Dear colleague and business partner,

This year the Deutsches Krebsforschungszentrum (DKFZ) celebrates the 50th anniversary of its research in cancer prevention, diagnosis and therapy – for a life without cancer. Technology transfer is an integral part of the DKFZ mission, translating research results and partnering with industry for the benefit of the patient.

This issue's featured technologies concern cell death and cancer metastasis. You will learn more about how to sensitize cancer cells with Chinese drugs and thus enhance cancer cell death. And how these drugs simultaneously protect normal cells from cell death due to chemotherapy. The second featured technology is a versatile and optimized in vivo system for monitoring metastasis of tumor cells in chicken eggs instead of using animal models.

As usual I invite you to browse our opportunities and news. If you are interested in any of our technologies I’ll be happy to connect you with the respective technology manager and researcher.

Cheers
Ruth
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Content:

Feature Articles about new approaches of traditional Chinese herbal medicines and on a fast and cost-efficient in vivo model to investigate tumor metastasis.

New Technologies: Therapeutics (8) Diagnostics (6) Research Tools (3) Devices (3)

Patents granted: 5 new patents were granted
New and Notable: Be sure not to miss the opportunity to meet us during the Upcoming Events

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Elucidating and exploiting the molecular mechanisms of traditional Chinese herbal medicines (P-822, P-1080, P-1128)

For many years, Professor Peter Krammer MD, renowned for his discovery work on programmed cell death, and his long-standing coworker Dr. Min Li-Weber, have focused their scientific interests on the traditional Chinese compounds Rocaglamides and Wogonin. Their aim is to implement traditional Chinese medicine (TCM) as an approved treatment in cancer therapy. They elucidated the direct mechanisms of action of these compounds as well as their interactions with other cancer drugs and revealed several promising new approaches for cancer treatment.

Krammer and Li-Weber were able to show that combining Rocaglamides with chemotherapeutic drugs e.g. 5FU, gemcitabine or substances that induce the extrinsic apoptosis pathway, e.g. TRAIL, dramatically increase the sensitivity of tumor cells towards these drugs. Importantly, normal cells were not sensitized. As regards the underlying mechanism, they showed that Rocaglamides down-regulate c-FLIP and up-regulate CD95L expression, and thereby enhance the TRAIL- and CD95L-mediated killing of cancer cells. Therefore, a combination of state of the art chemotherapy with Rocaglamides can reduce the drug dose and consequently reduce the side effects of the drugs, while retaining the effectiveness of the therapy. Also of great importance is the fact that Rocaglamides can even reverse TRAIL-resistance acquired during cancer treatment. [see technology offer P-822]

A further investigation of the co-application of Wogonin or Rocaglamide with Bcl-2 inhibitors (e.g. ABT-263) led to the finding that Wogonin and Rocaglamides can reduce the effective dose of Bcl-2 inhibitors and thereby reduce the risk of the development of thrombocytopenia during ABT-263 treatment. Both Chinese compounds dramatically increase efficacy of ABT-263 not only in leukemic cells but also in other types of tumor cells like colon, hepatocellular or prostatic cancer cells, which are normally resistant to ABT-263 treatment. Furthermore, the combination therapy can re-sensitize tumor cells that had acquired ABT-263 resistance during the treatment. [see technology offer P-1080]

Besides their sensitization activities in cancer treatment, Rocaglamides also have chemo- and radio-protective effects on normal cells. Krammer and his team were able to show that Rocaglamides prevent chemotherapy-induced death in healthy cells by inhibiting p53 expression at the translational level. This effect allows dose escalations up to 8-fold during cancer treatment and provides a wide therapeutic window. [see technology offer P-1128]

As all these inventions are highly promising approaches, DKFZ filed several patents to enable TCM to be used in cancer treatment in the future outside China as well.
Inventor profiles

Professor Peter Krammer MD has been the Division Head of Immunogenetics at DKFZ since 1989 and is board member of the National Center for Tumor diseases (NCT (Heidelberg). He is one of the leading scientists in the field of apoptosis worldwide and has received numerous prestigious awards and prizes, e.g. the Robert Koch Prize, the German Cancer Aid Prize, the Ernst-Jung-Prize for Medicine and the Lautenschläger Prize. His primary goal is to break the therapy resistance of tumors, based on novel immunotherapeutic strategies. Dr. Min Li-Weber is group leader in the Division of Immunogenetics and focuses on apoptosis sensitivity and resistance in cancer and identification of new anticancer drugs from natural products.

A fast and cost-efficient in vivo model to investigate tumor metastasis (P-1148)

Metastasis, the spread of a tumor from its primary site to other parts of the body, is the most significant problem in cancer treatment. Human-mouse xenografts and genetically engineered mice are often used to model the biological complexity that characterizes metastasis, as well as to study new treatment approaches to overcome metastasis. These animal models have the drawback of being costly and time-consuming.

Therefore, Professor Heike Allgayer MD and her co-worker Dr. Jörg Leupold developed a powerful in vivo model based on the chicken embryonic metastasis (CEM) assay, also known as the chorioallantoic membrane (CAM) assay. CAM is an established model to investigate the invasive properties of tumor cells. In short, tumor cells are grafted onto the upper CAM of a fertilized chicken egg. After different time points, the presence of tumor cells inside the chicken embryo, its germinal membranes, vessels and organs are measured to determine different aspects of the invasive and metastatic capacity of the tumor cells. With the CAM assay, spontaneous or experimental in vivo metastasis can be quickly detected in one week, a considerably shorter time compared to the 4 to 10 weeks required for typical murine models. Also, in contrast to most mouse models, the specific and essential step of in vivo intravasation can be differentiated specifically from local invasion and metastasis establishment in the CAM-model, at a high level of sensitivity.

Allgayer and Leupold combined the CAM assay with TaqMan probes that are highly specific for human genomic sequences and real-time reverse PCR, for accurate quantification of metastatic cells in different organs of the chicken embryo at a high sensitivity. As a consequence, no labor-intensive immunohistochemistry efforts are needed, as is typically required for murine xenografts. This makes the current method fast and cost-efficient with the tremendous advantage of not requiring animal test approval.

To date, Allgayer and Leupold have established CAM assay systems for colon cancer, melanoma, lung cancer, breast and pancreatic cancers. Furthermore, they successfully used the CAM assay to study the effect of potential therapeutic molecules in vivo. Since the chicken embryo is a closed system, the half-life of these potential therapeutic molecules is often much longer.
Quality control for CAM assay

compared to other animal models, allowing experimental evaluation also with limited quantities of substances.

Another application of the CAM assay developed by Allgayer and her team is the ability to isolate metastatic sub-clones of tumor cell lines.

DKFZ, in collaboration with the Mannheim Medical Faculty of Heidelberg University, offers this versatile and optimized in vivo system for monitoring the intravasation, invasion and metastasis of tumor cells as a service, for joint research purposes and for licensing (see technology offer P-1148).

Inventor profiles

Professor Heike Allgayer MD is the Departmental Head of Experimental Surgery at the Mannheim Medical Faculty of Heidelberg University, Germany, and also Head of the Molecular Oncology of Solid Tumors Unit at the German Cancer Research Center (DKFZ), Heidelberg. As a board-certified surgeon and molecular biologist she sees her mission as bridging basic research and the treatment of cancer patients as a dedicated translational researcher. Her major research interests include tumor progression, invasion and metastasis, molecular determinants of response to novel therapeutics, translational research, and molecular staging of cancer.

During his PhD and postdoctoral work at the DKFZ and the Mannheim Medical Faculty of University of Heidelberg, Dr. Jörg Leupold developed the CAM assay into a robust and quantitative in vivo method offering all the features and advantages described above.

NEW TECHNOLOGIES

Highly effective chemoprotective and radioprotective drugs (P-1128)

Chemo/radiotherapy-induced side effects limit the doses that can be administered during cancer treatment. In this invention Rocaglamide A (Roc-A) and derivatives are claimed to show chemo- and radioprotective efficacy in highly proliferating cells, slowly proliferating cells and quiescent cells. Roc-A and derivatives are highly specific for normal cells and do not protect p53-deficient/mutated cancer cells. Additionally, Roc-A has a wide therapeutic window and is highly potent (nM range). [see Feature Article]

Antibody specifically binding the enzymatically active form of Homeodomain Interacting Protein Kinase 2 (HIPK2) (P-1097)

The serine/threonine protein kinase Homeodomain Interacting Protein Kinase 2 (HIPK2) is an evolutionarily conserved regulator of cell death and cell growth during development, and in response to cellular stress such as DNA damage induced by UV irradiation, ionizing radiation (IR) and chemotherapeutic drug treatment. Like any other kinase, it is present in active and inactive states. To date, no modifications of HIPK2 have been identified that are suitable for predicting its kinase activity. The present invention therefore aims to provide an antibody that binds only the activated form of HIPK2.

Increased efficacy of Bcl-2 Inhibitors by co-application with wogonin or rocaglamide (P-1080)

The current invention provides a combination therapy of wogonin or rocaglamide, together with Bcl-2 inhibitors, leading to increased efficacy of
ABT-263 even in cancer cells which have acquired resistance to ABT-263, and without affecting proliferation of normal T cells and platelets. [see Feature Article]

**New spiroepoxide tetrahydrobenzo-triazoles and -imidazoles and their use as MetAP-II inhibitors (P-1068)**

Numerous studies have shown that selective inhibition of the MetAP-II subtype halts the growth of endothelial cells in culture, inhibits angiogenesis in animal models, and is a validated strategy 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. So the invention describes the design of the small molecules, which was guided by the chemical structure of fumagillin. The substances have drug-like substructures, exist in novel chemical space, and the active enantiomeric series has been identified.

**Armed oncolytic adenoviruses for combined viral tumor cell lysis and delivery of therapeutic antibody derivatives (P-1059)**

In the current technology the armed oncolytic adenovirus encodes an immunoRNase consisting of a tumor-targeting antibody fragment fused to an RNase toxicity domain. The oncolytic adenovirus will enter and specifically replicate in tumor cells. A new generation of oncolytic adenoviruses will be produced by the infected tumor cell. This results in lytic tumor cell death, release of virus progeny and infection of neighboring tumor cells. The infected tumor cell will also synthesize and secrete the virus-encoded immunoRNase. After it is taken up by tumor cells, the latter triggers cell death by RNA degradation.

**Receptor for Advanced Glycation End-products (RAGE) as a diagnostic and therapeutic target in liver cancer (P-1019)**

The receptor for advanced glycation end-products (RAGE) has been shown to play a central role not only in acute or chronic inflammatory diseases but also in distantly related fields such as cancer or neurodegenerative diseases. Our invention uses RAGE inhibition as a valid tool to significantly reduce tumor initiation and progression. The results were obtained by using Mdr2-/- and RAGE knockout mice as a model system. In addition the invention relates to a method for testing the RAGE status of a tumor in order to identify patients who will probably benefit from a therapy based on RAGE inhibition.

**New therapy against B cell lymphomas based on antibodies that recognize B cell receptors (P-997)**

The current invention provides a new and efficient treatment strategy for B cell lymphomas based on antigen-armed antibodies (AgAbs). The inventors showed that, after AgAb treatment, Epstein-Barr virus-transformed B cell lines and various Burkitt’s lymphoma cell lines were able to present antigens that efficiently induce T cell activation. The AgAb targeted the B cell receptors CD19, CD20, CD21 or CD22.
Harmless rocaglamide makes apoptosis-inducing drugs more effective (P-822)

The current invention is based on the finding that rocaglamide makes tumor cells more susceptible to anti-proliferative chemotherapeutic agents while leaving normal cells unaffected. This allows a dose reduction of apoptosis inducers and would therefore dramatically improve the patient’s condition during cancer treatment. [see Feature Article]

A list of all therapeutics technologies can be found here [Link].

DIAGNOSTICS

Human TERT promoter variants: Diagnostic and prognostic application (P-1140)

Activation of telomerase is a prerequisite of cancer cell development in order to compensate constant telomere shortening induced by cell divisions. In tumors originating from tissues with high self-renewal capacity, telomerase function is mainly up-regulated by epigenetic mechanisms while tumors originating from terminally differentiated tissues most frequently harbor mutations in the TERT promoter. The current invention identifies new mutations in the TERT promoter which qualify as diagnostic and prognostic markers.

MicroRNAs modulating the effect of glucocorticoid signaling (P-1137)

Glucocorticoid signaling plays a key role in diseases associated with metabolic syndrome, which are expected to become the major burden of human health in the 21st century. So strategies for treating such diseases are urgently needed. The current invention describes an miRNA which interferes with glucocorticoid signaling and can therefore be used as a therapeutic target for e.g. diabesity-related metabolic disorders.

A double-labeled probe for molecular imaging (P-1124)

The technology enables the direct and indirect detection of cancer tissue. It involves a pharmaceutical compound consisting of three subdomains: (A) for specific cell surface binding to neoplastic cells, (B) for binding radiometals via a chelator domain for e.g. PET, and (C) harboring a fluorescent dye moiety for optical detection. The combination of PET tracer and optical moiety enables the surgeon to localize the tumor preoperatively via PET/CT and intraoperatively through optical detection.

Linker modifications of conjugated Prostate-Specific Membrane Antigen (PSMA) inhibitors for prostate cancer diagnosis and therapy (P-1123)

The expression of PSMA on the surface of prostate cancer cells offers the opportunity to diagnose and characterize the primary tumor and corresponding metastases. DKFZ researchers developed a promising new series of low molecular weight imaging agents that target PSMA and allow rapid visualization and specific targeting of prostate cancer.
**Monoclonal antibodies against HDAC11 (P-1040)**

Modifications of histones are known to play a role in cancer, altering the accessibility of DNA for transcriptional processes. So detection methods for enzymes that modify histones are urgently needed. We established two hybridoma cell lines producing antibodies directed against HDAC11 and which are suitable for immunocytochemistry, chromatin IP, and Western Blot.

**The signature of WNT signaling in colon cancer (P-908)**

90% of sporadic colorectal carcinomas carry loss-of-function mutations in the adenomatous polyposis coli (APC) gene, which encodes a scaffolding protein mediating constitutive destruction of the β-catenin transcriptional co-activator in the absence of Wnt ligand. DKFZ inventors detected NKD1 and C10orf54 as biomarkers for identification of Wnt/β-catenin modulating compounds, such as small molecules, interfering RNAs, peptides and antibodies, and thus can be used for the development of a kit or an assay for detection of such compounds. This kit or assay can additionally be used as a companion diagnostic resource to identify patients in need of a treatment that modulates the Wnt/β-catenin signaling pathway (e.g. targeted therapy).

A list of all diagnostics technologies can be found here [Link].

**Non-ribosomal protein synthesis pigment fusion peptides (P-1126)**

Non-ribosomal peptides (NRPs) are secondary metabolites produced by microorganisms, e.g. bacteria and fungi. Unlike ribosomal protein biosynthesis, non-ribosomal protein synthesis (NRPS) does not require mRNA. NRPs are a promising source of functional molecules such as antibiotics. The technology allows for the identification, high-throughput screening and easy purification of engineered NRPs by optical measures.

**Scaffold-based organotypic culture for the long-term cultivation of human epidermal stem cells (P-876)**

The skin, as the largest organ in the human body, not only affords protection from the external world, but is also a target of many kinds of diseases, including cancer, psoriasis or wound closure defects. However, in vitro model systems of the skin suitable for long-term culture are not currently available. The aforementioned invention solves this problem and can be used for producing skin equivalents with a life span of at least 10 weeks.

**Assembly of absolutely quantified peptide and phosphopeptide solutions via element mass spectrometry (P-831)**

Most comparative proteomic studies deliver a relative quantification that expresses the changes in concentrations of a protein in the context of a different cellular stage. There is still an existing need to develop easy and convenient methods for determining the absolute concentration and the degree of phosphorylation of a peptide, and which contain fewer sources of error and are less time-consuming. DKFZ researchers have developed an easy-to-apply method that meets the above-mentioned requirements.
A list of all research tool technologies can be found here [Link]

**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. Since this promoter is methylated (epigenetically silenced), the reporter genes are not expressed. After the addition of demethylating agents, GFP or G418 can be used as a readout in a screening assay for epigenetic reactivation. The system has a z-value of 0.75 using G418 as readout.

**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.

**Control of radiation therapy devices via programmable logic controllers technology (P-996)**

Synchronization and control of linear accelerator, multi-leaf collimator, gantry system, patient support system and x-ray beam generation system at the same time is difficult to establish, particularly with hard real-time requirements. The presented technology comprises a control unit consisting of standardized programmable logic controllers for real-time operation of all subsystems of a radiation therapy device. Thus, the technology allows precise and dynamic patient treatment with high time resolution.

A list of all device technologies can be found here [Link].

**Personalized medicine through innovative tests by analysis of exosomes (P-779)**

The current invention provides a method for the enrichment of diagnostic target molecules based on CD24 positive exosome purification. CD24 is highly expressed on exosomes from cancers and those of fetal origin. This offers the possibility to enrich particular subpopulations of exosomes for cancer or fetal diagnostics. Patent granted in US and EP (DE FR, GB, IT, SE).

**Metformin for treatment of multiple sclerosis and graft-versus-host disease (P-778)**

Metformin is a well-known anti-diabetic drug. The current technology offers the
opportunity to use metformin, as a second-line drug, for the treatment of multiple sclerosis and graft-versus-host disease. Patent granted in US.

Multi-photon multi-spot scanning device (P-658)
DKFZ inventors developed a multi-photon multi-spot scanning device which is applicable especially in laser scanning devices such as confocal laser scanners and multi-photon microscopes. It can be used to speed up imaging of living cells which would be harmed by a stronger single beam. Patent granted in US and EP (DE, FR, GB).

Peptides for inhibition of the HPV-16-E6 oncoprotein (P-797)
The peptides identified by our inventors block the intracellular activity of the HPV16 E6 protein and thus increase sensitivity of tumor cells towards apoptosis. This effect is highly specific for HPV16-containing tumor cells. Patent granted in US and pending in EP.

Modulators of Kremen receptors of canonical Wnt signaling pathway as tumor (activation) and osteoporosis (inhibition) drugs (P-528)
The Wnt family of secreted glycoproteins mediate cell-cell interactions during cell growth and differentiation. Canonical Wnt signaling by way of the beta-catenin pathway is transduced by two receptor families. The transmembrane proteins Kremen1 and Kremen2 are high-affinity Dkk1 receptors that functionally cooperate with Dkk1 to block Wnt/beta-catenin signaling. Patent granted in IL, JP, US and EP (AT, BE, CH, DE, DK, ES, FR, GB, IE, IT, NL, SE). Patent pending in AU and CA.

Bayer and German Cancer Research Center (DKFZ) in Strategic Alliance against cancer
Bayer HealthCare and the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) have agreed on a five-year strategic research alliance against cancer. The two partners have already been collaborating since 2009 with the aim of jointly developing novel therapeutic options for cancer patients. Bayer and the DKFZ will together invest up to 30 million euros in their collaboration over the next five years to address the high medical need in cancer treatment and diagnosis.

Black sheep in the family: Why some infections with the Epstein-Barr virus cause cancer
Epstein-Barr viruses (EBV) are very common around the world; almost everybody is infected. In most cases an infection causes no harm, but sometimes the outcome is a serious disease. EBV may lead to infectious mononucleosis (Pfeiffer’s disease), which is common in Germany; in other parts of the world it even causes cancer. The reasons that EBV infections take such diverse courses have been unclear. Now scientists from a team headed by Henri-Jacques Delecluse at the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) have discovered that Epstein-
Barr viruses come in various strains that differ in terms of their aggressiveness. These findings are extremely important both for finding strategies to fight the diseases caused by EBV and for developing vaccines against infections with the virus. See technology offer P-989.

**How a secret friendship of two enzymes makes apoptosis possible**

When cells start growing out of control the body has a potent mechanism to protect itself from cancer: programmed cell death, or apoptosis. It is induced by an enzyme called HIPK2 and other molecules. Led by Dr. Thomas Hofmann from the German Cancer Research Center (DKFZ), a team of scientists from DKFZ, the European Molecular Biology Laboratory (EMBL) in Heidelberg, Germany, and the University of Trieste, Italy, have now discovered that HIPK2 depends on a second enzyme in order to become active: Pin1. This function of the Pin1 enzyme has been unknown until now. See technology offer P-1097.

**Defective packaging protein boosts gene activity in brain cancer cells**

In about half of all cases of high-grade malignant glioma in children, a mutation is found in a DNA packaging protein (histone) called H3.3. Scientists at the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) have now discovered that this mutation leads to reduced methyl labeling both in the histone mutant and in the DNA of the tumor cells. These two epigenetic changes increase gene activity in the cancer cells and may thus contribute to the aggressiveness of these tumors. See technology offer P-1012.

**New vaccine against papillomaviruses protects mice from skin cancer**

Scientists have suspected that non-melanoma skin cancer in patients who have received organ transplants can be caused not only by UV radiation, but also by simultaneous infection with specific types of human papillomaviruses (HPV). Scientists from the German Cancer Research Center (DKFZ) and the Charité University Hospital Berlin have now used a vaccine for the first time to protect mice against such skin tumors. The vaccine is even effective in animals with suppressed immune systems and mice that have previously been infected with papillomaviruses. See technology offer P-1168.

**Apogenix’ APG101 significantly prolongs the overall survival of patients with recurrent glioblastoma**

Apogenix has announced that its lead product APG101 demonstrates prolongation of overall survival in biomarker-positive patients in Phase II trial for the treatment of recurrent glioblastoma. ([www.apogenix.com](http://www.apogenix.com))

**Mint Medical GmbH to establish US subsidiary Mint Medical, Inc.**

Due to a significant increase in customers in the USA, Mint Medical GmbH has set up a new subsidiary in North America. Mint Medical, Inc. is a wholly-owned subsidiary of Mint Medical GmbH and is headquartered in Jersey City, NJ. ([www.mint-medical.de](http://www.mint-medical.de))
**AWARDS**

**DKTK Tübingen: Hans-Georg Rammensee receives 2013 German Cancer Aid Award**

German Cancer Aid (Deutsche Krebshilfe) presents its annual award to Professor Hans-Georg Rammensee, a collaborator in the German Consortium for Translational Cancer Research, for research in the area of cancer immunotherapy.

**DKTK Frankfurt: German Cancer Award for Simone Fulda**

Professor Simone Fulda, a pediatrician and cancer researcher in the German Consortium for Translational Cancer Research (DKTK) of the University Cancer Center (UCT) of the University Hospital Frankfurt, has been honored with the 2014 Cancer Research Award in the category “Translational Research.”

**Award-winning young researchers at DKFZ**

Four young researchers from the German Cancer Research Center (DKFZ) have simultaneously been honored with science awards. Dr. Irène Baccelli and Dr. Dominik Sturm shared the €4,500 Richtzenhain Award. Dr. Baccelli also received half of the €7,500 Lewenz Award, the other half of which was shared by Natalie Jäger and Dr. David Jones. The award ceremony took place on December 17, 2013, at the DKFZ.

**Helmholtz International Fellow Award for John Mendelsohn**

Following a nomination by the German Cancer Research Center (DKFZ), the Helmholtz Association of German Research Centers has distinguished U.S. cancer researcher Prof. Dr. John Mendelsohn with the Helmholtz International Fellow Award. The award gives Dr. Mendelsohn the opportunity to pursue a research visit at DKFZ and other Helmholtz research centers to intensify relations.

**German Industry Innovation Award 2014 for Abberior Instruments GmbH**

Abberior GmbH, founded in 2011 as a spin-off from the Max Planck Institute for Biophysical Chemistry in Göttingen together with DKFZ scientists, received the award for the first commercial development of a subdiffraction RESOLFT microscope. ([www.abberior.com](http://www.abberior.com))

**UPCOMING EVENTS**

We look forward to meeting you

- at the **Bio International Convention** in Boston, June 23-26, 2014
- at the **ASTP Annual Conference** in Oslo, May 14-16, 2014