Bayern Innovativ

FORUM LIFE SCIENCE 2007

International Congress and Exhibition

SPECIAL REPORT

FORUM LIFE SCIENCE 2007

Drug Development

Food and Nutrition

Industrial Biotechnology

5TH FORUM LIFE SCIENCE – ONE OF THE LEADING LIFE SCIENCES PLATFORMS IN EUROPE

Novel technologies, new products and the broad range of future applications of biotechnology in the pharma, food and chemical sector – these topics were the focus of the 5th Congress 'Forum Life Science' at the Technische Universität München in Garching.

The congress was designed and organised by Bayern Innovativ – the Bavarian centre for innovation and technology transfer – with the support of the Bavarian State Ministry for Economic Affairs, Infrastructure, Transport and Technology. On the basis of its multidisciplinary focus on 10 technologies and 10 industries, Bayern Innovativ developed the congress as a major platform for the exchange of information, interdisciplinary transfer of knowledge and for the instigation of cooperation in the Life Sciences.

More than 1,000 participants from 20 countries and 110 exhibitors reflected the great interest in biotechnology and in the growing potential for future applications.
66 speakers from industry and science, from Europe, North America, India and Australia, presented the latest technology and product trends in Life Sciences in the three sessions 'Drug Development', 'Food and Nutrition' and 'Industrial Biotechnology'.

The report highlights some of the most significant trends in biotechnology and Life Sciences and provides an overview about the results of the congress.

Erwin Huber
Bavarian Minister for Economic Affairs, Infrastructure, Transport and Technology

'Future oriented political guidelines build the framework for generating scientific results and their applications in new products and processes, thus strengthening Bavaria's competitiveness.'

Prof Josef Nassauer
CEO, Bayern Innovativ GmbH

'Due to viable networks in various disciplines and branches, Bayern Innovativ succeeded in bringing together experts from biotechnology, pharma, food and chemical industry on an international level.'

Prof Wolfgang A. Herrmann
President of the Technische Universität München

'The interdisciplinary orientation on natural sciences, engineering, medicine as well as on food and agriculture makes the TU München into one of Europe's leading research locations in the whole range of the Life Sciences.'

FORUM LIFE SCIENCE 2007 – FOCUS ON TRENDS AND INNOVATIONS IN LIFE SCIENCES

BIOTECH ENTERS INTO NEW INDUSTRIAL APPLICATIONS

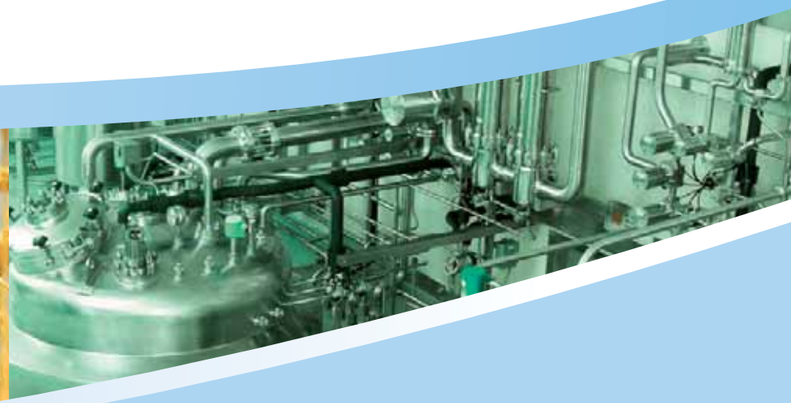
Biotechnology has led to a massive increase in understanding of molecular processes in living organisms. We have now attained a comprehensive knowledge about molecular principles such as genetic variability, interaction of biomolecules or synthesis and degradation processes. On the other hand, we are in the position to use these novel technologies on the basis of genomics, proteomics, bioinformatics, microbiology or enzymology as a toolbox for various industrial applications.

REALISING CONCEPTS ACROSS INDUSTRIES: PERSONALISED SOLUTIONS FOR FOOD AND PHARMA

The understanding of the impact of genetic variability together with different lifestyles, nutrition and environmental aspects of health and quality of life has led to new concepts for personalised products. Current knowledge allows for new approaches to medication with a specific drug and with the right dose, early diagnosis allows preventative intervention as well as the application of targeted nutritional concepts. Personalised medicine and personalised nutrition were major topics at the 'Forum Life Science'. The presentations indicate that biotechnology leads to a growing spectrum of common aspects between food industry with the development of nutrition with an added health value and the pharmaceutical industry, with early diagnosis and the development of specific therapeutics.

MAJOR CONGRESS TOPICS

- Upcoming Biotech revolution in the chemical industry
- Paradigm change in health care towards prevention and personalised medicine
- Creating healthy and good-tasting food



CONTENT

BIOTECH SOLUTIONS FOR MAJOR FUTURE CHALLENGES

KEY STATEMENTS OF THE PLENARY SPEAKERS

Dr Helmut Maucher, Honorary Chairman of Nestlé, was addressing three major future challenges in the world: The sufficient supply with water, energy and crop. He pointed out that novel technologies will be the key to cope with these challenges and that biotechnology will play a major role in this context. For example, biotechnology offers methodologies to develop crops with increased yields or to breed robust plant species. On the other hand, biotechnology can also be applied to develop processed well-tasting food with health benefits.

Dr Alfred Oberholz, Deputy Chairman of the Management Board of Degussa, emphasised that we are now on the 'eve of a biotech revolution' since the chemical industry will increasingly make use of nature's toolset and will apply enzymes and micro-organisms to produce amino acids, vitamins, cosmetic ingredients or biopolymers. Bioprocesses form the basis of increasing utilisation of renewable resources and decreasing petroleum consumption in the chemical industry.

Prof Günther Wess, CEO of the National Research Center of Environment and Health, presented the progression of chronic diseases, such as diabetes or COPD (Chronic obstructive pulmonary disease), causing, according to a WHO report, in 2015 about 60% of global deaths. Environmental and behavioural changes in combination with a genetic predisposition are the main reasons for this increase. On the other hand, the increasing understanding of disease mechanisms is the key for novel strategies for personalised disease prevention and respective drug development.

DRUG DEVELOPMENT

The session ‘Drug Development’ at the Forum Life Science highlighted major trends of the healthcare sector such as personalised medicine, biomarker development, target identification and cell-based therapies. Further focus was laid on strategies for cooperation along the pharma value chain.

PERSONALISED MEDICINE

TOWARDS A PHARMACODIAGNOSTIC STRATIFICATION

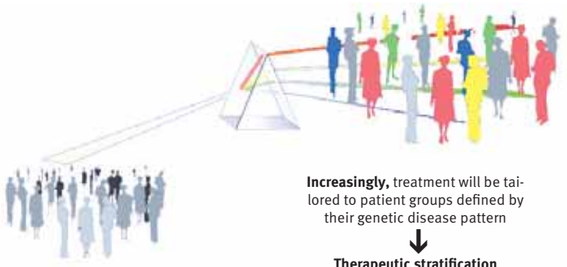
Still today, patients with the same symptoms and the same findings receive the same drug. But often these medications show different effects on the basis of the variability of diseases or of the drug metabolism or other reasons. In the future, treatment will increasingly be tailored to patient groups defined by their genetic pattern.
The benefits of this strategy are obvious: patients profit from fewer unnecessary treatments or fewer adverse side effects; reimbursers do not have to pay for the useless medication of non-responders and physicians will be enabled to give prognostic information and can provide the patient with more efficient therapies.

Personalised Medicine has been appearing in the headlines for the last 10 years. On the one hand, exorbitant expectations with one drug tailor-made for an individual patient and optimised for their genome can not be realised. But, increasing knowledge of the variation between individuals regarding their genetic profile and metabolism as well as the possibility to distinguish different types of one disease such as cancer or rheumatism offers a broad range of opportunities for the identification of a targeted population group which respond to a specific medicine.

The strategy of Roche regarding personalised healthcare was presented by **Dr Tim Jaeger**, Head Medical and Scientific Affairs at Roche. The industry will increasingly realise a therapeutic stratification, meaning that treatment will be tailored to patient groups defined by their genetic disease pattern. Existing drugs will be made more effective by additional diagnostic tools for the identification of subgroups which respond very well. In the future, there will be a further convergence between drug development and diagnostic development with a synchronization of these processes. Companion diagnostics, i.e. one drug associated with one specific diagnostic test, will be one but not the only strategy.
Healthcare companies such as Roche follow the strategy of possessing leading biomarker research and excellent diagnostic science in addition to their pharma research. Dr Jaeger emphasised that additionally the culture and the willingness for therapeutic stratification is a prerequisite for engagement in personalised healthcare.

Towards A More Personalised Healthcare

Using clinical differentiators to achieve optimal pharmaceutical efficacy and safety for the purpose of creating sustainable clinical benefits



(Source: Dr Tim Jaeger, F. Hoffmann-La Roche)

BIOMARKERS

ENABLERS OF PERSONALISED MEDICINE

Application areas of biomarkers
The paradigm shift of therapeutic approaches from treatment of disease symptoms towards a specific targeted therapy and predictive and preventative medicine means a massive change in the healthcare sector. On this basis, biomarkers will play a crucial role in the stratification of patient groups and to realise the promises of personalised medicine. Their application allows conclusions to be drawn about susceptibility, status of disease, clinical endpoints, efficacy of therapies, safety of drugs or mode of drug action.

Dr Andreas Weith, Director Functional Genomics at Boehringer Ingelheim, presented the application of biomarkers in the drug development process and highlighted methods for biomarker identification. Comparison of the expression of genes between patients and healthy individuals forms one well-established approach. For example, the different expression profiles of diabetes patients and healthy individuals obtained in *in silico* analysis indicate differently regulated genes. These genes could be candidates for target molecules for therapies or for novel biomarkers. A further approach is the identification of DNA based markers. One different single nucleotide in the DNA sequence (SNP) could be responsible, for example, for the variation regarding the efficacy of a drug and whether an individual will be a responder or non-responder.

Bavarian Blood Donor Biobank for biomarker evaluation
A promising approach for the identification and evaluation of biomarkers by using a biobank was presented by Dr Silke Martin, Blood Donor Service of the Bavarian Red Cross. The Bavarian Blood Donor Biobank has been collecting plasma samples and related data since 2001 on the basis of 400,000 blood donors. The unique concept of this biobank is the availability of plasma samples taken every 6 months on average over a period of 5 years from the same donor. In case of diagnosis of a disease, previous samples of the donor can be used to evaluate biomarkers indicating the onset of a disease at early stages. Currently, the Bavarian Blood Donor Service is running biobank studies for the development of cardiovascular and cancer biomarkers.

Biomarker:
A characteristic that is objectively measured and evaluated as an indicator of normal biological or pathogenic processes or pharmacological responses to a therapeutic intervention.
(Definition by FDA)

Current examples of biomarker-based diagnostics

Dr Thomas Baier, Head of Global Marketing, Roche Applied Science, presented current examples of the application of biomarker-based diagnostics to realise personalised medicine. Roche has developed, for example,

the AmpliChip CYP 450 Microarray to differ responders from non-responders to a drug. The test allows for the pre-selection of groups of patients for whom the therapy will be presumably successful as well as the adaptation of the right dose with respect to the individual metabolism to reduce an adverse drug effect. A specific therapy of sepsis with antibiotics requires an analysis of the pathogenic organisms. The traditional approach of cultivation of the organism in culture medium needs 3 – 4 days. PCR Diagnostics for detection and identification of the species of the pathogenic organisms delivers the result after 6 hours. A specific therapy with antibiotics can start much earlier increasing the chance for survival. A further prime example for personalised medicine is the treatment of HER2 positive breast cancer with the therapeutic antibody Herceptin. In 20 – 25% of the cases of breast cancer an overexpression of the growth factor HER2 occurs indicating a very aggressive tumour. In case of a positive test the medication with Herceptin will be promising and leads to a significant extension of lifetime.

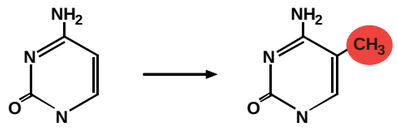
The cold storage facility of the Blood Donor Service in Wiesentheid provides the infrastructure for the logistics of blood samples of the Bavarian Blood Donor Biobank for biomarker research (Source: Blood Donor Service of the Bavarian Red Cross).

TARGET DISCOVERY

OPENING NOVEL APPROACHES FOR THERAPIES

The increasing understanding of molecular mechanisms of the cell and of interactions between pathways enables the identification and validation of novel disease-relevant targets. Some recent results in target discovery and subsequent development of a specific drug were one of the key topics within the session ‘Drug Development’ at ‘Forum Life Science’.

DNA-Methyltransferases – Targets for an epigenetic cancer therapy
Modification of genes can determine which genes of the cell will be switched on or off. For example, methylation of Cytosine – one of the building blocks of DNA – causes the silencing of genes which means switching off a gene without a genetic mutation. These alterations of the so called epigenetic markers affect gene expression without an accompanying change in the primary DNA sequence. Gene silencing is caused by an overmethylation of genes and can trigger tumour development. This could happen if tumour suppressor genes which are responsible for cell division and growth are in-activated by methylation. **Prof Frank Lyko** from the German Cancer Research Center in Heidelberg presented how these genes can be reactivated by demethylation. His team developed via an *in silico* screening approach a potent inhibitor of the DNA-Methyltransferase, the key enzyme which attaches methyl groups to the DNA. The substance enables indeed the demethylation of DNA and shows a great therapeutic potential in first in vivo tests.



(cytosine-5) DNA methylation catalyzed by DNA methyltransferases is the most stable epigenetic modification and plays an important role in human tumorigenesis (Prof Frank Lyko, German Cancer Center)

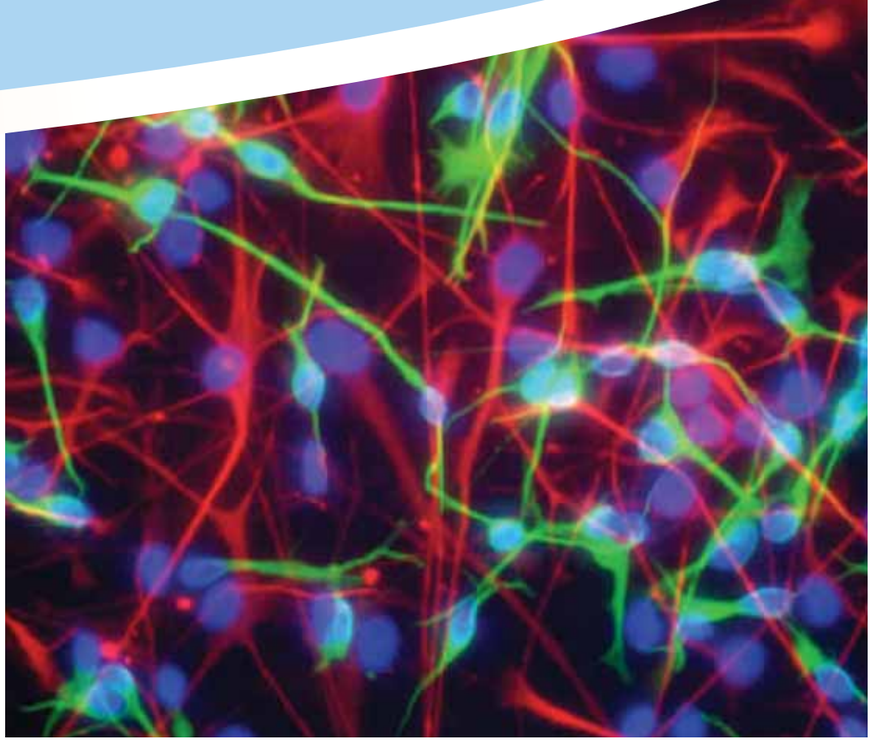
Toll-Like-Receptors (TLR) – Modulation of the immune system
DNA-Methylation pattern differs between human genes and genes of pathogenic organisms. The CpG motifs which are mainly modified by methylation in human genes are abundant in their unmethylated form in pathogenic organisms. This differentiation criterion is applied by the human immune system to recognise foreign invaders or pathogens. So-called toll-like receptors recognise pathogen-expressed patterns such as the CpG motifs. **Dr Christian Schetter**, Vice President of Coley Pharmaceuticals, presented the development of novel drugs stimulating the TLR-target. The TLR therapeutics on the basis of synthetic oligonucleotides bind to the TLR9-receptor on dendritic cells of the immune system and trigger a disease-specific immune response. This receptor stimulation initiates the expansion of tumour-specific lymphocytes and activates the immune response against cancer cells. Clinical trials in phase III of a first TLR9 agonist drug are currently being conducted.

REGENERATIVE MEDICINE

FIRST STEPS FOR STEM CELLS TO ENTER THERAPEUTIC MARKETS

Stem cells promise hope for otherwise untreatable diseases, such as Parkinson's disease, multiple sclerosis or cancer. While traditional pharmaceutical approaches act on symptoms of diseases, stem cell approaches aim to reverse the dysfunction by replacing the damaged or lost cells. Recent progress in the stem cell field has been reported on the development of cell-based therapies using hematopoietic, mesenchymal and neural stem cells.

Hematopoietic stem cells open new opportunities for combinatorial cancer therapy
Using an adoptive transfer approach **Prof Andreas Mackensen** from the University of Regensburg isolates T-cells from patients and specifically stimulates those using tumour-specific antigens. After selection and expansion, these cells are transferred back to the patient where they specifically target and eliminate tumour cells. T-cell priming can be achieved using dendritic cells or, as developed in Prof Mackensen's group, by immobilisation of the specific antibodies on beads. A phase I clinical study using dendritic cells resulted in a rapid tumour-specific cytotoxic response, an infiltration of T-cells into the tumour tissue and most notably a regression of metastasis. Future trends in immunotherapy will also aim to suppress co-inhibitory molecules and to implement this approach together with traditional tumour therapy, as well as conventional immunotherapy in a combinatorial cancer therapy.



Immortalised cortical cell line (CTXOA32); cultures are a mixed population of astrocytes (red) and neurones (green), in blue are nuclei (Source: ReNeuron)

Activation of endogenous mesenchymal stem cells for bone regeneration
Dr Andreas Schütz from Scil Technology in Martinsried and Prof Wolfgang Frieß from the Ludwig Maximilians University Munich collaborate to develop novel drug delivery systems for bone regeneration. Potential clinical applications comprise osteoplastic surgery, trauma and spinal fusion. The combination of suitable carrier material and bioactive growth factor molecule is required for efficient bone regeneration involving activation, proliferation and differentiation of mesenchymal stem cells followed by calcification and bone formation. Scil Technology has developed a technique to deliver a recombinant growth factor using highly porous, ceramic granules. The proprietary technology and unique material characteristics enable an adequate drug release. Advanced clinical pilot studies are underway on patients with periodontal diseases.

Stem cells *are relatively primitive cells that have the ability to continuously self-renew and are multipotent to give rise to more specialised cells of different lineages.*

Hematopoietic stem cells *are blood-forming stem cells that largely reside in the bone marrow.*

Mesenchymal stem cells *are derived from bone marrow and other tissue, such as umbilical cord and give rise to osteoblasts, chondrocytes, myocytes and adipocytes.*

Neural stem cells *reside in the central nervous system and can differentiate into neural tissue, such as neurons, oligodendrocytes and astrocytes.*

Transplantation of neural stem cells provides novel therapies for unmet medical needs

Dr Erik Miljan from ReNeuron (United Kingdom) presented the company's approach to target unmet medical needs. The heart of ReNeuron's technique uses a regulated overexpression system. The technique allows for the generation of stable, scaleable tissue-specific stem cell lines on a clinical grade. After transplantation these cells can replace damaged tissue in stroke, Parkinson's disease and diabetes patients. To overcome the challenge of packaging and delivering cells, cooperation with other Biotech companies has benefited ReNeuron, e.g. by using microcarriers or coating cells in alginate spheres. A Phase I clinical study is planned in stroke patients with ReNeuron's ReN001 cell line. This study will be pioneering in stem cell-based approaches for the treatment of major diseases of the central nervous system.

FOOD AND NUTRITION

The interaction of nutrition and health was the key topic of the 'Food and Nutrition' session. The focus was on novel bioactive ingredients, innovative products with health benefits, smart production processes as well as strategies towards a personalised nutrition. Technologies for the production of well-tasting food and current results in flavour research were highlighted in this context.

FOOD AND HEALTH

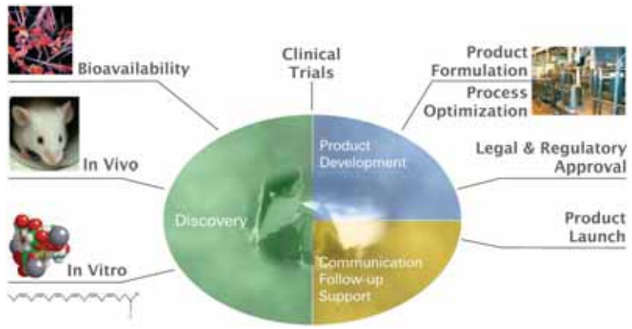
NUTRITION AS A BASIS FOR DISEASE PREVENTION

Changes in society such as an ageing population, increase in average weight and unhealthy lifestyle lead to a rise of chronic diseases, e.g. diabetes, cardiovascular diseases, osteoporosis and neurodegenerative diseases. In combination with increased health consciousness and consumer interest in wellness as well as disease prevention, opportunities open up for novel concepts to the food industry.

Hereby, one focus is set on disease prevention through a healthy diet. Many chronic diseases originating from metabolic imbalance can be targeted and prevented by nutrition – before medical care is required. Nutritional and medical prevention melt into each other and both disciplines will help to tackle health challenges particularly those concerned with an ageing population. In this the target groups differ: the pharma industry focuses on the unhealthy, the food industry on the healthy population driven by consumer pull.

Consumer demands and developments in society are identified by the food industry and targeted by the use of state-of-the-art approaches and technologies similar to those used in the pharma sector – molecular systems biology including biomarkers and 'omics' sciences.

The Product Development Pipeline for Healthy Foods (Source: Nestlé)



The strategy of the food industry hereby also shows similarities to the well proven research and product pipeline of the pharma industry during development, proof of effectiveness and production: in screening processes bioactive compounds are identified, selected, validated and tested in in vivo and clinical trials before product launch.

One of the challenges is to fulfil criteria such as flavour, taste and process ability while at the same time balancing the food composition by reducing components such as sugar, fat or lactose and by adding health-enhancing ingredients such as fibre, probiotic cultures or cholesterol-lowering compounds.

As one of the first corporates, Nestlé orientated itself towards Food and Health, regarding this sector as key driver of the future.
Prof Peter van Bladeren, Director of the Nestlé Research Center in Lausanne, presented insights on the development of health beneficial food by understanding and application of molecular approaches. Molecular sciences are used to identify functional ingredients such as bioactive proteins and to enhance their biological effect under physiological conditions.

Nevertheless, 'Functional Food' is one of the key words describing an ongoing trend: targeting physical weaknesses with the appropriate functional ingredients. Besides established health ingredients as vitamins, calcium, iodine and omega-3 fatty acids, novel nutraceuticals are in the pipeline. They specifically address the key areas of weight management, enhancement of physical and mental health, performance, healthy ageing and also addressing specific indications such as osteoporosis, hypertension or memory deficiency.

PERSONALISED NUTRITION

THE EFFECT OF GENETIC VARIATIONS ON METABOLISM

In line with the trend towards personalised medicine, food science is learning more and more about molecular interactions between genetic disposition, nutrition and health. This novel field of Nutrigenomics enables dietary advice and the customised development of nutritional products and supplements that fit individual genetic profiles and other factors such as age and lifestyle. In contrast to pharma, the food industry hereby addresses the healthy consumer wishing to improve his health and wellbeing as well as to prevent disease onset.

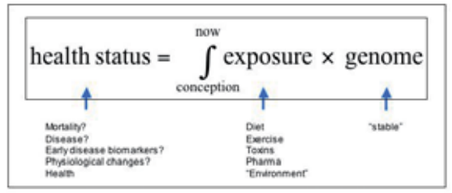
Even small differences in the individual genetic make-up can affect the activity of metabolic key enzymes. Specific variations of single nucleotides, so called SNPs (Single Nucleotide Polymorphisms), can lead to an altered enzyme structure and activity, e.g. in the gene of lactase resulting in lactose intolerance. SNPs play a role in the uptake of essential nutrients such as vitamins and minerals as well as in the underlying metabolism of chronic diseases such as diabetes and cardiovascular diseases.

Complexity of metabolism and personal health

Perspectives on personalised nutrition in research and industrial applications were presented by **Dr Ben van Ommen** from the Dutch research organisation TNO Quality of Life. Nutrigenomics as a novel field of science is still at the state of infancy, not yet sufficiently answering the question of how much of our health depends on the genome and how much on environmental factors such as nutrition and lifestyle.
Two major challenges need to be tackled in the future: the complexity of the metabolism with its network of biochemical pathways itself on the one hand and, on the other hand, the uniqueness of each individual metabolism. One research focus is hereby set on revealing the many little differences related to the early process of disease onset and designing 'personalised nutrition' that subtly interferes with the overarching metabolic processes in order to prevent disease onset. A further aspect is to take the little inter-individual differences that determine optimal health on a personal basis into account.

Individual nutrigenetic profile

Identifying health risk carried in the individual genome is no longer a scenario of the future. **Dr Rosalynn Gill-Garrison**, CSO of the US company Sciona, presented the latest consumer-focused strategies for personalised health and nutrition. SCIONA commercialises genetic tests and offers personalised nutrition recommendations based on an individual's unique genetic profile. The focus is set on genes



The suggested algorithm visualises the complexity and the yet not completely known influence of lifestyle and diet on disease outbreak and the processes of disease onset. (Source: Dr van Ommen, TNO)

that have an impact on an individual's response to diet, lifestyle and/or nutritional supplementation. Besides screens for nutrient uptake (e.g. calcium or folic acid) and for food intolerance (e.g. lactose intolerance), SNP variations can be determined in more complex relationships. Examples are genetically underlying causes of inflammatory processes which often can culminate into chronic diseases such as arthritis, inflammatory bowel diseases or cardiac diseases.
But, is there a market for personalised nutrition at all? The individual may not yet benefit from a tailor-made diet, but a huge variety of nutrient supplements are already available on the market in order to meet personal nutritional needs for groups such as the elderly, women, children, smokers, sportsmen, people with lactose or gluten intolerance and many others.

HEALTH INGREDIENTS

FUNCTIONAL ADDITITIVES AND RAW MATERIALS

Functional foods and nutraceuticals are already established on the market. Examples are probiotics and prebiotics in dairy products to create a healthy gut micro flora and improved immuno-resistance, enrichment with vitamin and minerals, fat exchange with unsaturated fatty acids, plant phytosterols or omega-3 fats in order to lower blood cholesterol or secondary plant metabolites in order to decrease cancer risk.

Probiotics and dairy products
The market for probiotics in dairy products has grown in the last years as indicated e.g. in significant growth of turnover from 75 million Euro in 1996 to 485 million Euro in Germany alone. In this competitive field, new generations of probiotics with additional health benefits are achieved by the use of molecular biotechnology tools such as 'omics' sciences, genotyping, reverse genetic engineering and high-throughput screening. Improved processes and delivery strategies such as encapsulation bring the microbes to the site of action remaining in a state of high vitality and biofunctionality.

Prof Tiina Mattila-Sandholm, Senior Vice President R&D at Valio, Finland showed new trends in functional milk products towards products beyond well-established healthy dairy products (e.g. lactose-reduced milk or dairy products with probiotics, calcium and vitamins). The major trends meet consumers' lifestyle and social needs such as achieving more on a physical and mental level, managing weight and fitness, healthy ageing and improving well-being during stress. Novel potential could lie in products such as 'brain-milk' which improves cognitive functions, 'masai milk' with an effect on growth, 'satiety milk' to counter appetite and a 'nightmilk' with calming peptides.

Inulin and Oligofructose
The health benefits of inulin and oligofructose were presented by **Dr Anne Franck** from ORAFTI, Belgium. Inulin obtained from chicories is enzymatically degraded into oligofructose. Inulin and oligofructose are well suited as health additives as they combine proven health benefits with little own taste. Amongst the proven health benefits are increased calcium absorption and bone health, prebiotic effect by selective stimulation of bifidobacteria for health of the digestive system and improved body resistance as well as the application as dietary fibre. Food products with inulin showed minimal impact on blood sugar and furthermore better control of satiety and food intake whilst at the same time being low in calories. Inulin and oligofructose are already applied in bread, cereals, bread spreads and chocolates.

Functional raw materials: grains
Instead of adding health beneficial ingredients, CSIRO in Australia works on the development of functional raw materials. Dr Bruce Lee, Director of the Food Futures Flagship, presented grains with half the starch content and at the same time a threefold increase in amylose within the starch. Amylose shows low glycaemic response which provides benefits in the area of bowel health, diabetes and obesity. Furthermore, amylose-enriched grains show potential to prevent colorectal cancer. A non-genetic modified barley variety is already available on the market. However in parallel to classical breeding, genetic technologies are used to achieve desired attributes. In experiments, the amylose content could be increased threefold by RNAi gene silencing. This approach is being further developed to come up with a non-GM mechanism for commercialisation.

FLAVOUR AND TASTE

FLAVOUR FORMULATION IN FOODS

Besides all health aspects, taste is the priority selection criterion for the consumer. With growing interest in health-beneficial products, the food industry is being challenged to preserve quality of taste and flavour although the composition of food is altered e.g. by the reduction of salt, fat or sugar.

Linkage between genes, receptors and flavour perception
Prof Hanns Hatt from the Department of Cellphysiology, Ruhr-University Bochum, presented the latest scientific insights revealing a strong link between genetic blueprint and flavour sensing. In general, three components comprise ‘flavour’ – taste, smell and the ‘trigeminal senses’.

The new high-temperature liquid chromatography method developed by Symrise allows researchers to separate aroma molecules and flavouring components from solutions and thus enables the simultaneous technical detection and human taste evaluation. (Symrise LC-TASTE™ Technology, Courtesy of Symrise)

Determining the sensoric threshold of fractions of food extracts (Source: Prof Thomas Hofmann, TU München)

For the sense of taste it is meanwhile proven that the cell ability to taste is not restricted to specific taste qualities on dedicated parts of the tongue but each taste receptor cell can only detect one quality of taste e.g. sweet or sour.
Furthermore, outstanding findings in the field of sense of smell revealed that in humans a family of 350 genes encodes for receptor proteins involved in smelling. The group of Prof Hatt elucidated about ten of those genes including the respective smell attributes. However, these receptor types are not highly specific and can be stimulated by similar molecules as well as inhibited by antagonistic molecules. This means the overall impression of a fragrance is always a combination of inhibiting and stimulating effects. Additionally, flavour components can lead to excitation of the newly revealed transmembrane channels of the Nervus trigeminus which innervates the upper and lower jaw as well as the eye region. These transmembrane receptor channels could be shown to function as temperature and chemosensors, thus taste sensations are perceived with a temperature aspect, e.g. coolness to mint or hotness to chilli. As only a small, dedicated temperature range is sensed, imaginable future food applications could stimulate e.g. the specific channel for 20-30°C and so create a sensation of warmth and well-being during the winter.

In a nutshell, the perception of taste and smell not only depends on cultural learnings, the contained aromas and flavours and their structural biochemistry but also on the individual genetic blueprint of receptors.

Prof Thomas Hofmann from the Institute of Food Chemistry and Molecular Sensory at the Technische Universität München presented new insights on the biochemistry of off-taste components and novel strategies for well-tasting products. Combining human psychophysics with analytical chemistry opens the possibility to identify and evaluate taste-active compounds contributing to the overall flavour of foods. Key taste compounds, their molecular structure and their tissue specific accumulation in plants can be identified. One example shown is the higher accumulation of

bitter compounds in carrot peel or varying bitterness in different carrot varieties. This information helps to improve taste and to avoid off-taste at a very early stage of the value chain via processing and selective breeding. Furthermore, experiments showed that biochemical interaction of flavour compounds with the respective receptor and thus final flavour sensation depends on the stereochemical structure. So for example, SAR (Structure Activity Relationship) studies on the taste-enhancing compound alapyridaine and its synthesised enantiomers revealed new lead molecules which open the possibility to improve the taste quality e.g. of sodium or glutamate reduced food products.
Dr Frank Ullrich, Director Global Research at Kraft Foods, presented applications of flavour research at Kraft Foods using the examples of instant coffee and chocolate. In this context, he showed a new method to assess the sensory impact of aroma fractions and/or single potent aroma compounds which could be used to enhance desired aroma aspects or to create new taste and aroma attributes by adding the respective naturally gained aroma component.

INDUSTRIAL BIOTECHNOLOGY

The trend towards an increasing use of biotech processes in the chemical industry was the focus of the 'Industrial Biotechnology' session. Biobased materials, novel technologies in biocatalysis as well as approaches for biorefinery concepts were discussed. The presentations highlighted also the perspective of the use of biomass and lignocellulosic feedstocks for the production of bulk chemicals.

PERSPECTIVES FOR INDUSTRIAL BIOTECHNOLOGY

SEIZING OPPORTUNITIES IN THE CHEMICAL INDUSTRY

White or industrial biotechnology, with a worldwide market of 50 billion Euro, has become an essential part of our daily life. Examples extend from consumer, food and health products to the supply with biofuels. The motor behind industrial biotechnology is the economy itself as biotech processes become more cost-effective and have a technological advantage to conventional chemical processes. The biotech approach makes processes possible that otherwise can only be achieved with difficulty or not at all by classical chemical methods. Furthermore, industrial manufacturing processes are often faster, more efficient and more sustainable. Therefore, industrial biotechnology gives companies the opportunity to realise benefits throughout the value chain.

White biotechnology will occupy up to 10 – 20 % of the entire chemical market by 2010. (Source: McKinsey & Company)

Biotech processes for bulk products

Current interest in industrial biotechnology is focused on fermentation and biocatalysis as well as replacing processes based on fossil resources with biobased feedstock. An example of the industrial use of renewable resources was given by **Dr Alfred Oberholz**, Deputy Chairman of the Management Board of Degussa, for the antiknock agent ETBE. The fuel additive was previously obtained form methanol, however, bioethanol has replaced it in ETBE on an industrial scale. Thus white biotechnology provides the opportunity to develop novel processes for the sustainable production of bulk chemicals independent of petrochemical resources. Degussa aims to base 15-20% of production on renewable resources by 2015, showing the significance of biotechnology for the future of the chemical industry.

Establishing a biotech-based value chain

The growing market for biofuels is of particular interest as it opens up new business opportunities for already well-established companies and the agro industry. Political endeavours in Europe are being made for biofuels to substitute 5.75% of the total amount of trans-

portation fuels by 2010 and the US aims to replace 15% of annual gasoline consumption by renewable and alternative fuels by 2017. The increased market demand for biofuels has enriched the product portfolio of companies as shown by Dr Andre Koltermann from Südchemie and Prof Markwart Kunz from Südzucker. Bioethanol production has become of strategic importance for both companies, as established technologies can directly be applied for the generation of biofuel. Südchemie accomplished this by using their expertise in adsorbents and catalysts, Südzucker by using their long-term expertise in fermentation technology to produce bioethanol. In both examples accumulated by-products are converted into products additionally contributing to the value chain of the process. In the near future not single conversions of raw materials but integrated biorefineries will play a key role in transforming crops and agricultural waste into multiple intermediate and end products for the energy and consumer market.

Bioethanol plant
(Source: CropEnergies)

TECHNOLOGIES

CREATING A COMPETITIVE ADVANTAGE

Biotechnology-based processes have the chance to replace conventional processes depending on their superior cost-to-performance ratio. The implementation of recent discoveries in molecular biology, 'omics' technologies and fermentation processing has significantly contributed to making industrial biotech applications economically competitive. In this respect the optimisation of biocatalytic processes is of particular commercial interest for many companies. Various tools for screening, metabolic engineering and process engineering are available to further increase the efficiency of biological applications.

High-throughput screening for new biocatalysts

The search for novel biocatalysts has led to the development of high-throughput approaches. Dr Mark Struhalla from c-LEcta presented the company's cluster screening method to identify highly active enzymes. The approach allows for the simultaneous screening of thousands of genomes of different enzyme classes (of up to 107 variants per day) in a cost-effective way. Mutation based engineering of proteins will not only help to optimise existing enzyme properties like temperature or solvent resistance, stability or specificity, but moreover it will make it possible to generate entirely new enzyme characteristics. In collaboration with Sloning Biotech a mutational library has been designed to screen e.g. for enzyme variants with new substrate specificities expanding the substrate spectra that could be used for industrial applications.

Metabolic engineering for high efficiency production

Metabolic design makes biotech based processes more efficient as shown by **Dr Oliver May** from the DSM for riboflavin production, an ingredient in food, feed and pharma products. Riboflavin production and crystallisation was significantly increased by targeted modification of the synthesis pathway in an optimised strain. Moreover, economical and ecological benefits go hand in hand: the biotechnological process requires reduced synthesis steps and no environmentally harmful substances or processing compared to chemical synthesis. As shown e.g. for the production of antibiotics, biotech based processes save 65% of energy and materials and reduce the costs by 50% compared to conventional synthesis.

Application of industrial biotechnology in our daily life. (Source: Degussa, CropEnergies, Henkel)

Gas-inducing millilitre-scale bioreactor system with 48 stirred-tank reactors arranged in a bioreaction block (Source: Prof Weuster-Botz, TU München)

Process engineering for faster R&D periods

Increasing R&D efficiency through shortened development cycles and optimised industrial fermentation processes are essential to speed up time-to-market. Advances in reaction engineering provide new tools to overcome the obstacle of time- and labour-consuming experiments by designing miniaturised and automated bioreactors. As shown by **Prof Dirk Weuster-Botz** from the TU München, the design of a block with multiple bioreactors allows for the simultaneous investigation and optimization of complex reaction processes. With the novel high-throughput bioreactor system, rapid, cost-saving and reproducible results can be achieved in order to increase the efficiency of industrial fermentation processes.

CHALLENGES AND FUTURE TRENDS

USING WOOD AND GRASS FOR BIOBASED PRODUCTS

Industrial applications of biotechnology have come within reach for biofuels, pharmaceutical intermediates, supplements in food and cosmetic industry as well as chemical products. The business interest is focused on high-volume markets with the potential to decrease production costs, increase yields and quality of products as well as the prospect of developing novel products. From a financial point of view industrial biotechnology is particularly interesting as it does not require high capital investments such as red biotechnology and can take advantage of already established technology and management platforms.
As stated by Hilmar Platz from Kayenburg AG,

Prof Martin Faulstich *chaired the session on Bioprocess Engineering, Materials and Products*

investments of 10 million Euro are already sufficient to set up substantial technology and marketable product portfolios.

Lignocellulose as future resource for biobased products

Industrial biotech applications will require large amounts of biomass. This offers new perspectives for the agro industry to cover in future not only the demand for food and feed but also for a wide range of other industrial applications. The search for sustainable and sufficient sources has drawn considerable attention to the usage of ubiquitous available plant material, the lignocellulose. Cell membranes represent 85% of the biomass and contain three polymers that can be converted to products: examples are glucose in cellulose for biofuel, xylose in hemicellulose for solvents and phenoles in lignin for adhesives.

In order to make use of the abundant plant material, new synthesis and processing strategies need to be developed. A lignin-based production line was presented by Prof Thomas Hirth from the Fraunhofer Institute for Chemical Technology (Pfinztal). Products from lignocellulose based raw material reach far beyond biopolymers and bioethanols and may also find application in the food, textile, automotive, health and hygiene industries. Although the future is undisputable, the economic usage of lignocellulose is still in a very early state of development. This is mainly due to costly and complex processes for the isolation, separation and extraction of the lignocellulose compounds. Future work will focus on tackling this challenge and making plants available as resource for multiple products.

Prof Bärbel Hahn-Hägerdahl from Lund University (Sweden) presented new strains of baker's yeast with the ability to ferment all lignocellulose-derived sugars. An example given is the use of lignocellulose raw material for bioethanol production, but it could also be applied for the production of pharmaceuticals, food and chemicals. Benchmarks that determine the industrial use of the yeast strains are process water economy, inhibitor tolerance, ethanol yield and specific ethanol productivity. In order to identify fermenting strains with tolerance to fermentation inhibitors and of high productivity, metabolic engineering helped to generate industrially suitable yeast strains.

Renewable resources for biobased products

Ecovio® is a biodegradable plastic developed from BASF based on renewable resources

PRODUCTS AND MATERIALS

CHALLENGING THE BIOTECH TOOLBOX TO GENERATE NEW BIOMATERIALS

Biotech based production of polymers is a promising innovative field to which to apply biocatalytic processes. For many years research has focused on the development of biodegradable polymers and now products are on the market based on renewable materials (e.g. starch, cellulose), generated by biotechnological processes (e.g. polylactic acid, PLA and polyhydroxybutyrate, PHB) or biodegradable polymers chemically synthesised (e.g. PHB). However, the production of biopolymers on an industrial scale is still in its infancy due to high production costs and undesirable material characteristics such as low stability. The challenge of future research and process development will focus on manipulating the polymer content of plants as well as improving extraction processes. Many global companies have already implemented biopolymers within their product portfolio, but the application for bulk products such as packaging materials and foils requires cost-effective processes.

Using nature as a model for the chemical synthesis of biodegradable polymers

Originally PHB is a natural compound produced by some bacteria as a carbon energy reserve. The product received the particular attention of the chemical industry since it shows similar properties as polypropylene, but with the major advantage that it is biod gradable. Although PHB can be produced by fermentation, this process is today still costly and economically not competitive compared to petrochemically produced polypropylene. Considering biological pathways, **Dr Gerrit Luinstra** from BASF AG and Prof Bernhard Rieger from the University of Ulm imitated the process by using classical chemical synthesis. For their discoveries the two scientists received the Philip Morris Award in 2006. The novel strategy for the synthesis of PHB uses a designed catalyst based on silicon, cobalt and nitrogen. The synthetically produced biopolymer has characteristics of biologically produced PHB, such as biodegradability. While biologically produced PHB is of rather low stability, the properties of the synthetically produced PHB can be adjusted according to the demand: depending on the composition of the catalyst the PHB has firm or soft characteristics and can be used for multiple products such as bags, cups, automotive parts or nappies. Most notably, PHB generated by chemical synthesis can eco-nomically compete with polypropylene and could in the long-term replace it in many applications.

Screening polysaccharide producing strains for industrial applications

An approach to increasing the yield and desired properties of biopolymers is to screen for new biopolymer sources. Degussa and BRAIN, represented by Dr Jürgen Eck and Dr Volker Sieber respectively, collaborate to identify novel polysaccharides of biological origin. In a primary screening approach carried out at BRAIN, strain and habitat collections were searched for potential microbes producing exopolysaccharides with specified biopolymer characteristics. In a second screening step performed at Degussa the suitability of the generated polysaccharides was further characterised for their additional industrial application in oil recovery and the concrete industry. After determining the flocculation and viscoelastic properties as well as the molecular weight and the sugar content, small scale fermentations were carried out to select appropriate strains. Strains with high potential for industrial applications were identified and further chemical structure analysis is currently underway.

FIRST TRANSATLANTIC EU-PROJECT

TRANSBIO BUILDING A BRIDGE TO NORTH AMERICA

North America is the world leading market in biotechnology and an attractive partner for biotech related companies of any step of the value chain. An exceptional opportunity for collaborations beyond traditional processes is offered by the transatlantic bridging activities of the EU Project TRANSBIO which brings together specifically pre-matched partners from Europe, Massachusetts and Quebec and in addition provides assisting services such as coaching and facilitating of collaboration.

Dr Mark Trusheim, former President of the Massachusetts Biotechnology Council and partner in the EU Project TRANSBIO, presented trends in the North American biotech and medical device industry, in particular for Massachusetts. Specific areas of interest are set on healthcare, in particular on diagnostics and therapeutics in the areas of diabetes, cardiovascular diseases and dermatology, agricultural techniques such as genetic engineering and with increasing importance of advanced molecular breeding tools and on biofuels.

As there is an increasing need to fill product pipelines, investments tend to be done already in early development stages in order to secure technologies. Furthermore, common strategy of the industry is to accelerate success by linking with top science worldwide whereas global cooperation pushes away competition with one-winner approaches. This situation opens up excellent prospects for Bavarian companies to access Massachusetts with its extraordinary density of more than 250 Biotech companies and global pharma headquarters as well as well-known universities such as Harvard University, Massachusetts Institute of Technology (MIT) and University of Massachusetts as well as subsequently the North-American market.

DRUG DEVELOPMENT IN INDIA

NEW STRATEGIES BEYOND BULK DRUGS AND FORMULATION PRODUCTION

Focus on generics and processes
The Indian pharmaceutical industry has evolved dramatically in recent decades. Before 1970, there was no indigenous Indian pharmaceutical industry and the market was dominated by multinational companies. In 1990, a generic drug industry was established in India with the main focus on reverse engineering. This was the basis for innovations and increasing know-how in associated technology sectors such as process chemistry. In the last 15 years, Indian pharmaceutical companies such as Ranbaxy and Dr Reddy's Laboratories have emerged on the global generic market. During this time, cGMP-based manufacturing plants have been established and with more than 80 FDA-approved cGMP facilities India today possesses the highest number outside the US.

Start of own Drug Discovery programmes
Today, under the influence of a new patent regime with the recognition of product patents, India's pharma industry is starting its own drug discovery programmes and seeking for technology partnerships with Big Pharma as well as with biotech companies. **Dr Ramani Aiyer**, Vice President of India's No. 4 pharmaceutical company Nicholas Piramal, highlighted at the 'Forum Life Science' their strategy in drug discovery showing an example of the current paradigm shift from processes to products at Indian pharma companies.

In addition to formulation production for the domestic market and manufacturing services for international clients, the drug discovery division at Nicholas Piramal with its R&D activities and its objective to develop new drugs

for the global market has become more and more important. To identify new lead substances, Nicholas Piramal's own compound libraries will be tested against relevant disease targets which have been already well defined. Natural resources such as microbes and plant extracts from different geographical regions in India or herbal products used already in traditional Indian food and medicine are sources for lead discovery and the drug development process. Today, drug discovery at Nicholas Piramal comprises 12 projects in preclinical and clinical phases I/II for therapeutic areas such as oncology, inflammation and infectious diseases.

Indian pharma market:
8 billion US $ turnover
8% of worldwide volume
13% growth p.a. of domestic market
Indian biotech industry:
340 companies
2 billion US $ revenues
about 35% growth p.a.
expected revenues in 2010: 5 billion US $
Clusters: Bangalore and Hyderabad

AUSTRALIA'S FLAGSHIPS

ADDRESSING NATIONAL RESEARCH PRIORITIES

Over the past 4 years, Australia has established six National Research Flagships as large-scale multidisciplinary research partnerships to tackle major challenges in areas such as water, food, health, energy or climate. Initiated by the CSIRO (Commonwealth Scientific and Industrial Research Organisation), the Flagship programme is one of the largest research endeavours ever undertaken in Australia. **Dr Bruce Lee**, Director of the 'Food Futures' Flagship described the goal to transform the competitiveness of Australia's agrifood sector through new technologies and add 3 billion A$ value until 2013. The highly interdisciplinary approach and intensive collaborative research along the whole value chain will be key factors for the success of the Flagships. For example, the Food Futures Flagship comprises disciplines such as tissue engineering, stem cells, biosensors, food processing and agriculture.

TOP INSTITUTES IN THE NETHERLANDS:

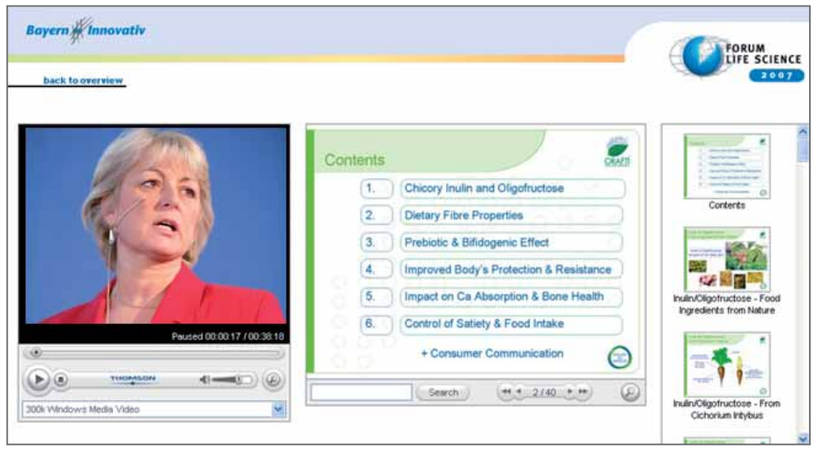
DUTCH GOVERNMENT ENFORCES INNOVATIVE RESEARCH AND DEVELOPMENT BY PUBLIC PRIVATE PARTNERSHIP

As a response to the increased complexity and multidisciplinary of research in different technological fields and the growing demand for financial resources and experts, the Dutch government initiated the concept of Top Institutes (TI) bringing together stakeholders from academia and industry. Outstanding examples are the Top Institute Food and Nutrition focusing on research and development of new, healthy foods with regard to major health concern such as obesity and metabolic syndrome and the Top Institute Pharma with the goal to accelerate the time-to-market and reduce the cost-to-patient of pharmaceutical products for a more efficient drug discovery process. Both institutes were founded as a public private partnership with funding from three sources: academia, industry and the dutch government. TI Pharma presented by **Prof Daan Crommelin** is pre-competitive and includes drug discovery processes from target identification up to proof of concept studies in clinical phases I/IIa, while later stages of the drug discovery process such as product development are beyond the institute's mission. Increased efficiency in the drug discovery process shall be achieved by higher structural collaboration between industrial and research teams based on an interactive platform accompanied by training courses in drug discovery, GMP production and business management. The concept is less profit orientated but rather aims to conduct ground-breaking and cross-disciplinary research and is devoted to priority medicines project of the World Health Organization.

CONGRESS TV 'FORUM LIFE SCIENCE 2007'

Presentations of the 'Forum Life Science' are available in the internet free of charge

www.bayern-innovativ.de/congress-TV



OUTLOOK

The biannual congress ‘Forum Life Science’ is a major platform of the international Network ‘Life Science Bavaria’.

The Network ‘Life Science Bavaria’ brings together partners from different disciplines and industries, joining a broad range of technology and application sectors within the interdisciplinary Life Science field.
It offers access to new technologies and facilitates contact between cooperation partners for the realisation of innovations.

Future activities of the network will comprise, e.g.

- Joint Stand ‘Bayern Innovativ’ at **Biotechnica**, Hannover, 9 – 11 October 2007
- **Transbio** Brokerage Event, Boston, 6 – 7 November 2007
- Panel Discussion **‘Drug Innovation’**, Würzburg, 19 November 2007
- Cooperation Forum **‘Drug Development’**, Würzburg, 20 November 2007
- Joint Stand ‘Bayern Innovativ’ at **Analytica**, München, 1 – 4 April 2008

Further information about the Network ‘Life Science Bavaria’ is available on:
www.lifescience.de

MARK YOUR CALENDAR FOR THE NEXT

FORUM LIFE SCIENCE 2009

International Congress and Exhibition

18-19 February 2009
Technische Universität München, Garching

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