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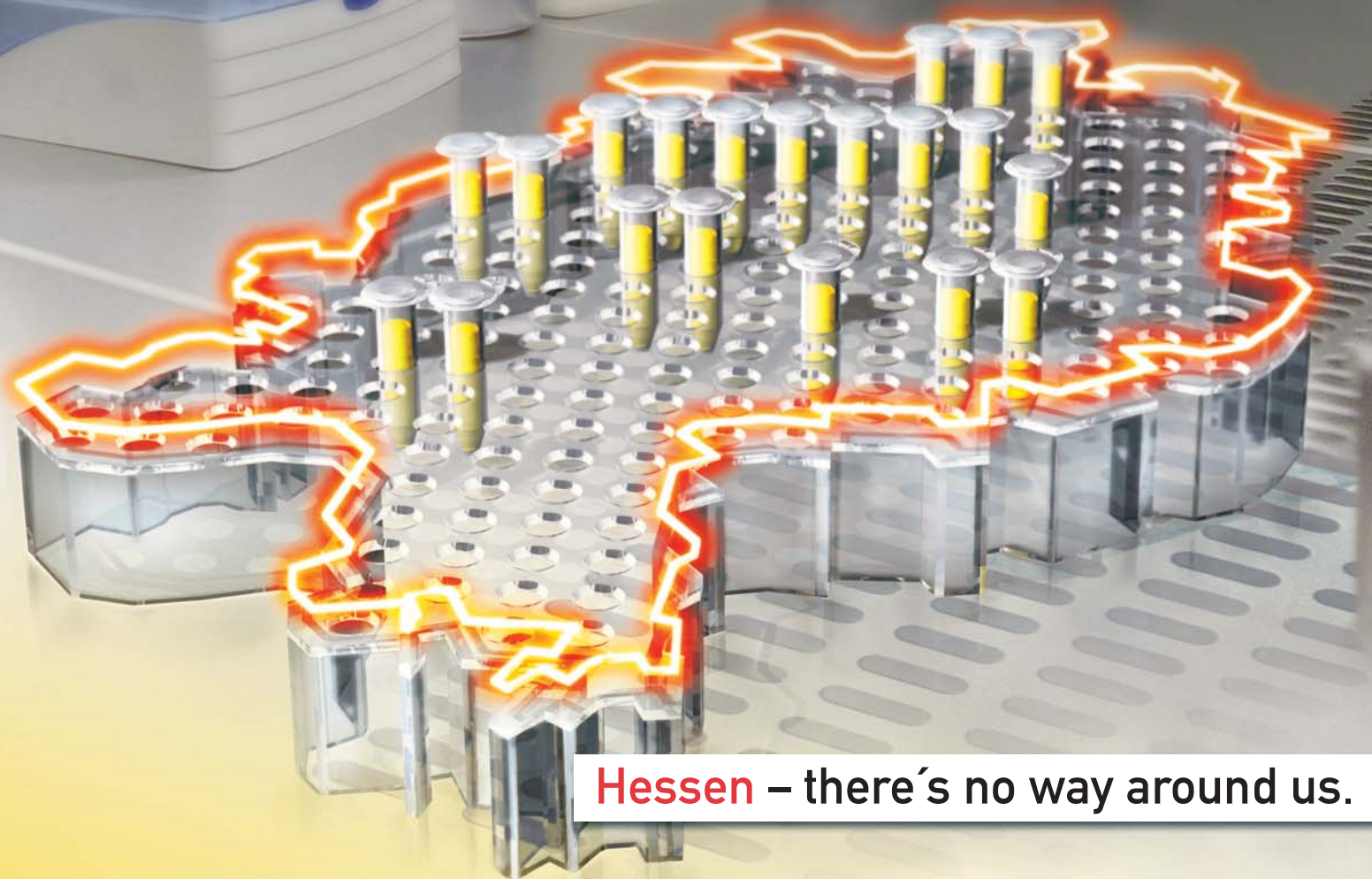
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HESSEN



Room for Innovations

Hessen - location for biotechnology



Hessen – there's no way around us.

Hessen

Biotech

Aktionslinie Hessen-Biotech, a project of the

Hessian Ministry of Economy, Transport, Urban and Regional Development

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Give impulses, pave the way – room for innovations in **Hessen, location for biotechnology**

The year is 1609: People use biotechnology to make wine or to bake bread, although the term itself does not even exist yet. They live in fear of witches and try to cure themselves with miraculous potions. Not exactly the best conditions to pave the way for two sciences. Still, it is in this very year that Moritz, landgrave of Hessen-Kassel, at Marburg University, establishes the first chair in the world for "chemiatri", predecessor to modern pharmacology and chemistry - an early example of promotion of economic development.

"Looking back on a long-standing tradition as a chemistry and pharmaceutical location," says Hessian Minister of Economics Dieter Posch, "we recognize a lot that still characterizes Hessen today: an excellent research landscape, commitment to promoting young researchers, and advancement of innovative technologies. These and other factors have contributed to Hessen being one of the leading biotechnology locations in Europe."

Course set for growth

Be it workforce or revenues - the industry's indicators are pointing up, as demonstrated by a 2009 study. A total of 225 enterprises generated revenues of over five billion Euros, with the majority expecting a continued growth in Hessen. As an international IT and traffic hub, it does not only offer excellent infrastructure, but also a high availability of skilled personnel and close networking of science and industry.

In order to further enhance business conditions and to advance development of this future-oriented sector, the federal state gives many impulses: The State Offensive for



“With its unsurpassed opportunities, Hessen as a location for biotechnology offers the industry’s stakeholders room for innovation. In order to foster their development and implementation, regional politics is constantly striving to give new impulses and pave the way for future growth.”

Dieter Posch | Hessian Minister of Economics,
Transport, Urban and Regional Development
Prof. Dr. Theo Dingermann |
Official Biotechnology Representative, Hessen

the Development of Scientific and Economic Excellence (LOEWE), for example, facilitates outstanding research activities. The start-up initiative Science4Life on the other hand supports budding life science companies. “In all our measures we attach great importance to the assessment by industry experts,” stresses minister Posch. “This is embodied, amongst others, in the unique institution of the Hessen Official Biotechnology Representative.” In this capacity, Prof. Dr. Theo Dingermann represents the future technology and makes his expertise available.

Explaining the potential of this key technology, the Frankfurt professor of pharmacology states that first of all, biotechnology is of the utmost economic importance. “The sector is going to expand, that is beyond question. In the future it will be next to impossible to identify fields where biotechnology is not applied - whether in the production of pharmaceuticals or consumer products, the food sector or medical diagnostics. When it comes to environmental protection, biotechnology is a showpiece technology.”

Crucial for this are advances in white biotechnology, i. e. its application in industrial production. Accordingly, com-

panies’ revenues in this field of application in Hessen have risen to over ten percent. While the contributions of green biotechnology - plant biotechnology and food technology - are somewhat smaller, traditionally one colour dominates the industry in Hessen: red. More than 80 percent of Hessian biotechnology revenues are generated in the medical field, especially in drug production. Taking Germany as a whole, Hessen supplies one third of overall manufacturing capacity in this area, making it a location of biotechnological production.

Writing success stories

Nonetheless, the sector is characterized by a balanced diversification into the different fields of activity. From research and development over production and services to marketing - the complete value creation chain is represented in Hessen. The companies’ structures are as multifaceted as their focus of activity. Besides many small enterprises that are mainly active in research, the state is characterized by a large number of companies that are active both in research and production. These unique characteristics prepare the ground for close networking: both among the companies themselves as well as with noted universities and research institutes that are available as cooperation partners in immediate proximity.

The Biotechnology Representative Professor Dingermann sums up: “Hessen offers stakeholders good conditions to write their individual success stories.” He is joined by minister Posch: “We give researchers and entrepreneurial personalities room for their innovations. Because they are the ones who breathe life into Hessen as a centre of biotechnology and they exemplify the diversity and the innovative power of the Federal State.”

Uniquely

"From the viewpoint of evolutionary biology, insects are clearly the most successful group. To me, as a researcher, their tremendous diversity makes them unique."

Prof. Dr. Andreas Vilcinskis | Acting Director of the Institute for Phytopathology and Applied Zoology, Gießen University

Uniquely successful

- learning from insects

Prof. Dr. Andreas Vilcinskis shares his workplace with a "very big bully" - and he is even downright thrilled about it. His enthusiasm for the rapidly spreading Asian lady beetle is based on purely scientific interest, though. Prof. Vilcinskis is an entomologist, meaning that his research at Gießen's Liebig-University is in the area of applied insect science. His passion: insect biotechnology, still widely unknown in this country but holding future promise.

These animals may be very small, and for lovers of cuddly toys they need a lot of getting used to - but already as a little boy Vilcinskis was enthusiastic about insects. Today, he is Acting Director of the Institute for Phytopathology and Applied Zoology at Gießen University and has turned this fondness into his profession. With more than half a million of species described, insects exhibit an enormous diversity, from the viewpoint of evolutionary biology, they are by far the most successful organisms on the planet. "This species diversity manifests itself also at the molecular level," explains Vilcinskis. "Hence, this group is ideal for the search for new molecules."

The entomologist is turning to the insect realm for answers to many kinds of problems in medicine, plant protection and

On the advance: insect biotechnology

The fledgling discipline of insect biotechnology approaches the diverse insect world with biotechnological methods. At the molecular level it investigates e. g. new active ingredients for medicine, substances for agriculture or for industrial production.

Given its numerous potential fields of application it is seen as a point of intersection between green, red and white biotechnology. In Asia, insect biotechnology has a long tradition: For around 5,000 years, the caterpillars of the silkworm have been used for silk production.

A home for bugs: In Gießen University's laboratory scientists are breeding insects for their work.



Different from indigenous lady beetles, their Asian relative's surrounding is free of bacteria (on the right).

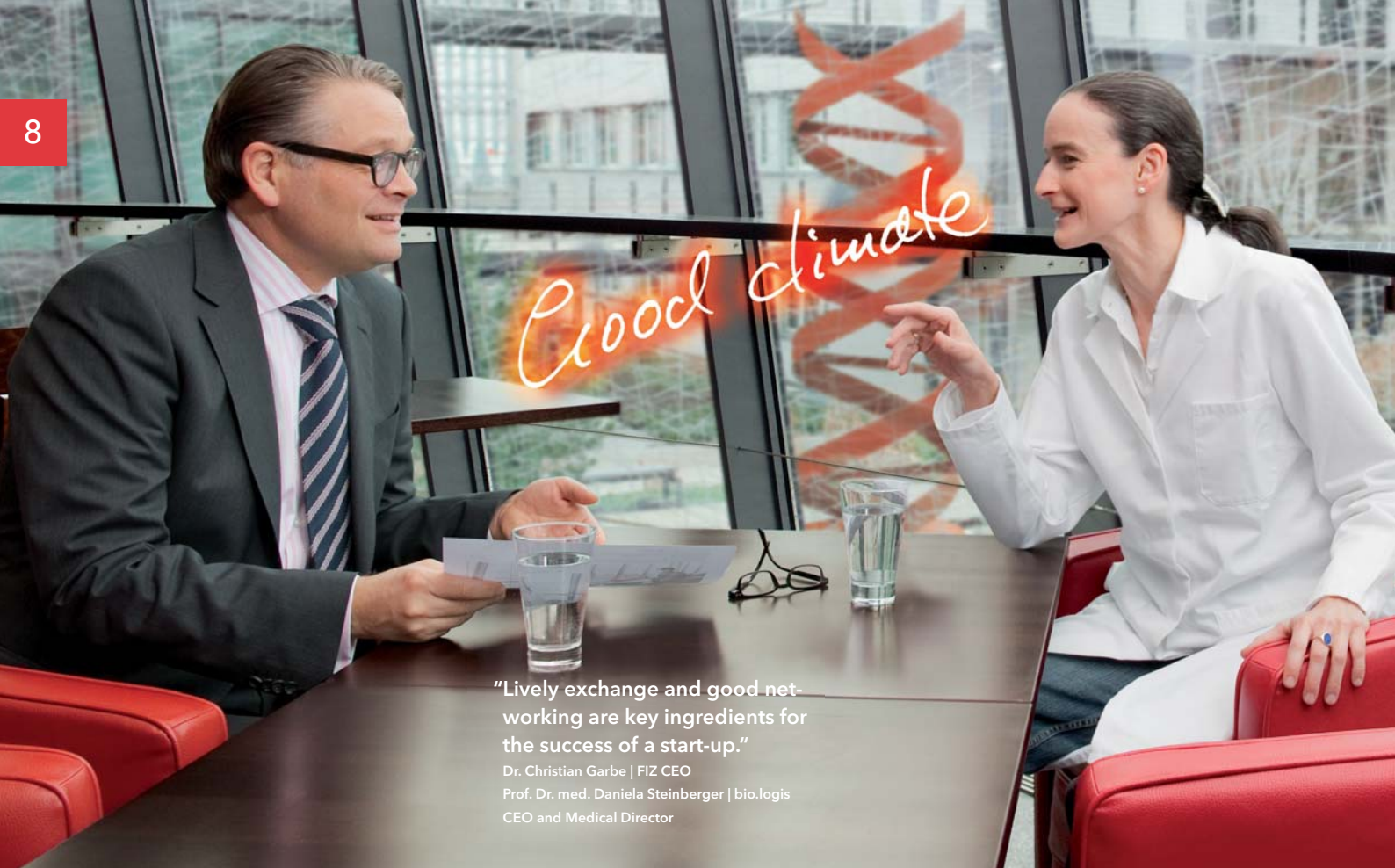


industry. His broad knowledge helps him to choose the relevant species, technological advances help to realize his projects. These hold so much promise that a new Fraunhofer project group "Bioresources" is being established at Gießen University. Supported by Hessen's LOEWE programme and directed by Prof. Vilcinskis, this group is to systematically develop and exploit insect biotechnology's potential. Vilcinskis states: "We are the only ones to cover the entire value creation chain in this area, to try and turn research results into applications."

Applications in plant protection have progressed far. In wax moth larvae the researchers found a peptide, i. e. a small protein molecule that protects very specifically against fungi. The task was to learn from such an efficient immune system: At first the Gießen scientists transferred the gene responsible for the production of the peptide Gallerimycin into tobacco plants, then, together with another insect gene coding for the peptide Metchnikowin, into barley. The latter peptide confers resistance against fungi that harm the plant without inhibiting fungi that are beneficial to the plant. Vilcinskis appears thrilled: "That is spectacular."

Besides agriculture, wax moths are also interesting for medical applications, although they are not the only bioresource by far. In fact, the path to new antibiotics occasionally leads the researcher into a slurry tank. The only animal living and feeding here is the rat-tailed maggot. Obviously, it possesses an extraordinary immune system, and indeed entomologists have hit upon different new molecules that could be a starting point for the development of antibiotics.

Similar expectations are placed in a small roommate at Gießen University: the Asian lady beetle. According to Vilcinskis, it has become a "really big bully", because it is spreading world-wide and is supplanting indigenous conspecifics. Getting around so much and hardly being harmed at all points to an exceptionally good immune system. The Gießen scientists could already show that the beetles release an extremely powerful antibacterial activity. Now the responsible substance is to be isolated. Maybe it holds the key to the production of new antibiotics? The Asian lady beetle might well be a lucky charm for Prof. Vilcinskis and many patients.



"Lively exchange and good networking are key ingredients for the success of a start-up."

Dr. Christian Garbe | FIZ CEO

Prof. Dr. med. Daniela Steinberger | bio.logis
CEO and Medical Director

Good climate for successful networking

Stereotypically, revolutionaries do not usually wear elegant trouser suits or lab coats. And yet Prof. Dr. med. Daniela Steinberger is one of them. "We are part of a fundamental change," the physician explains, "that in the end will entail a democratization of expert knowledge." We, that is bio.logis GmbH's 25-strong team which she leads together with Dr. Michael Lindemann and biologist Ulrike Groß. The company is based in a technology centre that carries its mission in the name: the FIZ Frankfurt Biotechnology Innovation Centre.

"Our strategy is based on bringing together the right mix of companies to enable synergies between experienced enterprises and start-ups and thus facilitate development of innovations," explains FIZ CEO Dr. Christian Garbe. In Science City Frankfurt-Riedberg, especially small and medium-sized enterprises in the life science sector find a platform that is close to the market and complete with lab and office infrastructure. The centre, initiated in 2002 by the Federal State of Hessen, the City of Frankfurt-on-Main and the local chamber of commerce and industry was opened in 2004, expanded in 2008 and now, as a base for 15 companies employing a workforce of around 300, is running at full capacity.

The existing network was one of the reasons for Prof. Steinberger to choose the FIZ as a site for her bio.logis GmbH, founded in 2008. The experts in genetic diagnostics recognized "the historic chance to be one of the first players worldwide to develop and launch a specialized, innovative service." Their business idea: Rapid advances in DNA analytics, in understanding diseases and in information technology are currently coming together. This opens up many new possibilities for diagnostics - yet the individual rarely benefits from it. To enable anyone interested to gain access to her or his genetic information, to process these results in a way that laymen can use them in a medically sound way - that is at the core of the new service from Frankfurt.

"bio.logis is an example how biotechnology revolutionizes the diagnostics market by tracing it back to the individual," Dr. Garbe sums up. At bio.logis in particular, as well as in general, according to Garbe, tangible sales opportunities and thus marketability are decisive for FIZ's positive development. In contrast to other innovation centres it focuses on certain areas of indication of red biotechnology, thus facilitating the exchange between companies in the FIZ and around the innovation centre.

"Real" genetic data - as they are being analyzed by bio.logis - contain a great deal of information based on which improved medical decisions can be taken: How does one's body process certain pharmaceuticals? Which drugs are expected to have adverse effects? At bio.logis, answers to these possibly vital questions are read from DNA samples and made available to its customers through a web portal. "As a physician I deal with a growing number of medically competent patients," says Prof. Steinberger. "To me, people's desire and ability to manage information about their health themselves and not having to rely on a doctor's access to the right medical record is an important improvement of health care. And with our service, we are adding a piece to that."

Searching for causes: genetic **diagnostics**

In humans, the genetic information carrier DNA harbours about 30,000 genes, and many diseases can be attributed to faulty genes. Science is learning more and more about the processes that are involved - valuable knowledge, because it is the foundation for constantly improving diagnostics and therapies.

The search for a molecular cause has already been successful for about 2,500 genetic diseases. Respectively, scientists discovered specific alterations in certain genes. Using genetic diagnostics the analysis of genetic material can yield information that can be relevant for the health state. This in turn can form the basis for important preventive or therapeutic measures.

The FIZ in Science City Frankfurt-Riedberg offers a platform for biotechnological innovation.



bio.logis GmbH is exploring new paths in genetic diagnostics - both in the laboratory and in data processing.





"Worldwide, there are only a handful of companies like BioSpring. So, if anybody anywhere in the world is looking for such a supplier, we usually get contacted."

Dr. Sylvia Wojczewski | BioSpring CEO

Specialties

from the clean room

From Frankfurt, specialties get shipped to all over the world. Some of them, unlike sausages or cider, are invisible to the naked eye. Yet, like all special products they are marked by their quality and their exclusivity. We are talking about: oligonucleotides. In BioSpring GmbH's laboratories in Fechenheim district they are investigated and produced for international customers.

"Virtually unlimited" - that is how Dr. Sylvia Wojczewski, CEO of BioSpring, describes the range of applications of oligonucleotides. Accordingly, individual customers' requirements with respect to composition, properties and quality of these short nucleic acid chains are highly specialized. BioSpring produces them on behalf of universities and research institutes, but primarily for biotech and pharmaceutical companies. Some customers, like sterna biologicals, are located in Hessen, around 80 percent, however, are based abroad - from Switzerland, the USA and Japan to India and Israel. "We are the only European manufacturer of oligonucleotides that is certified to produce active components for pharmaceutical applications," comments Dr. Sylvia Wojczewski on BioSpring's international success.

Know-how in the matter of oligonucleotides

Oligonucleotides are nucleic acid chains composed of only a few nucleotides (DNA or RNA). Their applications, mainly in molecular biology and in red biotechnology are diverse - they have become virtually indispensable:

They are applied e. g. in the polymerase chain reaction (PCR), a method for the amplification of DNA sections, or in diagnostics to detect viruses or to identify hereditary diseases. They become more and more important in therapeutics as an active drug component. Many development projects in this area are currently entering the clinical phase, so that a growing demand is to be expected.

But besides the required clean room facility that meets the highest quality requirements, the company has a further characteristic: No matter which oligonucleotides are to be produced, no matter the scale, the 25-strong team is able to offer the entire spectrum. Wojczewski: "We accompanied a number of customers from early research up to the clinical phase. And that is truly unique in the world."

While working at Frankfurt's Goethe University, Wojczewski realized early on that oligonucleotides would be indispensable one day and, together with co-workers and in parallel to her doctoral thesis work, founded BioSpring in 1997. Two years later they won a special award in the business plan competition Science4Life Venture Cup, and to this day the company benefits from the network they were able to intensify in the course. Building on that and in line with the corporate slogan "The Oligo Company" Wojczewski plans to expand BioSpring's top ranking position in the oligonucleotide sector. "We see a continuing demand here and want to grow accordingly."

Start-up initiative **Science4Life**

As an independent start-up initiative Science4Life offers nationwide free consulting, support and advanced training for emerging companies in the life science and chemistry sectors. It is initiated and sponsored by the government of Hessen Federal State and Sanofi-Aventis.

Year after year the initiative invites participants in these industries' biggest business plan competition in Germany, the Science4Life Venture Cup. In the process, a network of more than 120 companies and institutions supports the participating founders.

On the left: In the clean room BioSpring is producing particularly high-grade oligonucleotides for therapeutic applications.



On the right: Thanks to up-to-date technology, products can be synthesized in the laboratory at almost any scale.



Worldwide cure with concentrated knowledge

Like a modern cruise ship Æterna Zentaris GmbH's building is located on Campus Oberhafen, a traditional business and laboratory location in Frankfurt-on-Main. But whereas emigrants once used ocean liners to turn their backs on their home country, with Æterna Zentaris an overseas company has settled in Hessen: The biopharmaceutical company, one of the top players in Europe, is a 100 % subsidiary of the Canadian Æterna Zentaris Inc.

"We are the only German biotech company that is listed at the American and Canadian stock exchanges," Prof. Dr. Dr. Jürgen Engel puts the global bridge building in a nutshell. As president and CEO he carries responsibility for Æterna Zentaris' worldwide workforce of 100. The company was formed in December 2002 when the German Zentaris AG was acquired by the Canadian Æterna Laboratories Inc. Not only did Frankfurt, besides Québec and Warren, New Jersey, continue to be one of the company's sites - it is even the international headquarters, and new jobs were created.

A tradition of success

Analgesics, asthma or tumour drugs - traditionally the Oberhafen in Frankfurt stands for successful drug development. Already in the 1920s it was a centre for it, at the end of the last century it was home to ASTA Medica AG, Degussa's pharmaceutical subsidiary.

From it in turn emerged the spin-off Zentaris AG in the year 2001. With two products in the market, a well-loaded product pipeline and a library of over 120,000 active substances it was so attractive that shortly after the Canadian Æterna Laboratories Inc. indicates interest - the birth of Æterna Zentaris GmbH, which continues the pharmaceutical tradition in Oberhafen.

In the Frankfurt laboratories a constant supply of new molecules is generated and directly tested for efficacy.



Extraordinary library: More than 120,000 active substances are at Æterna Zentaris' disposal for research and development.





Worldwide cure

"We want to cure patients. That is our highest goal. In order to reach it, we ever strive to develop innovative pharmaceuticals."

Prof. Dr. Dr. Jürgen Engel | Æterna Zentaris
President & CEO

Today, with more than 80 employees, the majority is active in the Main metropolis, where the entire spectrum from early drug development to pharmaceutical production to application for approval can be covered. According to Prof. Engel, besides the excellent infrastructure, the good local opportunities for cooperation, e.g. with numerous biotechnology enterprises in the Frankfurt metropolitan area, decided in favour of the location. Also, the close proximity to scientific institutions like Goethe-University, the Georg-Speyer-Haus, the Max-Planck-Institutes and their Nobel laureate Prof. Dr. Dr. h.c. Hartmut Michel and to regulatory authorities like the Paul-Ehrlich-Institute is advantageous. But especially important: the skill of the specialists, because "to transfer the know-how to Canada would have been impossible".

"Committed to cure" - under this motto, Æterna Zentaris' staff develop products in the areas of endocrinology (hormone research) and oncology (cancer research). This mission statement has already materialized in two drugs that are successfully used in therapy: The Frankfurt company discovered and developed the first orally applied medicine against Leishmaniasis, one of the most dangerous tropical diseases after malaria. In the meantime, the drug against

this life-threatening disease is being marketed worldwide. Also, in over 90 countries, in a co-operation with Merck Serono, an Æterna Zentaris product used in in-vitro fertilization is marketed.

At the same time the Æterna Zentaris research team is constantly working on the development of new pharmaceuticals, many of which are already undergoing clinical trials. Captain Engels' wishes and goals for the company's near future are clear-cut: "We want to launch two more products for cancer therapy and hormonal diagnostics within the next two years." Thus, from its new building in Oberhafen, Æterna Zentaris will continue to gather way.



"At BRAIN we went our own way right from the beginning. Very early on, we banked on white biotechnology, a field that became immensely important only years later. This unique position was the foundation of our success."

Dr. Holger Zinke | BRAIN Chairman of the Board

Thinking out of the box for a clean future

Dr. Holger Zinke would not call himself white biotechnology's pioneer, but he would not object to that term, either. After all, pioneering work means to plough new fields and to prepare the ground for progress - and in Zinke's case, this can be taken almost literally. Today, the enterprise that he founded, BRAIN AG in Zwingenberg in southern Hessen is one of Europe's leading industrial biotechnology companies. The basis for this success: tiny single-celled organisms, millions of which occur in a thimbleful of soil.

In 3.5 billion years of evolution nature has developed solutions for a vast number of problems: Millions of microorganisms live under extreme conditions, convert substances, generate energy. In the few years since the foundation of BRAIN AG (Biotechnology Research And Information Network) in 1993 Dr. Zinke and his staff have recognized this potential and, using genetic engineering, have harnessed it for industrial applications. Already in 1998 this development was honoured with the Hessian Innovation Award: BRAIN had revolutionized white biotechnology at a time when the term did not even exist.

Zinke remembers: "Back then it was not foreseeable that industrial application of biotechnology would be on everyone's lips. Still, we have continuously worked on this subject. That, too, is part of our success." By now, when an industrial partner contacts BRAIN about a specific problem, the biotech-company can draw on a giant archive. Deep-frozen, it stores around 20,000 bacterial strains and millions of genes, proteins and metabolic pathways from heretofore unknown microorganisms. No other technology company possesses a comparable library of natural components.

Zinke went his own way, too, when developing his company's business model: "From the start we have worked in co-operation with chemical and pharmaceutical companies and developed a medium-sized concept, untypical for biotechnology." To him, as BRAIN AG's CEO, that means to sustainably support his staff of around 80 and, together with regional companies and universities, to get involved with professional training. It is no coincidence that Zinke chose a listed Bauhaus building as the company's home. This environment, steeped in history, is to stimulate the team's creativity and co-operation.

From Zwingenberg as a base, Zinke has already brought under way white biotechnology's development and that of its opportunities, amongst others, in the area of environmental protection. Did he receive the German Environment Award 2008 for this? "It is not as if I got the award because Zinke found a great enzyme, but rather for creating visibility and acceptance for these new technologies, processes and products even in large companies," is the awardee's comment.

More and more corporations rely on white biotechnology in their production processes because thanks to special bio-catalysts it is possible to save energy and reduce costs. Fossil resources are conserved and emissions are lowered. "Basically, we are facing a change of existing industries," is Zinke's conviction, "especially in the chemical, but also the consumer goods industry. And in this respect the biotech sector has gained a lot of potential and importance". Pioneer Zinke picks up the shovel again in Zwingenberg, metaphorically speaking. Research and development areas are being expanded and a new production facility is added. In future, BRAIN is not only going to develop new substances, but also to produce them - progressing from a purely technological to an industrial company.

From nature to the supermarket

Time and again, to walk through a supermarket is a pleasure for Dr. Zinke. Here, it becomes visible that white biotechnology has reached the consumers. Together with Henkel his company developed a washing agent that, thanks to an enzyme, already works effectively at much lower temperatures - laundry becomes clean in a way that is green.

Biological resources are also found in cosmetics. From a project by BRAIN, Symrise and AnalytiCon Discovery originated two novel cosmetic agents that are utilized, among others, in deodorants and in products for sensitive skin.

Together with the Kronberg based company Nutrinova, the Zwingenberg researchers developed biological sweeteners. Together with Südzucker, on the other hand, BRAIN is optimizing a biological manufacturing process for the production of a tooth-friendly sugar. Zinke: "Wherever we look, we see the biological transformation coming. Because the consumers demand sustainable products."



On the left: Many microorganisms cannot be cultivated in the laboratory. A "picking robot" helps in making their hereditary information available as a blueprint.

On the right: A glimpse into BRAIN's treasure chamber, specifically the collection of natural products.



"The recipe for success in our co-operation is short distances and team spirit, based on mutual, grown trust."

Dr. Joachim Bille | sterna biologicals
co-founder and Managing Director

Team spirit on the way to new therapies

It starts innocuously: a wrong step, snow starts sliding. The snow gathers mass, dragging along more and more, turning into a destructive avalanche. In the body, inflammations arise in a similar cascade. In the case of the skin disease atopic dermatitis, they become manifest in unpleasant symptoms like strong itching. Common therapies often fall short. What if already the first step could be prevented? Precisely that is the goal pursued by sterna biologicals GmbH & Co KG from Marburg and several partners.

The idea for novel drugs arose during many years of research by sterna Managing Director PD Dr. rer. nat. Holger Garn and Prof. Dr. med. Harald Renz, Director of the Department of Clinical Chemistry and Molecular Diagnostics at Philipps University of Marburg. In order to turn the idea into substances and subsequently into drugs, they founded sterna biologicals in 2006, supported by the Central Hessian TransMIT Gesellschaft für Technologietransfer mbH. Its focus: the causative treatment of inflammatory diseases like atopic dermatitis or bronchial asthma by intervention directly at the pathophysiological roots. To achieve this, the team is developing highly specific agents, so-called DNAzymes. First success is already becoming apparent, because an asthma drug is about to enter the clinical phase.

DNAzymes: custom-made efficacy

A look into the inside of a cell elucidates DNAzymes' mode of action: In the nucleus a specific part of the genetic material DNA is transcribed into a working copy, the messenger RNA which is then transferred out of the nucleus. Using the information contained, the cell's "protein factories" can now produce a specific protein.

Some proteins, however, can be unwanted under certain circumstances, may even become pathogenic: enter the DNAzyme. This custom-made short DNA molecule attaches to the messenger RNA and cleaves it - like an enzyme. After the job is done the DNAzyme dissociates, attaches to the next RNA, cleaves it, dissociates again... The result: The production of the unwanted protein is inhibited.

Ready for top level biotechnological research: RNA workplace at sterna biologicals.



Target-specific drugs are in focus for managing directors Dr. Holger Garn and Dr. Joachim Bille.



The development of a DNAzyme-based pharmaceutical against atopic dermatitis is still requiring a little bit more patience from sterna and its partners in this demanding project. Besides sterna biologicals, the pharmaceutical company Engelhard Arzneimittel from Main-Kinzig county is part of the co-operation. Additionally, the development of the new therapy is supported by Gießen-Friedberg University of Applied Sciences and Marburg University. All partners work together gladly and efficiently, the more so as "all of us are located relatively close to each other in Hessen" as sterna Managing Director Dr. Joachim Bille points out.

In Marburg, the company is developing the drug for the treatment of atopic dermatitis. That arises from a misguided immune response, i.e. the body reacts with an immune reaction to something that is actually nonhazardous. Like an avalanche, it starts rather small: Certain immune cells produce a specific protein. When it is formed, however, other cells become active and in turn produce proteins. Again, they activate more cells, so that the immune response becomes stronger and stronger. A drug in the form of a DNAzyme is intended to stop the protein from being produced. Dr. Bille: "That way, we stop the inflammatory avalanche very early on."

To enable the DNAzyme to become active at the proper site, the right route of administration (as a cream, ointment or tablet) has to be found - a task assigned to Gießen-Friedberg University of Applied Sciences. "In the first phase we could already show that we can bring the DNAzyme into a stable form," explains Prof. Dr. Frank Runkel, Deputy Managing Director of the Institute for Biopharmaceutical Technology. The efficacy of the "packaged" substance is then tested by the partners at Marburg University.

Engelhard Arzneimittel contributes its know-how on pharmaceutical-grade drug production. "The co-operation between a long-established medium-sized enterprise and a start-up is certainly not common practice," explains Director Richard Engelhard. "But Engelhard wants to continue what has been proven successful and at the same time watch out for future developments in our focus areas." One of them could be DNAzyme-based drugs. At sterna, initial preparations have been started to transfer the novel therapeutics for atopic dermatitis into the preclinical phase. There is a good chance that the development team's work is a step in the right direction to block the causative "slip" on the "snow slab".

Fertile ground for tasty ideas

Usually, one should not compare apples and oranges. N-Zyme BioTec GmbH's staff beg to differ: To them, fruit is fruit when it comes to developing new food components using biotechnological methods. "Apples, pears, grapes or peaches are all the same to us," explains Dr. Stefan Marx, the Managing Director of the Darmstadt based company. "What matters to us is to use fruit as a natural resource and to convert it to special products."

The optimization of fruit juices, lemonades and other beverages, that is what N-Zyme Bio Tec's staff are working on in the lab. With its business area new beverage bases the company, founded in 1999 as a spin-off of Darmstadt's university and technical university, bridges classical biotechnology and food industry. The second pillar, Bio-Products, is aiming at the development of natural cross-linking agents for broad industrial applications. There is always one goal, in focus, however: the creation of innovative technologies and products.

Indeed, yeasts have been helping in the production of beer and wine for millennia, but today N-Zyme is using microorganisms specifically in order to change beverage bases so that they fulfil unique functions. Dr. Marx: "Among others, we try to achieve special taste experiences or nutrition-physiological effects, such as sweetening without calories." Less calories through microorganisms? Put simply, that is indeed the case. Microorganisms, too, have a metabolism. Add them to beverage bases, they process sugar in order to grow - thereby reducing its content in the products. The trick is choosing the right microorganisms or enzymes.

In order to give a grapefruit flavour to future beverages, the Darmstadt researchers, in a co-operation with the Institute for Food Chemistry and Food Biotechnology at Gießen University, even studied mushrooms. An extraordinary beer whose characteristic is due to an N-Zyme BioProduct is already in the market: With the aid of transglutaminase - an enzyme acting as "biological glue" - the beer is devoid of gluten, a protein that many people

Naturally linked

True to the motto "linking nature and technology", N-Zyme BioTec has specialized in the development and manufacture of natural cross-linking products. There is great demand for these products across many branches of industry. For example, transglutaminases are applied as enzymatic cross-linkers in the food industry, and in future they might also be used in medicine. "Enzymes, being natural products, are influenced by environmental factors, however," explains Dr. Stefan Marx. "Accordingly, it is important to expand our portfolio by other cross-linker products, like our plant residues."

Using waste and at the same time devising environmentally friendly production processes - plant residues such as olive leaves have this potential. They are waste accumulated during olive harvest. N-Zyme uses them as a base for an extract with cross-linking properties that can be used as tanning agent in leather production. The result is a naturally tanned leather of high quality that can be used in the automobile, furniture and shoe industries. Given these favourable prospects, the company is already working on further plant residues - an innovation that, according to Dr. Marx, "makes N-Zyme BioTec somewhat one of a kind."



"We are constantly working on enlarging our portfolio of beverage components and natural cross-linker products. This variety is certainly also a fertile ground for N-Zyme BioTec's growth."

Dr. Stefan Marx | N-Zyme BioTec Managing Director



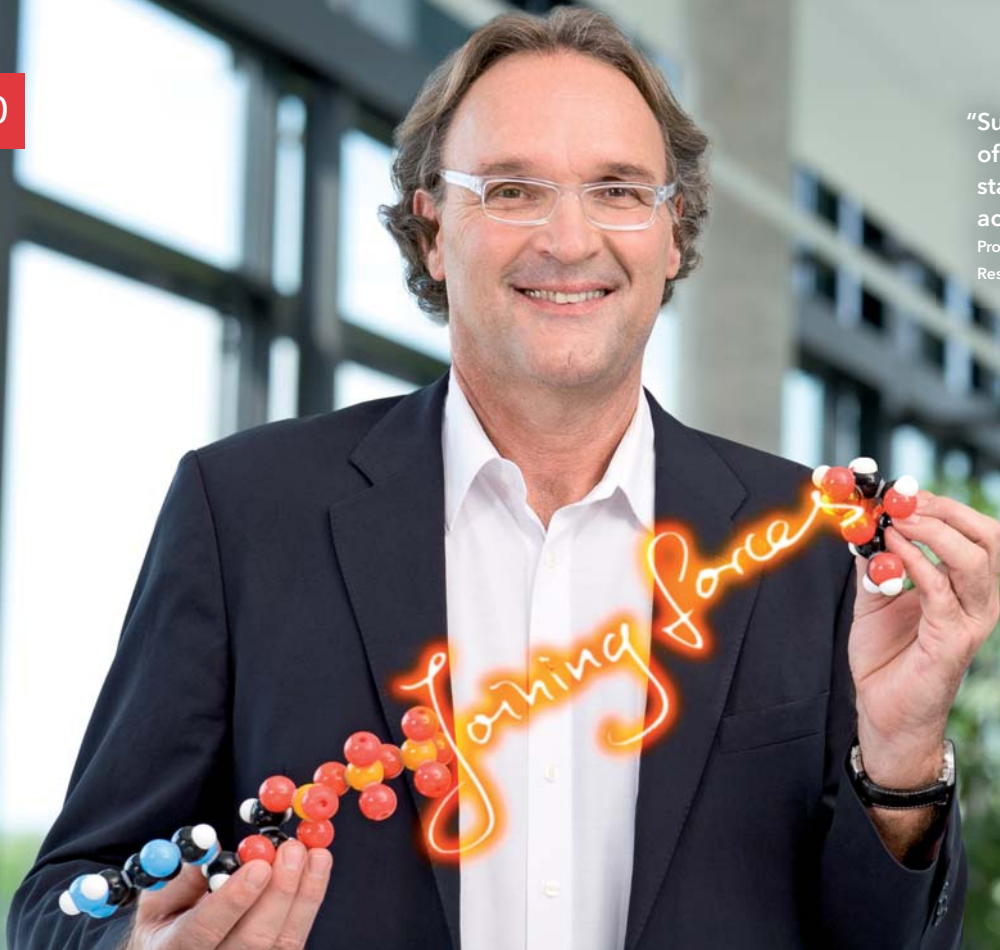
cannot tolerate. The transglutaminase cross-links the soluble gluten molecules, they become insoluble and can be removed before bottling. The brewing process itself is

not affected. When comparing the taste of regular and gluten-free beer, thanks to the innovation from Darmstadt, one does not have to compare apples and oranges.



On the left: Olive leaves accumulate as waste product during harvest, but they can be used to organise production processes in a more sustainable fashion.

On the right: In the laboratory, natural bases are processed into beverage components with special properties relating to health or flavour.



"Successful co-operation is the result of openness, trust, mutual understanding, shared enthusiasm, and accepting the other's expertise."
 Prof. Dr. Jochen Maas | Sanofi-Aventis Germany
 Research and Development Managing Director

Joining forces for tomorrow's drugs

„Every man takes the limits of his own field of vision for the limits of the world“, Arthur Schopenhauer, a Frankfurter by choice, used to say. Sanofi, one of the leading international health companies also chose Frankfurt as home to its German headquarters, but is taking a very different view. The globally operating enterprise is aware that going it alone will not meet the pharma sector's future challenges and thus repositioned its research and development. For Frankfurt-Höchst as the largest R&D location this means that all departments are in the same boat from the start. Furthermore, Prof. Dr. Jochen Maas, Executive Officer Research and Development of Sanofi-Aventis Germany GmbH, would like to increase the formation of research networks in order to continue to lead in the global competition for innovative drugs and therapies.

From first research approaches to shipping finished drugs, at its Höchst site, Sanofi provides all requirements for supplying the German market as well as 85 other countries with pharmaceuticals. "As the only integrated site in the Sanofi world we are able to cover the entire value creation chain. At the same time we are also involved in the global context and use our know-how and capacities to provide worldwide support for the corporation", explains Prof. Maas.

Due to regulation that is becoming ever more stringent and the ensuing increase in development costs, head of research Mass wants to overcome the "silo mentality" in the development of pharmaceuticals: "So far, research would create a molecule, throw it across the fence to development, and at the very end marketing would take over. Now we are bringing all three divisions together early on", clarifies the veterinarian and biologist. Of particular importance to him is to already look at research approaches from the clinical perspective. "We cannot just deal with targets. We treat patients, and they have to be at the centre, always." This principle is being implemented in divisions that focus on particular diseases. Since 2010, Höchst has been home to the global diabetes division. It is in charge of the worldwide diabetes business, of developing competences and comprehensive patient care. In so doing, it has not only levelled boundaries between individual departments, but also between different countries, so that specific market situations and regulations can be taken into account right from the beginning.

With about 51 active pharmaceutical ingredients, Sanofi has one of the most innovative and extensive research portfolios. Still, co-operation partners are being sought for

actively: "Early research yields the most innovative insights. But basic research is not the task of a large pharma corporation. Rather, it is our job to translate new approaches and results first into molecules and then into drugs", according to Maas. Therefore, the global player co-operates with small biotech companies, universities and science organisations such as the Max Planck Society, the Fraunhofer Society and the Helmholtz Association. In Hesse, for example, there are co-operations with Marburg University as well as others that originated through Gießen-Friedberg University of Applied Sciences. For such a co-operation to be successful, the partner's approach has to be understood. After all, the mindsets in academia, biotech and big pharma are quite different. For Maas it is certain: "We are not all experts in every field - the mutual acceptance of the other's expertise is essential on the way to new insights and drugs."

Höchst - a history of success

Approximately 130 years ago, in what is today Höchst industrial park in Frankfurt, the first drug was produced: From 1883 on, fever and pain could be fought using Antipyrin - this started the development of the Chemical Factory Meister Lucius & Co. to the proverbial "pharmacy of the world".

Today, Höchst industrial park is one of the largest European research and production sites, particularly in the pharmaceutical and chemical sector. The premises cover 460 hectares in the centre of the Rhein-Main-area. Excellent conditions then for around 22,000 employees of more than 90 companies to continue the site's success story.

On the left: Up-to-date facilities, enormous capacities - Frankfurt is one of the biggest insulin production sites worldwide.



On the right: Likewise, from Höchst industrial park, pens for the simple application of insulin go all over the world.



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