Interview
Only recently he has received the Life Time Achievement Award in recognition of his major contributions to neuroblastoma research: Professor Manfred Schwab. After almost three decades as head of the Division Tumor Genetics at the German Cancer Research Center, he has set out for a new challenge as chairman of the Alumni Association. In an interview with Stefanie Seltmann he talks about his research on the role of gene amplification in human cancers, personalized treatment of neuroblastoma, and his future plans for the Association.

Inauguration
With the attendance of Germany’s Federal Minister Annette Schavan and State Minister Theresia Bauer, the official launch of the German Consortium for Translational Cancer Research (DKTK) was celebrated in late October 2012 in Heidelberg. A major goal will be to achieve a prominent role in personalized oncology with special regard to pediatric tumors and glioma. The event was accompanied by a festive inauguration of the gantry, a unique beam guide system located at the Heidelberg Ion Beam Therapy Center (HIT).

Individualized Oncology
Tumors often vary from patient to patient. The elucidation of the molecular causes of the malignant disease in each individual is in the special focus of the newly established Heidelberg Center for Personalized Oncology (DKFZ-HIPO). The genomes of patient derived tumor cells will be analyzed for mutations thereby allowing a prognosis on disease progression related to a distinct mutation or mutation pattern. This will hopefully facilitate the decision which drug or drug combination might be most promising for the respective patient.
Dear Alumni, Colleagues, and Friends,

This Newsletter, once again in the layout designed by Dagmar Anders, reports on many of the events during 2012, both in our Alumni Association and in the German Cancer Research Center. The major event for the Alumni Association was our General Meeting in June comprising the symposium “Highlights in Cancer Research”, with some of the top scientists of our center as prominent speakers, and with a tour through “Heidelberg as a Science City”, visiting the National Center for Tumor Diseases Heidelberg, the Heidelberg ion beam therapy facility, and the old part of our town with its University Library. In our business meeting, the Honorary Memberships were approved for Nobel laureate and former DKFZ chairman Harald zur Hausen and for the founding chairman of the Alumni Association Peter Bannasch. Moreover, Manfred Schwab and Lindsay Murrells were elected as new members of the board. This was a prerequisite for the later election of Manfred Schwab by the Alumni Board as its future chairman.

A memorable event during the General Meeting of the Alumni Association was the reception at the Kurpfälzische Museum, where we presented for the first time the “Alumni DKFZ Awards” for young scientists, who had to complete their PhD or MD degree not more than three years ago and who had to be first authors of an article in a top-ranked international journal. Also during this reception, the certificates for honorary membership were handed over.

Major events and milestones at the DKFZ and the National Center for Tumor Diseases Heidelberg, which are addressed in this newsletter comprise the official opening of the nationwide alliance against cancer and the opening of the Heidelberg Center for Personalized Oncology (DKFZ-HIPO). Moreover, the Heidelberg Ion Beam Therapy Center (HIT) officially opened its doors, and a picture of the huge gantry is shown in this issue.

Interviews are presented by Stefanie Seltmann, head of the DKFZ press office, with our new chairman Manfred Schwab on his motivation and future plans for the Alumni Association, and with Carl-Henrik Heldin, long-term chair of the DKFZ Scientific Committee, on his pioneering research and his impressions during his work for the DKFZ.

A major challenge ahead for the DKFZ will be the next evaluation by an international review committee of the past, present and future research performance and planning. Since the center strongly relies on the “program-oriented funding” for the next five-year period by the Helmholtz Association, an extensive proposal with detailed plans for the program in Cancer Research has been submitted in November 2012 and will be evaluated during a site visit in spring of 2013. The main topics of this future program in Cancer Research are described in a brief overview in this Newsletter.

An important component of the activities of the Alumni Association has been organized by Gerhard van Kaick, who planned, together with Elfriede Mang, excursions to cultural, scientific, and industrial sites and centers easily reached from Heidelberg. Mentioned in this Newsletter are visits to the UNESCO world cultural heritage buildings of Maulbronn monastery and the imperial cathedral in Speyer, a visit to the famous Max Planck Institute for Astronomy, and tours to the BASF in Ludwigshafen, the world’s largest chemical industrial complex, and to the Mercedes-Benz Museum in Stuttgart.

These are just some of the topics and highlights covered in this Newsletter, and I hope that you will enjoy a look into this new issue.

With best wishes from Heidelberg,

[Signature]

The Alumni Association gratefully acknowledges financial support from MerckSerono.
From June 21 to 23, 2012, the General DKFZ Alumni Meeting took place for the 5th time in Heidelberg. On this occasion, Alumni and guest scientists from all over the world participated in the exchange on recent scientific issues and at the same time took the opportunity to refresh personal relationships.

After a warm welcome by Prof. Dietrich Keppler, organizer of Alumni DKFZ until October 2012, and an introduction into recent developments at the DKFZ by Prof. Otmar D. Wiestler, Chairman of the DKFZ Management Board, the meeting got straight to the point: Decisions of Life and Death were in the focus of Prof. Peter H. Krammer’s talk. The head of the Division of Immunogenetics gave insight into achievements in apoptosis and beyond. Prof. Peter Lichter, head of the Division of Molecular Genetics, highlighted the issue “Cancer Genome Sequencing” and led through the developments from genomics to clinical applications.

After lunch Prof. Andreas von Deimling, head of the Division of Neuropathology, talked about “Development and Application of Mutation-specific Antibodies Targeting Isocitrate Dehydrogenase 1 and BRAF”. Facts and Fiction on targeting tumor angiogenesis were discussed by Prof. Hellmut Augustin, head of the Division Vascular Oncology and Metastasis. The afternoon session of the Alumni meeting ended with a talk by Prof. Eric J. Stanbridge. The microbiologist who is distinguished research professor at the Department of Microbiology and Molecular Genetics, University of California, Irvine, presented “A Brief History of the Genetic and Epigenetic Basis of Tumor Suppression”.

Counterclockwise starting from top: Eric J. Stanbridge, Dietrich Keppler, Peter H. Krammer, Andreas von Deimling, Hellmut Augustin, Otmar D. Wiestler.
Should Auld Acquaintance Be Forgot...
A Ceremony for Important Achievements

After a day of stimulating scientific sessions and an informal get-together in the foyer of the Communication Center, the Alumni meeting was continued with a reception at Kurpfälzisches Museum in the Old Town of Heidelberg. Here, the guests awaited an award ceremony in a beautiful ambience with the delightful music of the Trio Flauto con bassi. Prof. Dietrich Keppler, chairman of the Alumni Association, presented the Alumni DKFZ Prize 2012 to Dr. Katrin Straßburger, nee Hahn, in recognition of her work published in *Cell Metabolism* in 2010. Dr. David Jones was also honored with the Alumni DKFZ Prize 2012 acknowledging his work published in *Cell* 2012 and in *Nature* 2012.

Prof. Peter Bannasch received the certificate as Honorary Member of the Alumni Association in recognition of his merits as a founder and long-term chairman of the Association. On a separate occasion, Prof. Harald zur Hausen, former Chairman of the DKFZ Management Board, had been elected Honorary Member of the Alumni Association of the DKFZ. Prof. Keppler emphasized his decisive role in the initiation and support of the Association.
Heidelberg as a Science City

On the second day of the General Alumni Meeting in June 2012, a large group of Alumni participated in a tour, which started at institutions in the Neuenheimer Feld and ended in the historical library of Heidelberg University in the old part of the town.

At the National Center for Tumor Diseases (NCT) Heidelberg, its director Christof von Kalle introduced us into the concept combining diagnostics, research, and patient therapy under one roof of a building with fascinating architecture. He explained the importance of genome sequencing and the resulting anticipated therapeutic consequences for an increasing number of cancer patients. Subsequently, he guided us through various sections of this new institution in which the Heidelberg University Hospital, the German Cancer Research Center, and the German Cancer Aid combined their efforts to make cancer therapy more efficient. Despite the short runtime of this comprehensive cancer center, it is becoming apparent that space of the building is not sufficient, therefore, plans are already underway for an expansion.

In the direct vicinity of the National Center for Tumor Diseases, the group visited the brand-new and impressive Heidelberg Ion Beam Therapy Center (HIT), which is described in more detail on page 8 of this newsletter. The tour passed by the new Children’s Hospital of Heidelberg University and the Max Planck Institute for Comparative Public Law and International Law, and made an enjoyable lunch stop in the old part of Heidelberg.

A pleasant walk brought us to the University Library, which is the oldest of its kind in Germany and was founded in 1386 together with the University (see photography of its main entry). Treasures of the library include the Codex Manesse and parts and copies of the famous Bibliotheca Palatina. Of course, the major activities today focus on the modern predominantly digital University Library, part of which is located in the Neuenheimer Feld next to the medical and scientific institutions.

GENERAL ASSEMBLY

The General Assembly of the Alumni Association was held on June 22, 2012, and comprised reports from the chairman and the treasurer, as well as unanimous votes of approval of the Board’s actions. The report from the chairman, Dietrich Keppler, mentioned the relaunch of the Alumni homepage, the new membership directory, a special e-mail address for DKFZ Alumni, and the receptions for members, colleagues, and friends at the Annual Meeting of the American Association for Cancer Research. He stressed the success of the program for guest scientists and of the Heidelberg Alumni Club organized by Gerhard van Kaick. The newly introduced Alumni DKFZ Award for young scientists was considered a valuable activity of the Association.

The treasurer, Konrad Buschbeck, reported on the favorable financial situation of our Alumni Association. He also showed that the number of members has been growing each year, however, in view of the size of the DKFZ, a further increase of the membership and voluntary contributions is clearly desirable.

Manfred Schwab and Lindsay Murrells were unanimously elected as new members of the Alumni Board, thereby replacing Dietrich Keppler and Wolfhard Semmler who announced their retirement in the near future. Unanimous votes supported the Honorary Memberships proposed by the Board for Peter Bannasch, founding chairman of our Alumni Association, and for Nobel laureate and former DKFZ chairman Harald zur Hausen who played a decisive role in the initiation of the Association.

Members of the Alumni Association can access the password-protected detailed minutes of the General Assembly on our homepage.

Dietrich Keppler
On entering Manfred Schwab’s office, your eyes instantly are drawn to an oversized Andy Warhol portrait of Dr. Mildred Scheel; a gift from the German Cancer Aid in recognition of his many years of service to the Dr. Mildred Scheel Foundation Fellowship board. During his time serving on the Board he reviewed countless research projects and interviewed numerous fellowship candidates. “Of course, the mission was to support young talents. This work always gave me great pleasure”. At the end of 2012, Manfred Schwab succeeded Dietrich Keppler as Chairman of the Board of the DKFZ Alumni Association. In this interview with Stefanie Seltmann he talks about his scientific background, his time as a researcher at the DKFZ and his plans for further development of the “Alumni”.

Seltmann: Professor Schwab, you came to the DKFZ in 1986; what influenced this decision?

Schwab: This goes back to a meeting in Urbino, Italy, I think in 1984. At that time I was working as a Heisenberg Fellow of the German Research Society in the laboratory led by the later Nobel Prize winners Mike Bishop and Harold Varmus in San Francisco. I had just identified the cancer gene MYCN and its amplification in the genome of neuroblastoma, which is one of the most frequent solid cancers developing from peripheral neural cells in young children. Harald zur Hausen also attended the meeting, and he asked whether I would like to return to Germany to the German Cancer Research Center.

Seltmann: And you accepted immediately?

Schwab: To be honest, no. The DKFZ at that time did not have the same reputation as it enjoys today, and I took some time to consider. My wife, our two sons and I had been very happy in San Francisco, and I had just been appointed Assistant Professor. But finally, after seven years we did decide to return to Germany, and I joined the DKFZ. By then the DKFZ structures were not comparable with current ones; accordingly, the early establishment phase of a research group was a bit bumpy. All in all, however, I am happy that I made this decision. The possibilities for the development of research programs, funding and the general organization and support at the DKFZ can only be described as outstanding.

Seltmann: Your research interests were, and still are, cancer genes; of limited general interest before you went to San Francisco, but now central to contemporary cancer research.

Schwab: Yes, that’s right. I had already successfully worked out genetic causes of cancer during my doctoral and postdoc studies. However, at that time it was done without the use of sequencing, PCR or molecular cloning – molecular genetics did not yet exist – but instead by employing classical Mendelian genetics: Using targeted crossings, we were able to show the activity of “tumor genes” and “differentiation genes” – now regarded as tumor suppressor genes – in the development of melanoma in fish of the platyfish/sword-tail system, in the absence of any apparent external stimuli. In the same context, during my habilitation project, I was able to describe a genetic susceptibility to neuroblastoma in the fish. At that time I did not anticipate that this would become a starting point for my future work on neuroblastoma in young children.

Seltmann: How did you get to the whole laboratory was working on chicken retrovirus when the whole laboratory was working on chicken retrovirus?

Schwab: I was not interested in chicken retroviruses. With the many postdocs already working there on retroviruses I did not see a place for a project of sufficient visibility. Therefore, I decided to analyze human tumor cells. On the basis of particular chromosome abnormalities in human neuroblastoma cells, I examined RNA expression profiles using an array of the known oncogenes and discovered the MYCN gene. Especially conspicuous was the overexpression and genomic amplification of the MYCN gene, with up to 500 additional gene copies instead of the normal two copies, in cells of particular clinical stages of neuroblastoma...

Seltmann: Neuroblastoma have varying courses of disease progression and occasionally, by spontaneous regression, disappears without therapeutic intervention...

Schwab: Exactly, that is what makes neuroblastoma up to today so fascinating for a researcher. The copy number of the MYCN gene is clinically relevant, as it may be normal or highly amplified. In early-stage neuroblastoma the copy number allows for prediction of future tumor development, independent of any other diagnostic clinical factor. Even in otherwise clinically benign tumors, the presence of amplified MYCN predicts a strongly increased risk of rapid spread, a normal gene copy number carries a more favorable prognosis. Therapeutic decisions are made on the basis of MYCN status. The analysis of amplified MYCN, now established as an international standard in pediatric oncology in Europe, Japan...
and USA, has clinical consequences for individual therapy design. The “New York Times” had referred to this finding as “Oncogenes’ Clinical Debut” – it is prototypic for the currently discussed efforts towards “personalized cancer treatment” guided by molecular markers.

Seltmann: Now, after almost thirty years of science, you will be giving up your post as Division Head at the end of May 2013. You have already taken up the chair of the Alumni Association. What attracts you to this new task?

Schwab: I am particularly excited about the prospect of further developing the Alumni Association. Of course, all considerations are based on the tremendous achievements by my predecessors in developing the association: Peter Ban- nasch as the founding father, and Dietrich Keppler who instituted trendsetting initiatives. The starting point for the future mission is already apparent in the term “Alumnus”: Alumnus means “scholar” or, using a more contemporary term, “trainee” – and we should pay particular attention to our scholars.

Seltmann: Why?

Schwab: The idea came to me recently during a visit to the Shanghai Cancer Center in China. There I met the Director of the National Natural Science Foundation of China; she did her doctoral work in Ulm and worked for many years as principal investigator at the Max Planck Institute, Munich. In further discussion, it became apparent that the Chinese Minister for Science had also studied in Germany and had worked for many years in the research and development department of a major automobile manufacturer. This perfectly demonstrates where a career path can lead to: The many young doctoral students from all over the world working at DKFZ will return to their home countries and, at least some, will become leaders in science, industry, media and politics. They are therefore perfectly placed to be enthusiastic ambassadors, heralds to spread the word of Heidelberg as a wonderful science city and particularly the DKFZ as an excellent and well-organized place for biomedical research. These contacts are of great benefit to the DKFZ.

Seltmann: Who can become a member of Alumni?

Schwab: Basically any DKFZ staff member may join; retiring from the DKFZ is not a prerequisite for membership. On the contrary, one of our goals is to increase the visibility and perception of the Alumni Association both within and outside the DKFZ, and raise the awareness that active DKFZ workers should become members. The involvement of active DKFZ members is essential. We cordially welcome trainees, including postdocs, graduates, masters, bachelors, apprentices and especially foreign associates and guest scientists.

Seltmann: What do you have to offer the newly recruited Alumni?

Schwab: Firstly, they are kept up to date on all new developments at DKFZ through our regular newsletter. Secondly, we invite them to our Alumni Meetings, which combine science- and alumni-related lectures with cultural excursions in the region. Thirdly, we take care of guest scientists at DKFZ to whom we like to present Germany in all its variety: Starting with Heidelberg Castle; visits to chemical companies and car manufacturers; further excursions, such as a trip to the TV broadcaster ZDF are planned for this spring; and finally, rounding off with culinary exploration of regional dishes...

Seltmann: You mean stuffed pig’s stomach, Bratwurst and liver dumplings?

Schwab: You may laugh, but that is exactly what we had at the conclusion of our last trip in a historic Heidelberg restaurant with guests from Asia and South America. There were no leftovers!
A Nationwide Alliance Against Cancer

With the attendance of Germany’s Federal Minister Annette Schavan and State Minister Theresia Bauer, the official launch of the German Consortium for Translational Cancer Research (DKTK) was celebrated in late October 2012 in Heidelberg.

The partnership of the DKFZ with seven German university hospitals will help to translate current research results even more swiftly into patient care. During the celebration, Prof. Otmar D. Wiestler, DKTK’s chief coordinator and Chairman of the DKFZ Management Board, expressed his wish to transfer the exemplary collaboration between cancer researchers and physicians already established at the National Center for Tumor Diseases (NCT) Heidelberg to the whole of Germany. He stressed that with the outstanding expertise provided by each consortium partner, Germany’s cancer research is well prepared to participate in networks across the border and to face the increasing challenges of international competition and be more attractive for young talents. A major goal of the DKTK will be to achieve a prominent role in personalized oncology. The consortium also aims to be at the forefront of translational research, focusing on acute myeloid leukemia, glioma and colorectal cancer in the implementation phase. Joining forces means to establish a research environment highly attractive for the best scientists and physician scientists, Wiestler explained. Furthermore, the consortium will encourage public-private partnerships with companies of the health care sector.

In the following panel discussion, scientists and oncologists of DKTK presented aspects of individual programs in the new consortium. The clinical communication platform of DKTK for instance will ensure that patients have the possibility to participate in clinical trials best suited for them anywhere in Germany. Using the example of pediatric cancer, researchers of the consortium finally explained the prospect of improved cancer therapies emanating from sequencing individual tumor genomes.

For more details on DKTK see Newsletter issue 2011, p. 1.

Celebration in the foyer of the National Center for Tumor Diseases Heidelberg with Prof. Harald zur Hausen at the speaker’s desk.
Starting a New Era of Ultrahigh Precision Radiotherapy

The Heidelberg Ion Beam Therapy Center (HIT) at the University Hospital started up its unique beam guide system (gantry) at a ceremony last autumn. Ion therapy at HIT is likely to benefit around 15 percent of the cancer patients whose tumor growth cannot be stopped with conventional therapy.

Treatment at HIT is part of the therapy concept of the National Center for Tumor Diseases (NCT) Heidelberg, which is jointly operated by the Heidelberg University Hospital and the German Cancer Research Center. The aim is to translate the results of basic research more quickly into clinical application and to provide interdisciplinary, individually tailored cancer treatment for every cancer patient. The ongoing advances in radiotherapy at HIT are an important contribution to this overall concept.

At the core of the huge radiotherapy facility is a unique gantry of astounding precision. The gigantic steel construction is 25 meters long, 13 meters in diameter and weighs 670 tons. The 360° rotating beam guide system can deliver heavy ions or protons to irradiate tumors very precisely and effectively from any angle, even if the tumors are located deep inside the body or at places surrounded by tissue that is highly sensitive to radiation. The ions reach the patients at up to 75 percent of the speed of light, can penetrate up to 30 centimeters into the tissue and still deviate from the target by no more than one millimeter. In addition, a robot-based treatment table is adjustable in six ways. Combining these two technologies enables an infinite number of beam entrance angles to be realized for the beam delivery.

HIT’s clinical operations run six days a week. Since an individual patient is irradiated around 20 times on average, some 750 patients can be treated per year in the three treatment rooms. While proton gantries are used at other international treatment facilities, especially in the United States, the Heidelberg gantry is now the world’s first facility to begin gathering experience with heavy ions.

At one of the treatment rooms, Federal Minister Annette Schavan (2nd from left) and State Minister Theresia Bauer, officially put the gantry of the Heidelberg Ion-Beam Therapy Center (HIT) into operation. Far left: Prof. Jürgen Debus, Scientific and Medical Director HIT; far right: Prof. Thomas Haberer, Scientific and technical Director HIT.

The huge gantry weighs 670 tons, of which 600 tons can be rotated with submillimeter precision. The beam delivery system enables the therapy beam to be directed toward the patient at the optimal angle.
The five Helmholtz Centers contributing to the Research Field Health, employ excellent basic research, driving the development of new approaches in prevention, diagnosis, and therapy, as confirmed by continuous reviews of their scientific portfolio. The centers have made particular efforts to extend their expertise into translational research by strengthening existing and establishing new strategic partnerships with university medical centers, academia, and industry. In the forthcoming funding period starting in 2014, the following programs will be further developed:

- Cancer Research
- Cardiovascular and Metabolic Disease
- Infection Research
- Diseases of the Nervous System
- Genes and Environment in Common Diseases

The issues of the program “Cancer Research” which is headed by Prof. Olmar D. Wiestler are commonly pursued by four Helmholtz Centers. DKFZ claims a leading role, but it is furthermore involved in the Helmholtz program “Cardiovascular and Metabolic Diseases” as there is increasing evidence for correlations between metabolic disorders and cancer.

Ongoing and future activities with regard to malignant diseases are reflected in the cancer research cycle. This encompasses a continuous exchange between excellent basic research, interdisciplinary studies to unravel mechanisms of cancer development and progression as well as translational activities from bench to bedside. Special attention is paid to so called “priority areas” which will be further expanded during the upcoming funding period. They comprise personalized oncology based on cancer genome sequencing and targeted treatment. The area of particle therapy and image-guided radiotherapy will concentrate on improving local tumor control by integrating spatial, temporal, and biological parameters towards personalized radio-oncology. Current research activities in applied tumor virology include the identification of new infectious agents associated with cancer and autoimmunity, the study of viral transformation mechanisms, the development of prophylactic and therapeutic vaccines against infection-induced tumors, and the use of viral vectors for oncolytic therapies. Activities in neurooncology focus on tumors of the nervous system. They constitute priority candidates for cancer genome sequencing, personalized oncology, and novel treatment approaches. Additionally, a number of topics are emerging as future research fields. One takes into account the association between the metabolic syndrome — obesity, hypertension, and diabetes — and increasing rates of multiple cancer types, while the immunotherapy program will be furtherexploited with regard to apoptosis and to central and peripheral tolerance in the immune system. Thirdly, DKFZ will place increasing emphasis on preventive oncology conducting research in (i) the identification of risk factors and biologic mechanisms, (ii) early detection and screening, and (iii) improving clinical outcomes of cancer patients with special regard to colorectal cancer, lung tumors, and cervical carcinoma. In view of the known demographic trends, it is also important to analyze the cost-effectiveness of future medical care for the population. A strong unit in health economics that focuses on tumor diseases will be established at DKFZ.

A flexible system of interdisciplinary cross-program activities has been implemented, focusing on drug research, metabolic dysfunction, systems biology, structural biology, biomedical imaging and radiation research. Interdisciplinary cooperation within the Helmholtz Association is also promoted through cross program activities planned under the leadership of the Research Field Key Technologies, which include Technology and Medicine, and Synthetic Biology.

DKFZ is aware that research performance critically depends on talented scientists. Therefore, a comprehensive career development program has been implemented that comprises high school and undergraduate education as well as international PhD programs and graduate training. Moreover, programs for postdoctoral education have been set up. Career perspectives also include the establishment of junior research groups. Tenure track options with special career tracks in translational research are implemented together with research professorships. Guidelines to grant equal opportunities are part of the activities, too.

Many of the major challenges faced in cancer research can only be met through active interdisciplinary cooperation. Within the program Cancer Research each topic has launched strategic partnerships. The aim is to share different expertise and jointly generate synergies for the benefit of cancer patients. Examples of such strategic partnerships are the German Consortium for Translational Cancer Research (DKTK), the Heidelberg Center for Personalized Oncology (DKFZ-HIPO) and the Heidelberg Ion Beam Therapy Center which are described in more detail in this newsletter.
Combined Approach for Individually Tailored Therapy

The newly established Heidelberg Center for Personalized Oncology (DKFZ-HIPO) is dedicated to the elucidation of the molecular causes of cancer in each individual. To this end the genome of patient derived tumor cells will be analyzed for mutations thereby allowing a prognosis on disease progression related to a distinct mutation or mutation pattern. This will hopefully facilitate the decision which drug or drug combination might be most promising for the respective patient.

DKFZ-HIPO integrates the expert research groups in functional genomics, systems biology, and translational oncology into a unified organizational structure. The center is coordinated by the HIPO Directorate (Prof. Peter Lichter (chair), Prof. Roland Eils and Prof. Christof von Kalle) and consists of three programs: (1) Genome analysis (Lichter), (2) Systems biology (Eils), and (3) Precision oncology (von Kalle). The mid- to long-term goal of DKFZ-HIPO is to readily translate latest research and technologies from the field of functional genomics and systems biology into clinical practice. A technology platform for high-throughput sequencing, data analysis, and imaging features requires technology for pursuing the center’s ambitious goals. In particular, it integrates the next-generation sequencing (NGS) platform (Genomics and Proteomics Core Facility; PD Dr. Stefan Wiemann and Dr. Stephan Wolf) with an envisioned annual throughput of more than 1,000 cancer genomes. This sequencing unit is complemented by a bioinformatics hub that hosts Germany’s largest data facility in the life sciences together with a very strong genome data analysis group that oversees the entire area of data analysis in all three projects of the International Cancer Genome Consortium (ICGC) in Germany. A mass spectrometry-based proteomics laboratory will add to these platforms. For a detailed, mechanistic study of deregulated pathways in vivo, a next-generation microscopic imaging platform is currently being established that will provide all imaging devices required for high-throughput, high-content analysis, and perturbation of cellular processes at a single cell level in an in vivo setting.

Within DKFZ-HIPO, collaboration with the University Women’s Hospital on the analysis of the RNA transcriptome from 200 breast cancer patients is envisioned. In summer 2012 the analysis of the exomes of patient-derived pancreatic carcinomas has started. Other projects jointly established with the Heidelberg University Hospital include research on brain tumors, tumors of the gastro-intestinal tract, and leukemia. Additionally, the whole genome of up to 100 striking cases (for example, if an unexpected positive therapy response occurs) will be analyzed for the underlying mechanisms. As a start, DKFZ supports this important center with annually 3.3 million Euros for a period of five years.
A Visit to the Shanghai Cancer Center

During a visit to Fudan University Shanghai Cancer Center in October, Manfred Schwab, the newly appointed chairman of the Alumni Association, not only gained insight into the expertise of the leading cancer center in China, but also experienced a remarkable hospitality. A celebration for the new Chinese Office of the Journal “Cancer Letters” complemented the stay in Shanghai.

Following an invitation by President Prof. Xiaomao Guo, Prof. Xianjun Yu, Chief of the Surgery Department, and Prof. Min Li, Director of the Pancreatic Cancer Research, Manfred Schwab travelled to Shanghai to learn about Fudan University Shanghai Cancer Center (FUSCC), which was established in 1931 and has been the first hospital specializing in cancer in China. After 80 years of development, FUSCC has become the leader among cancer centers in the People’s Republic in the field of radiation oncology, pathology, breast cancer and pancreatic cancer. Today, FUSCC is a triple A comprehensive cancer center under the auspices of the Ministry of Health. The work focuses on early diagnostics and treatment of cancer with multidisciplinary approaches that strictly follow international standards. Surgery, radiotherapy, chemotherapy, traditional Chinese medicine (TCM), intervention therapy and biotherapy are combined to yield optimal outcome. FUSCC staff currently comprises 1,139 medical professionals, 138 professors and associate professors. The center has 1,200 beds, with an annual out-patient visit load of 592,441 and an annual in-patient admission of 22,515. Yearly, there are 4,700 patients receiving radiotherapy, and 14,454 patients are treated surgically. The research activities of the comprehensive cancer center are directed towards elucidating the pathogenesis and etiology of different cancers, aim at developing early diagnosis and treatment measures and searches for the optimal strategies for prevention and combined-modality treatment. State-of-the-art equipment and technology in cell biology, molecular biology and genetics as well as animal facilities are available. A highlight is certainly the Fudan University Pancreatic Cancer Institute, the leading institute in basic scientific research and clinical practice in treatment of patients with these tumors in China. Further, the Fudan University Breast Cancer Institute has established an impressive record in angiogenesis research. Additionally, the Center for Radiation Oncology is of particular importance for FUSCC.

International alliances include the establishment of a sister institute with The University of Texas MD Anderson Cancer Center in 2003, The Cancer Institute Singapore Healthcare Group in 2005, Institute Gustave-Roussy near Paris in 2008, and the Japanese Cancer Research Institute of Kanazawa University in Japan in 2010. After the introduction to the FUSCC, Prof. Schwab in turn offered a glance at current and future research activities of the DKFZ. In particular, he presented recent findings on genetic instability in human cancer, particularly in neuroblastoma. Schwab’s introduction on “Writing Scientific Manuscripts” was met with particular interest among young Chinese scientists. Afterwards Schwab presented the journal “Cancer Letters”, for which he is Editor-in-Chief. A special occasion during the visit in Shanghai was the opening ceremony of a Chinese Office of Cancer Letters. The establishment of the office was made possible by the farsighted and tremendous support of FUSCC President Prof. Xiaomao Guo. The visit has established friendship with leading FUSCC scientists. Their warm hospitality has been impressive – not to mention the overwhelming range of Chinese dishes during lunch and dinner. Plans are underway to welcome FUSCC scientists in the near future at the DKFZ.
Since 1986, Carl-Henrik Heldin has been Branch Director of the Ludwig Institute for Cancer Research in Uppsala, Sweden. In 1992, he became Professor in Molecular Cell Biology at Uppsala University. His research interest is related to mechanisms of signal transduction by growth regulatory factors, as well as their normal function and role in disease. Heldin has served as a member of DKFZ’s Scientific Committee from 2002 till 2010 with the chair from September 2006 till 2010. From 2006 till 2010 he was also member of the Board of Trustees. At the end of 2011, an honorary doctorate of the Medical Faculty of Heidelberg University was conferred to this distinguished Swedish scientist.

In an interview with Dr. Stefanie Seltmann Prof. Heldin talks about his opinion on the past years of cancer research in Germany and how he rates the challenges and new approaches facing the global burden of tumor diseases.

Seltmann: Dr. Heldin, you served in the Scientific Committee of the German Cancer Research Center for many years. What are your impressions on cancer research in Germany?

Heldin: Well, I was very much impressed with what I saw when I was on the Scientific Advisory Board of the DKFZ; there is clearly a lot of excellent work being done here. It’s also an impressive concentration of cancer research in this place with many different academic groups of different directions and interdisciplinary medical approaches.

Seltmann: I am persuaded that eventual mastery of cancer will come only from intense and unremitting scientific exploration over decades”, says Daniel Ludwig, the founder of the famous Ludwig Institutes. Is that your opinion, too?

Heldin: Yes, definitely. As you know, during his presidency in the United States, Richard Nixon declared war on cancer in 1971, more than forty years ago, and this was sort of an important event, but, of course, it was not as easy as people might have thought at that time. Despite the large effort that was made, we still haven’t really been able to cure cancer. We should be realistic: A lot more work is required before this problem is solved and we can actually offer efficient therapies. Nevertheless, I am fairly optimistic that we gradually will be able to find ways to treat all tumor types.

Seltmann: What do you think are the most interesting and promising areas of cancer research in the coming years?

Heldin: The whole issue of cancer stem cells or tumor-initiating cells is very interesting, I think, and I guess this is also an area where we will learn much more in the near future.

Seltmann: You are a leading expert on signal transduction in cells, with special focus on the growth factors PDGF and TGF-β. What is their role in cancer?

Heldin: Platelet-derived growth factor (PDGF) stimulates cell growth and particularly cells of connective tissue origin. An overactivity of PDGF can then drive development of tumors that carry receptors for PDGF. But there are also mutations of the receptors which then make the receptors overactive in other types of cancers. So there can be direct proliferation, stimulation of proliferation by PDGF or overactivity of PDGF receptors. But PDGF also has a more general role in solid tumors where it can promote angiogenesis and it can also affect the stroma of tumors.

Seltmann: And what do we know about the other one, the TGF-β?

Heldin: Transforming growth factor beta (TGF-β) is a component which affects almost all cell types of the body and it displays both tumor-suppressing and tumor-promoting activities. In tumor biology TGF-β plays a complicated role. Initially it prevents us from getting cancer, but at later stages it promotes the formation of malignant cells.

Seltmann: So it might be difficult to influence these factors in order to see a positive clinical effect?

Heldin: Yes, PDGF is easier because if you inhibit PDGF or PDGF receptors, you can help tumor patients with an overactivity of these PDGF receptors. However, with TGF-β it is more tricky because you would
Seltmann: Is there a high risk for side effects as PDGF does not only play a role in cancer cells?

Heldin: Yes, however the side effects are rather small. The most dramatic effect is the edema, particularly around the eyes where the tissue is very soft. This is due to one of the normal functions of PDGF as a regulator of the interstitial fluid pressure in tissues. So if you inhibit TGF-β you’ll get edema. There are also other side effects, but they are fairly small.

Seltmann: Tumor cells learn rapidly, so if you inhibit one pathway the cell might escape via another one. How do you rate the problem of development of resistance?

Heldin: Indeed, this is a big problem, as you pointed out. Resistance of many tumor cell types occurs frequently, often caused by inhibition of PDGF. Most likely TGF-β will be associated with problems of tumor resistance, too. It seems that most people believe that you need to inhibit many pathways at the same time in order to increase the chances of a successful cancer treatment.

Seltmann: What does ‘difficult time’ actually mean?

Heldin: Well, the stock markets are now so volatile that the value of the fund can change very rapidly. And it’s also difficult to get any interest money as the interest rates are pretty low now. But if you deposited your money in a very safe way you would be subjected to even lower interests. So it’s a tricky situation to deal with.

Seltmann: Thank you very much for your insights.

like to inhibit only the tumor-promoting effects of TGF-β but not the tumor-suppressing influence.

Seltmann: Are there any drugs available yet, which are based on the knowledge of these pathways?

Heldin: Yes, indeed. And they are already in clinical use: A drug called Imatinib, or Glivec, which inhibits PDGF receptor kinases and is used for treatment of chronic myelogenous leukemia, as it also inhibits another tyrosine kinase, Ableson. But for those rare tumors in which PDGF receptor kinases are overactive this drug can help.

Seltmann: And for the other one, for TGF-β?

Heldin: For TGF-β there isn’t yet a clinical application, but there are approaches which aim at developing inhibitors for TGF-β, too.

Seltmann: So what does ‘difficult time’ actually mean?

Heldin: Well, the stock markets are now so volatile that the value of the fund can change very rapidly. And it’s also difficult to get any interest money as the interest rates are pretty low now. But if you deposited your money in a very safe way you would be subjected to even lower interests. So it’s a tricky situation to deal with.

Seltmann: Thank you very much for your insights.
The European Research Council (ERC) supports two DKFZ scientists with the prestigious ERC Advanced Grants for a period of five years with funds of 2.5 and 2.0 Mio. Euros, respectively. **Prof. Michael Boutros**, head of the Division Signaling and Functional Genomics, wants to investigate the interaction of all genes in a higher developed organism. **Prof. Bruno Kyewski**, head of the Division Developmental Immunity, received the grant for a project on tolerance mechanisms of immune cells towards the body’s own molecular structures.

**Dr. Ana Garcia-Saez**, head of the Junior Research Group Membrane Biophysics, was awarded an ERC starting grant for the project titled "The quantitative Bcl-2 interactome in apoptosis: decoding how cells escape cell death". The project will be financed by the European Scientific Council over a five-year period with 1.46 million Euro. The 35 year old scientist has recently accepted a full professorship at the University of Tübingen.

**Prof. Ingrid Grummt**, head of the Division Molecular Cell Biology II, received the prestigious “Prix International” for her life’s work from the French Institut National de la Sante et de la Recherche Medicale (INSERM). The institute honored the cell biologist for elucidating important regulatory mechanisms in gene expression. The presentation ceremony took place in December 2012 at the College de France in Paris in attendance of the French Minister of Health and the Minister of Research.

**Prof. Peter Krammer**, head of the Division Immunogenetics, was honored with the Deutsche Krebshilfe Prize 2011 (award of the German Cancer Aid) for his pioneering work on programmed cell death. He shares the prize with Prof. Klaus-Michael Debatin, University Medical Center Ulm. Krammer was additionally awarded the Johann Georg Zimmermann Medal for his commitment in fighting cancer.

**Prof. Peter Lichter**, head of the Division of Molecular Genetics, was awarded the Jacob Henle Medal by the Medical Faculty of the University Medical Center Göttingen for his contributions to tumor genetics that help to predict tumor progression more precisely. Lichter has also been honored with the ESHG Award of the European Society of Human Genetics. The organization acknowledges Lichters pioneering achievements in the fields of cytogenetics and genome structure, especially the development of assays to provide evidence for cancerogenesis.

**Dr. Armin Nagel**, Division of Medical Physics in Radiology, was honored with the Coolidge Award 2012 for innovation in the use of imaging techniques in diagnostics. The researcher used signals from sodium atoms for magnetic resonance imaging instead of the usually employed hydrogen atoms. Thereby, it becomes possible to visualize pathologic tissue alterations. Nagel shares the prize with Dr. Mirko Pham, a colleague at the Heidelberg University Hospital.

**Dr. Christiane Opitz**, member of the Helmholtz University Young Investigator’s Group Experimental Neuroimmunology at DKFZ and physician scientist at Heidelberg University Hospital, is this year’s recipient of the Hella Bühler Prize, which

Since September 2012, **Dr. Susanne Weg-Remers** heads the Cancer Information Service (KID). The physician followed **Dr. Regine Hagmann**, who successfully led KID as acting head for the last three years.

**Dr. Thomas Hofmann**, head of the Junior Research Group Cellular Senescence, is awarded the prize of the Berlin-Brandenburg Academy of Sciences and Humanities for his outstanding achievements in cancer research. The biologist unraveled mechanisms by which cells decide upon their future role following DNA damage.
is endowed with 100,000 euros. Opitz received the award in recognition of her ongoing and future research on a signaling pathway that enhances the progression of malignant glioma and impairs immune responses. Developing inhibitors of this signaling pathway might lead to new chemotherapeutic drugs.

A research team headed by Prof. Stefan Pfister received 450,000 US Dollar from the James McDonnell Foundation. The scientists from both DKFZ and Heidelberg University Hospital intend to develop a method to detect brain tumors in cerebrospinal fluid samples. The biology and the size—both decisive factors in determining treatment—will also be assessed using this method. Stefan Pfister heads the Pediatric Neurooncology Division at DKFZ and is a practicing pediatrician at the University Hospital.

Prof. Michael Platten, head of the Helmholtz University Young Investigator’s Group Experimental Neuroimmunology, is one of the two awardees that received the Chica and Heinz Schaller Research Award 2011. The distinction endowed with 100,000 Euro acknowledges Platten’s groundbreaking work in basic biomedical research. The scientist who is also affiliated to the Department of Neurooncology at the Heidelberg University Hospital elucidated the role of tryptophan metabolism in the growth of brain tumors.

The German Society for Medical Physics honored Prof. Wolfhard Semmler with the Glocker Medal. The award acknowledges his many years of commitment to Medical Physics. He is the third DKFZ scientist after Prof. Walter J. Lorenz and Prof. Wolfgang Schlegel to have received this medal. Semmler heads the Division Medical Physics in Radiology.

Prof. Gerhard van Kaick, formerly head of the Division Oncological Diagnostics and Therapy, has been awarded the Röntgen-Medal of the City of Remscheid. He received the award for his studies on the diagnosis and evaluation of long-term damages caused by radiation, as well as for his investigations into clinical application of imaging technologies.

In October 2012, Prof. Otmar D. Wiestler, Scientific Director and Chairman of the DKFZ Management Board, has been awarded an honorary doctorate of the Medical Faculty of the University of Tübingen.

Prof. Harald zur Hausen, former Chairman of the DKFZ Management Board and Nobel laureate in 2008, is one of three awardees honored with the Tsungming-Tu Award 2011 of the National Science Council in Taiwan and the Alexander von Humboldt Foundation. The distinction of 75,000 US-Dollar has been conferred for the virologist’s groundbreaking investigations that have led to the development of a vaccine against cervical cancer.

Obituary

Prof. Rudolf Preussmann, head of the Division Environmental Carcinogens from 1970 until 1993, died at an age of 84. Starting his career in Freiburg in toxicology, the chemist provided the basis for the seminal discovery of more than 60 nitrosamines and nitrosamides producing many types of cancer in laboratory animals. At DKFZ, he focused on chemical carcinogens in the human environment and the development of preventive measures. His outstanding achievements were honored by the Federal Cross of Merit on Ribbon (1981), the Honorary EACR-Membership, and the German Cancer Award (1992). Rudolf Preussmann will be commemorated not only as a great scientist but also as a colleague with remarkable integrity and high standing.

PD Dr. Angelika Riemer, head of the Junior Research Group Immunotherapy and prevention, has been elected member of the Young Academy, a joint project of the Berlin-Brandenburg Academy of Sciences and the Leopoldina, the German National Academy of Sciences.
Advances in Stem Cell Research and its Role in Cancer Development

The 7th International Heinrich F. C. Behr Symposium at DKFZ in Mid-October 2012 was dedicated for the fourth time to the exciting topic of “Stem Cells and Cancer”. A highly interactive meeting sparked by a panel of internationally renowned speakers gave the opportunity to discuss the role of tumor stem cells in the development of cancer and how they sustain tumors and cause metastasis. Catriona Jamieson, University of California in San Diego, for example, is searching for ways to track down and destroy blood cancer stem cells hidden in their “niche” in the bone marrow. Luis Parada from the University of Texas in Dallas reported on his latest findings on brain tumor stem cells while Owen Witte, University of California in Los Angeles, explained in his talk that prostate cancer also originate from tumor stem cells. Finally, in the last session Markus Wernig, Stanford University in California, reported how his group succeeded, based on the work of nobel laureate Shinya Yamanaka, in directly reprogramming skin cells into nerve cells without the detour via stem cells. The symposium was jointly organized by the German Cancer Research Center (DKFZ), the National Cancer Institute (NCI), Bethesda, and the German Academy of Sciences Leopoldina with generous support by the Heinrich F. C. Behr Foundation.

Concerted Action to Fight a Worldwide Burden

At DKFZ, Germany’s largest biomedical research center, more than 2500 staff members, including 1000 scientists, are actively involved in unraveling the basic mechanisms that lead to cancer, identifying cancer risk factors, developing cancer prevention strategies and translating the results from bench to bedside in order to improve cancer diagnosis and therapy. The brochure “Cancer Research at DKFZ” which will be published in February 2013 is a tour d’horizon of the research programs with its divisions and research groups as well as the core facilities. Many major contributions in recent years and current issues at the cutting edge of cancer research constitute the reputation of the center – the new publication gets it all straight to the point. No matter if you are PhD student, Postdoc, group leader or a full Professor – if you want to learn more or even join the DKFZ you will not be mistaken reading this concise compendium. The brochure, written in English, will be available soon as PDF and a printed version. For more information, please, contact presse@dkfz.de.

An Insight into Medieval History during a Visit to Maulbronn and Bretten

The famous monastery of Maulbronn belongs to the cultural highlights easily reached from Heidelberg. This made it an attractive destination for an excursion arranged by the guest scientist program of the Alumni Association.

Under ideal weather conditions our group arrived at the historical site founded in 1147 by Cistercian monks, and inscribed in the UNESCO world cultural heritage list since 1993 as the best-preserved medieval monastery complex north of the Alps. Early parts of the monastery of Maulbronn were built in the Romanesque style, while most other buildings, including the church and the convent showed a transitional Romanesque-Gothic architecture. The Duke of Württemberg who converted from the Catholic to the Protestant religion in the 16th century decided to turn the building into a protestant state monastery school. This school, founded in 1556, had well-selected scholars, many of whom became protestant priests later on. Famous scholars include the astronomer and mathematician Johannes Kepler (1571 – 1630), the poet Friederich Hölderlin (1770 – 1843), and the writer and Nobel laureate Hermann Hesse (1877 – 1962). With a short walk to the “deep lake”, which formerly served the monks as a source of fish for their meals on Fridays, the visit to Maulbronn ended.

On our way back we made a stop in Bretten with the history of the old town, particularly during the war between the French King and the Palatine (1688 – 1697). Bretten is famous for its former citizen Philipp Melanchthon (1497 – 1560), later professor at the University of Wittenberg. As a collaborator with Martin Luther, he played a decisive role in the Reformation process.

The excursion not only provided insights into medieval history of our region, but also supported a lot of interactions between the participants from many countries, including China, India, Iran, Nigeria, Poland, and the USA. At the end of the tour Gerhard van Kaick and his organizing team received a lot of appreciation for this successful visit of cultural treasures near Heidelberg.
excursions

An Entertaining Lesson in Regional History

An invitation to the exciting historical sites of the Rhine-Neckar area was well received: On a sunny day in late September a group of DKFZ Alumni and guest scientists from various countries started for a visit to the chemical company BASF in Ludwigshafen and afterwards to the old City of Speyer.

Established in 1865 as a manufacturer of chemicals necessary for dye production, BASF has meanwhile developed into a huge enterprise with international activities in the fields of Chemicals, Plastics, Performance Products, Functional Solutions, Agriculture Solutions, as well as Oil and Gas. Topics like production processes using living organisms, also called “White Biotechnology” and plant biotechnology were at the center of the presentations at BASF. In the afternoon, the group took the opportunity to gain some insight into the vivid past of the City of Speyer with its famous Cathedral. The history of Speyer began with the construction of a Roman camp around 10 BC. Around the year 500 AD the name “Spira” first appeared in written documents. A decisive event in the history of the town was in 1024 when Konrad II., a Salian from the Speyer district, was elected king of Germany, drawing Speyer into the center of imperial politics. In 1816 Speyer became capital of the district of the Pallatinate.

Worth visiting is the “Imperial Cathedral of Speyer” which was added to the UNESCO World Heritage List of culturally important sites as a “major monument of Romanesque art in the German Empire”. Based on the foundation walls of a former basilica, the cathedral was completed in 1106 after nearly 80 years of construction. During the following centuries, the cathedral served as a burial site for eight Salian, Stauffer and Habsburg Emperors and Kings. The Pallatinate War of Succession in the late 17th century as well as the Napoleonic Wars (1803-1815) have left their marks on both the cathedral and the City of Speyer. Yet, today an elaborately renovated medieval town with modern features awaits its guests.

Stuttgart Comes Up With Unique Technology and Great Nature

Have you ever been on a travel into the heart of motorization history, architecture and exotic wildlife? Guests of the Alumni Association did so when they joined an excursion to the Mercedes-Benz-Museum and the zoological gardens of Wilhelma in Baden-Württemberg’s capital.

On Saturday, May 5, more than 50 co-workers from different nations (China, Vietnam, The Netherlands, Turkey, Ukraine, Poland, Iran, USA, South America, Vietnam) entered the bus for Stuttgart. The first destination was the Mercedes-Benz Museum which opened in May 2006. The museum close to the main automobile production plant in Untertürkheim combines living history and future innovations in a unique architectural space. The building’s height and “double helix” interior contains more than 160 vehicles, some dating back to the very earliest days of the motor engine. In 1883, Gottlieb Daimler laid the foundations for a motorized society by developing the world’s first high-speed four-stroke gasoline engine. Between 1885 and 1888, Daimler and his companion Wilhelm Maybach used this engine to motorize a carriage, a ship, a handcar, a streetcar, a fire-fighting pump and an airship and not least, they built the world’s first motorcycle, the so-called Riding Car. It was the beginning of universal motorization on land, on water and in the air. Our group of visitors was quite captivated by the sophisticated presentation of the past, present and future of mobility in show rooms on nine floors.

Later, the lunch break gave the opportunity for the participants to taste Swabian meals like “Spätzle” and “Maultaschen”. Vivid discussions arouse when Professors Ada and Donald Olins who had been guest scientists at the DKFZ for several times exchanged their broad experiences with younger scientists.

The afternoon tour took us to the Wilhelma – Europe’s only large combined zoological and botanical garden that is home to over 8,000 animals from over 1,000 different species and exotic plants from over 5,000 species. Originally, the Wilhelma was a royal palace and reflects such buildings as the Alhambra Palace. Beside its exotic and extraordinary selection of animals and plants, the Wilhelma is also worth visiting for its architecture, which is intact from the mid-19th century. Being closed during World War II, Wilhelma was reopened in 1949 and started with an “Azalea Show”. Today, the zoo is famous for keeping all four kinds of great apes (bonobos, chimpanzees, orang-utans and gorillas) in families with offspring. Wilhelma has become a center for raising motherless apes from all over Europe. The participants enjoyed the day and many of them are already looking forward to the next excursion.

Gerhard van Kaick
A visit to the famous Max Planck Institute for Astronomy on the hills above Heidelberg gave impressions of the work of the institute as well a view of the exciting architecture of the new house of astronomy.