

# 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,

November is said to be a dreary month – at least in Germany with its cold and damp winter climate. However, it is also the month of partnering and deal-making as we can see from this year's BioEurope in Hamburg. November in other words is still a month of harvesting grapes and the fruit from seeds planted in the past. I have heard that this year's vintage was good. And long efforts eventually bear fruit.

In personalized medicine DKFZ is therefore very pleased to have added ROCHE as a strategic partner – at last, together with the Heidelberg-based National Center for Tumor Diseases and the Heidelberg University Hospital. With our partners we hope to make a difference for cancer patients. This is DKFZ's second pharmaceutical alliance after BAYER, with possibly more to come. Please watch us moving on to new horizons. And please check out our latest news and featured technologies – freshly unpacked just for you!

Cheers,

Ruth Herzog

E-mail: [r.herzog@dkfz.de](mailto:r.herzog@dkfz.de)

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[Feature Article](#) about the DKFZ spin-off Multiplexion GmbH

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

[New and Notable:](#) [Roche - new strategic partner of DKFZ](#); and more  
[Inside the office](#)

Feedback: [technologietransfer@dkfz.de](mailto:technologietransfer@dkfz.de)

Address: Deutsches Krebsforschungszentrum, Im Neuenheimer Feld 280, D-69120 Heidelberg, Germany,  
Phone: +49 (0)6221 422958, Fax: +49 (0)6221 422956

FEATURE  
ARTICLE

Dr. Markus Schmitt

MULTIPLEXION



Most common cell  
contaminations are  
19.9% Mycoplasma  
4.4% Interspecies

## Multiplexion GmbH – Quality control for your research!

**Multiplexion GmbH** is a limited liability corporation founded in 2012 as a spin-off of the German Cancer Research Center (DKFZ). It offers quality control services to researchers from academia or industry. CEO Dr. Markus Schmitt is deeply committed to helping researchers to obtain safe and consistent research results. To industrial partners who wish to establish their own in-house quality control unit, DKFZ offers non-exclusive licenses for assays and know-how from this promising new spin-off company.

Cell culture contaminations are a serious problem in biological research since they may lead to distorted and non-reproducible results. The usual reason for contamination is mishandling of cells during routine culture and cryopreservation but it may also be caused by **the lack of convenient tests for the quality control** of cell cultures. It is estimated that 15-30 % of cell lines in current use are contaminated or not what they are thought to be. In principle, cell lines can be contaminated by a wide range of agents including i) bacteria, ii) viruses and iii) other cell lines.

One of the Multiplexion's services is to **simultaneously detect contaminations from up to 25 viral, microbial and interspecies origins**. The so-called Multiplex Cell Contamination Test includes the detection of 12 Mycoplasma species, *Acholeplasma laidlawii*, SRMV and cross-contaminations with cells of 12 different species (e.g. human, pig, dog, *Drosophila*). Detection of contaminations after DNA extraction is done with specific primer sequences in a multiplex PCR and subsequent hybridization using specific oligonucleotide probes. As internal DNA quality control, the presence of the vertebrate PolA gene is tested in parallel. Moreover, several positive and negative controls are included to test PCR performance. The method has been successfully used at DKFZ for cell culture testing for more than four years. It is a cost-effective, high-throughput assay for production units as well as tissue culture labs. ([Technology offer](#)).

Additionally, the company offers the Multiplex human cell line authentication test using SNP-profiling. In this test, the complete genotype is compared to a reference database, comprising more than 570 distinct STR-profiling-authenticated human reference cell lines. In contrast to STR-profiling, widely used cell lines with mutations in their mismatch repair genes can also be robustly authenticated. The level of detection of cross-contaminating cells from another human cell line is as low as 3%.

### CEO profile Dr. Markus Schmitt

Dissatisfied by the presence of contaminated cell cultures in his own experiments, Dr. Markus Schmitt founded the DKFZ Core Facility "Contamination Control" in 2008, which he headed until 2012. Realizing that there is a serious need for this kind of service throughout the scientific community, he then founded Multiplexion GmbH, which he currently manages. In addition, he continues to work as post-doc in the Virus-Host Interactions of Polyoma and Papilloma Viruses group at the DKFZ, where he aims to translate his research results into diagnostic applications.

## NEW TECHNOLOGIES

### THERAPEUTICS



#### [Multi-modal cancer therapy using viral hitchhiking \(P-714\)](#)

The invention substantially enhances T-cell mediated killing of tumor cells marked with Newcastle disease virus (NDV). This effect is facilitated by a tri-specific fusion protein tsHN-IL-2-CD28 which elicits immune stimulatory effects by binding to the IL-2 receptor of immune cells. Additionally, it brings NDV-tagged tumor cells in close proximity to cytotoxic T-cells or dendritic cells, thereby increasing their killing efficiency.

#### [Means and methods for treating or diagnosing IDH1 R132H mutant-positive cancers \(P-987\)](#)

The IDH1 R123H mutation of human isocitrate dehydrogenase type 1 (IDH1) including an exchange of amino acid at position 132 from R to H is a frequent mutation in several cancer types. The invention relates to a peptide consisting of 10-20 amino acids including this mutation of the IDH1-gene. The peptide can be used for diagnosis, vaccination and subsequent immune monitoring of patients with various types of cancer without the need for cumbersome and potentially dangerous biopsy.

#### [HC toxin for treating advanced stage neuroblastoma \(P-695\)](#)

We have identified a small molecular compound for the treatment of childhood neuroblastoma, called HC Toxin. The compound elicits anti-tumoral effects in nanomolar concentrations and it is capable of inducing differentiation, growth arrest and apoptosis in neuroblastoma cells. Normal, non-transformed cells are not affected by HC Toxin. The anti-proliferative effect is based on inhibition of histone deacetylation and is particularly pronounced in N-myc amplified advanced stage neuroblastoma. Thus, the HC toxin may improve the success rate of the current standard therapy.

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

### DIAGNOSTICS



#### [Protein biomarker set for personalized treatment of ER \$\alpha\$ -positive breast cancer \(P-1035\)](#)

Luminal breast cancer accounts for 70-80% of newly diagnosed breast tumors. The histologic grade of luminal breast cancer is often determined by semi-quantitative methods describing morphologic features related to the differentiation states of the tumor specimen. In order to make a clear-cut classification of luminal breast cancer as either "grade 1" (= low risk) or "grade 3" (= high risk) tumors, DKFZ researchers have developed a 3-protein marker set.

#### [Reliable Prognostic Marker for HPV-driven Oropharyngeal Squamous Cell Carcinoma \(P-988\)](#)

Human papillomavirus (HPV) can be detected in 50-80% of patients with oropharyngeal squamous cell carcinomas (OPSCC). These patients have a



higher survival rate. DKFZ inventors have identified an RNA pattern, suitable as a reliable prognostic marker to deescalate cancer treatment of HPV-driven OPSCC patients.

#### [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) internal DNA quality and PCR performance control.

#### [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 has been validated and is ready to use in clinical studies. The technology is available as a non-exclusive license or as service.



#### [Diagnosis of glioblastoma and acute myeloid leukemia by \(D\)-2-hydroxyglutarate test \(P-977\)](#)

Diagnosis and monitoring of IDH1/IDH2/IDH3 dependent diseases such as: different types of brain tumors, acute myeloid leukemia (AML), chondrosarcoma, intrahepatic cholangiocarcinoma or angioimmunoblastic T cell lymphoma. The technology describes a patented test, which is a simple and robust enzymatic assay with readout in 3 hours. In comparison to established assays (e.g. GC-MS), this test is suitable for 96-/384-well format and high-throughput, making it less time-consuming and more cost-effective.

#### [Methods for the diagnosis and prognosis of a tumor \(P-937\)](#)

Researchers at DKFZ have developed an immunohistochemical assay to classify tumors based on differences in the metabolism of branched chain amino acids. In brain tumors the assay distinguishes tumors harboring mutations in either the IDH1 or IDH2 genes or both from tumors with wild type IDH1 and IDH2 genes. Thus the IDH1 status and activity of branched chain amino acid metabolism can be determined using tissue slides. The specificity of the immunohistochemical IDH1 and IDH2 status analysis is significantly increased from about 92% in known methods to 100% in our method. The assay allows the fast and reliable diagnostic and prognostic classification of tumors based on the activity of branched chain amino acid metabolism.



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

RESEARCH  
TOOLS

### [Oligonucleotide mixture for the detection of contaminations in cell cultures \(P-792\)](#)

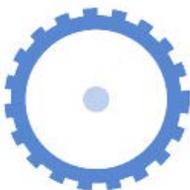
Since cell culture contamination cannot be totally avoided, regular testing is a key factor for good cell culture management. The present invention provides means and methods to simultaneously detect up to 35 viral, microbial and inter-species contaminations. It facilitates sensitive and reliable determination of cell line purity. The technology is based on multiplex PCR and Luminex detection. Especially production units can profit from this cost-effective high-throughput method. [[Feature Article](#)]

### [Inexpensive and flexible methods for quantification in mass spectrometry \(P-684-739\)](#)

DKFZ scientists have developed an easy and convenient MassSpec-based method for absolute quantification of molecules, proteins or peptides by means of permuted peptides. The method is useful for profiling of blood serum proteins, mapping and profiling of post-translational modifications of peptides in the cell, and identification of peptide-tagged pharmaceutical active compounds or drug metabolites in different cellular stages.

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

## DEVICES



### [Quadscanner for High Resolution Microscopy \(P-750\)](#)

Quadscanner for High Resolution Scanning Microscopes. The key facts are: (1) Fast, adaptive optical scanning device; (2) Completely free positioning of the scanning mirrors in relation to the conjugated back focal plane; (3) Applicable in STED microscopy; (4) Calibration with 4 galvanometers; (5) Application in high resolution microscopes (fluorescence, Raman, STED, localization)

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

NEW PATENTS  
GRANTED

### [Optical Tomography \(OT\) for multi-modality imaging \(P-706\)](#)

DKFZ has developed an optical imaging detector (25 mm x 100 mm photon sensor) for fluorescence and bioluminescence in small animal imaging, which is compatible for magnetic resonance imaging (MRI), computer tomography (CT), positron electron tomography (PET) and single-photon emission computed tomography (SPECT). Patent granted in US (additional application is still pending for EP, CA, JP).

### [Optical Tomography \(OT\) and MR combination for dual-modality imaging \(P-734\)](#)

DKFZ has developed an optical imaging detector for fluorescence and bioluminescence in small animal imaging, which is compatible for magnetic

resonance imaging (MRI). This technology makes it possible to study tracer/marker kinetics of optical (OT) and NMR induced signals simultaneously. Patent granted in D, CH, GB, NL, FR, JP and US.

**FAM: Fluorescence Activation Microscopy, a new Principle for 3-Dimensional Fluorescence Microscopy (P-803)**

FAM enables optical sectioning without the need for confocal optics or 2-photon excitation. The new method involves the use of a fluorophore which can be repeatedly activated temporarily by means of an optical transfer signal to label the structure of interest and the detection of the fluorophore by applying activation and excitation simultaneously through two opposing micro-objectives. Patent granted in D, CH, GB, NL, FR, S and US.

**Method for determining the ratio of two distinct peptides or polynucleic acids by quantitative proteomics (P-684)**

The exact ratio of two distinct target-peptides or -polynucleic acids is determined, using a compound-specific correction factor or by double ratio calculation. The innovative method can be performed using a variety of different analyzers (e.g. mass spectrometer, fluorescence-spectrometer or scintillation detectors). Patent granted in D, AT, DK, GB, NL, FR, IT and US.

**Roche – new strategic partner of DKFZ: Science and industry join forces to optimize cancer treatment**

Roche has concluded its first collaborative agreement on personalized healthcare with the National Center for Tumor Diseases (NCT), represented by its supporting institutions, the German Cancer Research Center (DKFZ) and Heidelberg University Hospital. The aim is to strengthen cooperation between all participating partners in the early stages of oncology research and development projects so that patients reap benefit from innovations sooner. Two projects are already underway.

**Nationwide Alliance Against Cancer**

With Germany's Federal Minister Professor Dr. Annette Schavan and State Minister Theresia Bauer in attendance, the official launch of the German Consortium for Translational Cancer Research (DKTK) was celebrated in Heidelberg. The consortium aims to enhance translational cancer research in Germany at 7 designated partner sites of the DKFZ.

**Biomarkers for virus-induced cancer of the oropharynx**

Patients with oropharyngeal cancers have a more favorable prognosis if their tumors are caused by human papillomaviruses. Scientists from the DKFZ and Heidelberg University Hospital have now identified biomarkers which enable them to differentiate cancer cases taking a favorable course from those with an unfavorable one. It may be possible to treat the two disease types differently. [please see also corresponding [Technology offer](#)]



NEW AND  
NOTABLE





**7.5 Million Euros for the Fight Against Cancer**

The Dietmar Hopp Foundation will fund the Heidelberg Institute for Stem Cell Technology and Experimental Medicine (HI-STEM) at the German Cancer Research Center (DKFZ) for another five years.

**Scientists Find Achilles' Heel of Cancer Cells**

Scientists from the DKFZ, Bayer Healthcare and Heidelberg University Hospital have identified the HDAC11 enzyme as a promising target for new cancer therapies. If this molecule is turned off, cancer cells stop growing and die.

SPIN-OFFS



**Apogenix's Apocept™ for Glioblastoma Multiforme Named One of "Top 10 Projects to Watch"**

Apogenix, founded in 2005 and developing novel protein therapeutics for the treatment of cancer and inflammatory diseases, announced that its lead product, Apocept™ (APG101), has been selected by Elsevier Business Intelligence and Windhover Conferences as one of oncology's "Top 10 Projects To Watch". ([www.apogenix.com](http://www.apogenix.com))

**Affimed raises €15.5 Million in a Series D financing round**

Affimed Therapeutics AG, founded in 2000 and developing therapeutic TandAb, announced the successful closing of a Series D financing round of € 15.5 million. The proceeds from this transaction will be used to fund the clinical development of Affimed's therapeutic pipeline that consists of two TandAb products, AFM11 and AFM13. The results of the trial are expected by December 2012. ([www.affimed.com](http://www.affimed.com))

INSIDE THE OFFICE



From left: Dr. Christian Schuster, Dr. Christian Kliem, Andrea Pörsel, Dr. Martin Siepmann, Dr. Natalie Watzke, Dr. Frieder Kern, Dr. Ruth Herzog, Dr. Dirk Kuck, Dr. Katja Beck, Inga Höche, Gabriela Hantke, Sandra Schuhmacher [Homepage](#)

Frieder Kern and Christian Kliem, two newly appointed licensing managers with acknowledged expertise market and license technologies to our industry partners, while three technology managers (Christian Schuster, Martin

Siepmann, Natalie Watzke) work as scouts with the researchers in order to patent technologies and assist them in concluding collaboration agreements. In addition, validation and drug development activities are coordinated by project manager Dirk Kuck. Assistance is provided by Andrea Pörsel (office management and marketing), Sandra Schuhmacher, Gabriela Hantke (patent administration) and Katja Beck (marketing, MTAs). The team relies on Inga Höche's legal expertise and counsel, including the head of the Office of Technology Transfer, Ruth Herzog.