dkfz. GERMAN CANCER RESEARCH CENTER IN THE HELMHOLTZ ASSOCIATION

Research for a Life without Cancer

DZG DEUTSCHE ZENTREN DER GESUNDHEITSFORSCHUNG

DKTK German Cancer Consortium

Fighting cancer together – the German Cancer Consortium (DKTK)

ANNUAL REPORT 2022

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The **German Cancer Consortium (DKTK)** is a national consortium of specialist oncological institutions and university hospitals. It is funded by the German Federal Ministry of Education and Research (BMBF) and participating German states.

Cover image:
Right: Colorectal carcinoma with PanCK+ epithelial cells (cyan), blood vessels (CD31+, red), collagen fibrils (gray), and immune infiltrate (calprotectin/neutrophils, magenta) and macrophages (CD68, yellow) (© Hartmann group)
Bottom: Invasive breast cancer with PanCK+ epithelial cells (green), collagen fibrils (gray), blood vessels (CD31+, red) and immune infiltrate (CD68+/macrophages, yellow; CD8+ T-cells, magenta; CD14+ monocytes, cyan) (© Hartmann group)
Left: Invasive lung adenocarcinoma with tumor cells (EpCAM+, cyan), glucose-6-phosphate dehydrogenase expression (magenta), and immune infiltrate (CD3e/T-cells, yellow; CD14/monocytes, green) embedded in extracellular matrix (collagen1A1, gray), and blood vessels (CD31+, red) (© Hartmann group)
Top: Colorectal carcinoma with PanCK+ epithelial cells (green), blood vessels (CD31+, red) and immune infiltrate (CD68/macrophages, yellow; CD3e/T-cells, cyan), and smooth muscle actin (gray) and the amino acid transporter ASCT2 (magenta) (© Hartmann group)
Middle: Tumor cell under the microscope (© studioworkstock)

Foreword

The German Cancer Consortium (DKTK) is a long-term, joint initiative involving the German Federal Ministry of Education and Research (BMBF), participating German states, and the German Cancer Research Center (DKFZ) as its core center. At the eight DKTK partner sites, scientists and clinician scientists from more than 20 university hospitals and academic research institutions with a particular track record in oncology have been successfully pooling their strengths in the struggle against cancer for ten years. As one of six German Centers for Health Research (DZG), each of which focuses on a different common disease, the DKTK aims to achieve important advances in the prevention, early detection, diagnosis and treatment of cancer.

Society and the healthcare system are both facing major challenges because of the continuing steep rise in cancer diagnoses, due primarily to changes in lifestyle and environmental impacts, but also to a general increase in life expectancy. The DKTK focuses largely on preclinical research topics – topics at the interface between basic research and clinical practice – in order to enable new knowledge to be transferred to clinical application in as targeted a manner as possible. This process is called "translation". The research approaches described, involving a wide range of specialist and methodological expertise, cutting-edge technology platforms and an established culture of collaboration between sites and disciplines, are essential for personalized oncology. Particularly since cancer is not a disease with a uniform disease pattern, but manifests in many different ways and with different tumors, depending on the affected tissue. This approach to developing and testing new strategies was once again singled out for special recognition by the DKTK's Scientific Advisory Board in 2022.

Support for a number of additional important translational research projects was achieved through competitive calls for proposals in the DKTK Joint Funding Program. More than 50 Joint Funding projects involving at least three partner sites have been launched since 2012. These joint projects offer both long-standing DKTK researchers and newcomers an important platform to establish innovative research approaches. Networking opportunities for early career researchers are provided in particular by the DKTK School of Oncology with its comprehensive training and professional development programs.

In all our scientific efforts at the DKTK, we place a high value on listening to patients and taking their wishes, ideas and suggestions on board at various stages of the research process. By establishing the DKFZ/DKTK Patient Advisory Council on Cancer Research early foundations were laid for this, and the dialogue with the patient representatives continued in 2022.

An anniversary event provided an opportunity to look back at the successes of the past ten years and forward to future goals. I would like to invite you to read more about developments at the DKTK in this annual report and hope you find it stimulating.

Prof. Dr. med. Dr. h. c. Michael Baumann
Spokesperson of the German Cancer Consortium (DKTK)

Cancer in figures

Around **500,000** **people are diagnosed** each year.

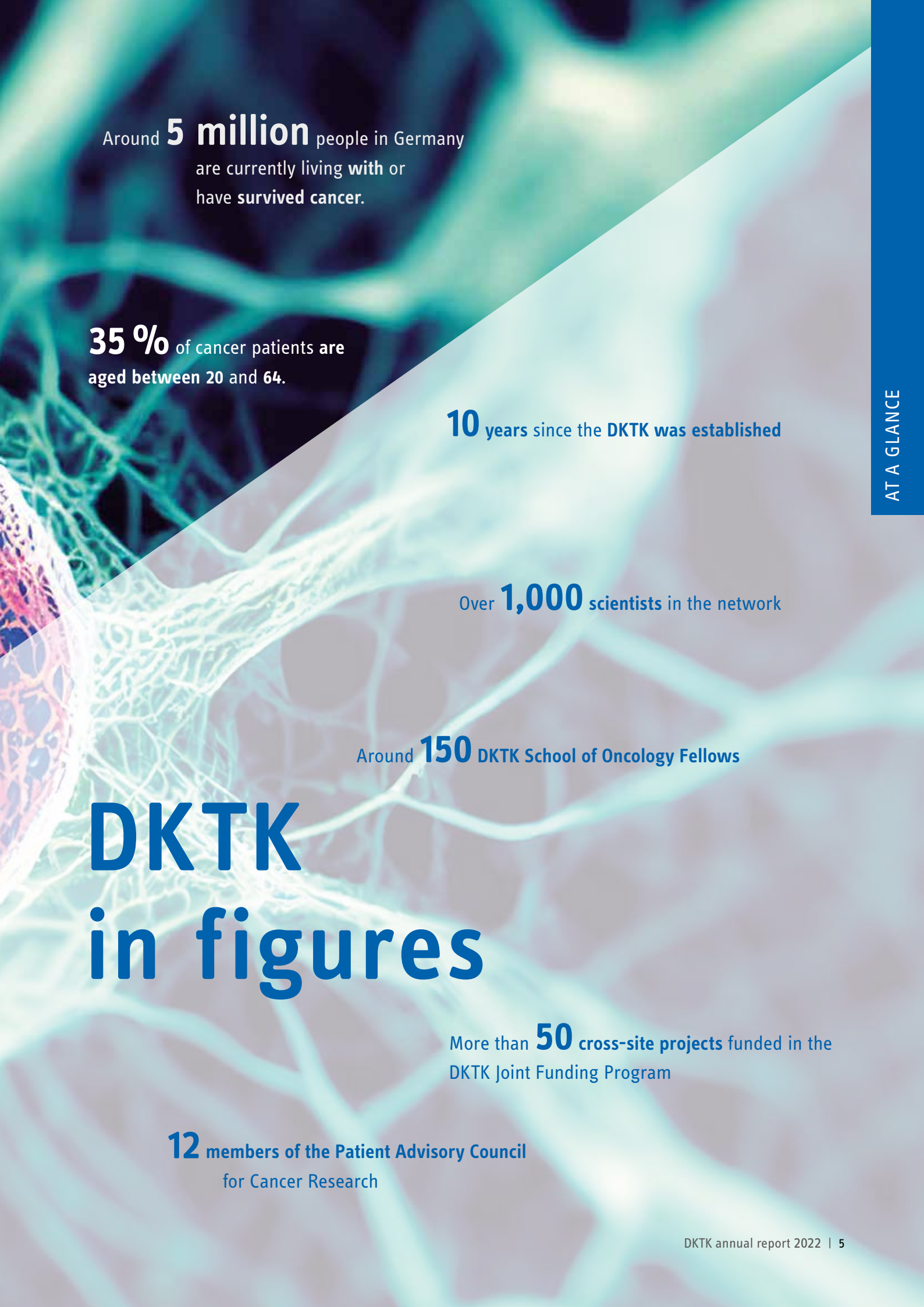
65 % **of patients survive** the next 5 years.

By 2030,
cancer incidence will
rise by **20 %**.

More than **200,000** **people**
die of cancer each year.

305 **positions financed**
by the DKTK in 2022

Since 2012, **13** **DKTK professorships,**
3 **DKTK-associated professorships,**
1 **clinical cooperation unit** and
12 **young investigator/junior research groups**



Around **5 million** people in Germany are currently living **with** or have **survived cancer**.

35 % of cancer patients **are aged between 20** and **64**.

10 years since the **DKTK was established**

Over **1,000 scientists** in the network

Around **150 DKTK School of Oncology Fellows**

DKTK in figures

More than **50 cross-site projects** funded in the DKTK Joint Funding Program

12 members of the Patient Advisory Council for Cancer Research

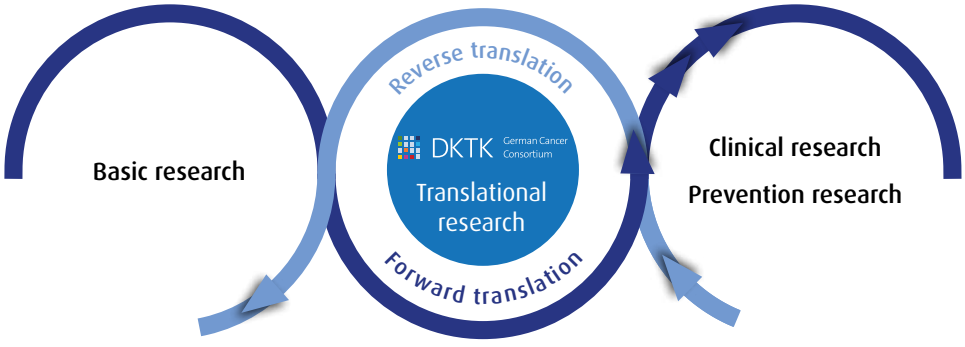
(© AdobeStock/Vladimir Borovic)

Bridging the gap between basic and clinical cancer research

About the DKTK

Despite the major advances that have been made in medical cancer research, there are still many types of cancer for which no optimal treatment or therapy is available. Basic research has delivered vital new knowledge about cancer over the past few decades. Scientists, physicians and regulatory authorities are working closely together so that this knowledge can be translated into clinical applications. The term “cancer” stands for a large number of different diseases, all of them caused by changes in the genomes of cells. These changes can affect practically any type of tissue cell and, depending on a wide range of other factors, such as environment and lifestyle, can lead to very individual clinical manifestations. In order to manage the heterogeneity of cancer and, ultimately, to develop personalized cancer therapies, it is essential to conduct scientific research on precisely defined tumor materials and to pursue interdisciplinary collaboration between basic research and clinical research.

The establishment of the DKTK in 2012 laid the foundations for a national cancer research network, bringing together leading institutions and expertise from different disciplines in clinically oriented cancer research through new long-term structures. The aim of this translational research is to speed up the transfer of promising laboratory results into clinical application in order to improve and personalize the early detection, diagnosis and treatment of cancer.

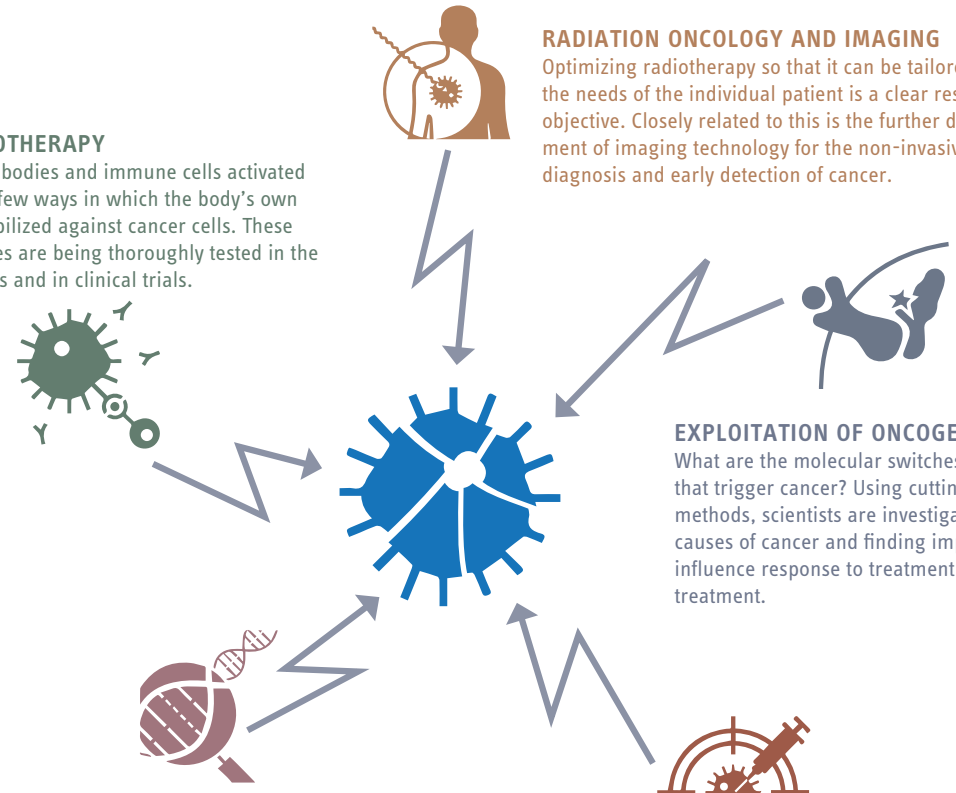


(© DKTK)

The German Cancer Research Center (DKFZ) in Heidelberg is the core center of the DKTK, collaborating with research institutions and hospitals with a particular track record in oncology in translation centers at eight partner sites. Institutional funding is provided via the DKFZ with 90:10 financing by the federal government and the participating federal states, securing long-term prospects for preclinical and patient-oriented research projects. In order to further strengthen close collaboration between all sites, researchers within the DKTK can apply for funds from the Joint Funding Program.

Effective translation of research into innovative clinical applications

The five DKTK research programs focus on integrating different phases of the translation process. This ranges from the discovery of cancer-related molecular changes to the development and testing of molecular biomarkers for prevention and diagnostics, through to the preparation of early clinical trials and the future application of new diagnostic and therapeutic approaches in patients. Observations from clinical practice, for example the development of therapy resistance, tumor recurrence, and metastasis, are fed back into experimental research in close consultation with clinicians (= reverse translation) and are investigated thoroughly. Research conducted in the DKTK focuses primarily on novel treatment approaches based on molecular analysis, such as the use of targeted therapeutics and combination therapies, cancer immunotherapy, advanced radiation therapy treatments and personalized surgical procedures. The harmonization of processes and workflows at all sites plays a key role in ensuring this research is conducted efficiently.



CANCER IMMUNOTHERAPY

Tumor vaccines, antibodies and immune cells activated in the lab are just a few ways in which the body's own defenses can be mobilized against cancer cells. These and other approaches are being thoroughly tested in the research laboratories and in clinical trials.

RADIATION ONCOLOGY AND IMAGING

Optimizing radiotherapy so that it can be tailored to the needs of the individual patient is a clear research objective. Closely related to this is the further development of imaging technology for the non-invasive diagnosis and early detection of cancer.

EXPLOITATION OF ONCOGENIC MECHANISMS

What are the molecular switches and genetic changes that trigger cancer? Using cutting-edge analysis methods, scientists are investigating the molecular causes of cancer and finding important indicators that influence response to treatment and the course of treatment.

MOLECULAR DIAGNOSTICS, EARLY DETECTION AND BIOMARKER DEVELOPMENT

Biomarkers can be used to detect cancer at an early stage, predict recurrence and assess more accurately whether a treatment will be successful. This also includes the further development of early detection and diagnostic methods, e.g. liquid biopsies, to provide reliable diagnoses without having to remove tissue.

MOLECULARLY TARGETED THERAPY

Researchers working on this program identify molecular weak points for targeted cancer drugs. Clinical trials then help develop these drugs further and bring them into clinical practice.

In many cases, effectively joined-up research at the DKTK has been made possible by new infrastructure and platforms. The consortium-wide, federated infrastructure of the Clinical Communication Platform (CCP) allows the DKTK community to link clinical data relating to cancer patients from research projects and information about biosamples, and to make them available to research within the DKTK, while complying with the highest data protection standards. This data collection of detailed clinical progressions of tumor diseases is one of the largest in Europe (for more information, see page 22).

Ongoing developments of the DKTK's RadPlanBio (Radiation DosePlan-Image/Biomarker-Outcome) platform are currently focusing on making data FAIR (findable, accessible, interoperable and reusable) and on participation in the LibreClinica community, helping to provide one of the few open-source systems that meets the requirements of good clinical practice for the conduct of clinical trials. In the field of imaging, the functionality of the DKTK Joint Imaging Platform (JIP) was extended to enable federated training of models. Additional central infrastructure includes equipment for the production of immunotherapeutics, high-throughput technology for genome screening to decode entire individual tumor genomes, and large bioinformatics data processing centers. In addition, the DKTK Organoid Platform, a strategic initiative, was launched in 2022 with the aim of pooling expertise from the eight partner sites and investigating the benefits of patient-derived tumor organoids for cancer research.

The DKTK supports the education and training of early career researchers in translational cancer research. In the DKTK School of Oncology, talented young professionals learn how to link research tasks to clinical requirements. Various events were held for this purpose in 2022, including the DKTK Young Academics Conference in May and seminar series, workshops and symposia on specific research topics, techniques and soft skills (for more information, see page 30/31).

Since the DKTK was founded, it has established a total of 13 jointly appointed DKFZ professorships at the DKTK partner sites, as well as three DKTK-associated professorships, one clinical cooperation unit and 12 young investigator/junior research groups. In Dresden, Dr. Jovan Mircetic took up the role of DKTK Junior Group Leader for Translational Solid Cancer Research on April 1, 2022.

Dr. Jovan Mircetic, new DKTK Junior Group Leader in Dresden since April 2022 (© Marie Brombach).

Other new strategic appointments were made by the university hospitals in the field of translational oncology. Through these appointments, the DKTK creates attractive career prospects in preclinical translational medical research for specialists with scientific and clinical experience, strengthening their collaboration at the interface between basic and clinical research.

Where are we now? Highlights of 2022

Numerous innovative translational cancer research approaches were developed into multicenter preclinical, trial-associated and pre-trial preparation research projects in 2022. Funding was approved for seven new projects through the DKTK Joint Funding Program, including the study-related research project on "Monitoring the Immune Modulating Effects in CRAFT" (MIMETIC), which aims to use cutting-edge scientific methods to gain a comprehensive understanding of immune-modulating properties of targeted combination immunotherapies. In addition, the tenth call for proposals of the UPGRADE funding line for translational research modules based on clinical trials was launched in the autumn, along with the eleventh call for proposals of the INNOVATION funding line for new translational, collaborative research projects (for more information, see page 27).

At the meeting of the Scientific Advisory Board on October 24, 2022, the members were very impressed with the progress in the year since the DKTK's internal evaluation and recommended further expansion and strengthening of the DKTK's preclinical translational research focus, its collaborations and shared resources. Prof. Ulrik Ringborg (former Chairperson), and Prof. Sir Alex Markham stood down after many years on the board. Prof. Elaine Mardis (Institute for Genomic Medicine at Nationwide Children's Hospital, Columbus, Ohio, USA) was elected chairperson of the Scientific Advisory Board at the meeting. As a result of five new members being appointed, the board now has 11 members (for more information, see page 43).

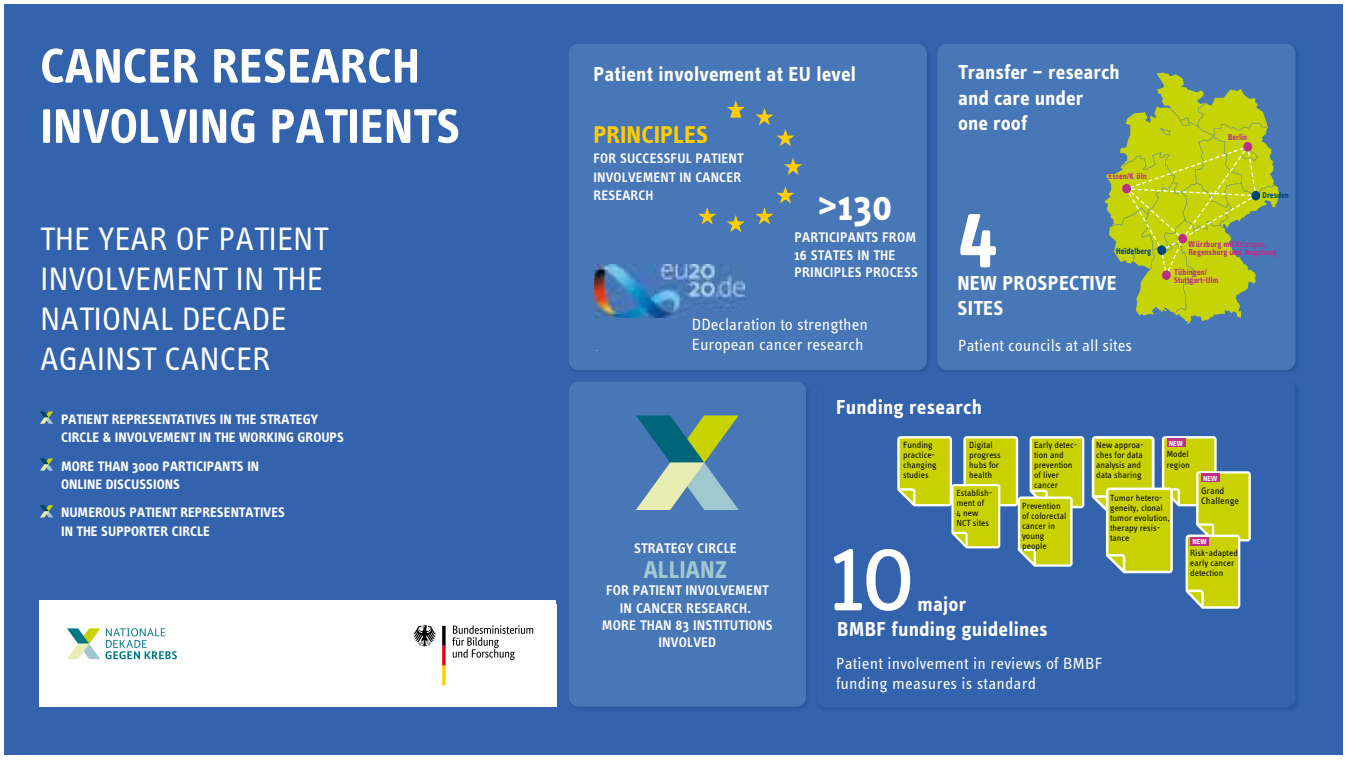
As part of the National Decade against Cancer, further progress was made in the ongoing process of expanding the National Center for Tumor Diseases (NCT) to four new sites: Berlin, SouthWest (Tübingen/Stuttgart-Ulm), WERA (Würzburg with

partners Erlangen, Regensburg and Augsburg) and West (Cologne/Essen). Together with the National Cancer Prevention Center (NCPC) in Heidelberg, which is also under development, the DKTK and NCT will make it possible to create a translational cancer research continuum. The established structure of the DKTK and its core center, the DKFZ, will open up significant opportunities for collaboration in this context and advance synergistic interaction with partners.

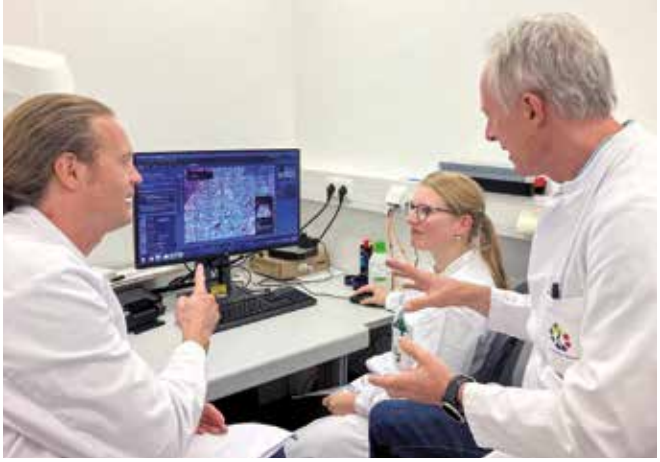
First national conference on Patients as Partners in Cancer Research at the DKFZ: (from left to right) Prof. Michael Baumann (DKFZ), Prof. Angelika Eggert (Charité Berlin), Rainer Göbel (moderator), Ulla Ohlms (PATH) and Dr. Klaus Schlüter (Vice President MSD SHARP & DOHME) during the panel discussion on Cancer Research in Germany – Overview/Current Situation. (© dkfz.de)

At a meeting on October 24, 2022, the members of the Scientific Advisory Board and Steering Committee said goodbye to Prof. Ulrik Ringborg (Chairperson, left), and Prof. Sir Alex Markham (right), who had been involved with the board for many years. (© J. Jung / DKTK).

More than 1,400 DKTK-linked scientific publications came out in 2022. The DKTK's achievements were also reflected in prestigious awards for DKTK scientists, including, for instance, the Deutsche Krebshilfe Prize (for more information, see page 40). The following chapters give an insight into new DKTK findings and research highlights for the early detection, diagnosis and treatment of cancer. For instance, novel bispecific CD28 antibodies were developed to strengthen T-cell antitumor immunity in prostate cancer. In addition, researchers were able to identify a mechanism by which, following chemotherapy, dying colon cancer cells play an active role in helping neighboring tumor cells to survive. Using artificial intelligence, a multicenter research team analyzed DNA methylation patterns to achieve a breakthrough in the diagnosis of nasal and paranasal tumors.



(© BMBF / National Decade Against Cancer)



Prof. Jens Siveke's research group at partner site Essen/Düsseldorf conducts research on pancreatic ductal adenocarcinoma (PDAC), among other things. In 2022, for instance, in collaboration with other researchers, it conducted a comprehensive morphogenetic analysis of the most common PDAC precursor lesions, opening up new approaches for the early detection of this extremely malignant form of cancer. (© Siveke group)

In the area of radio-oncology, biomarkers were improved so that they can be used to predict the radiosensitivity of specific head and neck tumors and so that radiotherapy treatment can be adapted to individual patients. Another project developed a preclinical model for leukemia that simulates the onset of acquired therapy resistance in the living organism, making an important contribution to the development of better, patient-specific treatment methods for resistant tumors (for more information, see page 12 onward)

The DKTK's Division of Radiopharmaceuticals Development at partner site Freiburg launched a collaboration with the Freiburg company 4HF Biotec GmbH in the field of innovative nuclear medicine therapy concepts. In the coming years, the researchers plan to identify innovative new active substances for the nuclear medicine treatment of lung and prostate cancer. The drugs will then be developed for clinical application through DKTK infrastructure facilities and the Department for Nuclear Medicine at University Hospital Freiburg. The Invest BW funding program led by the Baden-Württemberg Ministry of Economic Affairs is supporting this project with third-party funding.

The third HARPOON (HArmonization of Reporting in PrecisiOn Oncology) workshop on harmonizing molecular tumor boards was organized by the Heidelberg-based MASTER team in autumn 2022. The workshop provided a platform to exchange experiences and for intensive networking between precision oncology programs and molecular tumor boards in Germany.

A commemorative event was held in Berlin on May 19, 2022, to mark the DKTK's tenth anniversary with the theme "10 years of research for health". The DKTK and the three other DZG celebrating anniversaries – the German Center for Cardiovascular Research (DZHK), the German Center for Infection Research (DZIF) and the German Center for Lung Research (DZL) – celebrated with numerous guests from the fields of politics and science: Federal Research Minister Bettina Stark-Watzinger, Hessian Economics Minister Angela Dorn, Berlin State Secretary of Health Dr. Thomas Götz, former Federal Research Minister Dr. Annette Schavan, Prof. Christian Drosten, and BioNTech co-founder and medical director Prof. Özlem Türeci, who is also head of a DKFZ department, all offered their congratulations either online via video message or in person. The program included panel discussions with early career researchers and the board spokespersons from the four DZG with the facilitator on the work in the DZG, the translational research successes of the past decade and future desires and goals.

The DZG succeeded in carrying out an important project in 2022: the DZG Innovation Fund (DZGIF), a joint funding instrument for the support of DZG-wide research projects. Scientists can apply for funding for a project on a specific topic that involves at least three DZG. In the first call for proposals on the topic of "cell and gene therapy" researchers from the DKTK and four other DZG submitted a successful joint application. A second call for proposals on the topic of "microbiome" was approved for 2023 (for more information on DZG collaboration, see page 35).

COVID-19 and cancer research

Scientific exchange within and between the eight partner sites in 2022 took place online and, increasingly, in hybrid and in-person formats. This enabled direct personal interaction between DKTK employees so that they could continue with their activities. Events organized by individual sites also used a variety of formats, and enabled other sites to take part. Within the DKTK School of Oncology, most symposia and lectures were held online. The annual Cancer Core Europe Summer School in Translational Cancer Research took place in person again for the first time in October 2022 in Portugal.

At the start of the pandemic, the DKTK launched a strategic initiative on "Immune Reactions to SARS-CoV-2 in Tumor Patients" involving four of the DKTK partner sites. This project was completed in 2022. One of the research areas was antibody formation and T-cell response to different variants of SARS-CoV-2 in 60 patients with hematologic diseases, especially lymphoma and multiple myeloma, following three injections with one of the approved COVID-19 vaccines. Among other results, the researchers were able to show that a SARS-CoV-2-specific T-cell response was induced even in patients who did not form antibodies following the vaccinations, which means this group of patients is protected against severe COVID-19 progression.

Group photo of the speakers at the DZG 10th anniversary celebration on May 19, 2022. (© DZG)

SARS-CoV-2 research projects were also pursued at the individual sites, since people with cancer have an increased risk of severe COVID-19 progression if they become infected with the coronavirus. For instance, a team in Heidelberg showed in a clinical trial that the COVID vaccination is not associated with any particular risks when given to people with cancer during treatment with immune checkpoint inhibitors (immunotherapy). This finding supports the vaccination recommendation of the Robert Koch Institute.

The RACOON initiative (RAdiological COOperative Network on the COVID-19 pandemic), which launched under the umbrella of the National Network of University Medicine (NUM), has successfully installed instances of the JIP at all participating university hospitals in Germany for the structured recording of radiological data from COVID-19 cases. The RACOON-COMBINE project, which has been funded by the BMBF since 2021, is now pursuing further radiological research questions on the basis of this infrastructure, and the JIP represents an important component for the federated development and application of AI methods within the network.

Participants at the Cancer Core Europe Summer School in Translational Cancer Research in October 2022 in Portugal. (© DKFZ/NCT Heidelberg)

(© AdobeStock / eplisterra)

Exploitation of Oncogenic Mechanisms

The better we understand the extremely complex molecular basis of cancer, the greater our chances of being able to build on this understanding to develop new diagnostic methods and therapies. The mechanisms of cancer growth and spread, but also of treatment response and resistance, are particularly relevant.

In the DKTK's Exploitation of Oncogenic Mechanisms program, researchers investigate various levels of cellular communication and molecular regulation in cancer. These include a functional understanding of the impacts of genetic and epigenetic changes, signal processing in cancer cells, how cancer cells communicate with each other and with cells in the tumor microenvironment and, in particular, the immune system and the role of cancer stem cells. The primary goal of the program is to generate and test mechanistic hypotheses of cancer biology, and so to obtain new insights into molecular oncogenic mechanisms and therapy response. The researchers seek to identify the Achilles heel of the various different types of cancer, which can then be used to develop particularly promising diagnostic and therapeutic approaches in close collaboration with the other DKTK research programs.

Program coordination:

Prof. Sven Diederichs (partner site Freiburg)
Prof. Björn Scheffler (partner site Essen/Düsseldorf)
Prof. Dieter Saur (partner site Munich)

◪ ongoing project ☑ goal achieved

Developments in 2022

- ☑ Selective multi-kinase inhibition sensitizes mesenchymal pancreatic cancer to immune checkpoint blockade by remodeling the tumor microenvironment
- ☑ Inflammatory fibroblasts mediate resistance to neoadjuvant therapy in rectal cancer
- ☑ Identification of the proteogenomic subtypes of acute myeloid leukemia
- ☑ Deciphering bidirectional tumor-host interdependence in glioblastoma through spatially resolved multi-omics
- ◪ Concept development to initiate the strategic initiative DKTK Organoid Platform

Goals for 2023

- Carry out comprehensive functional characterization of the influence and predictive significance of cancer gene mutations on therapy response
- Use genetic and PDX mouse models, organoid and co-culture models to characterize the interaction of the tumor microenvironment, and immune system, with a focus on their influence on therapy response, including to immunotherapies
- Turn big data into smart data: Collect and use genomic, epigenomic, transcriptomic, proteomic and metabolomic data, including at single-cell level, to understand molecular signaling pathways and mechanisms in cancer
- Focus on functional genomics for comprehensive high-throughput characterization of genetic aberrations in terms of their influence on therapy response
- Develop drug combinations to prevent or overcome resistance to targeted therapies

Research highlight of 2022

Colon cancer – how dying cancer cells give neighboring tumor cells instructions on how to survive

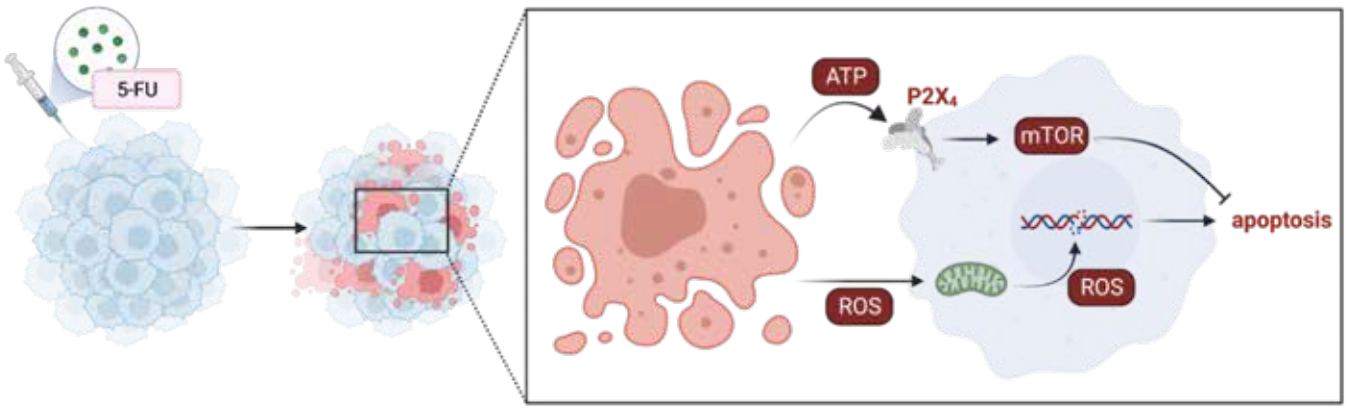
One of the biggest barriers in cancer treatment is the development of resistance to therapies that were once effective. A team of researchers at DKTK partner site Frankfurt/Mainz, under the leadership of Prof. Florian Greten, Director of the Georg-Speyer-Haus and spokesperson for the LOEWE Frankfurt Cancer Institute, has discovered a mechanism that leads to chemotherapy resistance in colon cancer.

It is a mechanism that could be described as "perfidious": The dying cancer cells killed off by the chemotherapy pass on instructions to the neighboring cancer cells – a signal that lets the neighboring cells reprogram their signaling cascades to resist the chemotherapy and survive. This signal is sent by the dying cells in the form of adenosine triphosphate (ATP), the cell's energy currency, which acts as a messenger in this context. The ATP binds to the receptor P2X4, activates a powerful survival signaling pathway and so cancels the cell death signal emitted by the chemotherapy. If this communication is interrupted, e.g. by inhibiting the P2X4 receptor, the tumors respond several times better to chemotherapy in preclinical models. As Greten explains: "We were surprised to see that the dying tumor cells play an active role in helping their neighbors survive a therapeutic 'attack'. At the same time, we see an opportunity to improve standard therapy in patients by interrupting the communication between these cells."

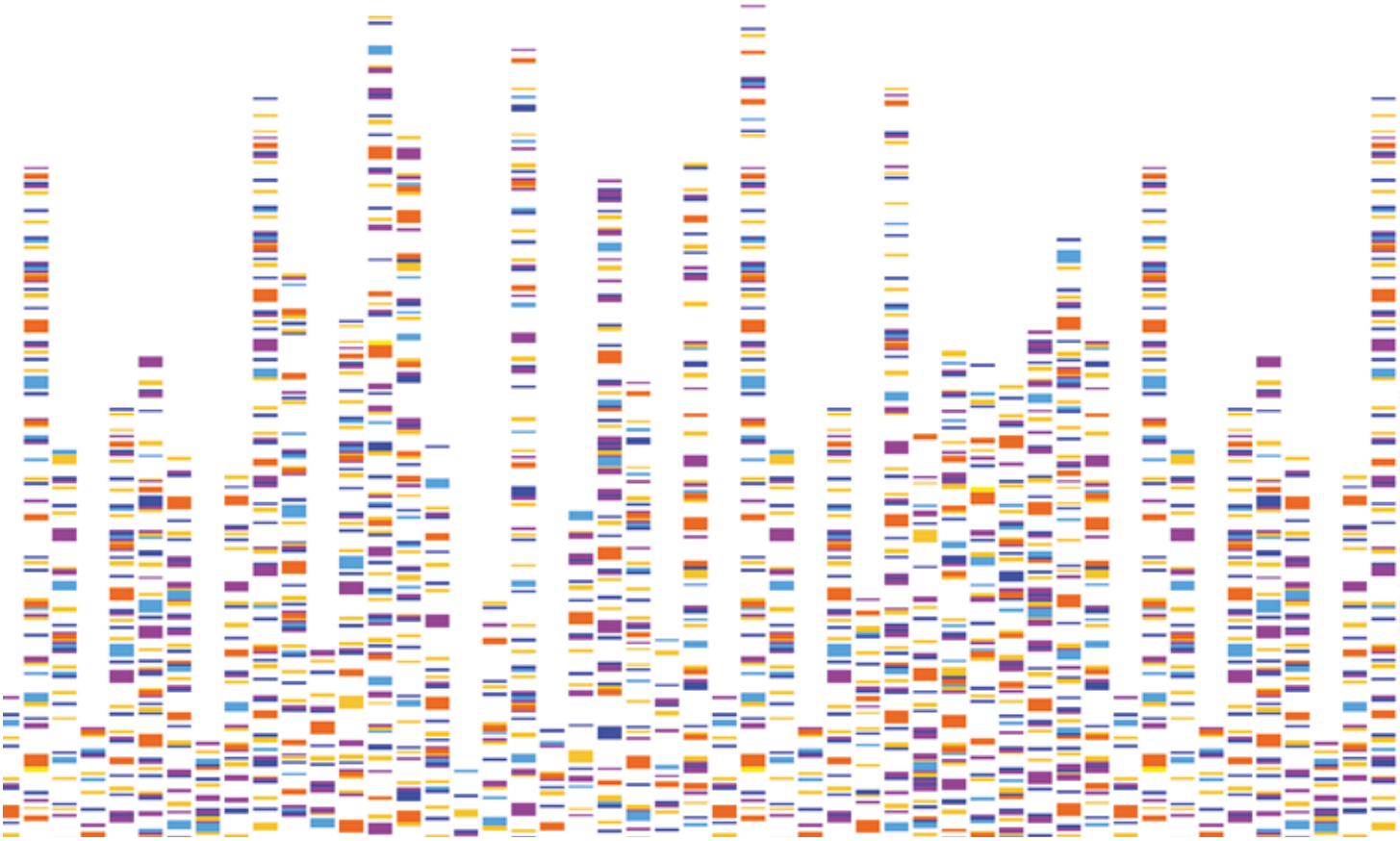
The signaling pathway involved in this communication is the mTOR signaling pathway, which has already been the subject of considerable research. In laboratory experiments, it can be inhibited with rapamycin, a substance that is already licensed as a drug for certain diseases, but which does have side effects. The researchers are working with industry partners to test another highly specific inhibitor for the P2X4 receptor so that this effect can be used in colon cancer patients in future and improved further. The overall aim of the research team is to develop a new treatment option from this approach for advanced colorectal cancer, which has until now been difficult to treat.

Further information:

Schmitt M, Ceteci F, Gupta J, et al. Colon tumour cell death causes mTOR dependence by paracrine P2X4 stimulation. Nature. 2022;612(7939):347-353.



Chemotherapy-induced cell death leads to cell death in neighboring tumor cells, induced by reactive oxygen species (ROS), called apoptosis. At the same time, extracellular adenosine triphosphate (ATP) released by the chemotherapy can activate the mTOR protein (mTOR = mammalian Target Of Rapamycin) through the P2X4 receptor, counteracting the pro-apoptotic signaling pathway in the neighboring cells. Consequently, inhibition of mTOR or P2X4 leads to the death of neighboring tumor cells that were not eliminated by the chemotherapy. (© F. Greten)



(© AdobeStock / yepifanovahelen)

Molecular Diagnostics, Early Detection and Biomarker Development

Not all tumors are the same, even if they occur in exactly the same part of the body in two different patients. Differences in the molecular structure of a tumor that are invisible under the microscope can cause one tumor to grow extremely aggressively, while another takes years to grow.

The DKTK's Molecular Diagnostics, Early Detection and Biomarker Development program is dedicated to the discovery of tumor molecular profiles and their application for cancer diagnosis, prognosis and prevention. To this end, the DKTK scientists develop new technologies that are implemented in research and in clinical practice. There is a focus on analyzing liquid biopsies to identify tumor cells and molecular tumor profiles in easily accessible bodily fluids. Faulty gene regulation and changes in the protein profile are also investigated. The aim is to develop reliable biomarkers that can be used to predict the progression of the disease and the response to a planned course of treatment as precisely as possible for each patient. In cancer prevention, the focus is currently on the further development of screening methods for the early detection of colorectal cancer.

Program coordination:

Prof. David Capper (partner site Berlin)
Prof. Thomas Oellerich (partner site Frankfurt/Mainz)
Prof. Hermann Brenner (Core Center Heidelberg)

◪ ongoing project ☑ goal achieved

Developments in 2022

- ◪ Successful continuation of two Joint Funding projects: MTBA for the harmonization of molecular tumor boards (MTBs) and EXLIQUID for the harmonization of liquid biopsy methods
- ◪ Harmonizing MTB approaches throughout the DKTK, in collaboration with the NCT
- ☑ Start of a pilot project for the reimbursement of costs for INFORM analyses by selected German health insurance schemes
- ☑ Identification of epigenetic biomarkers for the classification and prognosis of numerous classes of tumors
- ◪ Establishing long-range sequencing methods to identify structural variants and for rapid diagnosis
- ◪ Introduction of tumor classification based on DNA methylation in low- and medium-income countries

Goals for 2023

- Decipher the clonal architecture of acute myeloid leukemia (AML) with the help of single-cell technologies
- Conduct proteogenomic characterization of various tumor entities
- Identify differences in the composition of immune cells based on different tumor etiology and genomics
- Determine the composition of the immunological microenvironment in hepatocellular carcinoma (HCC) with the help of large-scale, highly multiplexed spatial immune profiling
- Conduct DNA methylation profiling of primary tumors and advanced tumors to analyze the potential predictive value of epigenetic changes
- Develop an *in vitro* diagnostic method based on the metabolic signature of pancreatic cancer
- Refine long-range sequencing methods for intraoperative diagnosis

Research highlight of 2022

Nasal cavity cancer: AI enables diagnostic breakthrough

Sinonasal cancer covers a broad range of different tumor types. They are difficult to diagnose because they often do not present a specific pattern or appearance. This is particularly true of the tumors known as sinonasal undifferentiated carcinoma (SNUC). A team led by Dr. Philipp Jurmeister and Prof. Frederick Klauschen from the Pathological Institute at LMU Munich and Prof. David Capper from Charité – Universitätsmedizin Berlin has succeeded in improving diagnosis considerably and differentiating reliably between these tumors.

The researchers worked with an artificial intelligence (AI) tool that reliably differentiates between the tumors based on chemical DNA modifications that play a key role in the regulation of gene activity. This includes DNA methylation, which adds an extra methyl group to DNA building blocks. Thanks to extensive international collaboration, researchers were able to record the DNA methylation patterns of nearly 400 sinonasal tumors.

Methylation array (front) that was used in the study. Behind it is the standard method used until now: tissue sections.
(© LMU / Philipp Jurmeister)

To analyze the methylation data, the researchers, working closely with Prof. Klaus-Robert Müller's Machine Learning group at Technische Universität Berlin and the Berlin Institute for the Foundation of Learning and Data (BIFOLD), developed an AI model that classifies the tumors. "Machine learning methods are essential because of the large volumes of data," says Jurmeister. "To spot patterns we had to analyze several thousand methylation positions."

The researchers found that it was possible to classify SNUCs that could not be differentiated using the previously available methods into four groups based on their DNA methylation pattern. They were able to confirm the results, for instance, using the protein profile. "These results also have clinical relevance, since patients in the four different groups have different prognoses," says Jurmeister. "In future, it will be possible to develop targeted new therapies on the basis of the groups' molecular characteristics. The algorithm is already being used in experimental clinical diagnosis in Munich and Berlin and in cooperating international institutions like New York University for the classification of SNUCs."

Further information:

Jurmeister P, Glöß S, Roller R, et al. (2022) DNA methylation-based classification of sinonasal tumors. Nat Commun. 2022;13(1):7148. Published 2022 Nov 28.

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Molecularly Targeted Therapy

The DKTK's Molecularly Targeted Therapy research program studies molecular pathways and target structures that can be exploited by cancer drugs. The aim afterwards is to be able to test these new drugs and therapy approaches, in combination with the relevant biomarkers, as quickly as possible in clinical trials and to introduce them into clinical practice. The program works closely with two other research programs: Exploitation of Oncogenic Mechanisms and Molecular Diagnostics, Early Detection and Biomarker Development. It covers both research directions: from model to patient (forward translation) and from patient back to improved models (reverse translation). In the latter case, repeat testing and further development in the laboratory is important to investigate why a drug is only effective in some patients. By using patient-specific cell culture and animal models, this research program also provides the extensive data packets needed for the approval of clinical trials, so that new molecular therapy approaches, preferably including knowledge-based combinations involving several active substances, can be tested in patients. It makes use of novel, optimized study designs in order to identify the most effective therapies faster.

Program coordination:

Prof. Stefan Pfister (Core Center Heidelberg)
Prof. Jens Siveke (partner site Essen/Düsseldorf)
Prof. Stefan Knapp (partner site Frankfurt/Mainz)

◪ ongoing project ☑ goal achieved

Developments in 2022

- ◪ Expansion of the available PDX and PDO models for genetic and pharmacological screening and investigation of therapy resistance, including preclinical models for interactions between cancer and the tumor microenvironment/immune cells
- ◪ Expansion of the workflow in INFORM to include (phospho) proteomic analyses and their integration in clinical decision-making, and development of Knowledge Connector, an internal software system that integrates and visualizes molecular and clinical data from the MASTER program with knowledge databases from precision oncology
- ☑ Consolidation of the preclinical platform ITCC-P4, an Innovative Medicines Initiative 2 (IMI2) project as a nonprofit company (gGmbH) based in Heidelberg with 15 academic partners and three contract research organizations (CROs) from all over Europe

Goals for 2023

- PROTAC (PROteolysis TArgeting Chimeras) evaluation in *in vivo* cancer models (e.g. Aurora A, ITK, CK1d/e, MLLT1/3, LIMK1/2, MYC interacting proteins)
- Exome sequencing vs. gene panel sequencing – impacts on diagnostic assessment for precision medicine in oncology
- Continue with the drug research programs (e.g. BET/HDAC, AKT, ALC1; microenvironment targets). Partnership with leading medicinal chemistry companies (DKFZ BAYER-Allianz) for high-throughput drug screening

Research highlight of 2022

New therapeutic vulnerabilities in resistant leukemia cells

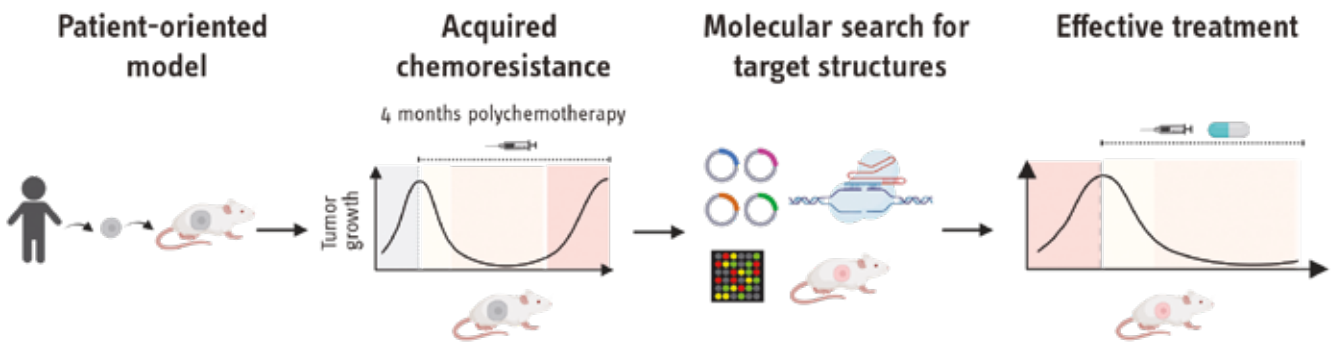
Leukemia or blood cancer, which is particularly common in children as well, is caused by abnormal precursor cells in the hematopoietic system. Despite the development of new, targeted therapies, conventional chemotherapy is still the main treatment component. However, the patients' recovery is often hindered by the development of resistance. "The underlying chemoresistance mechanisms in leukemia cells are not sufficiently understood," says Prof. Irmela Jeremias, a DKTK scientist at partner site Munich. In order to get to the bottom of this phenomenon, researchers in her research group on "Apoptosis in hematopoietic stem cells" at Helmholtz Munich developed a preclinical model that simulates the development of acquired therapy resistance in the living organism (1). In order to simulate the clinical situation in the patient as closely as possible, tumor cells from leukemia patients were transplanted into mice. These cells had previously been manipulated with lentiviruses so that the researchers could use imaging methods to follow the spread of the disease in the animals and the therapy response precisely (2).

In a novel approach, the animals were then treated over several months with a common type of chemotherapy, to which they developed resistance in the course of their treatment – as happens in human patients. The resistant tumor cells presented many different genetic changes of great heterogeneity. With the help of the resulting altered expression patterns, and genetic manipulation using "genetic scissors", the researchers verified a number of genes that play an important role in the development of chemoresistance. They then demonstrated the translational relevance of their findings: By inhibiting a previously identified "resistance gene" using drugs, they were able to lift the tumor resistance and bring about a drastic reduction in the tumor burden in treated mice that received the same chemotherapy compared with those that had previously developed resistance. The researchers are convinced that this new, preclinical model will be able to make an important contribution in future to the development of better, patient-specific treatment methods for resistant tumors.

Further information:

(1) Wirth AK, Wange L, Vosberg S, et al. In vivo PDX CRISPR/Cas9 screens reveal mutual therapeutic targets to overcome heterogeneous acquired chemo-resistance. Leukemia. 2022;36(12):2863-2874.

(2) Vick B, Rothenberg M, Sandhöfer N, et al. An Advanced Preclinical Mouse Model for Acute Myeloid Leukemia Using Patients' Cells of Various Genetic Subgroups and In Vivo Bioluminescence Imaging. PLOS ONE. 2015; 10(3): e0120925.



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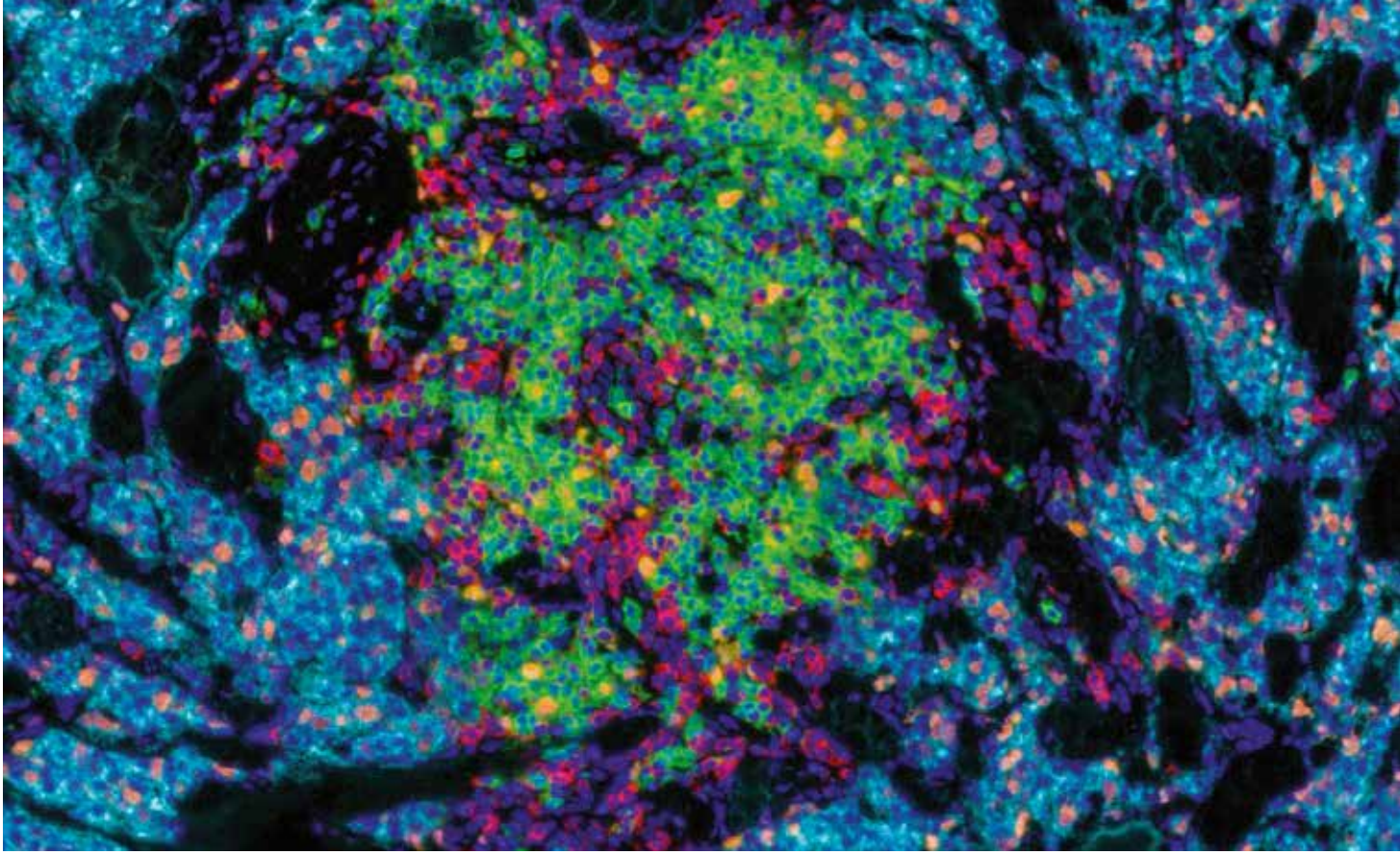


Multiplex immunohistochemistry: The image shows tertiary lymphatic tissue (TLS) in Merkel cell carcinoma. Tumor cells are dyed cyan, B-cells green and T-cells red. The cell nuclei are blue, with dividing cells also colored orange. This is a typical sign of B-cells in TLS and shows that the tumor cells are proliferating rapidly. The presence of TLS in tumors is often associated with a better response to immunotherapy. (© Becker group)

Cancer Immunotherapy

The human immune system is, in principle, capable of recognizing cancer cells and destroying them. This defense mechanism often fails in cancer patients, but the principle can still be used for cancer treatment. In the DKTK's Cancer Immunotherapy program, cancer researchers are investigating how the body's own immune system can be helped to fight cancer through a range of different approaches.

The researchers are focusing on developing innovative, targeted cancer vaccines, cellular therapies with various immune cells, such as cytotoxic T-cells and natural killer cells, tumor antigen-specific antibodies, and mechanisms to prevent immune escape – when tumor cells evade surveillance by the immune system. Other research areas include the further development of checkpoint inhibitors that have already been successfully deployed in clinical practice to activate the immune system, and research into cellular and molecular processes during immunotherapy as a basis for further improved therapy approaches, especially using combination therapies. This leads to increasing interactions with the other DKTK research programs.

Program coordination:

Prof. Jürgen Becker (partner site Essen/Düsseldorf)
Prof. Gerald Willimsky (partner site Berlin)
Prof. Helmut Salih (partner site Tübingen)

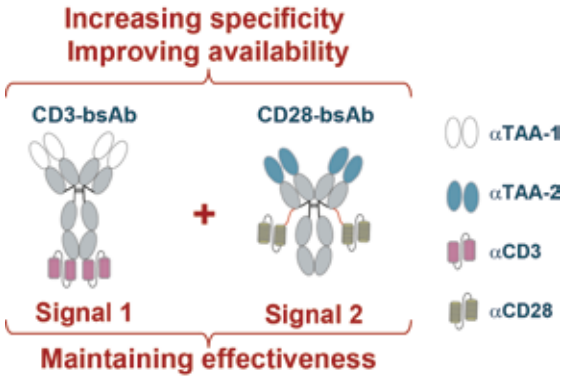
◧ ongoing project ☑ goal achieved

Developments in 2022

- ◧ Development of modular, adaptable, flexible adapter platforms for chimeric antigen receptors (CAR), called UniCAR and RevCAR, for highly specific cellular immunotherapy
- ☑ Discovery that patients who responded to immunotherapy with checkpoint inhibitors presented a diverse T-cell receptor repertoire
- ☑ Next-generation immunopeptidomics to identify naturally present tumor-associated antigens of neoepitopes (tumor-specific mutations, gene fusions and non-canonical transcripts), cryptic peptides (cell stress and senescence) and tumor-exclusive, high-frequency, non-mutated antigens
- ◧ In a first-in-human phase I trial, CAR2BRAIN is investigating local application of NK-92/5.28.z CAR-NK cells in patients with recurrent glioblastoma

Goals for 2023

- Combine multiplex immunohistochemistry, single-cell and spatially resolved transcriptomics/epigenetics of patient samples with preclinical models (organoids, living tissue parts, co-culture systems) to record the complexity of immune responses and to understand the heterogeneity and dynamics of the tumor microenvironment as a key actor in therapy response and resistance
- Validate the effectiveness of combinations of neoantigen-specific T-cell receptors and CARs in solid cancers and develop and validate in preclinical studies novel theranostic target modules with different structures and characteristics for CAR-based immunotherapy and diagnostic imaging
- Characterize immunological effects of targeted therapies and their relevance for the observed clinical effects



Kombinatorische Modulation von Signal 1 und 2 in T-Zellen: Die Kombination aus zwei funktionell voneinander abhängigen gegen CD3 (Signal 1) und CD28 (Signal 2) gerichteten bispezifischen Antikörpern (bsAb), welche gegen unterschiedliche Tumor-assoziierte Antigene (TAA) mit nicht überlappender Expression auf gesunden Geweben gerichtet sind, ermöglicht die Induktion einer nachhaltigen Immunantwort und gleichzeitig eine erhebliche Verbesserung der Tumorspezifität (© L. Zekri)

Research highlight of 2022

Novel bispecific CD28 antibodies to strengthen T-cell antitumor immunity

Bispecific antibodies (bsAbs) which trigger a potent immune response against tumor cells through T-cell signal 1 via CD3 show promising clinical results in hematologic neoplasia – malignant diseases of the blood and lymphatic system. However, so far, bsAbs have not been successful in solid tumors. Firstly, there are not sufficient specific target antigens in solid tumors, which leads to considerable side effects, and secondly, the T-cells do not have enough access to solid tumors and there is no physiological costimulatory signal 2 to sustain lasting T-cell activity to fight the tumor cells (1). "We have developed a PSMAxCD3 bsAb called CC-1 that is currently being investigated as a monotherapy in patients with prostate cancer," reports Dr. Latifa Zekri, a DKTK scientist and group leader of the Clinical Collaboration Unit for Translational Immunology at University Hospital Tübingen (2, 3).

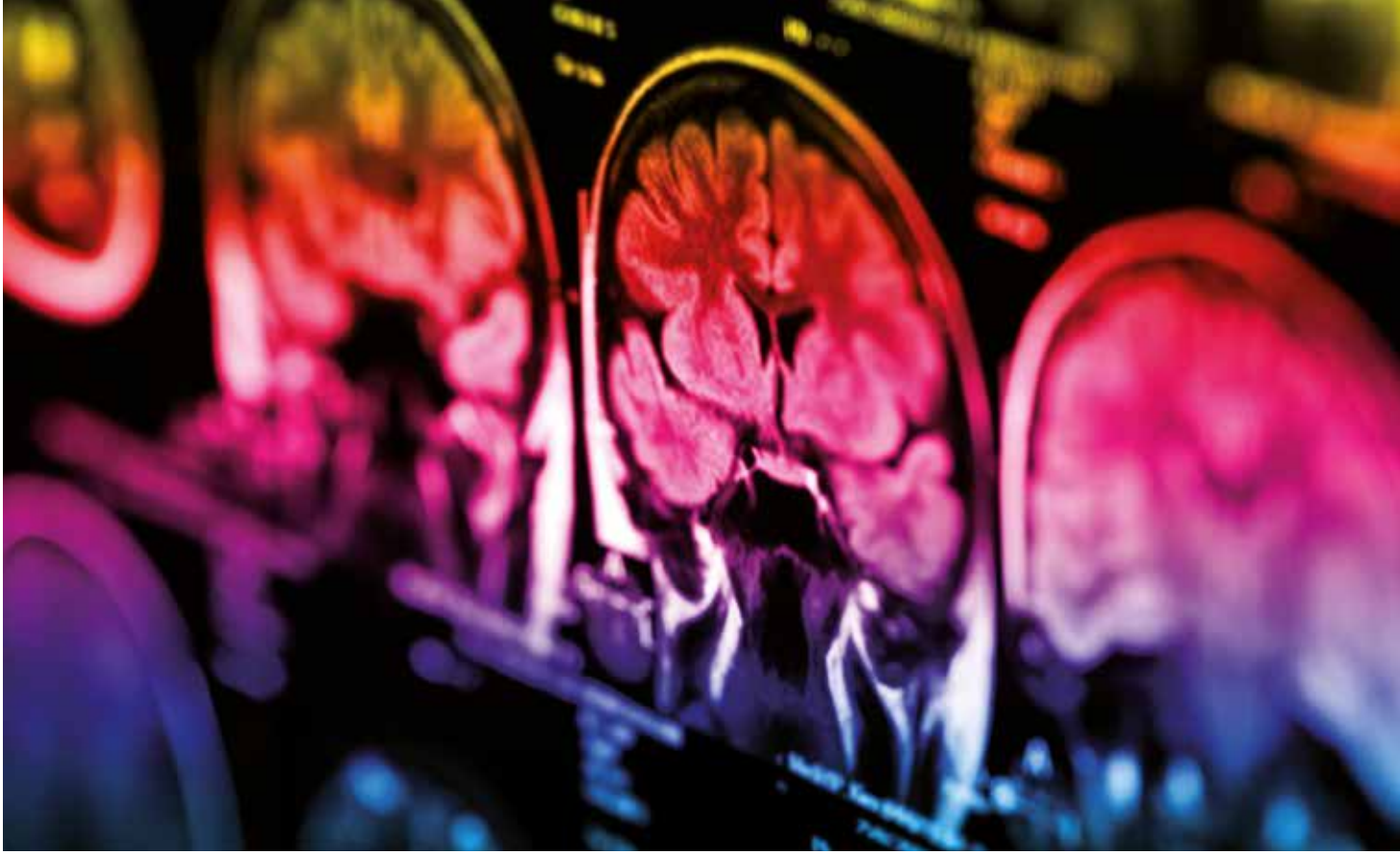
In patients with a high tumor burden, a clear but temporary response was seen in the form of a fall in the PSA value (trial NCT04104607). The PSA value indicates the amount of prostate-specific antigen (PSA) in the blood, and the risk of prostate cancer rises as this level increases. However, in people with biochemical recurrence of prostate cancer, i.e. when the PSA value increases again after initial diagnosis and treatment, and with a low tumor burden, the induced T-cell activity may be sufficient (trial NCT05646550). "In order to be able to combat a high tumor burden as well, we have developed an approach in which CD3-targeted bsAbs are combined with novel bispecific costimulators (BiCos) to activate CD28," says Zekri. "Unlike CD28 superagonists, our BiCos, as a single agent, do not induce activation of T-cells and so have no side effects." In combination with CD3-targeted bsAbs like CC-1, BiCos can enable greater tumor specificity by binding two different tumor-associated target antigens that are not expressed together on healthy tissues by means of the constructs' functional interdependence. As well as leading to more intense, lasting T-cell activity, simultaneous activation of CD3 and CD28 leads to T-cell proliferation and memory formation, which is important for combating large tumors and for lasting protection against recurrence. "In this way, our approach reduces side effects while simultaneously improving efficacy," says Zekri, summarizing the research. As a next step, the research team is planning a first-in-human clinical combination trial in prostate cancer patients at the end of 2023.

Further information:

(1) Salih HR, Jung G. The challenges of translation. EMBO Mol Med. 2019;11(12):e10874.

(2) Zekri L, Vogt F, Osburg L, et al. An IgG-based bispecific antibody for improved dual targeting in PSMA-positive cancer. EMBO Mol Med. 2021;13(2):e11902.

(3) Heitmann JS, Walz JS, Pflügler M, et al. Protocol of a prospective, multicentre phase I study to evaluate the safety, tolerability and preliminary efficacy of the bispecific PSMAxCD3 antibody CC-1 in patients with castration-resistant prostate carcinoma. BMJ Open. 2020;10(10):e039639.



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Radiation Oncology and Imaging

Radiotherapy, one of the oldest methods of treating cancer, is now one of the most innovative areas of cancer medicine. Moreover, modern imaging techniques provide the basis for diagnosis methods that would have been inconceivable in the past. The Radiation Oncology and Imaging research program brings together these disciplines that are vital for the diagnosis and treatment of cancer.

The DKTK's key focus areas in radiation oncology research are the technical optimization and biological individualization of radiation therapy and medical imaging. To develop new biomarker (signatures) for personalized radiotherapy, a unique, and internationally highly competitive network of all DKTK partner sites was formed: the DKTK Radiation Oncology Group (DKTK-ROG), which establishes and validates new biomarkers on shared patient cohorts. Investigating and further refining particle therapy and developing and funding innovative IT infrastructure are also important goals. In terms of imaging, the DKTK evaluates multiparametric imaging methods and imaging-based biomarkers. New, high-precision diagnostic methods are being developed for use in nuclear medicine that can often also be translated into therapeutic application as part of a theranostic concept.

Program coordination:
Prof. Mechthild Krause (partner site Dresden)
Prof. Matthias Eder (partner site Freiburg)
Prof. Amir Abdollahi (Core Center Heidelberg)

■ ongoing project ☑ goal achieved

Developments in 2022

- ☑ Identification of biomarker signatures for the stratification of patients with locally advanced head and neck tumors
- ■ Validation of these biomarker signatures in the prospective HNprädBio trial prior to potential application in clinical intervention trials
- ■ Establishment and cultivation of head and neck tumor organoids at several sites as a basis for joint trials
- ■ Guided surgery with PSMA-914 and other substances to identify tumor lesions during surgery
- ■ Positron emission tomography (PET) imaging of the tumor microenvironment using bicyclic peptide tracers
- ■ Multimodal imaging approaches with novel hyperpolarized agents
- ■ Identification and radiolabeling of biological substances in various formats for clinical trials
- ■ Reverse translation to investigate dose-limiting thyroid uptake of PSMA-617

Goals for 2023

- Develop and validate biomarkers for personalized radio-oncology
- Develop radiopharmaceuticals for improved tumor diagnosis and targeted radionuclide therapy (theranostics)
- Initiate further innovation studies on biomarker-based stratification of head and neck cancer patients in a matrix study
- Establish molecular radio-oncological tumor boards
- Establish a compound screening platform using head and neck tumor organoids
- Expand the JIP for tumor characterization and evaluation using artificial intelligence and pursue further the preclinical development of hyperpolarized contrast agents in MRI
- Use AI support for improved dosimetry and diagnosis in nuclear medicine and innovative AI technologies in oncological imaging

Research highlight of 2022

Another step towards clinical translation using combined biomarker signatures

For over ten years, the DKTK Radiation Oncology Group has been researching how to optimize radiotherapy for patients with head and neck tumors (HNSCC), taking into account individual tumor characteristics. In 2012, the first joint project involving all eight partner sites was funded through the DKTK Joint Funding Program. The focus was on developing biomarkers that can predict the radiosensitivity of individual tumors so that the radiotherapy can be adapted accordingly.

First of all, shared, retrospective patient cohorts were used to identify clinical parameters and biomarkers that showed a correlation with therapy response, e.g. the tumor volume, p16 status, the expression of cancer stem cell markers, other individual genes or hypoxia-associated gene signatures, the tumor mutation burden and certain single-nucleotide polymorphisms. In order to be able to use such biomarkers in clinical intervention trials, they must be validated externally – preferably on prospectively collected datasets. For this reason, two prospective trial arms of DKTK-ROG launched in 2014 for patients with locally advanced HNSCC who had completed their recruitment (HNprädBio trial).

For the subsequent validation, the identified, complementary biomarkers were combined into three different biomarker signatures in 2022. This means that the therapy result can be predicted more precisely than when individual markers are used. As well as a basic signature consisting of widely accepted parameters, two expanded signatures were developed with additional biomarkers from DKTK-ROG. These three signatures form the primary hypotheses for the prospective validation in the HNprädBio trial. Other biomarkers are used for secondary analyses, including radiomics signatures that were developed using machine learning methods and clinical imaging, and biomarkers from tumor methylome analysis.

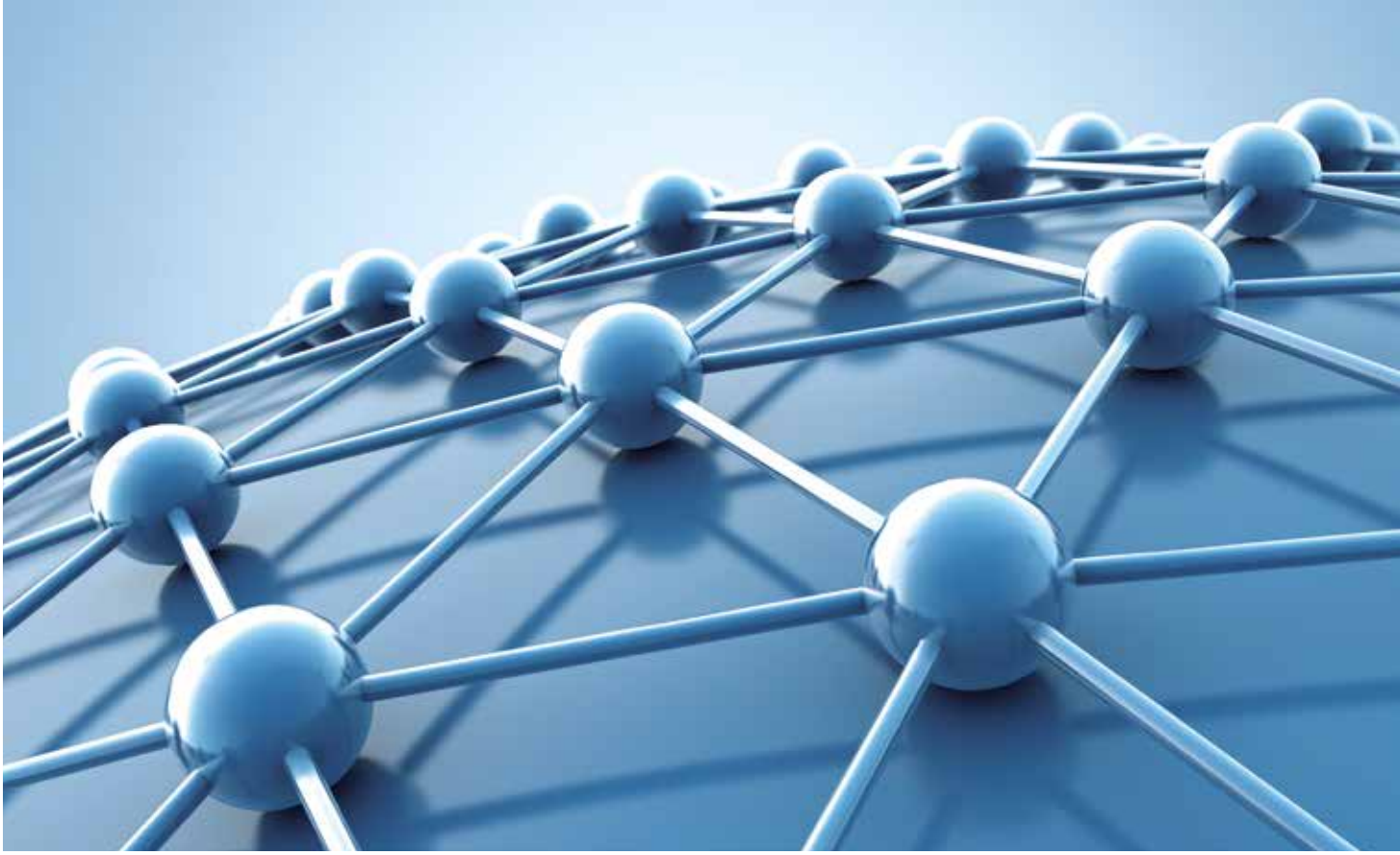
Following successful validation, it would be possible to move onto the next step: translation into an intervention trial. Already, the HPV status is being investigated in radiation oncology and, for example, dose reductions are being carried out within the first DKTK-ROG intervention trial (DELPHI trial) for the treatment of head and neck tumors with very good prognoses in order to reduce side effects. In future, a validated biomarker signature could further improve radiation of radiation-resistant tumors in selected patients by allowing the use of targeted dose escalation or a combination with immunotherapy.

Further information:

(1) Löck S, Linge A, Lohaus F, et al. Biomarker signatures for primary radiochemotherapy of locally advanced HNSCC – Hypothesis generation on a multicentre cohort of the DKTK-ROG. Radiother Oncol. 2022;169:8-14.

(2) Rabasco Meneghetti A, Zwanenburg A, Linge A, et al. Integrated radiogenomics analyses allow for subtype classification and improved outcome prognosis of patients with locally advanced HNSCC. Sci Rep. 2022;12(1):16755. Published 2022 Oct 6.

(3) Tawk B, Rein K, Schwager C, et al. DNA-Methylome based Tumor Hypoxia Classifier Identifies HPV-negative Head & Neck Cancer Patients at Risk for Locoregional Recurrence After Primary Radiochemotherapy [published online ahead of print, 2023 Apr 14]. Clin Cancer Res. 2023;CCR-22-3790.



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Clinical Communication Platform (CCP)

Developing and improving diagnostic procedures and personalized therapies for cancer requires a large amount of diverse patient information. The Clinical Communication Platform (CCP) offers federated IT infrastructure to link data from routine clinical care and research with biosample data and to make the data available to DKTK researchers. This oncological data collection of the DKTK partner sites is one of the largest in Europe and is supplemented through connections to other certified oncological centers as partner sites and through the addition of more data.

The central CCP coordination team is supported by IT, tumor documentation, biobank and data science expertise at the participating centers in the field of cancer research. The CCP collaborates with the DZG and various research and infrastructure initiatives, including the German Biobank Node/Alliance (GBN/GBA) and the Medical Informatics Initiative (MI-I), promoting standardization and harmonization of data structures in the German research landscape. The CCP bridgeheads also connect to sites in the national Network of Genomic Medicine for Lung Cancer (nNGM) and in the German Network for Personalized Medicine (DNPM, under development, 15/21 sites).

Various CCP components that are published as open-source data are re-used in MII/NUM data integration centers and by the German Biobank Alliance, BBMRI-ERIC, the Digital Progress Hubs for Health (LeMeDaRT) and the German Center for Infection Research (DZIF).

◪ ongoing project ☑ goal achieved

Developments in 2022

- ◪ Development of a web application for network-wide case number analyses and queries regarding patient data and biosamples
- ◪ Connection of liquid biosample data from biobanks to the CCP IT infrastructure
- ◪ Integration of certified oncological centers as CCP partners
- ☑ Multicenter cohorts: Completion of federated analysis of routine care data in the network in the context of the DKTK Clinical Data Science Group
- ☑ Redesigned CCP website and information campaign for DKTK Joint Funding Program applicants
- ☑ Development of a federated web application to monitor the prospective data and biosample collections in DKTK-funded projects

- ☑ Successful upgrade of the technical infrastructure to up-to-date, flexible and interoperable standards in consultation with all partner sites

Goals for 2023

- ↗ Finalize and roll out the web application for case number analyses
- ↗ Develop an application for federated data analysis (the analyses come to the data and not the other way round) for safe and fast data evaluation
- ↗ Link data from the CCP with patient data from routine care at the sites and use federated data analysis for various research projects
- ↗ Offer a range of information to the DKTK research community regarding new and existing CCP applications and services

Platform coordination:
CCP office and CCP Spokesperson: Prof. Janne Vehreschild (partner site Frankfurt/Mainz)
CCP-Bio: Prof. Michael Hummel (partner site Berlin)
CCP-IT: Prof. Martin Lablans (Core Center Heidelberg)

Highlights of 2022

Multicenter cohorts

The CCP infrastructure provides diagnosis, disease progression and treatment information relating to patients from a large number of sites for research purposes. For a description of these multicenter cohorts, federated analysis was performed on over 600,000 patient datasets from routine care to check their usability for clinical epidemiological research. Comprehensive documentation was available for around 233,000 patients. Detailed analysis showed that the cohorts are comparable with population research in terms of the distribution of cancer diagnoses and that they are also representative of the spectrum of highly specialized care at the 14 participating oncological centers (1).

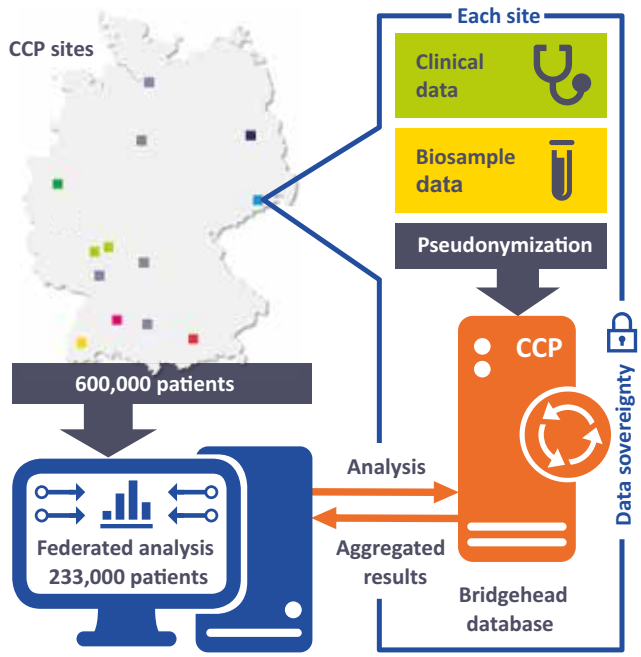
Information for researchers

In 2022, the CCP initiated completely new interactions with researchers in the DKTK and beyond. As part of an information campaign on DKTK Joint Funding Program applications, it organized two very well-received online seminars presenting the CCP and involving the RadPlanBio and JIP platforms. In addition, applicants received a flyer and personal advice on CCP support programs and on implementing the funding conditions. Following a comprehensive redesign with up-to-date content and images, the CCP web pages are now an attractive information platform (2).

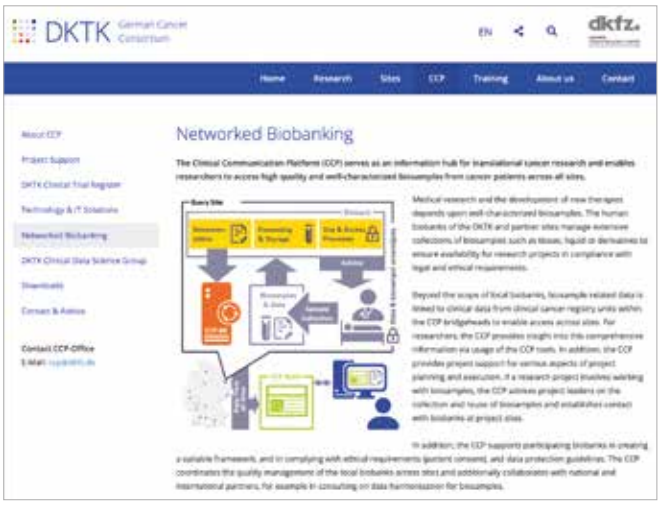
Further information:

(1) Maier D, Vehreschild JJ, Uhl B, et al. Profile of the multicenter cohort of the German Cancer Consortium's Clinical Communication Platform. Eur J Epidemiol. 2023;38(5):573-586.

(2) www.dktk.dkfz.de/ccp



The multicenter cohorts of the CCP, modified after (1).



Networked biobanking – one of the redesigned CCP web pages (2).

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Cancer Genome and Proteome Analysis Platform

Comprehensive analyses of the genome and molecular signaling pathways of cancer cells are vital in order to improve our understanding of cancer and to be able to treat tumors in a more targeted manner in the future. The DKTK's site-overarching Cancer Genome and Proteome Analysis Platform has special infrastructure dedicated to clinically oriented cancer research. A wealth of experience and expertise is combined here to investigate the genetic causes of cancer using the latest sequence analyses and to decode entire tumor genomes. Increasingly, because of the large volumes of data involved, artificial intelligence is able to improve treatment options. Modern bioinformatics also facilitates systems medicine research. For many aspects of molecular cancer research, it is also vital to consider the protein level, for example to measure the activity of certain cancer genes or cancer-relevant signaling pathways. And, at the same time, scientists can see how well cancer cells respond to a drug. Modern-day advances in proteomics – the analysis of the entire protein complement of a cell or organism at a particular point in time – make it possible to conduct unprecedented qualitative and quantitative research on cancer-related questions.

Platform coordination:
Cancer Proteome Analysis Platform: Prof. Bernhard Küster (partner site Munich)
Cancer Genome Analysis Platform: Prof. Stefan Fröhling (Core Center Heidelberg), Prof. Benedikt Brors (Core Center Heidelberg)

◧ ongoing project ☑ goal achieved

Developments in 2022

- ◧ Validation of a newly identified AML subtype that is responsive to BCL2 inhibitor venetoclax
- ☑ Proteogenomic mapping of lymphomas, e.g. diffuse large B-cell lymphomas and breast cancer entities
- ☑ Development of an automated pipeline for the preparation of proteome samples (autoSP3) that can be used for any type of clinical sample and improves data completeness in global and single-cell proteomics
- ◧ Development of a quality management system for the entire precision oncology workflow at the DKFZ with the aim of achieving full accreditation of the DKTK's precision oncology programs

- Continuation of molecularly stratified clinical trials within the DKTK and NCT (e.g. NCT PMO-1602/CRAFT, NCT PMO-1603/TOP-ART, NCT PMO-1604/Afatinib, SORATRAM, COGNITION-GUIDE) and translational research projects
- ☑ Initiation of regular MTBs to discuss the proteomic results and compare clinical recommendations on the basis of proteomic and/or genomic data
- ☑ Development of an in-house software system (Knowledge Connector) that integrates molecular and clinical patient data from the MASTER program with precision oncology knowledge databases and visualizes them in order to facilitate a semi-automated clinical decision aid

Goals for 2023

- ↗ Develop new proteomic work processes to characterize i) low sample quantities, ii) secretomes, and iii) bodily fluids, e.g. blood plasma and urine
- ↗ Characterize clinical cohorts of various entities with a focus on tumors of the nervous system, leukemias and lymphomas, sarcomas and prostate cancer
- ↗ Implement (phospho)proteomic profiling of patient samples to improve decision-making in MTBs at partner sites Heidelberg and Munich
- ↗ Continue ongoing precision oncology trials (see above) and projects (e.g. MARRIAGE, DECISIONS, MIMETIC) and initiate additional trials (e.g. RATIONALE) in the DKTK and NCT
- ↗ Complete the quality management system for the bioinformatic preparation, biological curation and clinical annotation of genome/exome and transcriptome data and accreditation of the entire precision oncology workflow by DakkS, the national accreditation body for Germany, in accordance with DIN EN ISO 15189

Highlights of 2022

Developments in the MASTER program

Key elements of the MASTER program in 2022 were the expansion of data structures and the development of additional tools for data analysis and data organization. The Knowledge Connector, a software system that integrates molecular and clinical data from MASTER patients with precision oncology knowledge databases and visualizes them in order to facilitate a semi-automated clinical decision aid, was incorporated into the MASTER MTB. To compensate for the absence of publicly accessible drug lists, the NCT Precision Oncology Thesaurus Drugs, a curated database of drugs, drug classes and drug targets in precision cancer medicine, was developed with the support of the DKTK and published recently. Other developments in the field of data include implementing new documentation software that reflects the relational character of the molecular and longitudinal clinical data generated in the MASTER program, a separate instance of the cBioPortal for Cancer Genomics that enables exploration of the molecular and clinical data of the MASTER cohorts, and making MASTER data available through the German Human Genome-Phenome Archive.

In the context of INFORM, a liquid biopsy pipeline was implemented for the improved diagnosis, treatment monitoring and early detection of relapses in pediatric cancer patients. Following a successful pilot phase, the creation of drug sensitivity profiles was incorporated in the INFORM MTB as an additional diagnostic component. The added value of the drug test was confirmed through individual case studies during the pilot phase and summarized in a manuscript that was recently accepted for publication.

Further information:

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(2) Möhrmann L, Werner M, Oleś M, et al. Comprehensive genomic and epigenomic analysis in cancer of unknown primary guides molecularly informed therapies despite heterogeneity. Nat Commun. 2022;13(1):4485. Published 2022 Aug 2.

(3) Jahn A, Rump A, Widmann TJ, et al. Comprehensive cancer predisposition testing within the prospective MASTER trial identifies hereditary cancer patients and supports treatment decisions for rare cancers. Ann Oncol. 2022;33(11):1186-1199.

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Identification of proteomic subtypes in AML

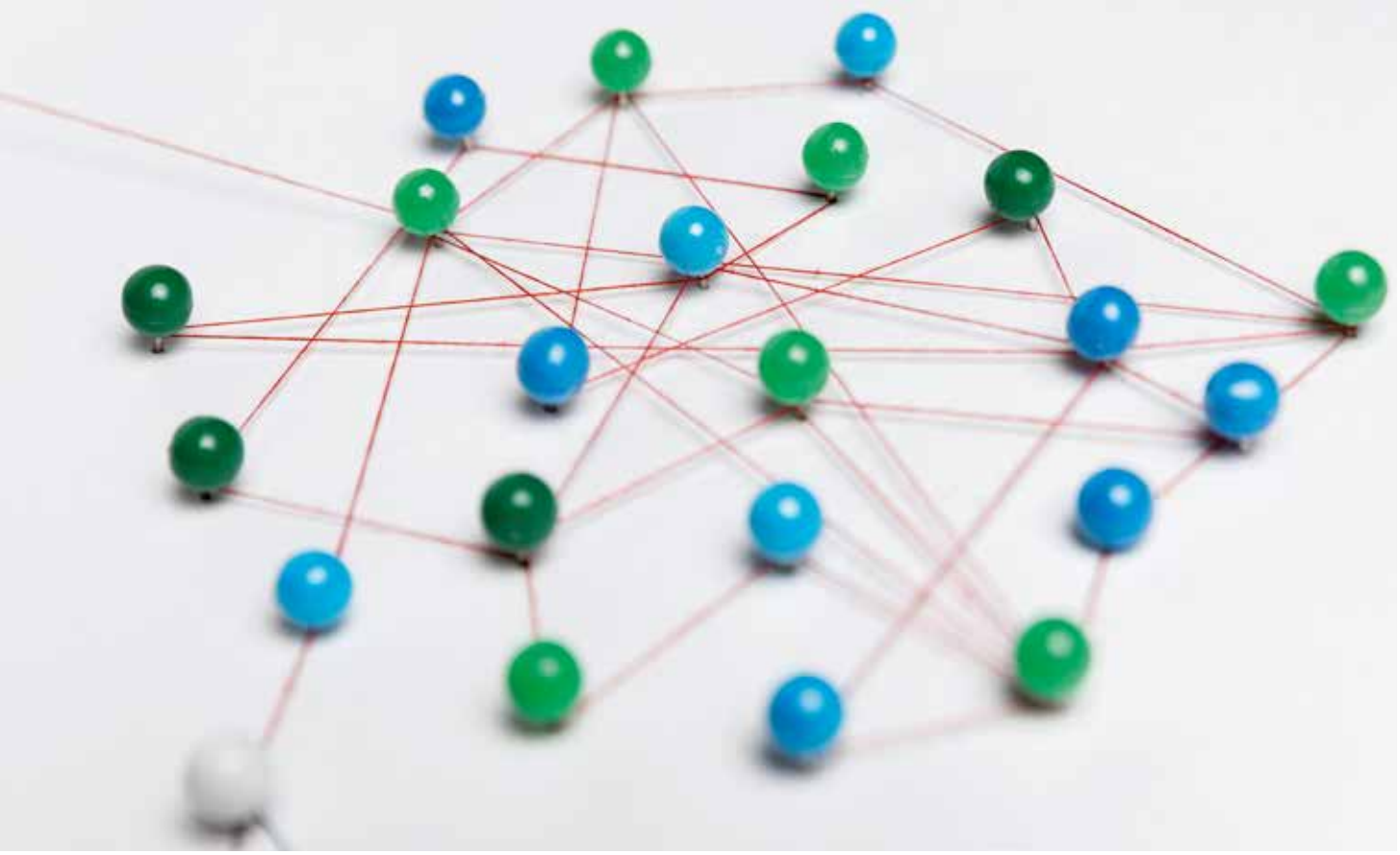
Acute myeloid leukemia (AML) is an aggressive type of blood cancer with a poor prognosis. In a large collaborative study that included DKTK researchers from Heidelberg, the research groups led by Prof. Thomas Oellerich, Prof. Hubert Serve (both DKTK partner site Frankfurt/Mainz) and Prof. Matthias Mann (Max Planck Institute of Biochemistry, Martinsried) were able to publish a comprehensive proteogenomic analysis of bone marrow biopsies from 252 AML patients who received the same treatment. These data bring the researchers closer to their goal of understanding the molecular pathophysiology of AML in order to develop future diagnostic and therapeutic approaches. The molecular profiles of the AML patients were comprehensively mapped – using both quantitative proteomics and cytogenetic profiling and DNA/RNA sequencing. Based on the proteomic data, five AML subtypes were identified that reflect specific biological characteristics. Two of these proteomic subtypes correlated with patient therapy success, but none of the subtypes was exclusively associated with specific genomic aberrations. Remarkably, a subtype (Mito-AML), which was only identified in the proteome, was characterized by high expression of mitochondrial proteins and led to a poor outcome, with a reduced remission rate and shorter overall survival rate when patients were treated with intensive induction chemotherapy. Functional analyses showed that Mito-AML is metabolically wired towards stronger complex I-dependent respiration and is more responsive to treatment with the BCL2 inhibitor venetoclax.

Further information:

(1) Jayavelu AK, Wolf S, Buettner F, et al. The proteogenomic subtypes of acute myeloid leukemia. Cancer Cell. 2022;40(3):301-317.e12.

(2) Fröhlich K, Brombacher E, Fahrner M, et al. Benchmarking of analysis strategies for data-independent acquisition proteomics using a large-escale dataset comprising inter-patient heterogeneity. Nat Commun. 2022;13(1):2622. Published 2022 May 12.

(3) Zecha J, Gabriel W, Spallek R, et al. Linking post-translational modifications and protein turnover by site-resolved protein turnover profiling. Nat Commun. 2022;13(1):165. Published 2022 Jan 10.



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Cross-site translational projects

A key focus area within the DKTK is working on interdisciplinary research topics at the interface between basic research and clinical practice, in particular funding the preclinical development of innovative therapy approaches and diagnostic methods. Through its INNOVATION funding line, the competitive DKTK Joint Funding Program finances collaborative research projects with a translational focus. In a multi-step selection process involving the DKTK's multinational Scientific Advisory Board, project proposals are evaluated, and projects of particularly high scientific quality that are also highly innovative, e.g. because they relate to tumor entities with insufficient therapy options, are selected for funding. Since 2017, the DKTK has been running a second funding line, UPGRADE, for research projects that build on or are associated with clinical trials to find answers to new scientific questions through experimental research, and to maximize the knowledge gained from clinical trials.

All Joint Funding projects involve at least three partner sites; some even involve all eight sites. Other, external partners can also support the projects with additional research contributions. Moreover, the program is used to address current topics of outstanding scientific and medical importance through a multicenter approach by providing targeted funding for strategic initiatives of the DKTK Steering Committee. Dedicated infrastructure facilities set up by the DKTK are of central importance for project implementation. They provide multifaceted technological support and, combined with the specialist expertise of everyone involved, play a key role in helping to connect preclinical and clinical research.

Since the DKTK was founded, more than 50 translational research projects, investigator-initiated early clinical trials and strategic initiatives have been funded through the Joint Funding Program. An overview on the DKTK website lists and describes these projects and offers a user-friendly filter function to view projects by site, entity, funding line and other categories (see https://dktk.dkfz.de/en/research/joint-funding-projects/projects).

Developments in 2022

During the ninth call for proposals of the DKTK Joint Funding Program's INNOVATION funding line in 2022, six new projects were selected. In autumn, two more new calls for proposals were launched: the 10th call for new research modules that build on clinical trials (UPGRADE 2023) and the 11th call for new translational cross-site research projects (INNOVATION 2023). In addition, work started on a new strategic initiative on organoids and a concept was drawn up with the participation of all partner sites.

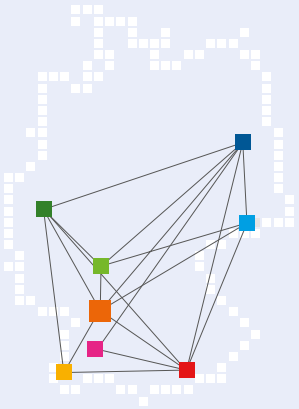

Table: All active projects within the DKTK Joint Funding Program in 2022:

Acronym	Description
Afatinib	This phase II study investigates the effectiveness of the pan-Erb inhibitor afatinib in advanced NRG1-rearranged malignant cancers once standard treatment has failed.
AMI2GO	This project accompanies the AMPLIFY-NEOVAC trial, using tumor tissue organoids to gain insights into the mechanisms of T-cell response and resistance following treatment.
AMPLIFY-NEOVAC	A multicenter trial assessing the safety and immunogenicity of a vaccine against a mutation of the IDH-1 protein in combination with immune activation via checkpoint inhibition in patients with a recurrent brain tumor.
ARMANI	A prospective trial assessing the safety and efficacy of a molecularly-guided anatomical resection compared with a non-anatomical resection of liver metastases in patients with RAS-mutated colorectal cancer.
CAR2BRAIN	This project enables detailed characterization of the changes to the blood, reservoir fluid and tumor tissue brought about by CAR-NK cell therapy in brain tumor patients in the trial of the same name.
CHOICE	This project investigates the role of bone and the bone marrow niche in the development of clonal hematopoiesis of indeterminate potential (CHIP) as a risk factor for stem cell-linked hematologic diseases in older patients.
EXLIQUID	This multicenter liquid biopsy project supplements the MASTER program and local programs at all eight DKTK partner sites. It is building a collection of blood samples before and during molecular, targeted therapies, and developing diagnostic tools.
IMMUNED	This project combines molecular analyses of tumor tissue samples with the characterization of immunological and tumor-specific biomarkers and clinical data from the IMMUNED trial to develop a prediction model for use in clinical practice.
INFORM	A register trial that aims to open up new treatment options for children with recurrent cancer who have run out of established treatment concepts. Researchers are analyzing the tumor genome for a potential use of new, targeted drugs.
INFORM/ MASTER-PRO	This project is testing how molecular characterization of tumors for personalized therapies, which is used in INFORM and in the MASTER program, can be supplemented and improved through the additional recording of (phospho)proteomic profiles.

Acronym	Description
IVAC-AN	This project, which builds on the IVAC-ALL-1 trial, characterizes in greater detail the T-cell responses triggered by peptide vaccination in patients with recurrent acute lymphocytic leukemia (ALL).
MARRIAGE	This project uses patient samples from the MASTER program and the TOP-ART phase II trial to study DNA repair systems and how they might be controlled for therapy purposes, and to incorporate them into therapy.
MASTER program	This DKTK-wide registry trial detects individual changes in the genome of cancer cells in young adults with advanced cancer and in patients with rare tumors, with the aim of developing a personalized therapy recommendation.
MEMORI	The aim of this project is to research molecular subtypes and tumor metabolic patterns in the MEMORI patient cohort with tumors of the gastroesophageal junction (GEJ), based on an integrated analysis of clinical, molecular and imaging data.
MIMETIC	Using cutting-edge methods, such as plasma proteomics and multispectral imaging, this project aims to gain a comprehensive understanding of the immunomodulatory characteristics of combined targeted immunotherapies for the CRAFT trial.
MTBA	This DKTK-wide project is associated with the MASTER program and aims to collate all local MTB datasets in one database and to harmonize workflows with other MTB initiatives in Germany.
NEO-ATT	This project is developing neoantigen-specific T-cell receptors for personalized T-cell therapy of solid tumors which will recognize new protein molecules that appear in the cancer tissue as a result of genetic changes.
NEOLAP/SUBPAN	Using image datasets, tumor samples and clinical information from the phase II NEOLAP trial, this project aims to identify biomarkers for subtype differentiation in locally advanced pancreatic ductal adenocarcinoma (PDAC) and to develop image-based algorithms for routine clinical use.
NextGenLOGGIC	In collaboration with the global phase III LOGGIC trial for pediatric low-grade gliomas (pLGGs), this project aims to generate preclinical data to create a basis for next-generation clinical trials.
PEVIDS	This project investigates the impacts at molecular level of personalized vitamin D supplementation on various health aspects in patients with colorectal cancer from the VICTORIA trial.
PSMAxCD3	The two phase I immunotherapy studies investigate the safety, tolerability and efficacy of the bispecific PSMAxCD3-CC1 antibody developed in the DKTK for prostate cancer or plate epithelial carcinoma of the lung.
RAMTAS	The aim of this project is to identify a molecular signature in metastatic colorectal cancer (mCRC) to predict how it will respond to anti-angiogenic therapy. To do this, the researchers are analyzing tumor and blood samples from the RAMTAS phase II clinical trial.
RiskY-AML	This project makes use of novel single-cell technologies and data analysis tools to develop new predictive biomarkers and therapeutic options that prevent or overcome resistance and recurrence in AML.
SI SARS-CoV2	This strategic initiative investigates the immune response to SARS-CoV-2 in order to deepen immunological knowledge across Germany, improve the clinical management of cancer with simultaneous COVID-19 infection, and harmonize the biobank structures.
SIGN-OC	This project is based on the international phase II TRUST trial and aims to identify characteristic molecular signatures in advanced ovarian cancer for personalized treatment decisions.
SORATRAM	This project is evaluating a new concept for treating a wide range of tumors in patients from the MASTER program with kinase-inactivating BRAF mutations.

Participants at the Cancer Core Europe Summer School in Translational Cancer Research in October 2022 in Portugal. (© DKFZ/NCT Heidelberg)

Early career support in the DKTK

Spokesperson: Prof. Mechthild Krause (partner site Dresden)

Excellent training of young scientists at the interface between patient-oriented, translational cancer research and the transfer of new diagnostic and therapeutic approaches to clinical practice is an important DKTK mission. Within the consortium, the DKTK School of Oncology contributes to education and training in translational cancer research through a wide range of programs.

In the School of Oncology, young researchers benefit from a nationwide network of interdisciplinary clinical competence, comprehensive expertise in the field of basic oncological research, and translational research infrastructure at the DKTK partner sites. The focus of the DKTK's early career support is on medical scientists – scientists with medical background/Postdocs up to 6 years after obtaining PhD – as well as clinician scientists – physicians in residency programs who are also amassing experience in cancer research. All members who are active in the DKTK School of Oncology are working on translational research projects in the DKTK or are involved in clinical trials. About 150 early career researchers are Fellows of the DKTK School of Oncology.

The School of Oncology program builds on the training offered by the Cancer Research Academy at the DKFZ and the DKTK partner sites. Fellows of the School of Oncology also have access to the DKFZ's PostDoc program, enabling them to benefit from consortium-wide networking.

Career prospects in the field of translational cancer research

- Several sites have offered scholarships to enable physicians in residency programs to take time off for research, so that they can devote themselves to a fixed-term research project.
- The DKFZ in Heidelberg has already completed its fourth selection round for the DKFZ Clinician Scientist Program.
- There are currently four DKTK young investigator/junior research groups at various partner sites.

Support measures and events in 2022

Whereas, in previous years, most events were held virtually because of the pandemic, in 2022 an increasing number were held in person again. Nevertheless, virtual and hybrid formats continue to facilitate regular nationwide networking among the Fellows and make it easy for people across all partner sites to participate in events. The **DKTK online seminar series on techniques in translational research (DKTK Tech Talks)**, which

launched in 2021, continued in 2022. Prof. Kirsten Lauber from the Molecular Radiation Oncology research group in the Department of Radiation Oncology at LMU Klinikum (University Hospital) in Munich spoke about comparing different assay formats to analyze clonogenic growth in vitro.

Event poster for the DKTK Young Academics Conference 2022. (© DKTK)

The **DKTK School of Oncology Young Academics Conference** took place on May 5 and 6, 2022 as a hybrid event in conjunction with the DKFZ Postdoc Retreat. As well as keynote lectures by Dr. Lisa Sevenich, Frankfurt, and Prof. Moritz Gerstung, DKFZ Heidelberg, the conference included workshops on "Storytelling", "On the Way to a Career", "Effective Communication" and numerous other talks and discussions relating to the research fields of the participating young scientists.

The annual **Cancer Core Europe Summer School in Translational Cancer Research** provides a dialogue platform to exchange views at international level with oncologists, cancer researchers and members of leading cancer associations on current topics in cancer medicine, to undertake further training and expand networks. Sixty-four ambitious doctoral researchers, postdocs and clinician scientists from 12 countries, and 29 international speakers met in Portugal from October 16 to 22. Among the participants were 14 DKTK School of Oncology Fellows. The focus of the research discussions was on personalized approaches in cancer medicine. Topics included immunotherapy, digital oncology, artificial intelligence, imaging, diet and physical activity in cancer prevention, ethics and health economics. The discussions were supplemented by workshops on clinical decision support systems, how to set up clinical trials, and project management, self-management and career development.

Within the joint DZG-wide early career support measures, the **Lunchtime Career Talks** seminar series continued, in which speakers – most of whom belong to one of the DZG – present different career paths in research and associated fields. On June 29, 2022, Dr. Uwe Raaz offered insights on "Founding and Working in a Startup". In addition, the DZG also organized their first joint symposium on "Single-Cell Analyses" in research and medicine. In this online event, held on November 10 and 11, 2022, 120 participants from basic and clinical research discussed projects and technologies with experts. The aim was to bring together young and experienced scientists from basic research and clinical practice from all the DZG for interdisciplinary discussions about the use of single-cell analyses so that they could learn from one another.

Event poster for the DZG "Lunchtime Career Talk" series. (© DZG)

Travel and lab rotation grants enable the Fellows to take part in scientific conferences or research residencies of up to three months in a host laboratory. Eight travel grants and two residencies in national and international partner institutions were approved in 2022.

Examples of other events and training offers in 2022:

- DKTK site retreats
- Young Investigator Club in Dresden
- Munich Cancer Retreat and DKTK Munich Cancer Colloquiums
- Essen Translational Oncology Symposium (ETOS)
- DKTK Freiburg Seminar Series
- Heidelberg Grand Rounds and initiatives of the DKFZ Postdoc Program and PostDoc Network
- Career Days at the DKFZ on "Clinical Research" and "Project Management"
- 4th Joint DZG Symposium Dresden

Goals for 2023

- Send out regular newsletters with information on events, seminars and funding opportunities
- Standardize further the application processes for the School of Oncology at the different DKTK partner sites
- Continue the virtual DKTK seminar series on the clinical relevance of preclinical research methods
- Expand DZG-overarching training measures in the field of translational research
- Support the participation of School of Oncology Fellows in (inter)national scientific events and facilitate external research residencies to obtain additional specialist expertise

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National and international cooperation and networking in the DKTK

Since the DKTK was set up, it has created a unique scientific environment in which DKTK scientists, clinician scientists and other associated experts collaborate in an interdisciplinary manner within the translation centers set up by DKFZ, as the core center of the DKTK, with leading German university partner sites. Through its preclinical translational research approach, the nationwide network of eight partner sites contributes to the faster transfer of new research findings into applications for patients. In particular, the DKTK also supports reverse translation, in which findings from trials that need further scientific investigation are studied in research projects.

As well as technology platforms that can be accessed by all the partner sites, the central Coordination Office at the DKFZ in Heidelberg and the scientific and administrative coordinators at the sites contribute to the successful development of the DKTK, providing central organizational support for researchers and creating effective communication processes and networking opportunities.

Multi-site collaboration

Initiating and cultivating collaboration between researchers at different partner sites within the consortium is one of the DKTK's central aims. It uses a number of different instruments for this, organizing regular retreats at the partner sites that aim to promote networking among the participants at the translation center in question, but also with partners from other DKTK sites. The DKTK also has a number of topic-based research groups that come together to investigate specific problems. The five research programs held strategy meetings in 2022 to work on the recommendations from the 2021 internal evaluation.

One of the most effective instruments offering targeted support for multi-site collaboration within the consortium is the DKTK Joint Funding Program, which identifies and funds innovative DKTK-wide research projects through competitive calls for proposals. External partners can also take part in the projects with supplementary contributions. A description of the program and a list of current projects can be found on page 27 onwards.

Expansion of the DKTK research structures

The consortium has established joint research infrastructure facilities and platforms, largely for use by DKTK scientists but also by external cooperation partners. For instance, the CCP is designed to enable the sharing of data that is important for research, while complying with the most stringent quality, ethics and data protection standards. Biological samples and clinical and experimental patient data are vital resources for medical research, in particular for the development of new personalized therapeutic and diagnostic methods. The human biobanks at the DKTK partner sites have extensive collections of annotated biological samples, including tissue, liquid samples and derivatives.

As an interdisciplinary, consortium-wide CCP research group, the DKTK Clinical Data Science Group (CDSG) serves as a forum for connecting researchers from different scientific and medical disciplines. It is only through continuous interdisciplinary collaboration between researchers from the fields of medicine, biology, informatics, statistics and data science that the added value of data-driven cancer research can be fully exploited and that data from routine oncological care can be used to support the development and implementation of healthcare-related, innovative research projects. The DKTK CDSG forms the basis for the low-threshold, continuous exchange of information needed for this process, and initiated a number of data-driven projects in 2022. Further information on current CCP developments can be found on pages 22 and 23.

The JIP also continues to develop very dynamically. It is a unique IT infrastructure platform based on decentralized evaluation of algorithms for the analysis of medical imaging methods (federated learning). This method is already used in several DKTK research projects but has also met with a great response from national and European research networks, including the RACOON network of the radiology departments of all the German university hospitals (www.netzwerk-universitaetsmedizin.de/projekte/racoon) and the Cancer Core Europe (CCE) DART initiative involving seven major European cancer centers (www.cancercoreeurope.eu).

The DKFZ/NCT/DKTK MASTER program and the INFORM program are core activities for personalized cancer research within the DKTK, and have established standardized protocols and procedures for deep molecular genetic analysis of tumor patients that can provide further information about diagnosis and novel therapy options. At the center of this process are the MTBs, interdisciplinary molecular tumor boards in which experts interpret the complex molecular data of individual tumor genomes and identify possible therapy options. Because of its long-standing experience in this area, the DKTK, together with the DKFZ and the NCT, plays an important role in the development of MTBs to ensure that these critical analyses are carried out to an extremely high standard.

Furthermore, the MASTER team organized the third DKTK HARPOON workshop (HArmonization of Reporting in PrecisiOn Oncology), at which more than 200 participants from all over the world, including from all the DKTK partner sites, came together to discuss the latest developments in precision oncology. Besides three international keynote lectures, the workshop provided a platform for an interdisciplinary exchange of ideas and offered insights into the current and future potential of versatile diagnostics and personalized therapy strategies.

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Projects with the pharmaceutical industry

In 2020, the DKFZ and DKTK partner site Tübingen joined forces with the University of Tübingen and investor Cullinan Oncology, LLC, in the USA to set up a company called Cullinan Florentine, which specializes in a bispecific antibody to treat patients with AML that was developed within the DKTK. The first tranche of Series B preferred stock financing raised over ten million euros. A second tranche of Series B preferred stock has since been sold to finance the remaining development steps of the clinical phase. A clinical multicenter trial is currently running at several hospitals in the USA with Cullinan Oncology as the sponsor, in which a bispecific antibody is administered to patients with relapsed/refractory AML or myelodysplastic syndrome (MDS). Following this successful startup, DKTK partner site Tübingen and Prof. Helmut Salih have created another spin-off: Bicony Therapeutics GmbH. Bicony receives an exclusive license for an even broader patent portfolio, with the aim of developing a combination immunotherapy, particularly for prostate, lung and colon cancer with two different formats of patented bispecific antibodies.

In addition, DKTK partner site Tübingen managed to secure financing for a pioneering project: Dr. Latifa Zekri-Metref received funds from beLAB2122, a partnership supported by Bristol Meyers Squibbs and Evotech, for her project to develop an optimized ACE2 fusion protein with improved activity against SARS-CoV-2 variants.

International cooperation and exchange

The DKTK's close contacts include the Cancer Core Europe (CCE) network, the European Academy of Cancer Sciences (EACS) and other organizations, and it was involved in setting up the EU Cancer Mission, among other things. In addition, several DKTK research programs have joined international research networks. For instance, the Radiation Oncology program works intensively with the European Particle Therapy Network of the European Society for Therapeutic Radiology and Oncology (ESTRO). Twelve countries are now involved in the INFORM program for molecular genetic analysis of pediatric tumors. Members of all DKTK research programs are regularly invited to give presentations at international conferences and workshops.

Dialogue with regulatory authorities

The Paul Ehrlich Institute (PEI), the Federal Institute for Vaccines and Biomedicines, is one of the key players in Germany when it comes to regulatory monitoring and the legally compliant conduct of clinical trials. The DKTK and the PEI have a long-standing partnership within the framework of the existing joint research program on "Regulatory analysis and optimization of the translation of development candidates in the DKTK". The PEI supports DKTK researchers and clinicians who want to translate their research results into human clinical trials, by providing regulatory expertise in the planning phase. As well as personal consultations on product-specific questions, there are kick-off meetings where interested staff members can find answers to general questions. The PEI also offered additional information and dialogue events in 2022, which were attended by DKTK members. Topics included new regulations for *in vitro* diagnostics and companion diagnostics, and the scientific and regulatory aspects of innovative drugs for novel therapies.

The National Decade against Cancer

The DKTK is an active driver and focal point for the further development of cancer research and cancer care in Germany. An example is the National Decade against Cancer that was declared jointly by the BMBF and the Federal Ministry of Health (BMG) in 2019, and in which the DKFZ, DKTK, NCT and many other partners are actively involved. Important decision-makers from politics, cancer research, research funding, healthcare, patient representative bodies, the economy and society pool their expertise on effective strategies to combat cancer. The Scientific Director of the DKFZ and Spokesperson of the DKTK, Prof. Michael Baumann, is Co-Chair of the Strategy Circle and, with other DKTK scientists, engages in a wide range of working groups and research initiatives and with the Strategy Circle of the National Decade against Cancer.

From September 30 to October 2, 2022, the first national conference on "Patients as Partners in Cancer Research" was held at the DKFZ with the theme "Learn. Cooperate. Change". The event was organized by patient representatives, including some from the NCT Patient Council and the DKFZ and DKTK Patient Advisory Council for Cancer Research, and aimed to advance the integration of patient perspectives in cancer research. The participants were able to discuss a wide range of aspects and take part in training activities – including talks on the assessment of research proposals and seminars on skills such as speaking and presentation techniques.

Fighting common diseases together

The main aim of the German government's health research program is to be able to tackle major widespread diseases more effectively. Together with the German Centers for Health Research, the BMBF and the federal states have developed powerful structures for this purpose. These long-term partnerships between non-university research institutions, such as the Helmholtz, Max Planck and Leibniz institutes, and universities and university hospitals pool existing expertise. The six DZG are dedicated to Cancer (DKTK), diabetes (DZD), cardiovascular diseases (DZHK), infectious diseases (DZIF), lung diseases (DZL) and neurodegenerative diseases (DZNE). Two more centers – for pediatric and adolescent medicine and for mental health – are in the process of being established. Strategic collaboration between the leading researchers in the DZG strengthens Germany's international standing as a research location and makes it considerably more visible and attractive in the field of translational research for early career scientists in Germany and abroad.

The six DZG have worked closely together since the beginning. Their regular meetings focus on the DZGs' strategic development and collaboration. In 2022, the DZG Board met quarterly with representatives of all DZG management boards and leadership teams, and in July and December there were additional DZG Forum meetings in which representatives from the BMBF also participated.

DZG collaboration has been expanded still further in recent years. The DZG Innovation Fund (DZGIF) is a joint DZG program that facilitates and provides financial support for promising DZG-wide research ideas that advance knowledge concerning the prevention and treatment of various widespread diseases. A proposal on "Cell & Gene Therapy" involving two DKTK scientists received funding following the DZGIF call for proposals in 2022. Scientists also form working groups to share knowledge and use joint structures. There are working groups on research IT, patient participation, regulatory aspects of clinical trials, promotion of young scientists, public relations and global health. Within the "promotion of young scientists" area, for instance, seminar series were organized (see pages 30 and 31), while two more issues of the joint research magazine were published in the area of public relations (see pages 36 and 37).

Fighting common diseases together: The three DZG based in Dresden (DZNE, DZD/PLID and DKTK) have been closely connected for years. At the joint DZG Symposium in 2022, young scientists once again received seed funding for new translational activities at the thematic interfaces between the Dresden centers. (© DZG Dresden)

The DKTK in the public

It is not only scientists who are asking questions relating to cancer research, but the general public as well. This is why the Coordination Office regularly tells the scientific community and interested members of the public about exciting research results, events, funding and awards through its website, social media accounts, press releases, articles in journals and magazines, various newsletters and events.

Cover of the DKTK Annual Report 2021 (© DKTK)

The DKTK newsletter appeared at regular intervals in 2022 in German and English, aimed primarily at researchers and research support staff at all DKTK partner sites. In May, the newsletter appeared for the first time in its new, updated design. Monthly event newsletters were also sent out with details of events that were relevant to, or organized with the help of, DKTK scientists. In addition, the BMBF reported in its June newsletter on the new WHO classification, which forms the basis for modern, precise cancer diagnostics worldwide and is based in part on DKTK research findings.

Insights into cancer research

In February 2022, the DKFZ ran an exhibition on cancer research and cancer prevention in a publicly accessible pop-up science shop in Heidelberg Old Town. In this "Science in the City" event, young researchers presented a different, exciting research project each day (the "topic of the day") to an audience of interested members of the public. On behalf of the DKTK, Heidelberg-based School of Oncology Fellow Dr. Thomas Walle presented the topic "How are modern computer models and machine learning supporting cancer medicine?" and illustrated the complex approach in a clear, easy-to-understand manner.

The DKFZ's einblick magazine also reported regularly on DKTK research: Issue 1/2022, for instance, contained a report on how, in the context of the National Decade against Cancer, DKTK researchers are involved in the BMBF-funded SATURN3 research consortium, helping to decode the molecular causes of therapy resistance in pancreatic cancer, breast cancer and colorectal cancer.

Heidelberg-based School of Oncology Fellow Dr. Thomas Walle presented the topic "How are modern computer models and machine learning supporting cancer medicine?" at a publicly accessible pop-up science shop organized by the DKFZ in February 2022 in Heidelberg Old Town. (© DKTK)

Scientific exchange

National and international congresses, conferences, symposia and other scientific events were held both virtually and in hybrid formats in 2022, and some in-person-only events were held for the first time since the start of the COVID-19 pandemic. DKTK researchers took part in local events organized by the DKTK partner sites, including the **Essen Translational Oncology Symposium** (ETOS) 2022, the 9th **Munich Cancer Retreat** and the **4th Joint DZG Symposium** in Dresden, and also in national conferences like the German Cancer Congress 2022 and the ESMO Congress 2022 of the European Society for Medical Oncology.

The DKTK scientific community also connected via social media. Individual researchers and entire research groups use Twitter, for instance, to share information and ideas, to network and communicate directly with one another. The number of followers has continued to increase. The Coordination Office regularly

Two events organized by DKTK partner sites in 2022: top the 4th Joint DZG Symposium in Dresden (©DZG Dresden) and bottom the 9th Munich Cancer Retreat (© DKTK Munich)

used Twitter to post news about cancer research and – as part of the DZG – about various common diseases and joint initiatives.

Cancer and other common diseases

The six DZG collaborate in many different areas – including public relations. Here they provided fascinating insights into translational research on cancer, cardiovascular diseases, lung diseases, neurodegenerative diseases, infectious diseases and diabetes. As well as joint social media posts, the DZG also publish a successful biannual joint magazine called SYNERGIE, which has as its motto "research for health". The magazine continued in 2022, with issues on "the immune system" and "clinical research" and was published both as a high-quality print magazine and online at www.dzg-magazin.de. In 2022, SYNERGIE won the iF Design Award in the communication category for its high-contrast, eye-catching design that helps make research into the major common diseases accessible to a wide audience.

In 2022, the DZG produced a joint corporate design manual, including a logo relaunch, color palette and fonts. The joint website for all DZG went live in May 2022: https://deutschezentren.de/. It publishes news and presents the individual centers, their disease areas and the DZG-wide working groups.

On May 19, 2022, four of the six DZG – the DKTK, the German Center for Cardiovascular Research (DZHK), the German Center for Infection Research (DZIF) and the German Center for Lung Research (DZL) – celebrated their tenth anniversaries with an event in Berlin. The program involved numerous political and scientific guests. A report and photos from the event are available on the DZG website:
https://deutschezentren.de/en/10-years-of-dzg/

Panel discussion involving the spokespersons of the four ten-year-old DZG at the anniversary event on May 19, 2022, in Berlin. (© DZG)

Print version of the DZG magazine SYNERGIE, Issue 7, on the immune system. (© DZG/WirDesign) The magazine won the IF Design Award 2022. (© iF Design)

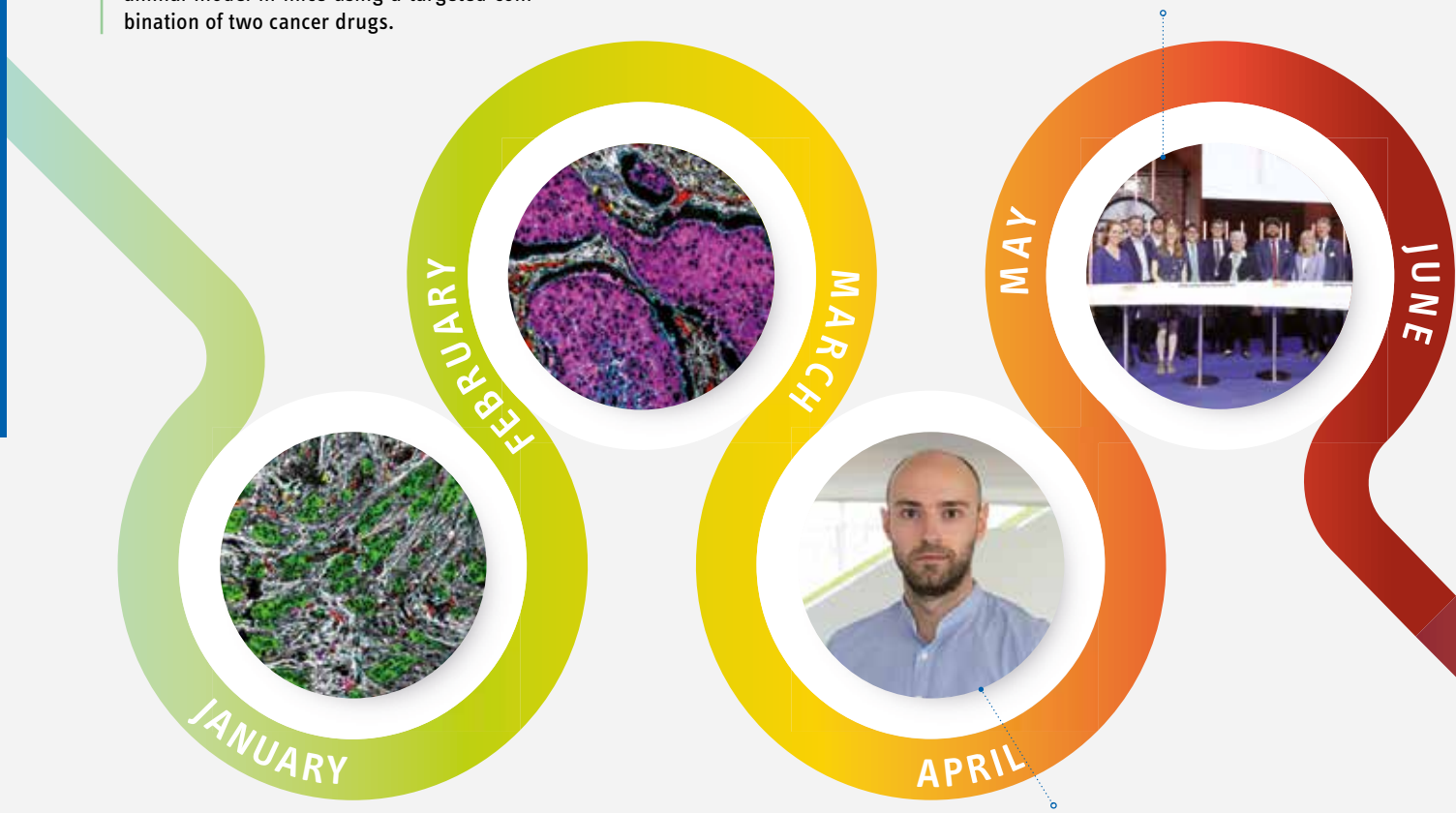
DESIGN AWARD 2022

Making pancreatic cancer responsive to immunotherapy

So far, there are no treatment methods for pancreatic cancer that are effective long term. Even immunotherapy is not usually successful. Researchers at DKTK partner site Munich succeeded in finding a way of making these immunologically inaccessible pancreatic tumors responsive to immunotherapy in a preclinical animal model in mice using a targeted combination of two cancer drugs.

10th DZG Anniversary

Four of the six DZGs celebrated their tenth anniversaries on May 19, 2022, with an event in Berlin, together with guests from politics and science. Federal Research Minister Bettina Stark-Watzinger, Hessian Research Minister Angela Dorn, Berlin State Secretary of Health Dr. Thomas Götz, former Federal Research Minister Annette Schavan, Prof. Christian Drosten, and BioNTech co-founder and medical director Prof. Özlem Türeci all offered their congratulations either in person or online.



New DKTK junior group leader in Dresden

Molecular biologist Dr. Jovan Mircetic and clinician colleagues are using CRISPR technology to investigate tumor resistance to standard therapies in tumor organoid models. Since April 2022, he has been developing this translational research approach further as a Junior Group Leader at DKTK partner site Dresden.

New resistance mechanism discovered in rectal cancer treatment

A research team in Frankfurt managed to identify a new resistance mechanism for rectal cancer treatment: Based on patient samples, they showed in the laboratory and in preclinical models that it was not primarily the tumor cells themselves but, surprisingly, the surrounding connective tissue cells that had been modified by inflammation that had a major influence on the response to radiotherapy.

Melanoma: Prolonging the rest phase and avoiding relapse

Melanoma cells change particularly fast. By contrast, persister cells follow a slow cycle and frequently do not switch to active cell division until cancer treatment has started. In lab experiments, researchers from partner site Essen/Düsseldorf successfully used a new drug in a cell culture model to keep the persister cells in the rest state, meaning they were vulnerable to treatment with drugs.

New subgroup of acute myeloid leukemia discovered

Using mass spectrometry, researchers have, for the first time, identified a proteomic subtype of acute myeloid leukemia, an aggressive type of leukemia. This discovery by scientists from partner sites Heidelberg and Frankfurt/Mainz and others could pave the way for new treatment options.

DKTK highlights of 2022

REVEAL – new potential vulnerabilities in metastatic colon cancer

REVEAL, the DKTK-funded biomarker trial coordinated by partner sites Munich and Berlin, demonstrated the serial analysis of mutation status and gene expression under standard therapy in patients with metastatic colon cancer. The trial offers a promising approach for understanding secondary resistance mechanisms.

DKTK EXLIQUID consortium – monitoring personalized cancer therapies in the blood

The blood of cancer patients can provide valuable tumor indications. The DKTK Joint Funding project EXLIQUID (Exploiting liquid biopsies to advance cancer precision medicine) aims to investigate the tumor DNA circulating in the blood to closely monitor response to treatment and identify in good time any new therapy resistance that emerges during the course of the disease. The researchers from all partner sites published their joint approach.

How brain tumors keep time – and why this makes them so dangerous

Glioblastomas are highly aggressive brain tumors. Researchers in Heidelberg discovered that individual, particularly well-connected cells in the tumor tissue take on the function of pacemakers. The consequences are serious: The tumor cell network's rhythm promotes tumor growth and resistance.

Comprehensive molecular analysis in CUP syndrome

A considerable proportion of patients suffering from cancer of unknown primary (CUP) syndrome could benefit from comprehensive molecular analysis and molecularly informed targeted therapies. These are the findings of a team of researchers from Dresden and Heidelberg using results from the DKFZ/NCT/DKTK MASTER program.

Baden-Württemberg promotes the development of innovative radiopharmaceuticals

The DKTK's Division of Radiopharmaceuticals Development at partner site Freiburg and Freiburg company 4HF Biotec GmbH launched a close collaboration in the field of innovative nuclear medicine therapy concepts. The Invest BW funding program led by the Baden-Württemberg Ministry of Economic Affairs is supporting this project with third-party funding to identify new drugs for nuclear medicine treatment of lung and prostate cancer.

First national conference on Patients as Partners in Cancer Research at the DKFZ

The first national conference on **Patients as Partners in Cancer Research** was held from September 30 to October 2, 2022. It was organized by patient representatives, particularly from the NCT Patient Council, and was held at the DKFZ. Among other things, the participants discussed how patient involvement in cancer research can be advanced, under the motto "Learn. Collaborate. Change."

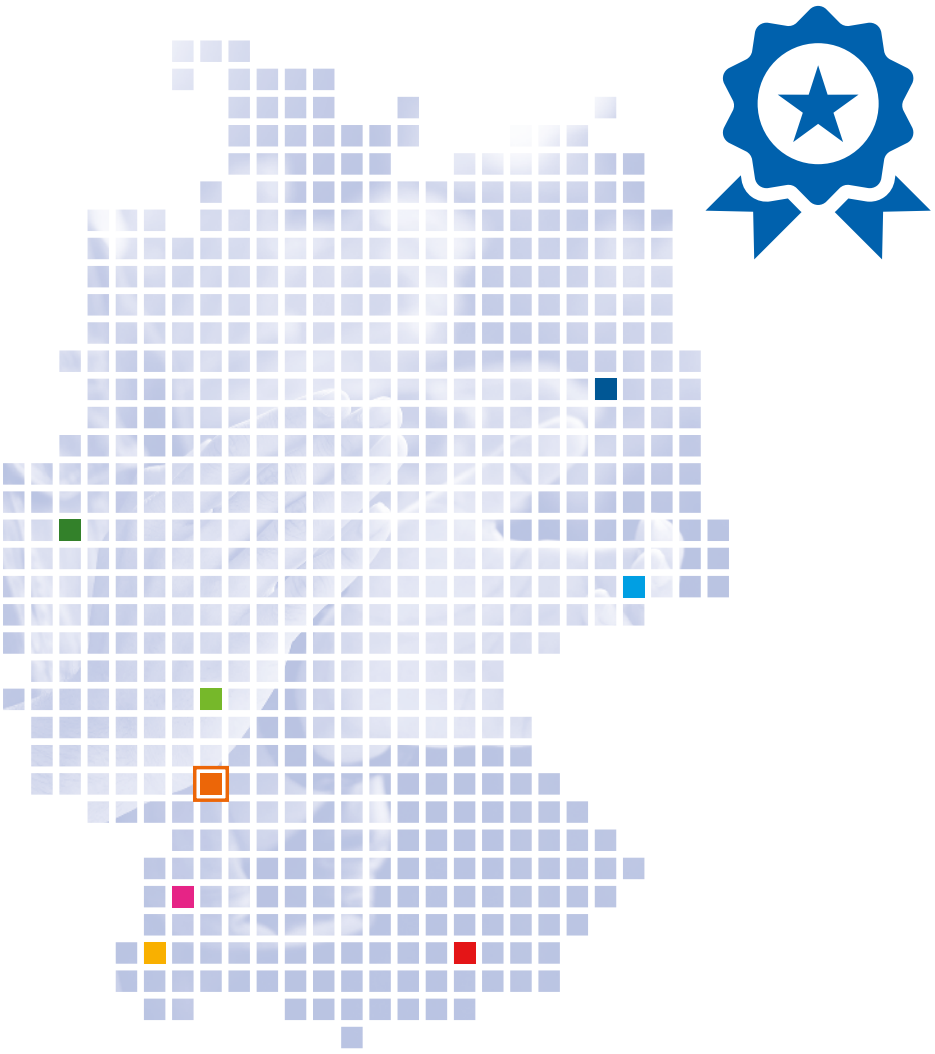
Tumorigenesis: What initial lesions in the pancreas reveal

Pancreatic ductal adenocarcinoma (PDAC) still has a poor prognosis, despite many years of research. Besides researching more effective drugs, better early detection can help. Since precursor lesions frequently become visible before the actual disease onset, a team at partner site Essen/Düsseldorf analyzed the most common PDAC precursor lesions using comprehensive morphogenetic methods. The results contribute to a better understanding of tumor formation in PDAC.

Scientific achievements and prizes

Selected prizes and awards 2022

Site	Prizewinner & award
Heidelberg	**Prof. Stefan Pfister:** State Research Award for Applied Research 2022
	Prof. Michael Baumann: Honorary doctorate from the Faculty of Health of Aarhus University, Denmark
Frankfurt/Mainz	**Prof. Claus Rödel:** Deutsche Krebshilfe Prize 2021
München	**Chiara Falcomatà (DI, DKTK PhD):** Helmholtz Doctoral Award
Dresden	**David Digomann:** Carl Gustav Carus Prize for outstanding dissertation
Berlin	**Prof. Ulrike Stein:** Women in Science Achievement Award of the Metastasis Research Society
Essen/Düsseldorf	**Dr. Phyllis Fung-Yi Cheung:** AIO Science Prize
Freiburg	**Prof. Robert Zeiser:** Prevention Prize 2022 of the German Society of Internal Medicine (DGIM)
Tübingen	**Dr. Judith Feucht:** Württemberg Cancer Award 2022
MASTER program	**Prof. Stefan Fröhling/HD, Prof. Hanno Glimm/DD:** Paul Martini Prize



DKTK publications 2022

In 2022, a total of 1,446 ISI or Scopus peer-reviewed scientific papers by authors affiliated to the DKTK were published (correct at March 31, 2023), of which 458 appeared in particularly high-ranking scientific journals with an impact factor of ten or more (impact factor in 2021). In 2022, DKTK-affiliated publications were cited 73,074 times. A PDF file containing the complete list of DKTK publications in 2022 can be found online at www.dkfz.de/zbi/nolink/Publikationen-DKTK-2022.pdf

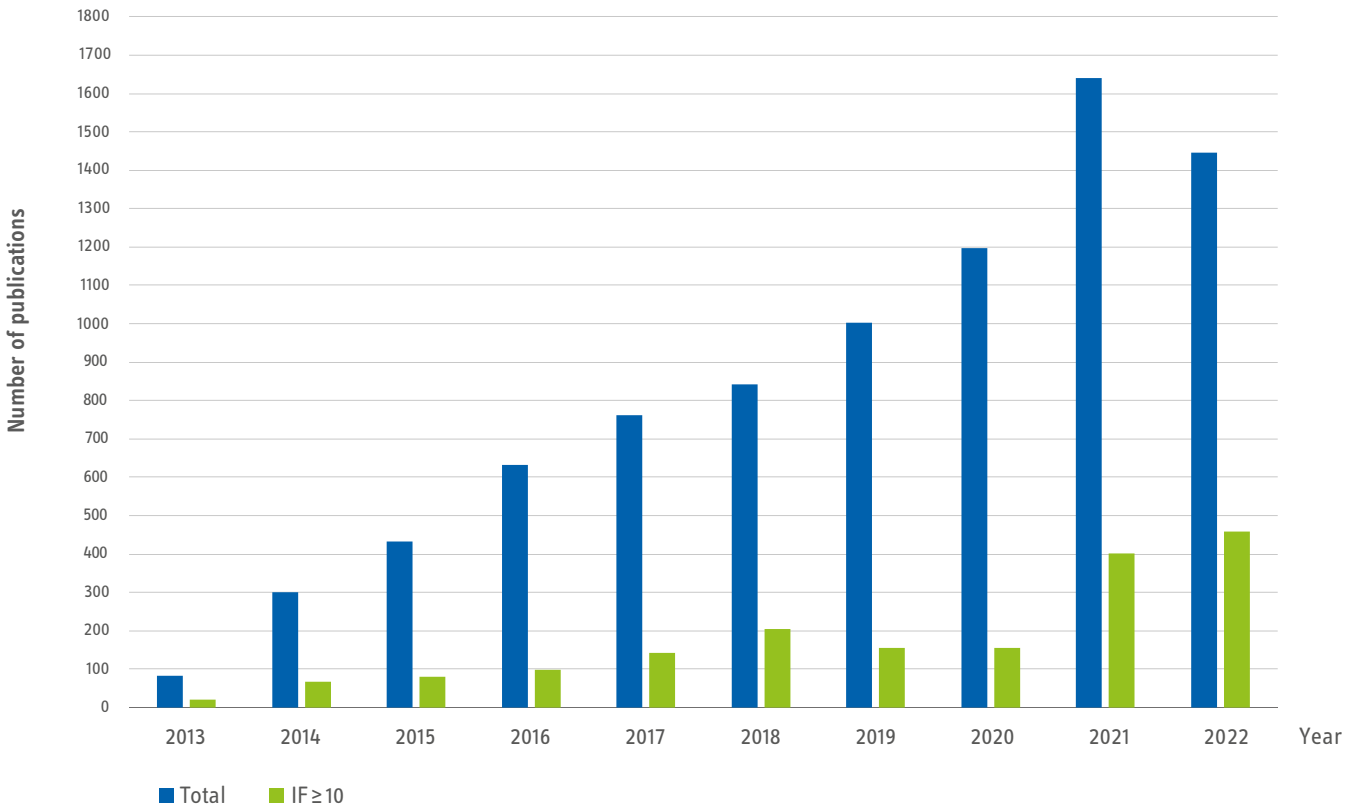


Chart showing the number of scientific publications by DKTK researchers mentioning their DKTK affiliation since 2013 (source: Web of Science, Scopus). Publications in particularly influential scientific journals (measured by impact factor [IF]) are listed separately. In 2013: 83 publications, of which 20 with IF ≥ 10; in 2014: 301 publications, of which 68 with IF ≥ 10; in 2015: 433 publications, of which 80 with IF ≥ 10; in 2016: 633 publications, of which 99 with IF ≥ 10; in 2017: 761 publications, of which 143 with IF ≥ 10; in 2018: 842 publications, of which 204 with IF ≥ 10; in 2019: 1,002 publications, of which 154 with IF ≥ 10; in 2020: 1,197 publications, of which 155 with IF ≥ 10; in 2021: 1,641 publications, of which 401 with IF ≥ 10; in 2022: 1,446 publications, of which 458 with IF ≥ 10.

DKTK structure and governing bodies

The German Cancer Consortium (DKTK) was set up on October 18, 2012. It is an unincorporated, public-law foundation having its registered office in Heidelberg and represented by the German Cancer Research Center. In translation centers at eight partner sites in Germany, the DKTK connects the DKFZ (core center) with research institutions and hospitals that have a particular track record in oncology. The eight sites are: Berlin, Dresden, Essen/Düsseldorf, Frankfurt/Mainz, Freiburg, Heidelberg, Munich and Tübingen.

DKTK governing bodies

Steering Committee

The Steering Committee is the foundation's central managing body and manages the foundation's activities. It consists of the two DKFZ directors and the spokespersons of the translation centers (see illustration, correct at December 31, 2022).

Board of Trustees

The Board of Trustees supervises the legal compliance, fitness for purpose and cost effectiveness of the foundation's activities and decides on the foundation's general research aims, its research policy and financial matters. The Board of Trustees consists of representatives of the DKTK's eight funding bodies:

- Federal Ministry of Education and Research (Chair)
- Ministry of Science, Research and the Arts of Baden-Wuerttemberg
- Bavarian State Ministry of Science and the Arts
- Berlin Senate Department for Higher Education and Research, Health and Long-Term Care
- Hessian Ministry for Science and the Arts
- Ministry of Culture and Science of North Rhine-Westphalia
- Ministry of Science and Health of Rhineland-Palatinate
- Saxon State Ministry of Science, Culture and Tourism

Scientific Advisory Board

The DKTK Scientific Advisory Board advises the Board of Trustees and Steering Committee on all important scientific matters. It is composed of up to 12 world-leading experts in the field of translational cancer research. In 2022, Prof. Ulrik Ringborg (SAB Chairperson), and Prof. Sir Alex Markham (SAB member) stood down after many years on the board. Prof. Elaine Mardis was elected as the new SAB Chairperson.

- Prof. Scott Armstrong, Boston, MA, USA
- Prof. Sir Michael Brady, Oxford, UK
- Prof. Kevin Brindle, Cambridge, UK
- Prof. Carlos Caldas, Cambridge, UK
- Prof. Amato Giaccia, Oxford, UK
- Prof. Rama Khokha, Toronto, CA
- Prof. Elaine Mardis, Columbus, Ohio, USA (SAB Chairperson)
- Prof. Holger Moch, Zurich, CH
- Stefanie Polat, Erlangen, DE
- Prof. Licia Rivoltini, Milan, IT
- Han Steutel, Berlin, DE

The members of the Scientific Advisory Board and Steering Committee during the meeting on October 24, 2022. (© J. Jung / DKTK).

Coordination Office

The DKTK Coordination Office at the DKFZ in Heidelberg supports the Steering Committee in its tasks following orders from the DKFZ Management Board. Its tasks include scientific and administrative coordination, committee work, helping with the strategic development of the consortium and the DKTK's press and public relations activities. There were two changes in the Coordination Office leadership team in 2022: In January, Dr. Philipp Gebhardt took over as Scientific Managing Director of the DKTK, following the retirement of Prof. Stefan Joos after many years of service. Dr. Melanie Viel took on the role of Administrative Managing Director in October, while Dr. Anette Reil-Held is in charge of administration of the DKFZ university medicine partnerships.

Patient Advisory Council for Cancer Research

The Patient Advisory Council for Cancer Research of the DKFZ and of its DKTK translational network consists of 12 members, led by Chairperson Rudolf Hauke. It held its 7th and 8th meetings in 2022. Within the Patient Academy, the patient representatives listened to talks on "Transfer of research results into society, the healthcare system and the economy" and took part in discussions with the presenters. The Patient Advisory Council also tackled the topics "Situation of oncological care during the two years of the COVID-19 pandemic" and "Data use and data protection rights". The first national conference on **Patients as Partners in Cancer Research** took place in autumn 2022.

Group photo of the members of the Patient Advisory Council for Cancer Research during the 8th meeting on September 30, 2022; from left, back row: Ralf Rambach, Uli Roth, Bastian Schwarz; middle row: Bärbel Söhlke, Karin Arndt, Stefanie Houwaart; front row: Rudolf Hauke, Dirk Hellrung (© J. Jung / DKFZ)

DKTK sites and associated partners

The sites at a glance

Berlin
- Charité – University Hospital Berlin

Charité Comprehensive Cancer Center (CCCC

Dresden
- Technische Universität Dresden
- University Hospital Carl Gustav Carus
- Helmholtz-Zentrum Dresden – Rossendorf (HZDR)
- Max Planck Institute of Molecular Cell Biology and Genetics (MPI-CBG)

National Center for Tumor Diseases (NCT) Dresden /
University Cancer Center (UCC), NCT/UCC Dresden

Essen | Düsseldorf
- University of Duisburg-Essen
- University Hospital Essen
- Heinrich Heine University Düsseldorf
- University Hospital Düsseldorf

Westdeutsches Tumorzentrum (WTZ)

Frankfurt | Mainz
- Goethe University Frankfurt am Main
- University Hospital Frankfurt
- Georg-Speyer-Haus (GSH), Frankfurt
- University Medical Center of Johannes Gutenberg University Mainz

University Cancer Center (UCT), Frankfurt and Mainz

Freiburg
- Albert-Ludwigs-Universität Freiburg
- University Hospital Freiburg
- Max Planck Institute of Immunobiology and Epigenetics (MPI-IE)

Comprehensive Cancer Center Freiburg (CCCF)

Heidelberg (Core Center)
- German Cancer Research Center (DKFZ), DKTK Core Center
- Associated partners: Paul Ehrlich Institute Langen

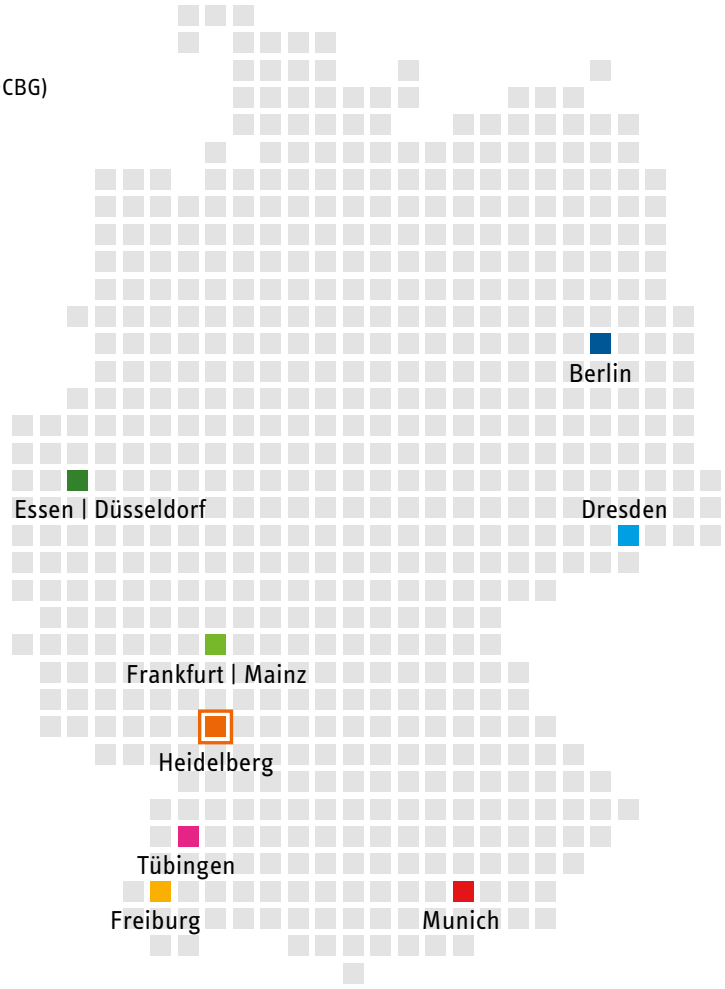
National Center for Tumor Diseases (NCT) Heidelberg

Munich
- Ludwig-Maximilians-Universität München (LMU)
- LMU University Hospital Munich (LMU Klinikum)
- Technical University of Munich (TUM)
- University Hospital rechts der Isar of the Technical University of Munich (MRI)

Comprehensive Cancer Center Munich (CCCM)

Tübingen
- University of Tübingen
- University Hospital Tübingen

Comprehensive Cancer Center (CCC) Tübingen – Stuttgart



Partner site Berlin

Charité Campus Mitte (© Charité – Universitätsmedizin Berlin)

Site Spokesperson:
Prof. Angelika Eggert, Director of the Department of Pediatric Oncology and Hematology, Einstein Professor, Charité – Universitätsmedizin Berlin

Deputy Spokesperson:
Prof. Ulrich Keilholz, Director of the Charité Comprehensive Cancer Center, Charité – Universitätsmedizin Berlin

DKTK Berlin Retreat 2022 – in person again at last (© Gudath / Charité – Universitätsmedizin Berlin)

Research profile

The DKTK partner site Berlin is integrated in Charité and cooperates closely with the Charité Comprehensive Cancer Center (CCCC). As Europe's largest university hospital, Charité not only contributes its scientific expertise to the DKTK network, but also the latest technologies for molecular tumor analysis and extensive clinical resources.

The partner site Berlin is dedicated to the early translational phase of personalized tumor medicine. Research at this site focuses on the preclinical development of new approaches to cellular cancer immunotherapy and on tumor evolution research as a basis for optimized molecularly targeted treatment approaches.

Other focus areas of research in the DKTK are cancer-related molecular signaling pathways, research on the interactions between a tumor and its environment, and the development of relevant preclinical models for various types of tumor. In terms of technology, the primary focus in Berlin is on molecular analysis methods at single-cell level and proteomic and metabolomic research, as well as the further development of liquid biopsies for precise diagnosis and cancer monitoring.

Developments in 2022

- **DKTK Berlin 7th Cancer Retreat**
  The DKTK Cancer Retreat took place in person once again, with more than 100 researchers taking part. Current research approaches and results were presented and discussed in three sessions (cancer immunotherapy, functional oncology and molecular diagnostics).

- **Funding approval for Gene and Cell Therapy Center**
  Charité, the Berlin Institute of Health in Charité (BIH) and Bayer are planning to develop a translation center for gene and cell therapy with funding from the BMBF.

- **Early career support**
  In the competitive DKTK Young Investigator Call, six young scientists were selected for funding to set up their own first research group.

- **Prizes & awards**
  Prof. Angelika Eggert (Pediatric Oncology) was admitted to the Leopoldina National Academy of Sciences. Prof. Anton Henssen (Pediatric Oncology) was awarded the Mildred Scheel Professorship for Functional Pediatric Cancer Genomics, Prof. Jalid Sehouli (Gynecology) received the Ernst Wertheim Prize for outstanding figures in gynecological oncology, and Prof. Ulrike Stein won the Women in Science Achievement Award from the Metastasis Research Society.

- **Publication highlights**
  Sinonasal cancer: AI facilitates breakthrough in diagnostics – researchers at Charité and LMU find four clinically relevant tumor groups (Jurmeister et al., Nat Commun 2022).

  State-of-the-art protein analyses reveal new treatment target for bone marrow cancer (Ng, Ramberger et al., Nat Commun 2022).

  Lymphoma: Researchers identify key signaling pathway involved in tumor formation (Schick et al., Nat Commun 2022).

Partner site Dresden

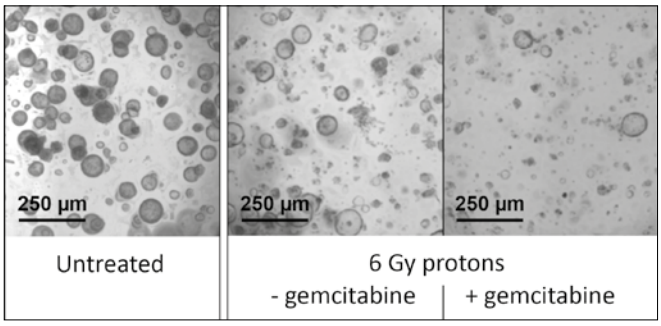
Proton therapy (© Ketchum Pleon / University Hospital Carl Gustav Carus Dresden)

Site Spokesperson:

Prof. Mechthild Krause, Director of the Department of Radiotherapy and Radiooncology and of OncoRay – National Center for Radiation Research in Oncology (NCRO) Dresden, DKTK Professor for Translational Radiation Oncology in the Carl Gustav Carus Faculty of Medicine, TU Dresden

Deputy Spokesperson:

Prof. Esther Troost, Dean of the Carl Gustav Carus Faculty of Medicine, Director of the Department of Radiotherapy and Radiooncology, Professor of Image-Guided High-Precision Radiotherapy at TU Dresden



Microscopy images of pancreatic cancer organoids with and without proton treatment. The combination with chemotherapy drug gemcitabine increases the therapeutic effect. (© Max Naumann et al., Cancers (Basel) 2022)

Research profile

Within the consortium, the DKTK partner site Dresden focuses on improving radio-oncological treatment, in terms of personalized and technically optimized cancer medicine, and is a world leader in this field. It focuses is on high-precision radiotherapy and, as one of four proton radiation centers in Germany, on optimizing particle therapy using protons. Imaging methods and radiation-specific biomarkers are combined for personalized cancer treatment in clinical and preclinical trials. Radiation methods are also used in combination with molecularly targeted drugs that can increase the effect of radiation in the tumor or reduce its effect in healthy tissue.

Dresden played a leading role in setting up the DKTK Radiation Oncology Group (DKTK-ROG), which continues to deliver internationally visible research results on biomarkers and patient stratification for personalized radiation therapy. It was in Dresden that the RadPlanBio platform was developed, which pools extensive information from imaging and radiation therapy for multicenter clinical and preclinical trials.

Developments in 2022

- **Biomarker signatures**
  Recruitment was completed for the HNprädBio prospective biomarker trial, so that validation of the biomarkers developed within the DKTK for personalized radiation oncology can now take place – an important step for the translation of the results into clinical practice. Researchers in Dresden also demonstrated that medical image characteristics can increase the prognostic value of genetic biomarker signatures.

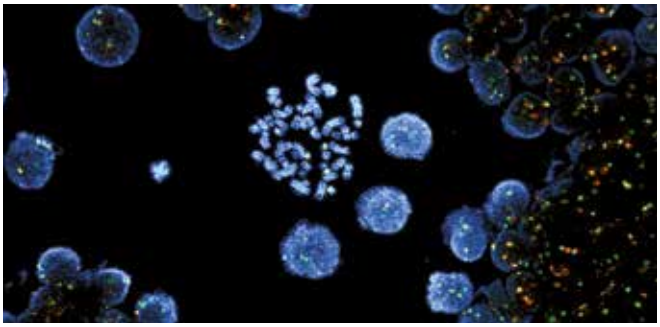
- **Proton therapy**
  In 2022, as in previous years, nearly all patients treated with proton therapy were included in clinical trials. A retrospective study showed increased sensitivity of brain tissue near the ventricles and a spatial correlation between image changes in magnetic resonance tomography (MRT) and the relative biological effectiveness (RBE) of proton beams. Patient-specific range prediction using dual-energy CT (DECT) was introduced into routine clinical practice.

- **Preclinical research**
  Organoid cultures of rectal and pancreatic carcinomas were irradiated on the experimental beamline to investigate the effect of radiosensitive substances. In cell culture models, a higher potential to combat cancer stem cells was found for protons than for photons.

- **New DKTK Junior Group Leader**
  As a new DKTK Junior Group Leader, Dr. Jovan Mircetic is using CRISPR technology with clinician colleagues since April 2022 to investigate tumor resistance to standard therapies in tumor organoid models.

Partner site Essen/Düsseldorf

WTZ research building (© Scheffler lab)



Fluorescence in situ hybridization (FISH) for BCL2L1, a cancer-related protein-coding gene (orange), and the centromere of chromosome 20 (green) in the metaphase of a Merkel cell carcinoma cell line (© Becker lab)

Site spokesperson:

Prof. Jens Siveke, DKTK Department of Solid Tumor Translational Oncology & Bridge Institute of Experimental Tumor Therapy (BIT)

Deputy Spokesperson:

Prof. Selma Ugurel, Department of Dermatology, University Hospital Essen

Research profile

The strength of the DKTK partner site Essen/Düsseldorf lies in designing and carrying out innovative clinical trials and patient-side translational research. Three DKTK departments are embedded in the West German Tumor Center (WTZ), a structure-forming institution and Oncological Center of Excellence of Deutsche Krebshilfe, along with the newly formed NCT West (including Cologne):

- Translational Skin Cancer Research (Prof. Jürgen C. Becker)
- Translational Neuro-Oncology (Prof. Björn Scheffler)
- Translational Oncology of Solid Tumors (Prof. J. Siveke) with the junior research group for Translational Genomics in Solid Tumors (Dr. Samuel Peña-Llopis)

and at University Hospital Düsseldorf the research group on:

- Pediatric Neuro-Oncogenomics (Prof. Marc Remke).

Three DKTK programs are (co)coordinated by partner site Essen/Düsseldorf (MDEB, CI, MTT).

The site focuses on three interrelated programs that are closely linked to the faculty's priority areas (including SFB1430, KFO337/2 and GRK2762, involving all DKTK departments): (i) Tumor evolution and plasticity; (ii) Tumor microenvironment; (iii) Drug research. Based on these, the DKTK faculty also focuses on methods for monitoring and predicting therapy response (AI, multimodal imaging, immune monitoring, liquid biopsies and multimodal therapy strategies).

Developments in 2022

- **New BMBF initiatives**
  Two initiatives for collaborative research on tumor heterogeneity launched with the site providing the spokesperson (SATURN3) or with the site's significant involvement (HEROES).

- **Brain tumor research**
  Therapy-resistant ALDH1A1+/ pAKT+ subclones were characterized in glioblastoma. The DKFZ BAYER Alliance, a DKTK pilot project for brain tumor drug candidates set up in 2019, was continued successfully.

- **Immunotherapy**
  Besides large multicenter trials (IMMUNED, ADMEC-O), the site also recruited for several low interventional trials (BONEMET, AliCe), with biomaterials from these being used for transcriptomic, epigenomic and TCR repertoire characterization of the therapeutically modulated immune response to solid tumors.

- **Tumors of the digestive tract**
  Results of the DKTK-funded multicenter MEMORI trial on PET-based therapy stratification in adenocarcinoma of the gastroesophageal junction were published. An immune escape mechanism was identified in pancreatic cancer. Several investigator-initiated trials (IITs) prepared through DKTK research are active (phase I/II: SEPION, COMBATBIL; phase III: METAPANC).

- **Tumor characterization and diagnostics**
  LncRNA HHIP-AS1 was characterized as a molecular driver of Sonic Hedgehog-activated tumors, including medulloblastomas. And new ddPCR-based diagnostic tests were developed for fast, sensitive molecular diagnosis of gliomas.

- **Radiopharmaceuticals**
  The prospective interventional IIT for 68Ga-FAPI-46 recruited 80% of its target patients in 2022. Data were published on the safety and efficacy of 90Y-FAPI-46. Successful participation in the Therapy ACceleration To Intercept CAncer Lethality (TACTICAL) award consortium of the Prostate Cancer Foundation (PCF).

Partner site Frankfurt/Mainz

Evaluation of the Frankfurt Cancer Institute in autumn 2022 by the Hessian Ministry for Science and the Arts (HMWK) (© Monika Schmitz)

Grounds of the University Medical Center of Johannes Gutenberg University Mainz (© University Medical Center Mainz)

Site spokesperson

Prof. Hubert Serve, Director of the Department of Medicine II, University Hospital Frankfurt

Deputy Spokesperson:

Prof. Thomas Oellerich, DKTK Professor for Translational Proteome Research in Cancer, Senior Physician, Department of Medicine II, University Hospital Frankfurt

Research profile

Frankfurt and Mainz play complementary roles in the DKTK partner site. Under Frankfurt's leadership, the site develops new cancer drugs and innovative therapeutic strategies. Its main research areas are tumor pathogenesis, the tumor microenvironment and therapy resistance, molecular diagnostics, data science and the development and validation of new therapy strategies.

Under Mainz's leadership, the site contributes an innovative immunotherapy program with a focus on novel immunotherapy approaches, including next-generation mRNA vaccines and tumor antigen-specific antibodies. Cell therapy is another shared focus area.

The DKTK site has considerable experience in clinical translation, particularly in the areas of leukemia, lymphoma, pediatric tumors, brain tumors, colorectal carcinoma and stomach and breast cancer. With the aim of facilitating cross-site access to research-relevant data, Frankfurt is working with the CCP to develop and coordinate a federated data storage and search concept for the entire DKTK.

Developments in 2022

- **Colorectal cancer therapy**
  Research by Prof. Florian Greten's group (Nicolas et al., Cancer Cell 2022) formed the basis for the ACO/ARO/AIO-21 trial under the clinical leadership of Prof. Emmanouil Fokas and Prof. Claus Rödel. The trial is investigating whether the tumor microenvironment can be reprogrammed using IL-1 receptor blockade and then combined with radiotherapy to improve the therapy success for rectal cancer.

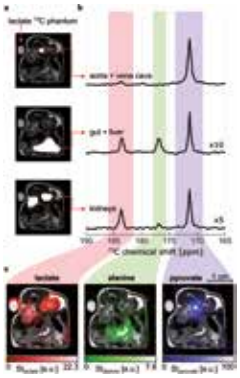
- **Proteomics and bioinformatics**
  In close collaboration with Frankfurt DKTK Professors Thomas Oellerich and Florian Büttner, the site was able to identify a new, clinically relevant subtype of acute myeloid leukemia using proteogenomic analyses and innovative bioinformatics (Jayavelu et al., Cancer Cell 2022).

- **Successful continuation of the FCI**
  In autumn 2022, the Frankfurt Cancer Institute LOEWE center (FCI, 2023–2025, Spokesperson: Prof. F. Greten) was extended, following a successful evaluation. The FCI creates important synergies with local and national DKTK activities.

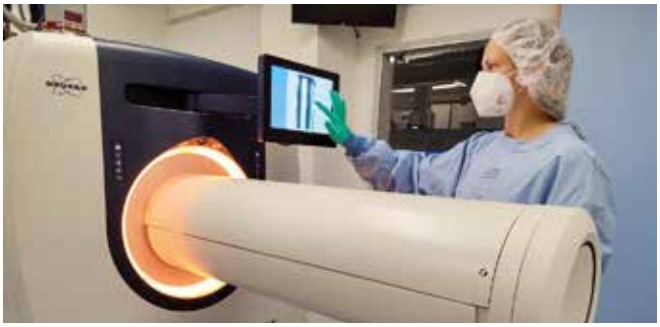
- **DKTK Joint Funding Program**
  The site coordinates two DKTK Joint Funding projects that focus on cell therapy and immunotherapy: NoviCARAZA (led by Prof. Evelyn Ullrich) and MIMETIC (led by Prof. Tobias Bopp).

- **New Mainz Collaborative Research Center**
  A new DFG Collaborative Research Center/Transregio on "Heterogeneity and functional specialization of regulatory T-cells in distinct microenvironments" was set up to exploit the full potential of regulatory T-cells for personalized immunotherapy (Spokesperson: Prof. Ari Waisman).

Partner site Freiburg



In Vivo Mouse Metabolic Conversion MRI of [1-13C]Pyruvate-d3 Hyperpolarized by Reversible Exchange with Parahydrogen. (© Maissin, H. de et al., ChemRxiv. Cambridge: Cambridge Open Engage 2023, under CC BY NC 4.0 License)



DKTK employee Lisa Domogalla working on a small animal PET/MRT system that was installed in the Radiopharmaceutical Development Division in 2021. The imaging system supports translational projects at the interface between preclinical development and clinical application of newly discovered radiopharmaceuticals for application in nuclear medicine. (© M. Eder/DKTK Freiburg)

Site spokesperson::

Prof. Christoph Peters, Scientific Director of Comprehensive Cancer Center Freiburg (CCCF), Director of the Institute of Molecular Medicine and Cell Research, Center of Biochemistry and Molecular Cell Research

Deputy Spokesperson:

Prof. Anca L. Grosu, Director of the Department of Radiation Oncology, Center for Diagnostic and Therapeutic Radiology, University Hospital Freiburg (UKF)

Research profile

Through the CCCF, the DKTK partner site Freiburg makes a point of integrating interdisciplinary partners from basic and clinical research to accelerate transfer between laboratory and clinic and to explore questions in the area of oncogenic signaling pathways, newly discovered mutations and epigenetics. This integration is supported by research networks, including Collaborative Research Centre CRC 1479 on oncogene-driven immune escape, CRC 992 on medical epigenetics, Priority Programme SPP 2177 on radiomics, the SATURN3 consortium on tumor heterogeneity in hard-to-treat cancers and the Medical Informatics Initiative, which has led to various translational projects and clinical trials. One of the supporting structures is the MTB, which makes interdisciplinary and personalized therapy recommendations using advanced molecular diagnostics and data analysis, and serves as a jumping-off point for the discovery of new findings through translation and reverse translation.

Application-oriented DKTK research projects in the field of radiopharmaceutical development also benefit from the site's proximity to and interaction with the Department of Nuclear Medicine and the CCCF. Additional core competencies at the site include targeted molecular therapeutic approaches, innovative data analysis and the further development of diagnostic methods using molecular imaging, e.g. the PSMA diagnostic method in prostate cancer.

Developments in 2022

The DKTK partner site Freiburg's three key research areas (Epigenetics & Oncogenic Signaling, Imaging & Radiation Therapy and Functional & Translational Genomics) achieve important results in the context of translation for the five DKTK programs.

- **Expansion of infrastructure and platforms**
  The Freeze-O organoid platform was introduced. It interacts closely with the DKTK Organoid Platform, a strategic initiative of the DKTK, to strengthen the focus on patient-derived organoids and reverse translation. In addition, the integrated data analysis platform (Börries group) enables integrated processing, analysis and interpretation of data from various sources with the help of AI-based methods in bioinformatics, supporting the generation of new hypotheses.

- **Funding in nuclear medicine**
  The Radiopharmaceutical Development Division (Prof. Matthias Eder) and Freiburg-based company 4HF Biotec GmbH will be working together to identify innovative new drugs for nuclear medicine treatment of lung and prostate cancer, which will then be developed for clinical use via infrastructure facilities of the DKTK and the Nuclear Medicine Department of University Hospital Freiburg. The Invest BW funding program is supporting this project with €1.6 million.

- **DKTK Joint Funding Program**
  Launch of DKTK Joint Funding project HYPERBOLIC (Coordination: Dr. Andreas Schmidt). This collaborative DKTK project is establishing an expert panel for the efficient translation of new developments in hyperpolarized MRT (HP-MRT) into preclinical research and clinical applications, and facilitates insights into tumor characteristics that are urgently needed for disease monitoring, personalized therapy and future diagnostics.

DKTK Core Center Heidelberg

DKFZ main building (© Tobias Schwerdt / DKFZ)

The DKTK Scientific Advisory Board (SAB) met at the DKFZ in Heidelberg on October 24, 2022. (© DKTK)

Management Board of the DKFZ and DKTK Core Center:
Prof. Michael Baumann, Spokesperson of the DKTK, Chairman and Scientific Director of the DKFZ, Ursula Weyrich, Administrative Director of the DKFZ

Spokesperson of the DKTK Translation Center Heidelberg:
Prof. Wolfgang Wick, Managing Director of the Department of Neurology at University Hospital Heidelberg and Head of the Clinical Cooperation Unit Neurology at the DKFZ

Deputy Spokesperson of the DKTK Translation Center Heidelberg:
Dr. Christiane Opitz, Head of the Metabolic Crosstalk in Cancer Division at the DKFZ (since 01/2023)

Research profile

The DKFZ plays a dual role within the DKTK: It is i) the core center of the DKTK and home to the central DKTK Coordination Office that coordinates the scientific activities and administrative and site-overarching processes in the DKTK, and ii) part of the DKTK's local translation center in Heidelberg, together with NCT Heidelberg, the National Center for Tumor Diseases run by the DKFZ, University Hospital Heidelberg and the Heidelberg University Medical Faculty. The DKFZ is a member of the Helmholtz Association, the largest biomedical research institution in Germany, and is one of the world's leading cancer research centers. Together, the Heidelberg Medical Faculty and University Hospital form one of the largest and most successful university medical centers in Germany. The NCT brings together patient-related research and patient care under one roof.

The Heidelberg site covers the entire portfolio of translational cancer research – from basic research to clinical, prevention and outcome research. One particular focus area is the systematic further development of personalized oncology and the conception of future oncological topics, such as cancer neuroscience. Other research topics that are relevant to the DKTK include personalized radiation oncology, the use of machine learning methods to interpret oncological imaging data, pediatric oncology, therapy resistance and cancer immunotherapy, particularly in the context of combination therapies.

Developments in 2022

- **DKTK Joint Funding Program**
  Six projects were selected during the 9th call for proposals: CD276xCD3, INVENT4GB, PerVision, HYPERBOLIC, NoviCARAZA and PredictAHR, and a trial-associated project (MIMETIC) was also launched, all with the involvement of the partner site Heidelberg. The DKTK Organoid Platform, a strategic initiative, was initiated.

- **Infrastructure**
  Within the CCP databases, work continued on the new technology for federated searches of sensitive patient data. Several multicenter projects are currently at various stages. In the autumn, the third HARPOON workshop on harmonizing molecular tumor boards was organized by the Heidelberg-based MASTER team.

- **Patient involvement**
  The DKFZ and DKTK Patient Advisory Council for Cancer Research met regularly. And the first national conference on "Patients as Partners in Cancer Research" was held at the DKFZ from September 30 to October 2, 2022.

- **Early career support**
  The central coordination team of the DKTK School of Oncology organized DKTK-wide lecture series, workshops and symposia, for instance in collaboration with the DKFZ Postdoc Program and the other DZG.

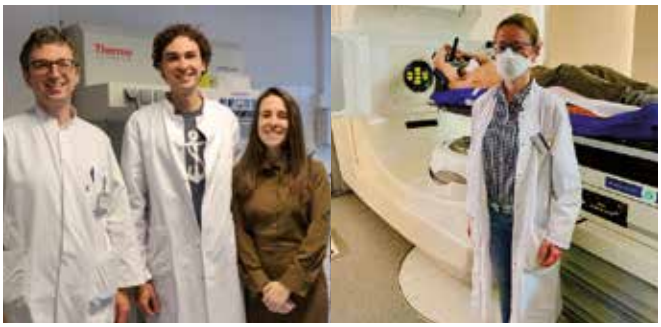
- **Communication**
  The Coordination Office kept the DKTK scientific community and interested members of the public informed through its website, press releases, articles, newsletters and other channels. Central events and regular meetings were also organized between the partner sites.

Partner site Munich

Official opening of the patient building at CCC Munich (© LMU Klinikum)

Site spokesperson:
Prof. Wilko Weichert, Director of the Institute of General and Surgical Pathology at TUM

Deputy Spokesperson:
Prof. Michael von Bergwelt, Director of the Department of Medicine III at LMU Klinikum



Munich OncoTrack – DKTK School of Oncology Fellows crossed the river to visit specialist departments at University Hospital rechts der Isar (MRI): left in the Surgery Department with Paul Kerbs from LMU Klinikum (center), Carmen Mota Reyes and I. Ekin Demir (© Paul Kerbs), right in the Radiation Oncology and Radiotherapy Department with Susanne Flach from LMU Klinikum and a patient (© Susanne Flach).

Research profile

Understanding the altered signaling pathways in cancer cells is one of the key joint research areas being worked on by researchers and physicians at the DKTK partner site Munich. Their approaches are based on the functional characterization of cancer in preclinical model systems, with the aim of explaining new molecular cancer mechanisms.

The findings are translated into molecularly targeted therapies for patients that are precisely tailored to the individual tumor. The two core areas of mechanistic modeling and molecularly targeted therapy are supplemented by new research approaches that use cells and mechanisms of the immune system to fight cancer (immuno-oncology).

The partner site Munich specializes in gastrointestinal cancers, such as pancreatic cancer, stomach cancer and colorectal cancer, as well as leukemia and malignant lymphoma.

The regular DKTK Cancer Colloquiums and the annual DKTK Munich Cancer Retreat provide opportunities for joint discussions about the latest findings from research and clinical trials. In 2022 the **Munich Cancer Retreat** was held in a hybrid format, with keynote lectures on how artificial intelligence can be integrated into data science and medicine (Prof. Joachim Schultze, DZNE Bonn) and on new therapy approaches in AML based on epigenetics and epitranscriptomics (Prof. Carsten Müller-Tidow, Heidelberg).

Developments in 2022

- **Munich OncoTrack**
  Munich Fellows of the DKTK School of Oncology take part in Munich OncoTrack, a program of short-term exchanges between University Hospital rechts der Isar (MRI) and LMU Klinikum (University Hospital). The three-year program gives them insights into areas outside their own oncological specialism (see illustration).

- **Patient house opened**
  In April 2022, the “patient house” was created as a new support center for cancer patients and their relatives (see illustration). Here, in addition to their conventional treatment, they can receive comprehensive advice and support in the areas of psycho-oncology, nutrition and complementary medicine.

- **New publications in 2022**
  Researchers in Munich made the greatest advance of the decade in mapping the mouse proteome as an oncological model organism (Giansanti et al., Nat Methods 2022), investigated the effect of AP4 as an oncogenic target gene on chemoresistance in colorectal cancer (Chou et al., Mol Cancer 2022), and discovered that pancreatic cancer can be sensitized to drugs by modifying the tumor environment (Falcomatà et al., Nat Cancer 2022). In the MASTER trial, researchers from Munich and other DKTK partner sites demonstrated testing options for therapies in rare and hereditary cancers (Jahn et al., Ann Oncol 2022).

- **International Immunotherapy of Cancer Conference**
  The 9th Immunotherapy of Cancer Conference (ITOC) took place in September 2022 as a virtual event chaired by Prof. Michael von Bergwelt, with speakers and participants from all over the world.

Partner site Tübingen

Mass spectrometry-based immunopeptidome analysis to identify tumor-specific antigens (© Beate Armbruster / University Hospital Tübingen)

Bottled peptide vaccine for trial purposes (© Britt Moulien/University Hospital Tübingen)

Site spokesperson:

Prof. Klaus Schulze-Osthoff, Head of Department in the Interfaculty Institute of Biochemistry, University of Tübingen

Deputy Spokesperson:

Prof. Juliane Walz, W3 Professor for Peptide-Based Immunotherapy and Medical Director of the Translational Immunology Clinical Cooperation Unit

Research profile

The DKTK partner site Tübingen specializes in the development of personalized vaccines and innovative antibodies for cancer treatment. The researchers also develop cell-mediated therapies (CAR T-cell therapies) and oncolytic viruses (virotherapy). Besides its emphasis on immuno-oncology, the partner site also focuses on the areas of functional and multiparametric imaging and functional genomics and academic drug development. In order to develop personalized vaccines, the researchers identify each patient's tumor-specific antigens (cell surface structures that are recognized by the immune system). The efficacy of the immunotherapy is monitored by an immune monitoring unit. The development and application of optimized monospecific and bispecific antibodies are other areas that are being pursued intensively. They promote interaction between immune cells and cancer cells to target the latter. As well as antibodies that are ready for application, there are a number of promising antibody formats in development.

Developments in 2022

- **DKTK Joint Funding Program**
  A first-line evaluation of CC-1 took place in patients with biochemical recurrence of prostate cancer. Funding was approved for two new projects coordinated in Tübingen: CD276xCD3 (Prof. Helmut Salih) and PerVision (Dr. Martin Ebinger).

- **Bispecific antibodies**
  Recruitment started for the first-in-human (FIH) trial with bispecific antibody CC-1 (PSMAxCD3) in patients with castration-resistant prostate cancer. In addition, a FIH trial was established for the evaluation of bispecific antibody CC-3 (B7-H3xCD3) in colorectal carcinoma. And new immunocytokines were developed from Fc-optimized CD19 and CD20 antibodies in combination with an optimized form of IL-15.

- **Peptide vaccines**
  A phase I trial was prepared to evaluate a peptide vaccine against a DNAJB1-PRKACA-fusion-based neoepitope in combination with immune checkpoint inhibition. In addition, the phase II trial to evaluate the COVID-19 T-cell activator CoVac-1 in cancer patients with antibody deficiency was completed.

- **Personalized cancer vaccines**
  The spin-off company ViferaXS was established to develop personalized cancer vaccines and peptide-based T-cell activators.

- **Senescence marker**
  A phase I trial started with a new proprietary PET senescence marker to detect therapy-induced senescence in solid tumors.

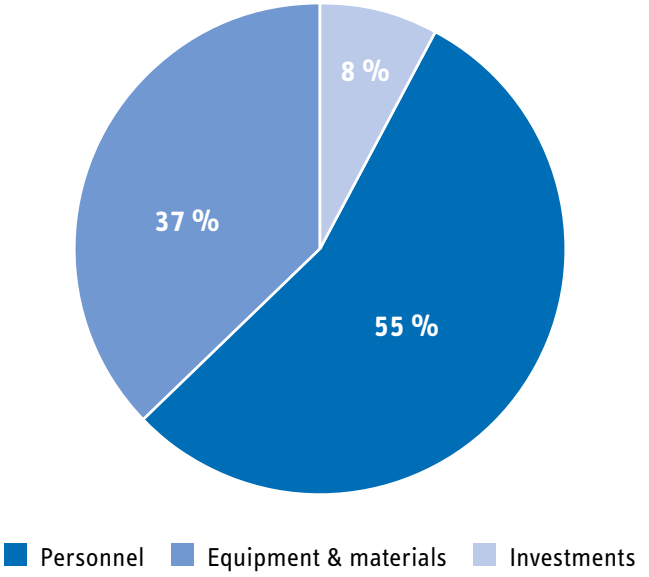
- **Drug development**
  As well as the academic development and early clinical testing of various low-molecular substances and kinase inhibitors for targeted cancer therapy, a phase I trial to test an MKK4i inhibitor developed by Tübingen start-up HepaRegeniX was successfully completed.

Finance and personnel

The DKTK is funded by the federal government (90 %) and the federal states in which the DKTK partner sites are located (10 %).

Expenditure

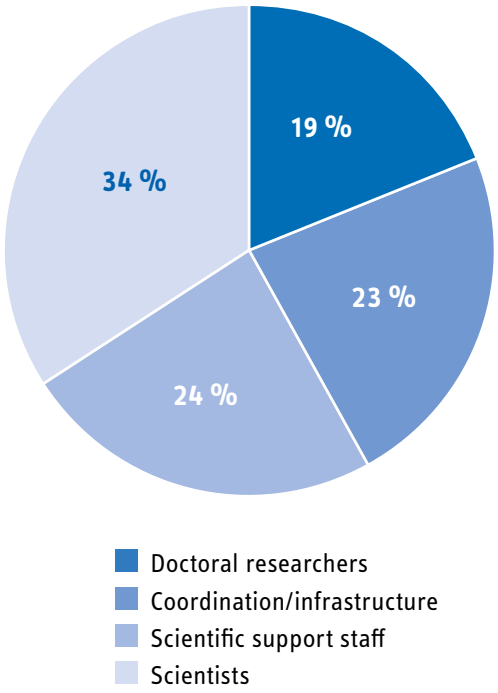
In 2022, expenditure in the DKTK amounted to € 29.9 million. More than half (55 %) went on personnel. Around a third of expenditure went on equipment and materials (37 %) and eight percent on investments.



Breakdown of DKTK expenditure 2022

Personnel

In 2022, the DKTK financed 305 individuals or 243 full-time equivalents (correct at: December 31, 2022). Scientists made up the largest proportion (34 %). Doctoral researchers accounted for 19 %. Around a quarter of DKTK-funded employees (24 %) are scientific support staff, e.g. technical assistants, and 23 % of staff work in coordinating functions and infrastructure facilities.



Staff composition

The DKTK workforce is international. Around 28 % of employees come from other countries, with 37 nationalities represented. Of the staff members financed by the DKTK, 63 % are women. In the DKTK's governing bodies, the proportion of women is 30 % in the Steering Committee and 36 % on the Scientific Advisory Board. As well as the DKTK-financed employees, many other researchers work in the DKTK who are financed by DKTK partners. In total, more than 1,000 scientists and clinician scientists are active in the DKTK.

New professorships and young investigator groups

Dr. Jovan Mircetic took up the role of DKTK Junior Group Leader for Forward Genetics for Translational Solid Cancer Research at DKTK partner site Dresden on April 1, 2022.

List of abbreviations

AI	artificial intelligence
AML	acute myeloid leukemia
BMBF	Federal Ministry of Education and Research
CAR	chimeric antigen receptor
CCC	Comprehensive Cancer Center
CCP	Clinical Communication Platform
DKFZ	German Cancer Research Center (Deutsches Krebsforschungszentrum)
DKTK	German Cancer Consortium (Deutsches Konsortium für Translationale Krebsforschung)
DZG	German Centers for Health Research
INFORM program	INdividualized Therapy FOr Relapsed Malignancies in Childhood – precision oncology program for advanced cancer in children
JIP	DKTK Joint Imaging Platform
LMU	Ludwig Maximilian University of Munich
MASTER program	Molecularly Aided Stratification for Tumor Eradication – precision oncology program of the DKFZ, NCT and DKTK for advanced rare cancer in adults
MTB	molecular tumor board
MRT	magnetic resonance tomography
NCT	National Center for Tumor Diseases
NK cells	natural killer cells
PDO	patient-derived organoid
PDX	patient-derived xenograft
PEI	Paul Ehrlich Institute, the Federal Institute for Vaccines and Biomedicines
PET	positron emission tomography
RACOON	Radiological COOperative Network for the COVID-19 pandemic
RadPlanBio	RadiationDosePlan-Image/Biomarker-Outcome-Platform
TUM	Technical University of Munich
WTZ	West German Cancer Center Essen

Imprint

Published by:
Deutsches Konsortium für Translationale Krebsforschung (DKTK)
Deutsches Krebsforschungszentrum (DKFZ)
Stiftung des öffentlichen Rechts
Im Neuenheimer Feld 280
69120 Heidelberg, Germany

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Layout:
Piva & Piva
Studio für visuelles Design, Darmstadt

German version printed by:
CITY-DRUCK Offsetdruck GmbH
Heidelberg

www.dktk.org

With thanks to our funding bodies:

Bundesministerium für Bildung und Forschung
Baden-Württemberg MINISTERIUM FÜR WISSENSCHAFT, FORSCHUNG UND KUNST
Bayerisches Staatsministerium für Wissenschaft und Kunst
BERLIN Senatsverwaltung für Wissenschaft, Gesundheit und Pflege
HESSEN Hessisches Ministerium für Wissenschaft und Kunst
Ministerium für Kultur und Wissenschaft des Landes Nordrhein-Westfalen
RheinlandPfalz MINISTERIUM FÜR WISSENSCHAFT UND GESUNDHEIT
STAATSMINISTERIUM FÜR WISSENSCHAFT UND KUNST
Freistaat SACHSEN

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DKTK German Cancer Consortium

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Research for a Life without Cancer