors globally. An official welcome was followed by a presentation of a film which detailed the history and the complete range of products that Merck manufactures throughout the world today. Besides chemicals and pharmaceuticals, another important field is 'Liquid Crystals'. Back in 1904 they were offered as a pure substance and subsequently were manufactured by Merck. It was really very fascinating to see the historical development of 'Liquid Crystals' from a plant product which was scoffed at to large scale manufacture and current widespread application in liquid crystal displays in televisions, PC monitors, notebooks, mobile phones etc.

As we were from a cancer research center, the next two speakers focused on pharmaceuticals, which included oncological products, (some interesting data on a recently cleared drug for targeted cancer therapy were presented), generic drugs and health care products such as vitamins, minerals and food supplements. They introduced us to the timeline and various steps a compound has to go through before it can actually be marketed and also gave an idea of the approximate costs involved. The sessions were rounded up with several queries from the audience, some of them quite pointed, but the answers and explanations appeared to be reasonably satisfactory.

By now everybody was having hunger pangs and the invitation for lunch was welcomed by one and all. Another bus ride took us through the vast complex, and some of the newly constructed, state of the art departments were pointed out by our guide. After lunch it was time for visiting the actual works. The first stop at the warehouse was very impressive. This computerised modern building is supposedly the largest automated chemical /pharmaceutical products storage and retrieval facility, with a distribution center for shipment to wholesalers and pharmacies. Afterwards, we were divided into several smaller batches, each to visit one of the departments, like the tablet making plant, quality control division etc. We learnt that the equipment represented the state of the art and was supposed to be upgraded periodically.

In the quality control division we were shown several of the important quality checks that a batch of tablet has to go through. This included the importance of the tablet strength, the pH dependent dissolution of the tablet, depending on the target, several analytical instruments to measure the amounts of the drug, the microbiological quality control etc.

All too soon the time was up. On our way back we took the opportunity of exchanging impressions of the different departments. Overall, we got a very interesting and educative glimpse into the working of a pharmaceutical giant.

The enthusiasm for the German Team during the world cup infected junior researchers, senior scientists and technical staff at DKFZ equally. Somehow, science seemed to be only second best...

World cup fever

Many sport fans eagerly awaited the first game for the world cup. The DKFZ was not excluded from this fever either. On Friday, June 9, 6 p.m. the first game was shown on a huge screen in the Foyer of the DKFZ. Many fans were enthusiastic about the first goals. Despite the rainy weather several days before, on the very day of the opening of the World Championship on soccer, bright sunshine and a blue sky pleased the spectators in many German cities, including Heidelberg. Here and elsewhere people gathered to watch the game on screens in common places. It was an atmosphere of a huge fair, and after the game was finished car parades crowded the streets.

However, every medal has two sides. There are also people who felt disturbed by this mania. Switzerland asked women who are tired of soccer watching to escape by making holidays in this nice country. Every time one listened to the radio or watched TV there were news on the teams, the wives of the players, e.g. Victoria Beckham, or how the German team has slept last night.
Despite my concerns after termination of the world cup, I can summarize this event as mainly positive: many different nations met in Germany and made friends, public viewing was a summer pleasure and despite the German Team not winning the World Cup the team was greeted enthusiastically when they said good-bye to their fans in Berlin.

Elfriede Mang

Obituary

Professor Gustav Wagner, former Director of the Institute of Documentation, Information and Statistics of the DKFZ from 1964 until his retirement in 1988, passed away at the age of 88. He was the Chairman of the Board of Directors (1966/67), was re-elected (1972/73), and became provisional Scientific Chairman of the Management Board of the DKFZ in 1982, thus strongly influencing the appearance of the DKFZ from its very beginning. Gustav Wagner was a pioneer in his discipline, promoting its reputation at the national and international level as a leading researcher and author, as longstanding President of the "Deutsche Gesellschaft für Medizinische Dokumentation, Information und Statistik", and as editor of the journal "Methods of Information in Medicine". He maintained close connections to the DKFZ up to the last few weeks, and will be commemorated as a personality full of life with an unforgettable laugh.

Imprint

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p. 1:	Mieczyslaw Chorazy
p. 4 - 9:	Gerhard van Kaick
p. 2:	left: DKFZ, right: Heinle, Wischer und Partner, Freie Architekten, Stuttgart
p. 3:	left and bottom: Yan de Andres, right: Brigitte Engelhardt,
p. 11:	Andrey Korshunov
p. 12:	private, except bottom left: Yan de Andres
p. 13:	private, except top row, left: Heidelberg University/ Dagmar Welker, middle row, left, bottom row, left and middle: Yan de Andres,
p. 14, 16:	Yan de Andres
p. 15:	left: Merck KGaA, Darmstadt, Germany, right: private