Biotechnology in Bavaria PROFILES PORTRAITS PERSPECTIVES

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THE SUCCESSFUL INNOVATION CENTRE MADE IN REGENSBURG

Health Industry of Regensburg

→ 1.8 billion Euro turnover

→ 20.000 employees

Cluster BioRegio Regensburg

- → 55 companies (Life Sciences)
- → 3.980 employees

BioPark Regensburg

- → 18.000 sqm area
- → 38 companies, 608 employees.
- → 64 start-ups since 1999
- → flexible leasehold concept & single offices
- → direct motorway connection
- → located on the University Campus
- → own day-care facility
- conference rooms and theatre

A company of the City of Regensburg

Member of CLUSTER BIOTECHNOLOGIE



2019

1999



Editorial

Biotechnology – added value for society

The transformation of experimentally based inventions and innovations into diagnostic concepts and therapies are the basis of modern biotechnology.

It is therefore no coincidence that this issue gives adequate space to "industrial" biotechnology, with perspectives on new projects, products and procedures.

With regard to the laboratory of the future in terms of data availability, increased efficiency and safety, personalized medicine plays a special role.

The following issues are also shaping the future of the biotechnology industry:

- Where are new developments and trends from all biotechnology areas accurately portrayed?
- Why are young entrepreneurs and company founders increasingly locating to the Innovation and Start-Up Centre (IZB)?
- What prospects does the "DigiMed" network offer for the medicine of tomorrow?
- Who supports and sustainably expedites the transfer of technology from the laboratory to the market?
- What role does the new, future-oriented network "bayresq.net" play towards a powerful and innovative life science landscape?

• Are genetically modified pigs the last therapeutic resort for damaged organs?

Modern biotechnology provides strong impulses for the economy: See for yourself!

Walter Fürst, Managing Director

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Preface Prof. Horst Domdey

Biotechnology is a multidisciplinary science-based technology and finds its application in various fields, like medicine, food, agriculture or industrial production.

Biotechnological processes such as brewing beer or fermentation have existed for thousands of years. But only this year, the term ,biotechnology' celebrates its 100th anniversary.

Today, modern biotechnology provides a strong impetus for the economy, the research landscape and, above all, the health care sector. In Germany, we have produced a respectable number of very successful biotech companies, such as Qiagen, Evotec, MorphoSys, Miltenyi and many others who have become global leaders in their field. This also holds true for Bavaria: one of the four companies mentioned above is based in the greater Munich area. In 2018, MorphoSys became one of the few companies to have a dual listing on the Frankfurt stock exchange and, more recently, the US Nasdaq. Having raised more than USD 200 million with their IPO in New York, the company can continue with its clinical development in late-phase trials.

Besides the many drug developing biotech companies located in Bavaria, we can also be proud of the many companies that supply the so-called tools for pursuing research - the Tools for Life Sciences'. Many of these companies operate globally, and some are even leaders in their field. To achieve this, they had to and must rapidly adapt to the expectations of their customers, e.g., by integrating artificial intelligence and implementing machine learning in the instruments they are developing and bringing to the market.

And now we are witnessing how the shift from experimentally based inventions and innovations to the creation of new diagnostic concepts and therapies based on the use of big data is - albeit still slowly taking off. With the help of DigiMed Bayern, a EUR 22.5 million program funded by the State of Bavaria, we have taken the lead in Germany in this field. The data of thousands of patients suffering from atherosclerosis will be collected, analyzed and interpreted, thus enabling physicians to select the most reliable diagnostic tool and best treatment. Though

DigiMed Bayern is currently an academic project it is clear that this academic ,experimental setting' will eventually evolve into an economically driven application in the industry.

I am in no doubt: At this 100year mark, the transformation in and with biotechnology has only just begun. With the biotech companies and the scientific landscape of which we can boast in Bavaria and all the partners in the Bavarian Biotechnology Cluster, I am confident that we can add value not only to our economy but also to our society, while coming closer to our vision: Bavaria – the place for the medicine of the future.

Sincerely yours Horst Domdey

Under

Prof. Dr. Horst Domdey CEO of Bio^MBiotech Cluster Development GmbH and spokesman of the Bavarian Biotechnology Cluster



PELOBiotech – Your partner for cells and media

Be one step ahead - together with competent cell experts

Biotechnology is one of the key factors in academic and clinical research. Especially in the development of drugs, cancer, immune, cell and gene therapies, it has become indispensable. At the same time, the pressure on scientists to deliver faster, more reliable results is increasing.

With over 25,000 products PELOBiotech GmbH is one of the leading distributors specialized in primary, stem cells and cell culture media. Based at the German Biotech hotspot Martinsried in Munich area, PELO-Biotech offers everything from tissue dissociation, 3D technologies to cryopreservation. "We want scientists to be able to focus on their actual research work," says Dr. Peter Frost, CEO of PELOBiotech. "That's why our expertise enables us to offer simple solutions that lead to success quickly and reproducibly. Just give us a call."

PELOBiotech also has a long history of success in the field of 3D models: co-founder Dr. Frost has already successfully introduced several 3D systems to the market. In addition, PELOBiotech has access to a worldwide network of competent and innovative partners.

"We are involved in several cooperations with companies and universities. This enables us to optimize our products constantly, exceed the highest quality stand-



ards and know where the real challenges are, in the laboratory," adds Dr. Lothar Steeb, CSO of PELOBiotech. He has developed a number of products of PeloBiotech's premium brand Cellovations. "Defined media are getting more and more attention in leading institutes," says Dr. Steeb.

Therefore, many cell cuture products are also available in GMP quality for clinical applications, but also as equivalent R&D products at significantly more favorable conditions. The advantage is that customers do not need to test these systems again - saving time and money.

Besides their comprehensive portfolio PELOBiotech can also offer customized cells from rare donors, "so that scientists can conduct their research targeted and efficient finally again" says Dr. Frost.



Choose from over 25,000 cell relevant products. Competent, Simple processes, Ready-to-use

- Cell isolation: highly purified enzymes (collagenase / dispase) for optimal and standardised isolation of various cell types, in particular islet and liver cells.
- Cell culture: human and animal primary cells, iPS, stem cells, labelled primary and stem cells, "Diseased" cell systems; CITES-compliant monkey cells; customized cells
- Cell Culture Media and Reagents: Corresponding to Cells, Media animal-free, xeno-free, chemically defined
- Cooling and freezing media: Gold standard, DMSO-containing and DMSO-free, costfriendly media
- Products for Genomics/Proteomics
- 3D Models: 3D co-cultures, hydrogels, scaffolds and scaffold-free systems for the production of spheroids and 3D ring structures as well as ECMs
- Cell Culture models: angiogenesis, 3D tumor spheroids and 3D liver microtissue and media
- Tools: Cytokines, growth factors, antibodies and assay systems such as MicroMatrix Assay, protein labeling reagents for microscopy, FACS, HTS (TR-FRET).

Follow our blog or on LinkedIn: www.pelobiotech.com https://www.linkedin.com/company/ pelobiotech-qmbh/

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Immunic: From Inception to NASDAQ in only 3 Years

Immunic is a clinical-stage biopharmaceutical company developing selective oral therapies aimed at treating chronic inflammatory and autoimmune diseases, including ulcerative colitis, Crohn's disease, relapsing-remitting multiple sclerosis, and psoriasis. The Company's development pipeline consists of three small molecule products: IMU-838 is a selective immune modulator that inhibits the intracellular metabolism of activated immune cells by blocking the enzyme DHODH; IMU-935 is an inverse agonist of the transcription factor RORyt; and IMU-856 targets the restoration of the intestinal barrier function by inhibiting a new and yet undisclosed target. In November



Immunic team (Source: Immunic) **=**

2018, Japanese pharma company Daiichi Sankyo granted Immunic an exclusive global option to license IMU-856 and related molecules.

Immunic's lead development program, IMU-838, is in phase 2 clinical development for ulcerative colitis and relapsing-remitting multiple sclerosis, with an additional phase 2 trial in Crohn's



Immunic develops best-in-class therapies for the treatment of chronic inflammatory and autoimmune diseases (Source: Immunic)

disease planned for 2019. An investigator-sponsored proof-ofconcept clinical trial for IMU-838 in primary sclerosing cholangitis is planned to start at the Mayo Clinic during summer 2019.

Immunic AG was founded in 2016 with headquarters in Planegg-Martinsried, Germany. Since April 2019, the company has been operating under the name Immunic, Inc. with its registered office in the United States and has been trading on The Nasdaq Stock Market under the ticker symbol "IMUX." The listing followed a reverse takeover transaction with US based Vital Therapies, Inc., as announced in January 2019. The company's research and development activities continue to be conducted in Germany.

Concurrent with the closing of the transaction, an investor syndicate that comprises LSP, Omega Funds, Fund+, LifeCare Partners, Bayern Kapital, High-Tech Gründerfonds and IBG Beteiligungsgesellschaft Sachsen-Anhalt, invested EUR 26.7 million in the company. This is expected to be sufficient to fund Immunic's development activities into the third quarter of 2020. In September 2016, Immunic completed a series A financing round of 31.7 million euros.





Dr. Daniel Vitt CEO and President of Immunic (Source: Immunic)

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IBB NETZWERK GMBH: Driving force of Industrial Biotechnology

Developing biobased and at the same time degradable plastics; converting greenhouse gas carbon dioxide into environmentally friendly products; replacing conventional, petroleum-based goods with renewable raw materials - what almost sounds like visions of the future are in reality the fields of work of industrial biotechnology. Since 2008, Industrielle Biotechnologie Bayern (IBB) Netzwerk GmbH has been actively committed to the associated change towards a sustainable society and greater independence from fossil raw materials. Similar to a catalyst, the network and service company supports and accelerates technology transfer from laboratory to market.

The ideal of sustainable economy is an ambitious goal, which IBB Netzwerk GmbH has been actively supporting for over a decade now with various instruments and measures.

The ,classical, technology transfer

IBB Netzwerk GmbH promotes technology transfer with all known means: whether scientific and market-relevant research, the selection of suitable financing sources, support in (grant) applications or networking with suitable partners for research and development projects.

Through these supporting activities, IBB and its partners have raised over 70 million euros in funding for Bavaria in recent years. In total, the network has already acquired over 100 million euros in funding and invested around 270 million euros in equity capital. But the IBB is also active in a number of other areas.

<u>Competence network of the</u> Industrial Biotechnology

,Motley' is the IBB network, in which biotechnological companies and research institutions are joined by companies from the engineering, automotive, aerospace, chemical and lubricant industries, paper, adhesive and environmental technologies, nanobiotechnology, bioinformatics and a number of other sectors. The current 111 network partners are located mainly in Bavaria, but also in almost all other federal states and in neighbouring countries such as France, Austria and the Netherlands.



Fig. 1: IBB's competence network operates in a large number of different industries



<u>Operating consortia</u> -The ,sub-networks' of IBB

The competence network IBB prepares the ground for disruptive innovations. If a new thematic focus emerges, IBB Netzwerk GmbH then establishes so-called ,sub-networks⁴. These ensure short and efficient routes to new projects, products and processes for participating members. IBB Netzwerk GmbH currently manages four such specialized sub-networks in addition to the large competence network:

- The **,BioPlastics**' partners are dedicated to the aim of developing innovative, bio-based and at the same time biologically degradable, marketable polymers.
- The **,Waste2Value**' network processes residual and waste materials from various industry sectors and converts them into higher-value products.

- In the ,UseCO₂' network, the name says it all: the harmful greenhouse gas carbon dioxide is used as a raw material for various products and energy sources.
- At **,MoDiPro'** digitization is making its way into biotechnology. There, the network develops digital models for diagnostics and process optimization.

Strength through strategic partnerships

It is well known that the strength lies in the community. This is why IBB Netzwerk GmbH also networks with domestic and foreign clusters, networks and associations within the industry and in related subject areas. Through this ,network of networks', thousands of relevant groups of people are reached and the opportunity for successful cooperation can be further increased.

IBB as partner in two European projects

In some cases, IBB Netzwerk GmbH also assumes the function of a project partner, e.g. in the two EU-funded projects "SUNLIQUID" (FP7, No. 322386) and "LIGNOFLAG" (BBI JU, No. 709606).

The two project consortia are working on the enzymatic conversion of plant residues, such as straw, to bioethanol. This conversion is to be established on an industrial scale. In both projects, IBB will be responsible for disseminating the progress achieved at events and via various media channels. It will also acquire further stakeholders.

In concrete terms, workshops for Romanian farmers who act as straw suppliers have been and are being organized, or parliamentary evenings in Brussels and Berlin with relevant politicians and stakeholder.



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20 Years of BioPark Regensburg



In 1999 BioPark Regensburg kicked into action with its first building and today with 18,000 m² is the second biggest center of its type in Bavaria. Together with its subsidiary enterprise TechBase, currently over 30,000 m² of floor space is available in the technology and startup centers on the university campus in the city on the Danube with 166,000 inhabitants. For years prognostic studies have counted Regensburg as being amongst the most dynamic and fastest growing municipalities in Germany. A reason for this was and is the consistent economic promotion of the city, which with its active business and cluster policy has had a significant influence on the innovative location on-site.

BioPark Regensburg

"Small but fine" has been the motto time and again succeeding in bringing the decision makers spanning different parties in the cathedral city to the table and bringing them together on the way towards innovative projects. All of the building projects were able to be realized by funding from the EU, Federal Government, State of Bavaria, City of Regensburg and private equity. As an enterprise of the City of Regensburg BioPark Regensburg GmbH has been able to constantly further develop its cluster policy in the Regensburg BioRegion beyond its sole leasing business. It is a region certified in East Bavaria with a Silver Label in accordance with the European Cluster Excellence Initiative. In particular the interdisciplinary linking of biotechnology with other industries such as sensory technology has led to new industry branches at the location.

Today over 50 companies with almost 4,000 employees are active in the Regensburg BioRegion, a good ten times more than 20 years ago. In this period of time we have successfully been able to bring 64 startup companies to the Business Plan Competition for North Bavaria. To date the companies have acquired 661 million \in , half as private equity and a quarter of this as venture capital or funding.

The success has many parents. The location is directly on the university campus surrounded by two universities and four clinics. The consistent support by the City of Regensburg and the State of Bavaria. A self-supporting BioPark Regensburg GmbH. The stakeholders on-site from university and businesses and of course the successful startups with their innovative applications.

With our youngest project "Healthcare Regensburg – managed by Bio-Park" we are just now expanding the next interdisciplinary cluster in healthcare in the region with the support of the State of Bavaria. For this we have produced a Healthcare Masterplan which denotes the potentials and recommendations for action for Regensburg and the Region in this field. One point of specialty is of course digitalization. For the "Digital Health Initiative Regensburg" we are organizing innovation days e.g. in caregiving or supporting the networking of regional stakeholders for the exchange of data for multiprofessional and interdisciplinary care in the whole of East Bavaria. With an incubator in the field of medical engineering and accelerator in the field of healthcare we are promoting innovation and startups in regional healthcare.





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DigiMed Bayern for the medicine of the future

Bio^M, the network organization of the biotechnology industry in Munich and Bavaria, will help shape tomorrow's medicine with its latest project "DigiMed Bayern". At the end of 2018, the DigiMed Bayern lighthouse project was launched with 22.5 million euros in funding from the Bavarian State Ministry of Health and Care (StMGP). The aim of the project is to integrate P4 medicine (predictive, preventive, personalized, participatory) into clinical routine in the exemplary indication of atherosclerosis. Finally, disease risk prediction, targeted prevention, diagnosis and therapy are to be improved.

The scientific leader of DigiMed Bayern is Prof. Heribert Schunkert, Director of the Department of Cardiovascular Diseases at the German Heart Centre Munich. Bio^M Biotech Cluster Development GmbH is responsible for management and project coordination. The consortium embraces further worldwide leading partners from Bavaria such as clinics, patient organizations and research institutions. ■

Using digital data to combat atherosclerosis

One of the most promising developments in medicine is the integration and analysis of clinical data, research data and patient real-world information. DigiMed Bayern focuses on atherosclerosis, the deadliest disease in industrial civilizations. The five-year pro-



Kick-off meeting of the partners of DigiMed Bayern on October 1, 2018.

ject combines comprehensive clinical and epidemiological data from patients diagnosed with atherosclerotic diseases, such as coronary heart disease and stroke, and/or with genetic risk factors. This dataset will be further enriched through state-of-the-art molecular "multi-omics" characterization. For integrative analysis of the resulting "big data", an ethically and legally compliant, highly secure and sustainable digital infrastructure is required. This will be fundamentally designed and be implemented with a focus on balancing privacy with sharing of sensitive medical data. Statements were obtained from the ethics committee and the state data protection officer early on and will be continuously considered throughout the entire project.

The greater vision is to then generate real-life improvements in disease risk prediction, targeted prevention, health care management, diagnosis and therapy. DigiMed Bayern also wants to create an exemplary integrated digital infrastructure. Highdimensional medical approaches and digital solutions promise to pave the way for other similar activities and finally help shape the medicine of the future.

<u>Germany ranks second last</u> in digitization in health care

The current detailed country comparison #SmartHealthSystems, commissioned by the Bertelsmann Foundation, reveals mercilessly how much Germany lags behind in the digitization of the health care system. In the study, an overall index was formed from the three areas of policy activity, readiness and actual data use. Of the 17 countries analyzed, 14 of which are in Europe, Germany ranks second last with only a score of 30. Estonia leads with a score

DigiMed Bayern



The leadership team of DigiMed Bayern at the kick-off meeting: Prof. Heribert Schunkert (German Heart Centre), Prof. Horst Domdey (Bio[™]), Dr. Huber (StMGP), Dr. Georg Münzenrieder (StMGP), Dr. Anand Schwenk-von Heimendahl (StMGP), Dr. Jens Wiehler (Bio[™]) (from left to right). ■

of 82. 13 countries have above 50 points and mostly significantly more. The study confirms the urgent need for activities such as DigiMed Bayern.

Learning from the European leaders: DigiMed Bayern lecture series The DigiMed Bayern consortium anticipated the situation



Prof. Jan Baumbach from TU Munich started the public lecture series with the topic "Systems Medicine: A big data driven disruptive view on current medicine".

already in the conception phase of the project and addressed the topic with a public lecture series "DigiMed Bayern Public Seminar". On seven dates from January to April 2019, nine renowned pioneers of P4 medicine from leading European countries presented their projects. The aim was to determine the current situation, provide orientation assistance and international networking for players in the Bavarian and German health system. A focus was on big data infrastructures for applicationoriented medical research and development.

About Bio[™]

Since 1997, Bio^M is the central network organization for the biotechnology sector in Munich and Bavaria, supporting the community in a variety of ways with its extensive network. The nonprofit cluster management offers centralized access. As a central point of contact, Bio^M connects Bavarian life science companies with relevant national and international partners. Furthermore, Bio^M organizes a broad range of training courses, events and network meetings. Especially for start-ups the network organization also provides comprehensive consulting services and specialized coaching, training and mentoring programs. Finally, the information portal at www.biom.org offers an extensive company database, news and events updates as well as a popular job forum.

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IGZ Würzburg – where knowledge becomes business

Würzburg has huge potential to offer when it comes to the health industry, biomedicine and biotechnology as well as medicine and medical technology. The "Innovations- und Gründerzentrum" IGZ Würzburg (innovation and business incubation centre) is a major player in developing, profiling and networking the local scientific and business community.

IGZ Würzburg is the largest business incubation centre in Lower Franconia. Opened in December 2001, it has since provided some 2,500 m^2 lab and 3,000 m^2 office space to technology-oriented entrepreneurs in their formative stages at competitive prices. All labs have high-tech equipment and can be upgraded to the higher security standard S2. It also provides conference and seminar facilities as well as consultancy services, which are currently being used by 28 companies with some 310 employees. The centre aims at safeguarding jobs, creating networks and synergies as well as promoting the region scientifically and economically. The facility is run by separate operating company whose shareholders include the city and district of Würzburg, Sparkasse Mainfranken (savings bank) and the Würzburg-Schweinfurt chamber of commerce (IHK).

Würzburg – a force to be reckoned with in life sciences

With its research centres, research groups, and postgraduate schools of medicine and life sciences, the Julius-Maximilian University ranks among the most successful universities in Germany. The Rudolf-Virchow Centre for Experimental Biomedicine is one of the DFG-funded centres of excellence focussing on the identification of new target proteins in cancer, cardiovascular, auto-immune and inflammatory diseases,



IGZ, the innovation and business incubation centre, is located in the science park on the Würzburg-Ost industrial estate (Gewerbegebiet). \blacksquare

which can be the basis for improved diagnosis and treatment. The dual centre of internal and operative medicine (Doppelzentrum für Innere und Operative Medizin) of the University clinic Würzburg the University Clinic Würzburg has excellent technical equipment and offers ideal conditions for patient care as well as basic and clinical research. Located in the immediate vicinity is the Com-



The enrolment of patients for the clinical phase 3 was started in August 2016 based on the very good results in clinical phase 2: the test substance Ronopternin (VAS203) of vasopharm GmbH from the IGZ Würzburg affects the increase in cranial pressure in traumatic brain injury patients

prehensive Heart Failure Centre (CHFC), an integrated research and treatment centre for cardiovascular diseases, which moved to a modern new building in 2016. The Comprehensive Cancer Centre (CCC) was established at Würzburg university

hospital in 2011 and is recognised as a centre of excellence for oncology by German Cancer Aid (Deutsche Krebshilfe). The interdisciplinary bank of biomaterials and data Würzburg (ibdw), established in 2013, is one of five nationwide databases which are an important prerequisite for a better understanding of diseases and disease mechanisms. The Fraunhofer project group for the investigation of regenerative technologies for oncology was integrated in 2014 after a positive evaluation in the newly founded "Regenerative therapies for Oncology and Musculoskeletal Diseases" translational centre, which is funded by the Free State of Bavaria. Within the scope of the Nordbayern initiative, launched in 2014, Würzburg's scientific excellence is being further expanded in the life sciences. This includes, among others, the establishment of a Max Planck research group for system immunology to investigate the immunotherapy of cancer and other diseases, the establishment of a Helmholtz Institute for RNA-based Infection Research (HIRI) as well as the "Center for Computational and Theoretical Biology (CCTB)".

IGZ Würzburg

Networking - locally and in Bavarián clusters

At the IGZ Würzburg, a structured program is pursued above all in order to further develop the potential of life sciences in the region. Start-up companies, company relocations and existing companies are promoted and given intensive support in cooperation with the Bavarian Ministry of Economic Affairs, the Würzburg university colleges, BayStartUP GmbH and the city of Würzburg economic development department. The incubation centre promotes the networking of regional companies and research institutions in the field of biotechnology and medical technology and supports their visibility through the platform BioRegion Würzburg (www.bioregion-wuerzburg.de). Furthermore, as regional partner in Lower Franconia, it ensures efficient networking with the Bavarian biotechnology cluster, the Medical Valley in Erlangen and the excellence initiative m4 in Munich.

Support for entrepreneurs

Together with local universities, IGZ Würzburg has developed a comprehensive program for promoting start-up activities in the region. Young scientists are offered advanced trainings courses with an economic and branchspecific focus. Technology scouts at colleges and research institutions in the region are screening research results for new business concepts with high economic potential at early stages. Once promising concepts and entrepreneurial teams are identified and motivated, they will be supported on the way to their own company through intensive coaching, consulting and networking. As member of the "Three Business Centers in Würzburg" (www.gruenderzentren-wuerzburg.de), the IGZ Würzburg works closely together with the "Technologieund Gründerzentrum" TGZ Würzburg (Technology and Startup Center) and the "Zentrum für Innovationen" Digitale ZDI Mainfranken (Center for Digital Innovations).

The new initiative "Gründen@ Würzburg.de" (www.gruenden. wuerzburg.de) supports the networking of founders and startups in Würzburg.

Start-up support bears fruit

In recent years, in close cooperation with universities and Bay-StartUP, IGZ Würzburg has done the initial work for creation of many new jobs at the incubation centre. Successful support by the IGZ and partners is reflected in the scoring of various Würzburg start-up projects in the

IGZ Würzburg has a comprehensive service package for young companies:

- Hire of 3,000 m² office space and 2,500 m² lab space at competitive prices
- Flexible rental possible from small units to building tracts
- High-tech equipment, labs can be upgraded to the S2 security standard
- Support in preparing and updating business plans, grant applications and initiating collaborations
- Advice on business strategies, business models, patent and brand strategies, quality management and quality assurance and corporate management questions
- Advice on financial planning and financing, support in investor talks and financing rounds as well as when negotiating with strategic, licensing and cooperation partners.

Other tasks include the following:

- regional and supraregional networking
- networking academic and industrial partners
- collaboration in the creation and further development of a constructive climate between regional companies and institutions in Würzburg and the Mainfranken region

Northern Bavaria business plan competition: since 2007 prize-winners have come regularly from Würzburg life sciences with the teams CALPORTIN Pharmaceuticals, CoBaLT, SmartmAb, Mablife, Cherry Biolabs, RealT-Vac, and AIM Biologicals. In order to promote business ideas, it was possible to gain over 16 million Euros in public funding (4x GO-Bio, VIP, m4 award, medical valley award, EXIST-Forschungstransfer and EXIST-Gründerstipendium). Four startup companies that have emerged from the pre-seed start-up programs have moved into the IGZ. Further start-up companies are expected in the coming years.





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Dr. Jennifer Gehring Project Manager





Research network in Bavaria: New Strategies Against Multi-Resistant Pathogens by Means of Digital Networking (bayresq.net)

Working together against multi-resistant pathogens

Where do we stand today?

Multi-resistant pathogens are already causing more than 6'000 deaths per year in Germany. While this number amounts to 23'000 in Europe, an estimated 700'000 victims are seen on a global level with rising tendency. In 2050, we will be looking at the inconceivable number of 10'000'000 deaths worldwide as projected by the Inter Agency Coordination Group on Antimicrobial Resistance. In 2013, the US Center of Disease Control and Prevention published calculations based on which the associated economic cost amounts to 300

payresq.net

billion USD annually, taking into account charges to the health system and loss of productivity. Meanwhile, these or similar reports from the media are seen on a nearly daily basis. It is high time for us to make all means available in order to suspend the imminent catastrophe and to develop novel concepts which will help face and oppose these

developments. The Bavarian government has since reacted and taken first steps in the right direction with the joint action plan against antibiotic resistance and the foundation of the recent network program "New Strategies Against Multi-Resistant Pathogens by Means of Digital Networking". In recent years, specific measures have been taken to improve the conditions for research in Bavaria, resulting in a high-performance and innovative life science landscape for the Free State of Bavaria. This has created the preconditions for a rapid reaction to international trends in the area of molecular biology, alongside the initiation and promotion of key areas of research. The already implemented programs such as the Bavarian Genome Research Network (Bay-



Fig. 1: In 2009, bacteria could not grow around the antibiotic spots. In 2019, bacterial growth will hardly be stopped by the antibiotic spots
spots

bayresq.net

Gene), the Bavarian Network for Immunotherapy (BayImmuNet) and the Bavarian Research Network for Molecular Biosystems (BioSysNet) are convincing examples.

The current program has issued a call for applications in May and has thereby launched a new network that will address the challenges associated with the rapid development of multi-resistant pathogens (Fig. 1). Of course, this global threat is also being perceived on an international level and by now, many other funding programs are being initiated by national and international organizations. Their focus lies primarily on hospital hygiene, antibiotic stewardship, the development of antibiotics of last resort and the discovery of novel pharmaceutical compounds. In addition, methods for faster diagnostic detection, for which the technical foundations are already in place, but which have so far not reached the clinics due to high costs, are being explored by a range of programs. All of these are indeed important approaches in order to avoid - at least for some time - a further worsening of the situation. However, none of the known programs acknowledges the fact that fundamental research in the area of infectious diseases has been neglected for many years. This is based on the widely held notion that antibiotics are easily available, therefore bacterial infections are treatable and consequently this research area is considered economically unprofitable. This is a big mistake, as it now turns out. We evidently require intensive basic research with regards to the following questions

- host-pathogen interactions
- composition of and interaction with the human microbiome
- development and spread of resistances
- immunological and other hostbased approaches (as well as their deeper understanding for the prevention and control of infection)

as a basis for the later development of innovative strategies to face the emerging problems. This is why this



Fig. 2: In bayresq.net, interdisciplinary groups and modern data management are to be combined into a new entity \blacksquare

new Bavarian funding program is such an important component of our research landscape. Only by gaining a better understanding of fundamental processes and novel insight into causal relations, will we be capable of developing effective solutions for this highly relevant and complex issue in the future.

The focal point of this program is an interdisciplinary approach that allows exploring completely new paths. Many processes which take place between host and pathogen, such as the question of how the existence of other microorganisms affects a beginning infection, are not yet understood on many levels. Research approaches regarding the therapy of infectious disease with means other than antibiotics have been neglected for many years. However, precisely those methods providing an alternative to antibiotic treatment are now becoming increasingly important. Another process is threating to emerge: more and more pharma companies are withdrawing from research and production of novel antibiotics. The time from development to production is considered too long for companies to be able to cover the development cost through subsequent sales, especially since newer compounds are initially given only in extremely threatening cases. That is not exactly an incentive for companies to invest large sums of money into the development of new substances.

Digitization

Alongside the efforts made in the area of life sciences, concrete approaches to specifically implement shared data management from the early phases of knowledge generation onwards are needed. This is the only way how to ensure an effective interdisciplinary cooperation and therefore lay the foundations for successful collaboration in order to remain competitive on an international level. Therefore, deliberate application of modern data usage and data networks on behalf of the project partners in the network is a new aspect of bayresq.net compared to previous networks. The challenge consists in creating the right conditions for the network projects so that all partners involved in the data network can access the jointly developed

data in an individual and user-friendly way. To this end, the bayresq.net main office plans to offer, maintain and optimize superordinate data management for all project partners. The targeted implementation of modern data networks and data usage among project partners should provide all scientists with the opportunity to access, analyze, manage and use newly acquired data immediately.

All of this forms the basis for creating a sustainable and digital added value, that could potentially benefit the wider public, the field of medicine, professional users and public institutions, for example in the form of web services or apps.

Information on the new program

bayresq.net will be funded by the Bavarian State Ministry of Science and the Arts with more than 10 million Euro in total over a period of five years. The plan is to finance up to interdisciplinary research seven groups from universities across Bavaria. Each research group is composed of 2-3 collaboration partners, it is also possible to include central academic core facilities from areas such as sequencing, proteomics or metabolomics within the cooperation. Prof. Dr. Horst Domdey, managing director of the BioM Biotech Cluster Development GmbH and BioM AG in Martinsried, has been appointed scientific director of bayresq.net, while Dr. Ulrike Kaltenhauser will lead the main office at the gene center in her capacity as managing director. An international panel of experts, the "scientific advisory board" of the network, evaluates and accompanies the program and particularly makes recommendations regarding the research groups' performances.

Preconditions in Bavaria

The high core competency of Bavarian universities in the areas of life science and data management is an important prerequisite for the proposed program. The same holds true for the area of infection research, as we have proven expertise in the sector of immunotherapeutic research, microbiome and epidemiology. This can be seen in the leading-edge cluster m4 of BioM, the research networks mentioned above, the German Center for Infection Research (DZIF), the Research Center for Infectious Disease in Würzburg, research groups at outstanding Bavarian universities as well as numerous other projects at many more Bavarian institutions. As important research teams are established at all of these important centers, the challenge now is to connect and to consolidate their expertise in the areas of both basic research and establish a joint data management, in order to collectively find solutions to the upcoming challenges (Fig.2). Only by staying up to date on all levels of research, can we compete with research institutions such as the ETH Zürich or elite universities in the UK or the US and remain visible as collaboration partners on an international level.

Outlook

Nowadays, the risk derived from antibiotic resistant pathogens has reached global awareness. Many of the application-oriented funding programs that are currently available to scientists may contribute to momentary relief in this critical situation. However, bear in mind that we must anticipate a severe worsening of the situation based on microorganisms developing many new resistances in the future. Only based on highly motivated basic research, using all available technical means and at the same time bringing together specialists through joint data management, can we hope to establish new treatment and prevention opportunities for infectious disease, which will contribute to facing the imminent threats. As long as basic research does not deliver new results, we won't be able to provide new strategies of application.

By funding this program, the Free State of Bavaria intends to make a regional contribution to provide novel strategies for this international challenge in the future. Sooner or later, collaboration on a global level will be necessary to prevent greater harm to humanity. Therefore, we require fast and uncomplicated information channels connecting all scientists. Precisely this aspect lies at the center of the new program. A large proportion of industrial companies has been relying on digital systems for many years to ensure a smooth and safe flow of information between all qualified partners within the value chain. This trend is now also becoming increasingly important in science. Through bayresq.net, this process will be greatly accelerated and optimized in the Free State of Bavaria. For all of the reasons mentioned above, Bavaria is given a unique opportunity with bayresq.net to refocus on the neglected developments of basic research in this area and thereby take a lead. Basic science and the knowledge on correlations between detailed facts are the prerequisite for novel solutions, which are dearly needed in the future. Although we should be aware that the problem of antibiotic resistances cannot be solved on a permanent basis, we can at least aspire to lay the foundation to manage it in the long term. \blacksquare



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Truth the basis for best medicine.



"Stop this sham" says communications expert Beatrice Sonntag, when she established the internet portal Kindermedizin.info in 2015. It was obvious for the Munich native, who spent many years in medical research at the LMU Munich and at Harvard University, Boston, and who studied at the Bavarian Academy of Advertising e-Marketing at the end of the 1990s, that something had to change.

"Fake news in the healthcare arena can do a lot of damage. Especially young parents become extremely distressed. "Nobody wants that, "says Beatrice Sonntag with great conviction.

Kindermedizin.info is gaining more and more recognition and real advocates, without financial help from outside. It just makes sense in the name of health. Because the range of news, unintentionally published in good faith and lies deliberately distributed into the world – are an increasing danger to the wellbeing of the body, mind and soul. In World Wide Web and social media in all probability about 90 percent of incorrect and misleading promises and statements



A little smile for a big goal. With the girl's face as key visual kindermedizin.info is fighting against Fake News in children's medicine.

which are circulated are old news, but still worth mentioning.

False information in the healthcare field items is as plentiful as cells in the human body, says Beatrice Sonntag. The spectrum ranges from nutrition and diet to fitness and psycho training, to acute and chronic diseases. And then there are the very drastic examples of Fake News in the medical field. And those can have potentially fatal consequences, as shown in a 1998 in the British top journal "The Lancet" published manipulated work shows. Based on falsified evidence, it was claimed

Kindermedizin.info



F.I.t.r. Dr. Nadine, Gerth, Beatrice Sonntag, Dr. Frank Bienenfeld

that a measles-mumps-rubella vaccine significantly increases the risk of autism and colitis and is therefore dangerous. As a result, the vaccination rate in the UK dropped dramatically.

How many children were not vaccinated as a result of this "study", who later became ill, died of complications or still suffer from permanent damage is unknown.

The fear of illness, the desire for health, the hope for recovery – which affects almost all people in more or less pronounced form, plays an important part in the marketing strategies of both small and large businesses in the medical arena.

"We will continue our educational work in the upcoming months," says Dr. Frank Bienenfeld. The creative director and text coach has been partner of Kindermedizin.info since 2018, as

Passionate Communicators

Since its founding in 2015, the health portal Kindermedizin.info has been reviewing, examining and connecting information on child medicine and provides annotated, verified contents. Users will see the source of the information and that the contents trustworthy and valuable.

Kindermedizin.info is an ownermanaged and independent company. As nutrition specialists, communication professionals and biologists, the initiators Beatrice Sonntag, Dr. med. Frank Bienenfeld, and Dr. Nadine Gerth bring a good mix of creativity and know-how for this important work. A network of medical professionals, editors, conceptual and web designers supports their work. the communications work of the portal is becoming increasingly important and extensive. In addition, starting in fall of 2019, kindermedizin.info will supplement its range of services with seminars and Coaching on verbal and non-verbal communication.

It begins with several text seminars. The target groups are principally those who work in the healthcare industry and daily interact with patients. Nevertheless, all of those interested from other professional groups have the opportunity to become more educated due to the creation and conception of well formulated and structured texts. Courses with new knowledge about body language complete the seminar series. Special feature of all courses is that the course contents are presented in an easily understandable, clear and humorous fashion.

Frank Bienenfeld: "If we present educational materials in a fun and entertaining manner it remains easily understandable and longer in the participants memory."

"We are breaking new ground in knowledge transfer. And the success corroborates to continue this way." Beatrice Sonntag adds: "We already accomplished and achieved a lot. But we will even more significantly increase our activities against Fake News in the future. We owe this commitment to our society and especially to the children of the world.

Kindermedizin.info Good knowledge, Better health.

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Lydia HD new concept for lymph node analysis in cancer diagnostics

Cancer is the leading cause for death in the western world and the number of cancer-associated deaths is steadily increasing making effective treatment options an urgent yet unmet need. Numerous new treatment options have become available and personalized therapies are emerging. To define the most effective therapy for a specific patient (group), precise predictive diagnostic assays are essential. Here, two aspects are becoming increasingly relevant. Firstly, as a result of a continuing genetic evolution, the molecular heterogeneity of cancer cells during the course of the disease and specifically during progression from local to systemic disease is limiting therapeutic efficacy by therapy escape of certain cancer cell clones. This opens the question on the best timing and selection of the best fitting, possibly stage-specific therapy for each individual patient. Secondly, the increasing number of new therapeutic options raises questions about their combination, sideeffect in patients and interference with other treatments. Short-term and long-lasting side effects in cancer survivors are currently completely under-investigated.

The diagnostic relevance of systemically disseminated tumor cells.

Ninety percent of carcinoma patients don't die of the primary disease but of metastases. Metas-

tases are caused by few cancer cells, the so called disseminated tumor cells (DTCs) that have disseminated and lodged before surgical removal of the primary tumor into distant organs and were not eliminated by the possibly applied therapy. These DTCs continue their genetic evolution at the distant site and consequently differ significantly on a molecular basis from cancer cells in the primary tumor [1, 2]. Despite this fact, current therapies are still selected according to the molecular characteristics of the primary tumor and not the target cells of therapy, the DTCs. To track the molecular evolution of cancer over time, the genotype and phenotype of cancer cells have to be assessed longitudinally, which is technically challenging as the frequency of disseminated cancer cells in organs/tissues that are accessible by biopsies can be very low. This is specifically true in the early phase of the disease when patients present with no or only few metastases.

Diagnostic assays to detect disseminated tumor cells in lymph nodes

In metastasized patients the molecular diagnosis of a systemic disease can be done by testing for the presence of circulating tumor cells (CTCs) or cellfree tumor DNA (ctDNA) in blood. Such a liquid biopsy has the advantage over conventional tissue-biopsies that the compliance of patients especially with regard to risk and safety is much better and hence much more suitable for longitudinal tracking of the patient's disease. However, the low number and amount of CTCs and ctDNA, respectively, limits this approach especially for the diagnosis of early disease patients and makes the development of new and innovative analytical tools necessary.

Individualized therapeutic decisions on surgery, irradiation, chemotherapy or other therapies in early disease patients mainly depend on the extent to which the disease is already systemically present and are guided by parameters such as the size of the primary tumor, whether dissemination to lymphnodes or other organs has occurred and the geno-/phenotypic changes of cancer cells over time. To determine whether dissemination has already occurred, lymph nodes are extirpated at the time of surgery of e.g. breast- or lung cancer patients. These lymph nodes are then sectioned and evaluated by microscope-assisted histophathology for the presence or absence of DTCs. This approach is very laborious as up to 70 lymph nodes per patient have to be analyzed depending on the cancer type. Moreover, sectioning of lymph nodes for histopathology is not standardized and due to limits in time and personnel only



Fig. 1: The impact of the sentinel lymph node for personalized cancer therapy. Dissemination of cancer cells from the primary tumor into other organs like lymph nodes happens already early during tumor development, when the primary tumor is still small and often not yet clinically detectable. During/shortly after surgical removal of the primary tumor, sentinel lymph nodes are extirpated. Extirpated lymph nodes are examined for the presence/absence of disseminated cancer cells. In some patients only single, isolated cancer cells are found which did not yet form a colony or metastasis. In other patients, small cancer cell colonies or even metastasis can be found. Therapeutic targets can differ for each disease-stage (isolated cancer cells, colony or metastasis) as cancer cells continue their genetic evolution also after dissemination and consequently require stage-specific, personalized cancer therapies enabling elimination of cancer cells that have disseminated to other organs than lymph nodes and thereby preventing the onset of lethal metastasis.

some sections are investigated but not each complete lymph node, which reduces the sensitivity of the approach. Although it is known that the histopathologysensitivity increases proportionally with the number of analyzed slides [3, 4], cancer cell clusters can be missed even with very extensive protocols and consequently lead to a false-negative diagnosis. Another disadvantage of the current histopathologic approach is the necessary formalin-fixation of tissues hampering down-stream molecular/genetic analyses. However, determining the presence or absence of therapy-relevant mutations in detected disseminated cancer cells is essential for the selection of modern, personalized and targeted therapeutics [5] and will increasingly become relevant in the near future, especially for therapy of tumors for which just recently new therapies have become available (Figure 1). To improve the current lymph node

diagnostics, we applied principles and technologies of the liquid biopsy: extirpated lymph nodes are mechanically put into single cell suspension and screened for the presence or absence of disseminated tumor cells. Using this method, w conducted a study on malignant melanoma over the course of eight years involving more than 1800 lymph node samples from more than 1000 patients [6]. Lymph nodes were bihalved, one half was subjected to routine histopathology, whereas the other half was put into single cell suspension and stained for the melanoma-specific marker gp100. This immunocytologic approach was found to be more sensitive than routine histopathology (Figure 2) and revealed a link between the presence of few, single DTCs and the poor prognosis of these patients. Already as few as one to three DTCs per million of lymph node cells increased the risk of patients to die of melanoma and a ten-fold increase in the number of DTCs doubled the risk emphasizing that each cell matters [6]. When additional prognostic factors such as age and localization of the primary tumor were included, the number of DTCs in the lymph nodes had a higher prognostic relevance in multi-variate analyses than diagnostic results obtained by routine histopathology. Moreover, based on the DTCnumber determined by our new immunocytologic approach, a statistical survival model could be established which predicted the survival-prognosis more precisely than current clinical staging guidelines of the AJCC (American Joint Committee on Cancer) [7].

Clinical relevance of lymph node diagnostics

In addition, we could recently show that dissemination into tumor-draining (sentinel-) lymph nodes occurs already very early, namely at a primary tumor thickness of less than 0.5 mm [1]. At this time-point, disseminated melanoma cells still have relatively few mutations. Numerous mutations necessary required for their ability to grow out are just acquired at the distant site, in our case in lymph nodes.

Melanoma cells having acquired these characteristic changes not only grow in immunodeficient mice, but also increase the risk of patients to die of melanoma. These characteristic changes include mutations in the BRAF proto-oncogene and gains and losses in the chromosomal regions harboring the tumorsuppressor CDKNA2 or the oncogene MET. In summary, identification of patients with disseminated cancer cells harboring this colonization signature could help in the future to more specifically direct patients into clinical studies with the ultimate goal to enable improved new therapeutic options for malignant melanoma.

Lymph node analysis



increases the risk of e.g. melanoma patients to die of their cancer (Ulmer PLOsMedicine 2014). Detected cancer cells can be isolat ed for further molecular profiling to identify relevant therapeutic target molecules by single cell genomics or panel-sequencing of selected mutations. Immunocytology-based lymph node diagnostics has a higher sensitivity than current routine histopathology. Especially small cancer cell deposits or single, isolated cancer cells are detected more frequently as the immunocytology approach examines the complete lymph node and is independent from the number of tissue-sections or the location and distribution of the cancer cells (B, C).

Improvement of the strategy for routine pathology

In order to optimize the clinical use of the above described lymph node diagnostics and to develop an automatized method for lymph node diagnostics we initiated together with Fraunhofer-groups the interdisciplinary project Lydia HD-Diagnostics. The group for Automation in Medicine and Biotechnology of the Fraunhofer Institute for Manufacturing Engineering and Automation IPA in Mannheim has developed the Tissue-Grinder, a device which gently separates cells without affecting their viability. It also allows the simultaneous, but independent processing of numerous lymph nodes, which is an absolute pre-requisite for its utility in routine pathology. In the next step, cancer cells are identified with a specific immunocytologic staining, detected and quantified by microscopy. This last step was relying so far on manual inspection of diagnostic specimen by specifically trained personnel and was therefore very time and personnelintensive. Through the collaboration with the Fraunhofer Institute for Integrated Circuits IIS in Erlangen, we could fully automatize these steps significantly reducing time and costs which is mandatory for a broad application in routine pathology. To subsequently decide on the optimal therapeutic regimen for individual patients, detected cancer cells can be individually isolated and analyzed for molecular changes. These molecular tests have already been developed at the Division Personalized Tumor Therapy at the Fraunhofer Institute for Toxicology and Experimental Medicine ITEM-R in Regensburg together with the Chair of Experimental Medicine and Therapy Research of the University of Regensburg. The method is based on the

Lymph node analysis



Fig. 3: LyDia HD work-flow.

The flow-chart shows the individual steps in the work-flow of LyDia HD (A). The work-flow covers all necessary steps from sample arrival at pathology up to diagnostic reporting on single cell level and incorporates four innovations that were developed within the consortium (B, pictures Tissue Grinder © Fraunhofer IPA, pictures Mikroskopysystem SCube © Fraunhofer IIS, Picture Cellisolation © Fraunhofer ITEM, Picture Merlin/IT ©Marc Arends/Fraunhofer IPA)

amplification of the DNA of single cells and has been already commercialized as Ampli1TM WGA (Menarini Silicon Biosystems). All processes in the workflow of Lydia HD-Diagnostics are supported and accompanied by the software Merlin, which was specifically developed by the IPA and includes assessment and documentation of the individual steps in the work-flow from processing of samples up to a medical report (Figure 3).

Summary

The new automatized LyDia HD-Diagnostic does not only provide a more exact, but also faster and economic work-flow than current diagnostic methods and enables reliable and sensitive diagnostic of the disease also in patients presenting with only few disseminated cancer cells. This work-flow in combination with genetic information from disseminated cancer cells will enable doctors to select the most suitable therapy for their patients. The newly developed diagnostic tool LyDia HD-Diagnostic is an important step towards the future development of effective personalized medicine.

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Industrial Biotechnology and Sustainable Economy in Bavaria: Data, potentials, trends

The economic sectors of (industrial) biotechnology and sustainable economy are flourishing in Bavaria. On top of this, Bavaria has been leading the ranking of the federal states in terms of the number of dedicated biotechnology companies for years. Directly after North Rhine-Westphalia, the state with the highest population, Bavaria provides the most jobs for biotech industry. In the entire secondary economic sector, the ,biologization of industry' is progressing and does not even stop at the mining industry. These positive developments are based on clever political decisions, excellent research by academic institutions and courageous industrial development projects. The balanced triad of academy, economy and politics prepares the ground for extraordinary biotech products and sustainable processes ,Made in Bavaria'...

A development is sustainable if it satisfies the needs of the present without compromising the ability of future generations to meet their own needs.' This sentence was already written in 1987 in the report of the Brundtland Commission and accurately describes the core of sustainability, which can only be achieved through the consistent application of the concepts of efficiency, consistency and sufficiency.

Thanks to the continuously increasing use of industrial biotechnology and ,sustainable economy' in more and more economic sectors, Bavaria is making an important contribution to preserving essential resources for future generations.

Political Initiatives

With the start of the ,Cluster Offensive' in 2006, proclaimed by the Bavarian Ministry of Economic Affairs, the rise of biotechnology and other future-oriented industries in Bavaria began. As a result of this political initiative, several clusters emerged with the aim of strengthening both high-tech industries and traditional key sectors of the Bavarian economy. At present, 17 clusters, in just as many different fields of competence, support the five megatrends defined for Bavaria: energy, health, digitization, materials and mobility.

In 2008, the ,BioIndustry 2021' cluster competition initiated by the federal government gave rise

to today's Industrielle Biotechnologie Bayern (IBB) Netzwerk GmbH. The network and service company based in Martinsried near Munich focuses specifically on the promotion of industrial biotechnology and sustainable economy. Initially fully co-financed by the federal government, the state and industry, since the end of 2013 the Free State alone has supported the company from public side. Currently, IBB Netzwerk GmbH finances itself to a large extent with about 75 percent of the turnover from acquired projects and own funds (more about the company on page 12). Since 2015, the early economic policy decisions have been joined by a new committee: the Bavarian

Industrial Biotechnology in Bavaria

Bioeconomy Council of Economic Experts, which was convened as part of the ,Initiative Bioeconomy for Bavaria'. It is currently elaborating a Bavarian bioeconomy strategy, which is to be published in 2019.

Industrial Research and Development

In Bavaria, many products and processes from the field of industrial biotechnology have already lost their infancy within just one decade. Although this does not mean that all market barriers have already been overcome, but the young industry can boast some successes.

Bavarian industrial companies such as Fritzmeier Umwelttechnik, Thermo Fisher Scientific Geneart, UPM, Clariant Produkte (Deutschland), Wacker Chemie, Freudenberg Chemical Specialities, Südzucker and Saint-Gobain Performance Plastics Biolink are driving developments in the industry and conquering more and more economic sectors.

They ,biologize' products or process paths traditionally based on fossil raw materials and purely chemical-physical processes. The spectrum of topics ranges from the fermentative production of polymers or aromas, synthetic biotechnology, the production of special or basic chemicals with the aid of enzymes, or from residues or wastewater, respectivley, sustainable adhesives, dyes and additives to fuels whose production does not compete with food. However, a large number of small and medium-sized companies and start-ups in Bavaria also have ,industrial biotechnology' in their portfolio. These include UnaveraChemLab, Electrochaea, Silantes, AMSilk, LXP Group, Naturhaus Naturfarben, DustBiosolutions, Polymaterials, Cascat, 2mag, Fabes, PreSens and Susteen Technologies.







Processes and products of industrial biotechnology have now found their way into many everyday consumer goods, such as cleaning agents and textiles, food and feed or in form of bioplastics.

Taken together, the Bavarian companies already reach dozens of industries. For example, they develop sustainable processes or products for the cosmetics, pharmaceutical, textile and food industries, for the paints, coatings, cleaning and lubricants industries, the construction and bioenergy sectors and the automotive and aviation industries.

Research Landscape

As intensively as on the industrial side, the majority of Bavarian universities and research institutions are dedicated to the tricky issues of industrial biotechnology and sustainable economy. With often astounding results, they continuously prove that they are an abundant source of innovative ideas and, as creative partners for research and development projects, can deliver important scientific findings.

At the Technical University of Munich, for example, a large number of professors work with this key technology across several faculties and locations. These include the Chairs of Chemistry of Biogenic Raw Materials. Microbiology, Biotechnology, Biological Chemistry and Bioprocess Engineering, as well as the WACKER Chair of Macromolecular Chemistry and the Werner Siemens Chair of Synthetic Biotechnology.

Almost all other Bavarian universities and colleges, such as Ludwig-Maximilian-University,

Munich University of Applied Sciences, Bayreuth University and the University of Erlangen-Nuremberg also conduct excellent research on industrial biotechnology.

Intensive research is also carried out at non-university research institutions such as the Max Planck and Fraunhofer Societies or the Helmholtz Centers.

It is therefore hardly surprising that the sheer number of research topics has now reached an enormous dimension, to name just a few:

- Biopolymers from renewable raw materials or from CO₂
- Fuels from agricultural residues and algae
- Thickening and binding agents from bacterial storage materials or proteins
- novel materials for tanks or coatings
- and much more. ■

Infrastructure

In industrial biotechnology, engineering sciences, process engineering, mechanical engineering and plant construction play a central role. It is only by upscaling production to industry standards that processes can be produced cost-efficiently and products can be competitive.

Concept*

Industrial biotechnology, sustainable economy, bioeconomy - these terms are often used synonymously, but there are very different concepts behind them. At its core, industrial biotechnology focuses on the technical transformation processes (biotechnologiwhile bioeconomy cal), focuses more on the raw materials (biological). For industrial biotechnology, it is therefore ,irrelevant' which starting materials are used if they are only converted biotechnologically, just as it is inverse for the bioeconomy which processes are used to process the biological starting materials.

Sustainable economy can be understood to mean an intersection of industrial biotechnology and bioeconomy, i.e. when biotechnological processes for the conversion of biologic raw materials are used sustainably. The greatest potential for a sustainable and environmentally friendly economy is expected from this intersection.



*The definitions described here merely reflect our understanding of the terms used in this article, serve as a basis for common understanding and make no claim to completeness or consensual recognition. Especially in industrial biotechnology, which works with living organisms and sometimes very heterogeneous starting materials, the leap from laboratory to industrial scale is very demanding and cost intensive. Small companies and start-ups in particular are often unable to finance this step on their own.

Bavaria also offers solutions for this development step so that a new approach can still reach mass production maturity. In March 2011, the TUM Technical Centre for White Biotechnology was opened at the Technical University of Munich. The University and the State of Bavaria invested four million euros in the construction and basic equipment of this facility, which is unique in the international university scenery. Biotechnological processes up to the cubic meter scale can be carried out there, and highly pure products up to the kg scale can be obtained.

According to a study by Ernst & Young in 2013, Bavaria still lacks a flexible pilot or demonstration plant that is open to all market participants. This need is now being considered. The construction of a multi-purpose demonstration plant in Straubing is expected to begin in 2019/2020. With this plant, the Free State of Bavaria is creating an opportunity, especially for smaller companies, to scale biotechnological processes up to industrial suitability. Due to its broad technical equipment and modular structure, the plant will be able to scale countless products and processes.

Cross-Clustering

As mentioned at the beginning, a total of 17 clusters in Bavaria are working on implementing the five major megatrends. The activities of the clusters speak for themselves: around 8,500 players cooperate in their networks, of which around 6,500 come from

Bavaria. Since their introduction, these clusters have held more than 12,000 events with over 640,000 participants and initiated more than 1,800 projects between companies and/or research institutions.

In the future, it will therefore be even more important to tap innovation potential at the intersections of different clusters and to initiate cross-cluster projects. This should enable the best possible use to be made of synergies for the further development of the Bavarian economy.

Clusters and networks that are of great relevance for industrial biotechnology and sustainable economy are the ,Chemie-Cluster', the ,Umweltcluster', the ,Medical Valley', the clusters in the fields of nutrition, nanotechnology and new materials as well as the ,Cluster Forst und Holz'. The list is not exhaustive, as there are also intersections with other clusters, initiatives, networks and associations in which still lies great potential.

<u>Trends</u>

In addition to the digitization of biotechnology, for example ,Internet of Things' (IoT), the ,cross-linked laboratory', and modeling of biotechnological processes, competitive biotechnological processes are needed that can be achieved above all through intensive optimization. Furthermore, the areas of synthetic biotechnology and ,omics' technologies, among others, still have large, untapped potential.

<u>There's always a job</u> to be done...

In the near future, tax incentives for research will be introduced in Germany. For Bavaria's and Germany's competitiveness in the international context, this instrument should be firmly anchored in the funding scene, in addition to project funding, even after a possible test phase.

Industrial Biotechnology in Bavaria



Some examples of Bavarian clusters, network management organizations and European associations in the field of industrial biotechnology and sustainable economy are shown here. More intensive cooperation between the clusters, but also stronger networking with European and international structures, should bring further advantages for Bavaria as an industrial location in the future.

Over and above, venture capital for start-ups in Germany - especially in the biotechnology sector - is still very difficult to obtain compared to other countries. Therefore, it will also be a great challenge in the future to promote start-ups in industrial biotechnology and sustainable economy in the best possible way.

The Future

The aim is to make the country fit for the future with state-of-the-art products and processes and to secure prosperity and jobs with them. Bavaria is on the right track.

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The biennial event brings together all stakeholders of the bioentrepreneurial and health tech ecosystem to inspire and to celebrate life science entrepreneurship.

- Be part of the bioentrepreneurial ecosystem !
- Don't miss key trends shaping the industry and the future of medicine !
- Meet exciting pre-seed and start-up showcases !
- Learn from peers, experienced entrepreneurs and industry leaders !
- Be inspired by key notes and captivating panel discussions !
- Participate in workshops, clinics and other interactive formats !
- Enjoy the m⁴ award ceremony !





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