

CaRe2B

Cancer Research to Business
e-Newsletter of the German Cancer Research Center

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EDITORIAL



Dr. Ruth Herzog

Dear colleague and business partner,

"Spring lets its blue ribbon flutter again in the breeze..." This is how a famous German poem by Eduard Mörike begins. Spring heralds the arrival of new and pleasant things. My long-planned publication resulting from my Master's thesis arising from the inspiring technology transfer symposium at Keio University in Japan was published in March and is presented in the "Inside the Office" section. And it is our pleasure to welcome Bayer Healthcare to the new joint laboratory established in the DKFZ premises in Heidelberg, thereby intensifying our longstanding collaboration in the field of immunotherapy.

This issue features antibodies as research tools and diagnostics, and highlights some of our licensing successes – hopefully generating a substantial revenue stream in the future which will be re-invested in cancer research.

Our next issue will appear at the end of summer! Enjoy the season and explore your opportunities!

Cheers

Ruth Herzog

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Content:

[Feature Article](#) about the DKFZ antibodies available for out-licensing

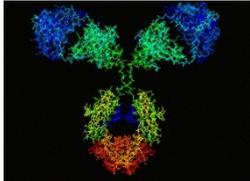
[New Technologies:](#) [Therapeutics \(3\)](#)
 [Diagnostics \(4\)](#)
 [Research Tools \(2\)](#)
 [Devices \(2\)](#)
 [Software \(3\)](#)
 [Vaccines \(1\)](#)

[Patents granted:](#) 4 new patents were granted

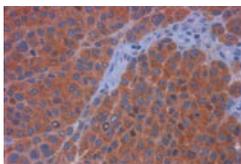
[New and Notable:](#) Awards and latest news from DKFZ

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FEATURE
ARTICLE

An antibody also known as an immunoglobulin is a large Y-shaped protein produced by B-cells.



Melanomas stained with BRAF V600E specific antibody



Immunostaining with IDH1 R132H specific antibody of a tissue array with different brain tumor entities

Antibodies developed at the DKFZ - as research tool, diagnostic markers or therapeutics

Over the last three decades since they were discovered in 1975, monoclonal antibodies have made a dramatic transformation from research tools to powerful human therapeutics and diagnostic markers.

The use of monoclonal antibodies for the therapy of cancer is one of the great success stories of the past decade. This success builds on a long history of basic research, including antibody serology, target selection, antibody-receptor function and immune regulation.

Today, monoclonal antibodies account for a third of all new treatments. These include therapeutic products for breast cancer, leukemia, asthma, arthritis, psoriasis, transplant rejection and dozens more that are in late-stage clinical trials. Approximately 30 therapeutic monoclonal antibodies are currently marketed in the United States and Europe in a variety of indications, still with an upward trend.

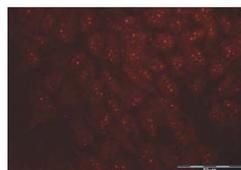
DKFZ success story I – BRAF V600E antibody as diagnostic marker

In 2012 Ventana Medical Systems, Inc., (www.ventana.com) a member of the Roche Group, signed an exclusive license agreement with the DKFZ and University Hospital Heidelberg to commercialize a **novel immunohistochemistry (IHC) antibody that detects the V600E BRAF mutation** protein. BRAF plays a key role in regulating cell signaling, and its mutation V600E has been shown to be a driver mutation in many human cancers (colorectal, thyroid, brain, and non-Hodgkin lymphoma). The antibody will be further developed by Ventana Medical Systems, Inc. as an in vitro diagnostic marker as well as a companion diagnostic. These products are expected to be the first validated, commercially-available IHC antibodies capable of detecting specific BRAF mutations.

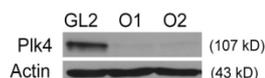
DKFZ success story II – IDH1 R132H antibody as diagnostic marker

In 2009 Dianova (www.dianova.com) signed an exclusive license agreement with the DKFZ and the University Hospital Heidelberg to commercialize a **novel immunohistochemistry antibody that detects the R132H IDH1 mutation** protein. IDH1 is implicated in malignant brain tumors, specifically in gliomas. **The ability to perform IDH1 R132H immunostainings are indispensable for any institution involved in glioma research and diagnosis.**

In this CaRe2B issue we introduce you to DKFZ's updated antibody list ([dkfz-antibodies](#)) containing our monoclonal antibodies available for out-licensing. Five examples from this brand new list are presented below.



Immunocytochemistry with HDAC11 antibody using BE(2)-C cells



Western blot analysis using Plk4 antibody; U2OS cells were transfected with either control siRNA (GL2) or Plk4 siRNAs (O1, O2).

NEW TECHNOLOGIES

THERAPEUTICS



[HDAC11 antibody as research tool \(P-1040\)](#)

DKFZ researchers established two hybridoma cell lines producing antibodies directed against histone deacetylase 11 (HDAC11) which are suitable for immunocytochemistry, chromatin IP and western blot analysis. A patent has been filed.

[Neurofibromin antibody as research tool \(P-897\)](#)

Neurofibromin is a diagnostic and prognostic marker for glioma treatment. DKFZ researchers established the proof of concept for a monoclonal antibody against neurofibromin using human biopsy material. The antibody is suitable for immunohistochemistry and Western blot analysis.

[MCPH1 antibody as research tool \(P-871\)](#)

Microencephaly is a malformation causally related to mutations in the MCPH1 gene. DKFZ developed a hybridoma cell line expressing a monoclonal antibody against microcephalin (MCPH1) which can be used for western blot analysis and immunofluorescence-based applications. A utility model has been filed.

[Plk4 as research tool \(M-334\)](#)

Polo-like kinase 4 (Plk4)/Sak has been identified as a crucial regulator of centriole biogenesis. DKFZ established a monoclonal antibody against Plk4 which can be used for western blot analysis, immunofluorescence and immunoprecipitation.

[CD19 as research tool \(M-10\)](#)

CD19 is a B-lymphocyte specific antigen. DKFZ generated a hybridoma cell line expressing a monoclonal antibody against CD19 which can be used for western blot analysis and immunohistochemistry. It is the first CD19 antibody that works on paraffin sections.

[Spiroepoxide tetrahydrobenzo-triazoles and -imidazoles as MetAP-II Inhibitors \(P-1068\)](#)

The invention describes the design of small molecules guided by the chemical structure of the antibiotic fumagillin. The novel substances show drug-like substructures, and an active enantiomeric series has been identified. The selective inhibition of the methionine aminopeptidase MetAP-II subtype inhibits the growth of endothelial cells and angiogenesis, and is a validated target for anti-angiogenic cancer therapy. In addition, MetAP-II has also emerged as a promising target for other indications, including malaria, rheumatoid arthritis, pulmonary hypertension, and obesity.



[Inhibitors of Receptor for Advanced Glycation-End products \(RAGE\) for treatment of liver cancer \(P-1019\)](#)

RAGE has been validated as a target that plays a central role not only in acute or chronic inflammatory diseases but also in several cancers and neurodegenerative diseases. Our invention uses RAGE inhibition to significantly reduce tumor initiation and progression.

[Antagonists of R-spondin 3 for treatment of bone disorders \(P-881\)](#)

Partial deficiency of Rspo3 leads to a significant increase in bone mass. These results indicate a major role for Rspo3 as a bone anabolic marker and/or target. Thus, Rspo3 antagonists are drug candidates for the treatment of osteopenia disorders, particularly in conditions associated with increased bone resorption.

A list of all therapeutic technologies can be found here [\[Link\]](#).

DIAGNOSTICS



[Histone mutations as markers for glioblastoma \(P-1012\)](#)

This technology resulted from a cooperation between McGill University and DKFZ. Brain tumors, such as the highly aggressive glioblastoma multiforme (GBM), are currently the leading cause of cancer-related mortality and morbidity in children. Current diagnosis of brain cancers involves MRI, PET and CT scans, angiographies, followed by biopsies performed either during the resection of the tumor or as a separate procedure via a burr hole. A blood-based test would provide a more economical, i.e. accessible, and less invasive diagnostic tool.

[New PDK1 phosphorylation site as therapeutic and prognostic marker \(P-1002\)](#)

The present invention relates to a method for identifying a cancer patient as being amenable to treatment with PI3K inhibitors (phospho-inositide 3-kinase). The underlying marker is a newly detected phosphorylation site of PDK1 (3-phosphoinositide-dependent protein kinase-1), which makes downstream signaling of PDK1 independent of PIP3.

[Multiple HPV Infections – Calculating the risk for prevalent cervical lesions \(P-954\)](#)

The current technology provides a method for differentiating between a severe and mild form of multiple human papillomavirus (HPV) infections, allowing the doctor to distinguish clearly between women with cervical lesions and those with normal cytology.



[Prediction of recurrence for bladder cancer by a protein signature in tissue samples \(P-985\)](#)

This invention pertains to the field of bladder cancer prediction. Specifically, it is a method for predicting the risk of recurrence of bladder cancer for a patient after treatment of bladder cancer by determining the amount of at least one specific biomarker selected from a set of biomarkers, and comparing the

RESEARCH
TOOLS

amount found with a reference.

A list of all diagnostic technologies can be found here [\[Link\]](#).

Please take a closer look at the [Feature Article](#) about available antibodies.

[Cell line for screening demethylating agents using an endogenous epigenetically silenced reporter \(P-1045\)](#)

The invention provides a high-throughput screening system for agents that influence DNA methylation. Using the Zinc Finger Nuclease (ZFN) technique, EGFP and G418 resistance genes were stably integrated in the genome of a human cell line under the control of an endogenous promoter.

[High-throughput method for determining the presence of papillomavirus-neutralizing antibodies in a sample \(P-938\)](#)

The invention is based on papillomavirus pseudovirions consisting of L1 and L2 proteins encapsulating Gaussia luciferase as a reporter system. Using HeLaT K4 cells as target cells, the screen can be performed in a high-throughput format without the need for time-consuming manual pipetting steps.

The method is validated and can be used for clinical studies generating approval-relevant data.



A list of all research tool technologies can be found here [\[Link\]](#)

DEVICES



[Personal dosimeter for magnetic field monitoring \(P-1032\)](#)

By using Hall effect sensors and electromagnetic induction coils, the magnetic flux density, the change in magnetic flux density, and the change in magnetic flux can be monitored simultaneously. The compact measuring sensor is connected to the supply and data storage device via a signal cable and can be attached to any body part. A fully functional prototype has already been constructed and tested.

[Navigation system for CT-guided radiofrequency ablation of the liver \(P-819\)](#)

The invention provides a needle-based navigation system for CT-guided radiofrequency ablation of the liver. The key facts are: (1) Precise intervention and navigation aid for soft tissue surgery; (2) Real-time observation and supervision and (3) Inexpensive hardware/software.

A list of all device technologies can be found here [\[Link\]](#).

SOFTWARE



Pseudonymization of patient identifiers for translational research

(P-1060)

The invention presents a new method for pseudonymizing e.g. patient identifiers in which the pseudonymization service provider is unable to derive the patient identifier from the pseudonym, but rather this ability is assigned to an authorized third party (Ombudsman).

Measurement of protein mobility and interactions in living cells by 3PEA

(P-991)

The presented technology is thought to be suitable for use in all confocal laser scanning microscopes (no additional hardware is needed) and would allow automated high throughput FRAP experiments.

Navigation for interventions: incremental real time recording of tracked instruments (P-632)

This invention describes a simple and robust navigation aid for physicians in bronchoscopy or similar interventional surgery (angiography; implantation of vascular stents and cardiac pacemakers).

A list of all software technologies can be found here [\[Link\]](#).

VACCINES



Improved DNA Vaccines: Shuffled Early Genes of the Human Papillomavirus Type 1 (P-974)

Development of a therapeutic DNA vaccine directed at tumor-specific antigens of the human papilloma virus (HPV) type 16. The invention is based on a "shuffled gene" technology that uses a combination with adjuvant genes to enhance synergistically immune responses by DNA immunization for the treatment of cervical cancer.

A list of all vaccine technologies can be found here [\[Link\]](#)

NEW PATENTS GRANTED



An oligonucleotide mixture for improved detection of human papillomavirus genotypes (P-760)

The "ready to use kit" offers the possibility of (1) simultaneous detection of up to 51 HPV genotypes in a single reaction, (2) homogeneous detection limits with no underestimation of individual genotypes; (2) reliable quantification of the different genotypes; (3) predefined high viral load cutoffs to identify cervical abnormalities and (4) with internal DNA quality and PCR performance control.

Patent was granted in CH, D, FR, GB, IT, NL and US (CN, JP and CA are still pending).

Bone morphogenetic protein 4 (BMP4) for treating advanced stage neuroblastoma (P-804)

Specific inhibition of histone deacetylases by BMP4 efficiently restores aberrant signaling pathways and biological features in experimental neuroblastoma at nanomolar concentration without unfavorably targeting untransformed cells. In addition, recombinant manufactured BMP4 is already established for other indications (osteoporosis and type 2 diabetes), which



NEW AND NOTABLE



SPIN-OFFS



should support the approval for this new indication.
 Patent was granted in US, CH, GB, D and FR.

Optical Tomography (OT), SPECT and CT combination for multi-modality imaging (P-560)

DKFZ has developed an optical imaging detector for fluorescence and bioluminescence in small animal imaging that is compatible with single-photon emission computed tomography (SPECT).
 Patent was granted in US ([US8361440](#)), CH, GB, D, FR and JP.

Manufacture of patient mask for positioning patients in radiotherapy by rapid prototyping (P-806)

A method for deriving anatomical and/or pathological structures from non-invasive imaging technologies is provided.
 Patent granted in US, a PCT is pending ([US8369928](#)).

Immunotherapies against cancer: German Cancer Research Center to broaden strategic alliance with Bayer HealthCare

The German Cancer Research Center (DKFZ) and Bayer HealthCare (Bayer) will extend their successful strategic research alliance in search of novel cancer therapeutics by establishing a joint laboratory focusing their activities on the field of immunotherapy.

Apogenix Receives FDA Orphan Drug Designation for Apocept™ to Treat Myelodysplastic Syndromes and Initiates Clinical Phase I Study

Apogenix announced that its lead product, Apocept™ (APG101), has been granted orphan drug designation from the US Food and Drug Administration (FDA) for the treatment of myelodysplastic syndromes (MDS). MDS are clonal hematopoietic stem cell disorders characterized by ineffective hematopoiesis leading to blood cytopenias, especially anemia. (www.apogenix.com)

PEPperPRINT: Nature Product Focus lists PEPperCHIP® platform among the "Hottest New Technologies" in 2012

Nature Product Focus listed PEPperPRINT's new peptide microarray platform PEPperCHIP® among the "**Hottest New Technologies**" in Nature issue 491 (2012). The product spotlight on 2012's latest technologies takes a look back at top 15 hot new technologies that emerged during 2012. (www.pepperprint.com)

AWARDS



[German Cancer Award for Stefan Pfister](#)

Professor Stefan Pfister, a molecular biologist and pediatrician, studies the molecular characteristics of brain cancer in children. Over the past few years, Stefan Pfister and his team have discovered a number of biomarkers for disease progression and treatment response. Some of these are already being applied in clinical practice.

[DKFZ awards Richtzenhain Prize and Dr. Emil-Salzer Prize](#)

The jury at the German Cancer Research Center (DKFZ) chose two outstanding young researchers, Matthias Eder and Mathias Heikenwälder, whose research findings can be directly translated into clinical practice.

[Thomas Hofmann Wins the Prize of the Berlin-Brandenburg Academy of Sciences and Humanities](#)

Dr. Thomas Hofmann, junior research group leader at the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ), is awarded the €10,000 prize for his outstanding achievements in cancer research. Hofmann, a biologist, unraveled the mechanisms by which cells decide upon their further fate following DNA damage. His findings help to understand how cancer cells respond to therapies involving DNA damage.



[International Research Award for Ingrid Grummt](#)

The French National Institute of Health and Medical Research (Inserm) has awarded its prestigious "Prix International" to Ingrid Grummt this year. The scientist from the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) is honored for her life's work. Grummt studies the role of RNA molecules that regulate gene expression.

[Felix Burda Awards for Commitment to Colorectal Cancer Screening Presented to Researchers from DKFZ and NCT](#)

The Felix Burda Awards have been presented for the eleventh time. The award in the category "Medicine and Science" went to Dr. Christian Stock, Dr. Michael Hoffmeister and Professor Hermann Brenner of the German Cancer Research Center (DKFZ). The award in the new category "Best Prevention Idea" was given to Cornelia Ulrich, Dr. Ulrike Bussas and Clare Abbenhardt of the National Center for Tumor Diseases (NCT) Heidelberg. This year there were 57 submissions for the awards, which were presented in five categories.



INSIDE THE OFFICE

[Managing Life Science Innovations in Public Research Through Holistic Performance Measures](#)

How much research money should be spent on patenting and commercialization and how can we measure success in technology transfer? These questions are being asked increasingly by science managers, politicians and the public. This is why I chose the performance measurement of technology transfer as the topic for my Master's thesis, which I completed in

2011. Thanks to the invitation of the highly prestigious Japanese Keio University, some answers can be found in Chapter 8 "Managing Life Science Innovations in Public Research Through Holistic Performance Measures" in the book "Fulfilling the Promise of Technology Transfer Fostering Innovation for the Benefit of Society". The book is available online on an open access basis and will appear in book form in May.