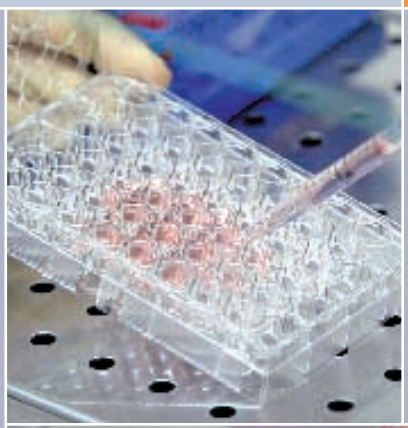
Science & Research

in the Rhineland



BioRiver Science

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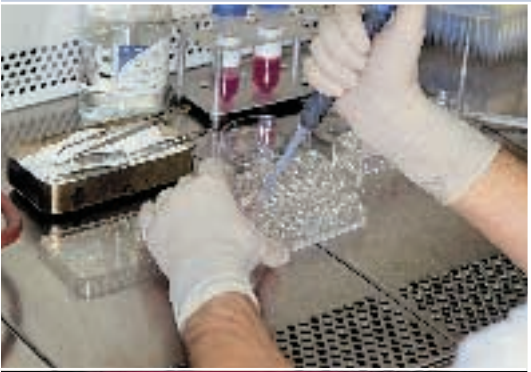
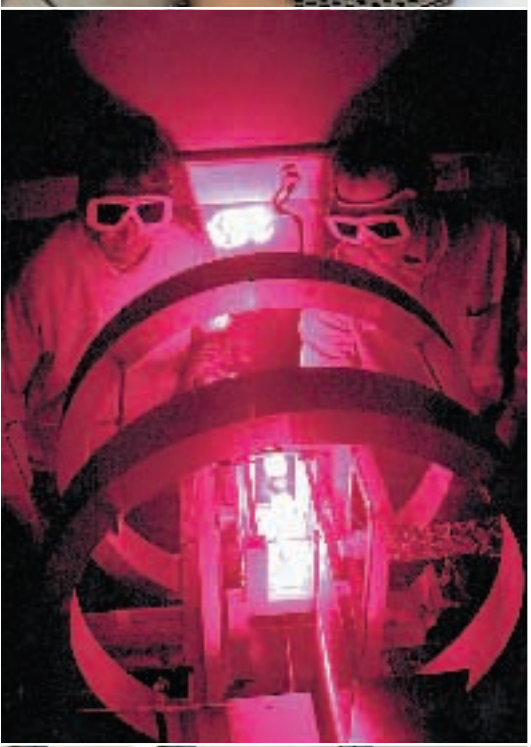
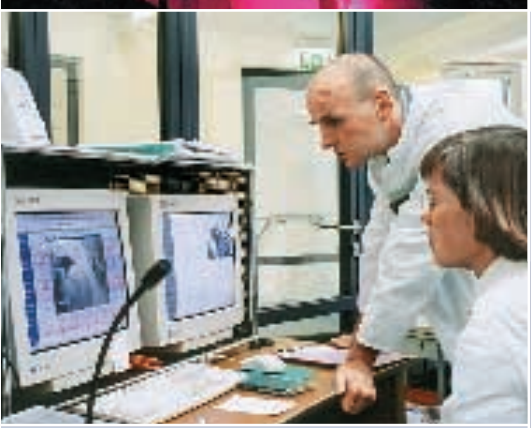






Imprint

Publisher:
The Rectorships of the Universities of Aachen, Bonn, Cologne and Düsseldorf,
and the board of the Research Centre Jülich

Contact:
University of Bonn/Dezernat 8 – Transfer and Public Relations
Nußallee 15a, D-53115 Bonn

Realization, Design and Production:
muehlhaus & moers kommunikation gmbh, Cologne

Editorial Works: Frank Luerweg, University of Bonn

Photography: Frank Homann; Eric Lichtenscheidt; Professor Dr. Helmut Reul, Institute for Biomedical Technology, Aachen University; Judith Bienen, Karin Görlitz, IZKF "BIOMAT", Aachen University; Manfred Bovi, Institute of Pathology, Aachen University; Peter Winandy; Professor Dr. Thomas Schmitz-Rode, Diagnostic Radiology, Aachen University; Clinic and Polyclinic of Dermatology and Venerology, University of Cologne; Institute of Biophysics, University Düsseldorf; Research Centre Jülich

Print: DIBA-Druck, Diefenbach GmbH, Cologne

Dear Reader,

The BioRiver region between Aachen, Bonn, Cologne, Düsseldorf and Jülich (the ABCD region) is one of the most intensively active areas for research and technology in Europe. As a result of the unparalleled concentration in this area of a great many public and private educational and research institutions, it is one of the leading regions for science in Germany. At the same time, around 150,000 students make the BioRiver region one of the most important areas for higher education in Europe.

Situated on the Rhine, our region has established itself world-wide as a center for life sciences, and thus the stream through Germany has become a "BioRiver". This river is fed from many sources: the universities in Aachen, Bonn, Cologne and Düsseldorf and the Research Centre Jülich. Top-ranking scientists are a guarantee of professional expertise, from research into fundamental principles right through to the development of new products. As a result our institutions are much sought after as partners for cooperative projects by higher educational establishments and companies all over the world. Professional scientists with first class qualifications in the life sciences and associated disciplines can be more readily found here than anywhere else. Geographical proximity facilitates the transfer of knowledge and cooperation on all levels. Important factors that qualify the BioRiver region as a leading region for life sciences are the favourable conditions for the foundation of new companies, and the proximity to reputed centers of expertise in the field of bioethics.

People are at the core of any scientific advance. The good reputation of the BioRiver region as a region for life sciences and biotechnology stands on the shoulders of outstanding individuals engaged in research. We would like to introduce you to some of these leading lights, as ambassadors for this leading life sciences region.

We invite you to discover what our region has to offer in matters to do with life sciences.

University of Aachen
Professor Dr. Burkhard Rauhut

University of Bonn
Professor Dr. Klaus Borchard

University of Cologne
Professor Dr. Tassilo Küpper

University of Düsseldorf
Professor Dr. Dr. Gert Kaiser

Research Centre Jülich
Professor Dr. Dr. Joachim Treusch

Contacts between Highly Specialized Cells Make the Difference in the Brain

Every human cell contains a complete set of stored information. However, depending on cell specialization, only some of the information is called up. Neuroscientists are asking questions like: How and when are certain parts of the cell activated and how can cells exchange information? In the BioRiver region experts of universities and industry are working closely together to find answers to these questions.

Brain research is among the most exciting but also most challenging fields in biomedical research. An understanding of normal brain functions will be an important prerequisite to develop novel diagnosis and treatment strategies for disorders of the central nervous system, many of which put a major burden on both the society and the medical systems. The BioRiver region is in an excellent position to take up this challenge. All participating universities support major programs in the neurosciences. In addition, the Helmholtz Research Centre in Jülich, the Max Planck Institute for Neurological Research in Cologne as well as various pharmaceutical and biotechnology companies considerably strengthen the local expertise. In this brief article, two of the centers (i.e. the Neuroscience Centre at the University of Bonn and the Helmholtz Research Centre in Jülich) will be portrayed. Information on brain research at the other BioRiver sites has been summarized in the boxes.

Many cells in the brain work like a good secretary: they make sure that only important images from our senses reach our mind. Unimportant signals are filtered out. "Disturbances of this automatic filter can cause severe mental illnesses," explain Professor Dr. Christian Elger and Dr. Thomas Grunwald. Brain researchers of the University of Bonn together with colleagues from Yale University are investigating how these cognitive filter processes function. To this end, many patients with epilepsy have electrodes implanted directly on the surface of the brain or in the brain itself. Using these electrodes, doctors can localise the origin of the attacks. Furthermore, the electrodes also enable scientists to identify the regions of the brain where the filter processes occur. Electrical responses that specific stimuli induce in the brain can be recorded immediately. Using this method, the participating scientists locate cells in which information processing occurs and investigate them in more detail.

Public-private partnership in brain research

A model institution, the research and development platform LIFE & BRAIN is being constructed at the medical campus in Bonn. LIFE stands for integrated research and development in the life sciences and BRAIN relates to the focus on neuroscience. One of its characteristics is close contact to partners from the industry that are going to work with the scientists from the Bonn University under the same roof. "Industrial and academic researchers interact and jointly develop new diagnostic and treatment modalities," explains Professor Dr. Otmar

"We hope that a treatment for diseases can be developed."

(from left) Professor Dr. Christian E. Elger, Professor Dr. Otmar D. Wiestler and Professor Dr. C. Oliver Brüstle, LIFE & BRAIN Research Platform, University of Bonn.

Research on brain diseases relies on expertise from many fields. Important tools include neuroimaging studies (top), neurophysiological recordings from patients' brains (bottom right) and molecular neurobiology (bottom left).

Wiestler, brain researcher from Bonn. Everyone benefits from the "everything under one roof" strategy: academic research because partners from the industry cover a part of the costs; the employees of the research platform gain experience from contact with the industry and the participating companies benefit from access to clinical data which would otherwise be inaccessible to them. Modern core units for the areas of genome research, transgenic models for central nervous system diseases, stem cell research, functional brain imaging as well as bio- and neuroinformatics will implement some of the key technologies used in brain research.

Interdisciplinary teams focus on brain disorders

It is not by chance that Venusberg is the location for the research platform: The University of Bonn with its Neuroscience Center, the Epilepsy Center and its Institutes for Neuropathology and Human Genetics is among Germany's high profile sites in the area of brain research. In addition to epilepsy, major topics include research ▸

Neurosciences

Aachen University

Collaborative Research Centers (SFBs)
SFB 542: Molecular Mechanisms of Cytokine Mediated Inflammatory Processes: Signal Transduction and Pathophysiological Consequences

Research Groups (DFG-funded)
450: Molecular Physiology of Ion Channels. 3D structure and Cellular Function; 112: Normal and Disturbed Attention and its Therapeutical Consequences: Basic Mechanisms and Clinical Application

Other Major Institutions
IZKF Aachen (Interdisciplinary Centre for Clinical Research, BMBF): Biomaterials and Material-tissue Interactions

University of Bonn

Collaborative Research Centers (SFBs)
SFB/TR3: Mesial Temporal Lobe Epilepsies; 400: Molecular Basis of Central Nervous System Disorders

Research Groups (DFG-funded)
427: Pathogenesis of Spinocerebellar Ataxia Type 3 (SCA3)

Graduate Colleges
246: Pathogenesis of Diseases of the Nervous System

Competence Networks
Stem Cell Network North-Rhine Westphalia; National Genome Research Network (BMBF), Neuronetz Bonn; Competence Networks "Schizophrenia", "Depression", "Parkinson's Disease" and "Dementia" (BMBF)

Other Major Institutions
Biomedical Research Platform LIFE & BRAIN GmbH; Institute for Science and Ethics e.V. (IWE); German Reference Centre for Ethics in the Life Sciences (DRZE); National Brain Tumour Reference Center (DGNN); Endowed Chair and Institute for Reconstructive Neurobiology (Gemeinnützige Hertie-Stiftung); Endowed Chair and Institute for Genetic Medicine (Alfried Krupp von Bohlen & Halbach-Stiftung)

University of Cologne

Research Groups (DFG-funded)
1088: Age-dependent Macula Degeneration

Research Centers
Molecular Mechanisms of Synaptic Processes in the CNS (IZKF); Coordination Centre for Clinical Studies Cologne (KKS Köln); ZVFK: Zentrum für Versorgungsforschung Köln; Institute for Neurological Research

Competence Networks
Stem Cell Network North-Rhine Westphalia; Competence Networks "Schizophrenia" and "Stroke" (BMBF); Network for Efficiency and Standardization of Dementia Diagnosis; EPOS European Prediction of Psychosis Study

Research Centre Jülich

Collaborative Research Centers (SFBs)
194: Function and Dysfunction of the Nervous System; 575: Experimental Hepatology

Research Groups (DFG-funded)
Normal and Impaired Attentional Processes: from Basic Neuroscience to Clinical Applications; Molecular Physiology of Ion Channels; Molecular Sensory Physiology

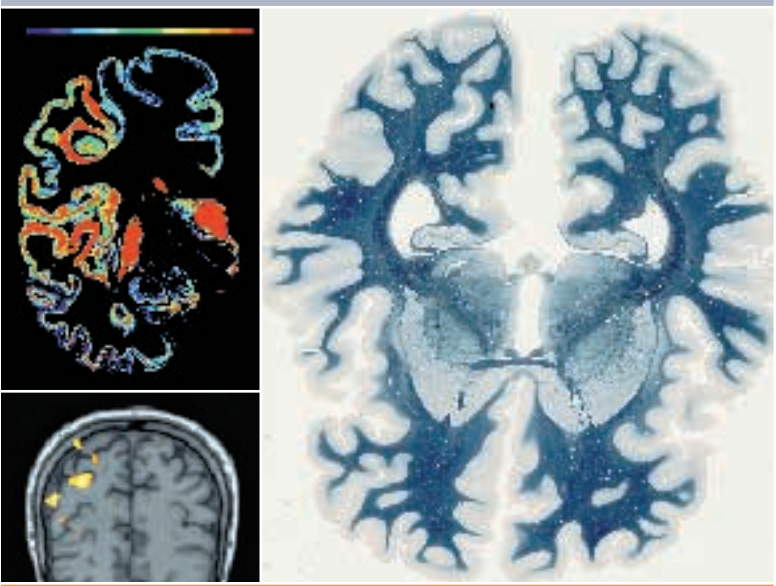
Research Centers
Brain Imaging Center West BICW (BMBF) together with Universities Aachen, Bonn, Cologne and Düsseldorf

Graduate Colleges
320: Pathological Processes of the Nervous System: from Gene to Behaviour

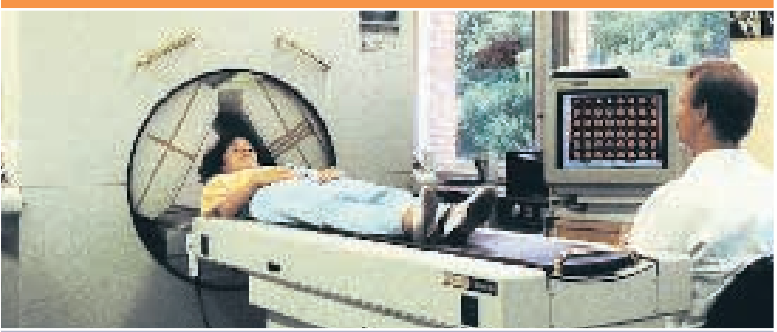
Competence Networks
Network "Schizophrenia" (BMBF); Network Bipolar Depression (BMBF); Therapy Network-TSE (Transmissible Spongioforme Encephalopathy); Human Brain Project (NIHM Grant) ▸

"Brain research is necessary because of the increasing life time of the populations."

Professor Dr. Karl Zilles, Institute of Medicine, Research Centre Jülich



Horizontal section of a human brain (above). Transmitter-receptor distribution (cholinergic receptors) in the human brain (left). Functional MRI – evidence for localized brain activation during spatial attention (left bottom). Positron emission tomography scanner (below).



► Neuroscience

University of Düsseldorf

Collaborative Research Centers (SFBs)
194: Dysfunction of the Nervous System

Research Groups
Neurodegenerative Diseases

Graduate Colleges
320: Pathological Processes of the Nervous System

Research Centers
Biological-Medical-Research-Center: Brain Function

Competence Networks
Dysfunction of Neuronal Networks (VW) (BMBF); Therapeutic Control of Feeding and Sleeping Disorders (EU)

on psychiatric diseases such as schizophrenia or depression, the investigation of inherited nervous system diseases, and of brain tumours as well as stem cell research. The participating scientists are generously supported by major funding organizations including Deutsche Forschungsgemeinschaft (DFG), the Federal Ministry of Science (BMBF), the local state, Deutsche Krebshilfe and Alfried Krupp von Bohlen & Halbach Stiftung. Also to mention: the Professorship for Reconstructive Neurobiology. Financially supported by the Hertie Foundation, this chair is unique for Germany and will considerably strengthen a new area of research in Bonn: tissue replacement with the help of stem cells.

New perspectives from stem cell research

Human embryonic stem cells (ES cells) can be developed in the Petri dish into precursors of many different tissue types. In collaboration with colleagues from the United States, Professor Dr. Oliver Brüstle who holds the foundation chair has recently succeeded in generating neural precursor cells from human embryonic stem cells. US scientists isolated neural precursors from stem cell cultures. They implanted the cells into newborn mice and sent the tissue on a long journey to Bonn, where Brüstle and his colleagues continued the experiment. "The transplanted cells migrated to different regions of the brain and matured into glial and nerve cells," explains the neuroscientist, who performed similar experiments with ES cells from mice in 1999 already. Brüstle hopes that a treatment for diseases such as multiple sclerosis can now be developed.

From molecules to complex neural systems

Basic research and the development of novel methods for diagnosis and therapy of neurological and psychiatric disorders are the goal of the Research Centre Jülich. "Brain research is not only an exciting exploration of an uncharted continent, but necessary because of the increasing life time of the populations, and thus increasing problems caused by these disorders", says Professor Dr. Karl Zilles from the Institute of Medicine.
The Institutes of Biological Information Processing, Structural Biology, Medicine and Nuclear Chemistry in Jülich analyse the function and dysfunction of the nervous system from the level of single molecules to that of

complex neural systems. They cooperate in national and international research programs, e.g. the Human Brain Project of the National Institute of Mental Health, USA, DFG-supported collaborative research centers (SFBs) and clinical research groups, the BMBF-supported National Network of Competence "Schizophrenia", and the recently granted (BMBF) Brain Imaging Center West (BICW) with international partners and colleagues of the universties in Aachen, Bonn, Düsseldorf and Cologne. Major clinically relevant topics are the molecular basis and pathophysiology of Parkinson's and Alzheimer's diseases as well as schizophrenia, epilepsy, consequences of stroke, diagnostics of brain tumours, and developmental and metabolic disorders of the human brain.

Concentration of most advanced research facilities

The structures and mechanisms of biological machines in cells, e.g. enzymes and transporter proteins are analysed in the Institute of Structural Biology at the level of atomic resolution. High resolution structures of intermediate states are obtained by using protein crystallography, multidimensional nuclear magnetic resonance and spectroscopy. "If you want to elucidate how diseases of the nervous system develop, you first need to understand the normal function of a nerve cell," says Professor Dr. Benjamin Kaupp, Director of the Institute of Biological Information Processing. The electrical and biochemical signalling in nerve cells is amazingly complex. Key to advances in our understanding of these cellular processes are exquisitely sensitive electrical and optical techniques that allow the observation of single biomolecules in a cell. These microtechniques provide fascinating novel insights into the cellular machines and pathways that enable us to see, to smell, and to taste.

The structure and functions of the living human brain are analyzed in the Institute of Medicine. Transmitter receptor molecules, major components of the signalling systems between nerve cells, are studied using positron emission tomography (PET). For these studies, radioactively labelled molecules are required, which are synthesized in the Institute of Nuclear Chemistry. These organic molecules are indicators of the concentration and localization of receptors in the living human brain. The development of such radioindicators is performed on the basis of physiological concepts and requires a multi-step process. The necessary radioisotopes with very short half-life time are generated using a particle accelerator. Finally, the radiolabelled molecules are extensively tested in pharmacological and preclinical trials before they are applied to healthy volunteers or patients.

Professor Gereon Fink from the Institute of Medicine analyzes, in cooperation with the Neurological Hospital of the University of Aachen, the neural mechanisms of cognitive and sensorimotor processes in the living normal or diseased human brain using functional magnetic resonance imaging (fMRI). A highlight amongst the large scale imaging systems in Jülich is the recently installed 4 Tesla high field, a whole body magnetic resonance scanner, which is an imaging facility unique in Germany. The research potentials of this scanner will be further developed by a group of physicists headed by Dr. Jon N. Shah. A further highlight of the biomedical research program in Jülich is the synchronization tomography using magnetic encephalography (MEG). This method has been developed by Professor Peter Tass, and allows the study of interaction of different regions in the normal or diseased living human brain at a time resolution of milliseconds. Furthermore, he is developing, in cooperation with the Department of Stereotaxic Neurosurgery of the University of Cologne, a novel demand controlled brain pacemaker for patients with intractable movement disorders, e.g. Parkinson's.

Network of neuroscience institutions

In addition to the centers in Bonn and Jülich, which have been portrayed in some detail, the region harbours other excellent facilities for neuroscience. In Cologne, these include the University and the Max Planck Institute for Neurological Research specializing in the development of novel therapies for Parkinson's disease and in research on stroke. At the University of Düsseldorf, renowned groups are working in the areas of neuroimmunology as well as degeneration and regeneration in the nervous system. The Medical Centre at the University of Aachen has profound expertise in research on central nervous system injuries and in the development of new treatment modalities for brain tumours.

A priority goal for the coming years will be to strengthen the network of neuroscience institutions in the BioRiver region. ■

Miniaturization of Medical Devices and a Repair Workshop for the Human Body

In the BioRiver region, researchers from the medical and natural sciences as well as technical engineers are working in close collaboration to develop advanced implants and medical devices. The results of this interdisciplinary work are impressive: Implants that are made from the body's own resources and are therefore better accepted as well as ever smaller technical appliances with superior performance in the patient.

The world's first heart valve to be composed solely of a patient's own tissue has been developed by a team working at the Interdisciplinary Center for Clinical Research "Biomaterials and Material-Tissue Interactions in Implants" (IZKF "BIOMAT") located at the Aachen University Clinics. The advantage of this novel heart valve replacement is two-fold: It is not rejected by the body's immune system and it can grow. Therefore, this novel tissue-engineered implant offers hope to children with heart disorders, as it saves them many cumbersome and painful operations required for the adjustment of the growing valve leaflets during childhood. This devlopment is just one example of the IZKF "BIOMAT"'s commitment to the emerging technology of tissue engineering: the replacement of malfunctioning body parts with the body's own materials combined with advanced synthetic materials.

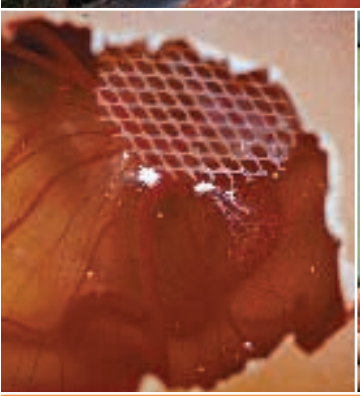
Speeding up the healing process

Further successful implants and devices, which were developed at the Centre, include vitreous body implants, bone and cartilage replacement materials, bioresorbable urethral stents and tissue implants ("meshes") for the support of hernia surgery. "What interests us most about implants is the interaction between material and tissue and, in particular, how we can harness the molecular processes of wound healing to improve the long-term performance of implants," explains Professor Willi Jahnen-Dechent, director of the post-graduate teaching program of the IZKF "BIOMAT". "We want to find out whether we can speed up the healing process by coating implants with endogenous messenger substances. We closely cooperate with basic scientists from a local center of excellence (collaborative research center 542), which is entirely devoted to the study of the molecular mechanisms of inflammation."

The protection of tissues in general and of the heart muscle in particular are major themes in a third research area pursued by the IZKF "BIOMAT". Major goals are the improvement of coronary vascularization, and the development of gentle, non-invasive methods for the regeneration of heart and vasculature in patients with occlusive cardiovascular disease. In addition, experts are examining the risks of future therapies with stem cells – particularly to find out whether disadvantages may arise from a prior treatment of blood vessel stenoses with endovascular prostheses (so-called stents).

Making synthetic materials biocompatible

A long standing cooperation exists between of the IZKF "BIOMAT" and the Aachen Competence Centre for Biomaterials (bwA). Here, the researchers are working on modifying the surface structure of implants. Coating with bioactive substances renders synthetic materials biocompatible and ensures that these materials are not rejected by the human body. The coating process has been successfully applied to plastics, textile structures and even metals. Coating agents include proteins of the extracellular matrix, growth stimulating or inhibiting signal molecules, so-called cytokines, differentiation factors or anti-inflammatory substances. Materials are tailored by choosing the right coating for a particular purpose. For example, coils for the closure of dilated blood vessels (aneurysms) are coated by thrombogenic substances, or vascular stents for recanalization of stenosed vessels are coated with growth inhibitors to prevent excessive cell proliferation and hence the clogging of freshly repaired vessels, a process called restenosis. Researchers have also developed a textile attachment apparatus for a synthetic cornea, a so-called keraprosthesis. The textile fibers are coated with the extracellular matrix molecule, fibronectin, to improve



The combination of engineering, natural science, and medical expertise provides an outstanding platform for interdisciplinary research and product development in the BioRiver region.

Medical Technology and Biomaterials

Aachen University

Collaborative Research Centers (SFBs):
440: Assembly of Hybrid Microsystems;
542: Molecular Mechanisms of Cytokine Modulated Inflammatory Processes: Signal Transduction and Pathophysiological Consequences

Research Groups (DFG-funded)
333: Surface-NMR of Elastomers and Biological Tissues

Research Centers
Interdisciplinary Center for Clinical Research "Biomaterials and Material-Tissue Interactions in Implants" (IZKF "BIOMAT");
Working group Helmholtz-Institute for Biomedical Technology;
Fraunhofer Institutes for Molecular Biology and Applied Ecology (IME), for Laser Technology (ILT) and for Production Technology (IPT);
In preparation: Institute for Technology and Development of Medical Products (ITEMP);
German Wool Research Institute

Graduate Colleges
Detection and Interfaces – Induced Control of Biomolecular und Cellular Functions; Regenerative Energies – A Cooperative Approach from Biologists and Engineers; Biofunctional Interfaces (in preparation)

Competence Centers and Networks
Aachen Competence Centre for Medical Technology (AKM);
Aachen Competence Centre for Biomaterials (bwA);
FORUM LIFE SCIENCES;
ALSA – Applied Life Science Aachen;
Retina Implants (BMBF), together with the Universities of Bonn and Cologne

University of Bonn

Research Groups (DFG-funded)
367: Keratinocytes – Proliferation and Differentiation in the Epidermis

Research Centers
Bonn Forum Biomedicin (BFB)

Other Major Institutions
Postoperative Intestinal Pathophysiology: Molecular and Cellular Mechanisms

cell attachment and hence fixing of the keratoprosthesis to the outer eye. Other BioRiver universities are also highly involved in research and development of biomaterials. Researchers from Düsseldorf successfully test new filling materials for bony defects. A research group at Bonn University investigates the interaction of biomaterials with epidermal cells.

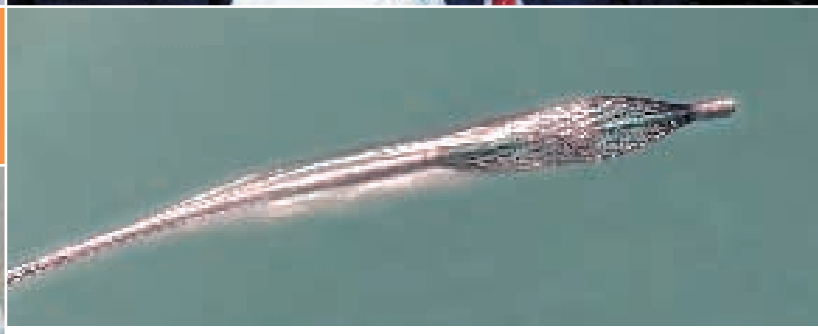
Developing medical instruments, devices, systems

The development of new biomaterials, however, is only one of the BioRiver research topics at the Aachen University. Another one is medical technology for development of highly integrated and miniaturized medical instruments, devices and systems.
Here, the Aachen University, with its combination of engineering, natural science and medical expertise of the University Clinic, provides an outstanding platform for interdisciplinary research and development. The benefits of bringing together a range of competences and capacities should lead to a fast rate of product development. Thus, in 2000, the Aachen Competence Centre for Medical Technology (AKM) was founded, supported by the Federal Ministry for Education and Research (BMBF). Here, in interdisciplinary projects, medical ▸

“Networking for biomaterials and medical devices.”

(from left) Professor Dr. Hartwig Höcker, bwA, FORUM LIFE SCIENCES, Professor Dr. Thomas Schmitz-Rode, AKM, and Professor Dr. Willi Jahnen-Dechent, IZKF “BIOMAT”, Aachen University

Miniaturized devices and instruments reduce trauma and minimise the risks of procedures.



technology products and processes are developed from initial concept to the market place. Ideas are provided by clinicians and scientists, institutes of the Aachen University and the three Fraunhofer Institutes for Production Technology, for Laser Technology and for Molecular Biology and Applied Ecology near the Clinic support development of the medical products, and young medical technology firms surrounding the university produce the end products. The regional industrial support agency (AGIT) and venture capital investors are also involved in this process. A spin-off company offering comprehensive services for the development of medical products is in its founding stage.

Minimizing the risk of complications

The AKM primarily promotes miniaturized medical technical systems. The tinier and preciser the instruments and implants are, the smaller is the negative impact on the patient. “In this way, we can minimize the risks of possible complications and greatly reduce the length of the recovery period,” says Professor Dr. Thomas Schmitz-Rode, chairman of the AKM. Special areas of interest include cardio-vascular and tissue therapy. Here, for example, scientists have developed blood pumps which support the heart and, at three millimetres, are so small that they can be positioned via puncture of a groin artery. Other development examples include blood pumps for replacement of the heart-lung-machine in heart surgery. The first models are already on the market, while others are currently in the test phase. Further projects are: a mini ablation tool for the treatment of heart rhythm disturbances, a tension sensor which helps to optimize surgical stitches, and an expandable mini-basket with which clots can be removed from pulmonary blood vessels.

The working group Helmholtz Institute for Biomedical Technology also carry out interdisciplinary work in the fields of medical technology and biomaterials research. The aim of this alliance of seven professorships (Medical Technology, Medical Information Technology, Biomaterials, Applied Medical Technology, Tissue Engineering, Cellular Engineering, and Molecular Imaging) is a combination of basic research and development in conjunction with the clinical application of the newest technologies for the benefit of the patient.

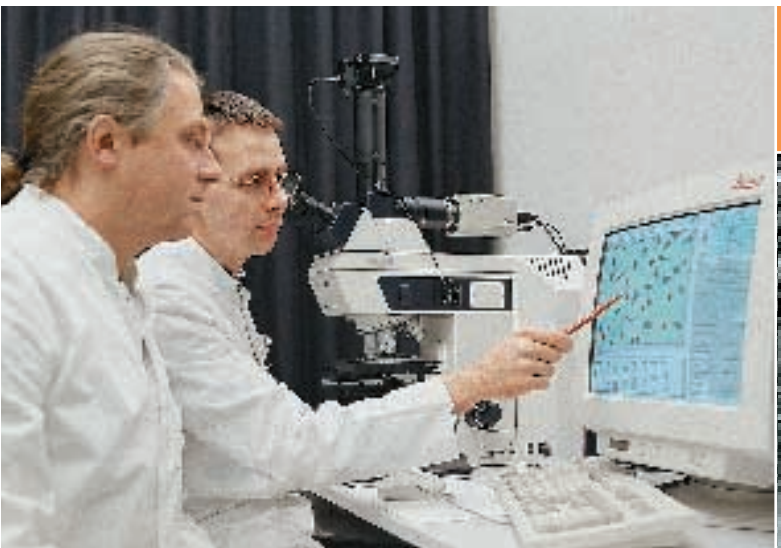
Education in medical technology and biomaterials

The students of the BioRiver region profit from the intensive interdisciplinary co-operation and remarkable research successes. Besides numerous interdisciplinary lectures and practical courses at the Aachen University, the University Clinic and the corresponding institutions, a master course in “Biomedical Engineering” is now

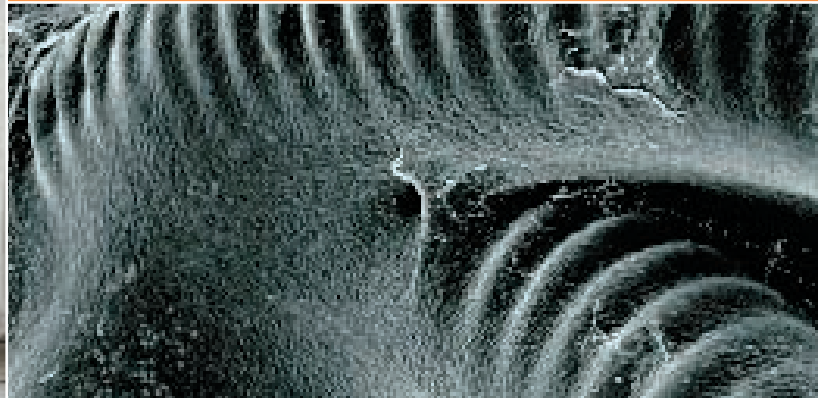
being offered. In addition to the basics of engineering, natural sciences and medicine, key specialized topics such as tissue engineering, artificial organs and devices, and image guided therapy constitute part of the syllabus. After four semesters, the graduates are ideally prepared for the international demands of both industrial and university research. Also, IZKF "BIOMAT" regards the continuing education of students at the pre- and post-graduate level as an essential part of its responsibilities. The educational programs offered, enable young scientists to acquire the knowledge and research techniques which make them desirable candidates on the university and industrial job market.

Building synergy in the life sciences

The interdisciplinary forums at the Aachen University stimulate cooperation and dialogue. This unique approach abandons strict boundaries between classical disciplines in order to find applied solutions. Innovation transfer into industrial applications is a major goal of this enterprise. Competences in the life sciences were brought together in the FORUM LIFE SCIENCES, which was founded in 2002. The FORUM LIFE SCIENCES is headed by Professor Dr. Hartwig Höcker, director of the German Wool Research Institute and chairman of the bwA. As an umbrella organisation for all life science centers, research plans, initiatives and major projects, the Forum seeks to promote medical technology and biomaterials research in the area of student teaching by the establishment of new graduate programs and in the area of basic research by founding special research areas. Thus, the Forum ensures that the BioRiver region takes full advantage of possible synergies in medical technology and biomaterials science. ■



"What interests us most about implants is the interaction between material and tissue."



From Basic Research to the Design of Novel Therapeutic Strategies

Treating complex diseases such as chronic inflammations or cancer calls for innovative and well-designed patient-tailored therapies. Such strategies require detailed information on the pathophysiology of these diseases. Modern medicine must therefore be able to integrate a large number of individual parameters, in particular when dealing with tumors, infections or inflammatory disorders.

"To develop and apply optimal treatment, we first need to identify the cause of the disease", says Professor Dr. Thomas Krieg from the Center for Molecular Medicine and the Department of Dermatology at the University of Cologne. "If, for example, diseases are caused by genetic alterations, ideally we could repair defective genes or turn them off. Unfortunately, for most diseases we do not have sufficient knowledge to perform such therapy yet ", he adds. At present, scientists in the BioRiver region can intervene at later stages of the disease or alter symptoms rather than cause of diseases. How do scientists address complex diseases such as cancer, infectious diseases or inflammation? In recent years, functional genomics and comparative genome analysis have made it possible to analyze genomes of entire organisms. Experts first analyzed the genomes of simple organisms, such as worms or flies before tackling the more complex human genome. With current genomic technology it is now possible to unveil complex interactions and to understand inflammation, cancer or infectious diseases at the molecular level. This can be exemplified for chronic inflammation: Inflammatory cells release mediators that activate receptors on adjacent cells. Changes are thereby induced in the cellular metabolism of these cells resulting in further disturbances. Ensuing inflammation could come to a halt if scientists were able to identify and inactivate the particular mediator. However simple this may sound, this poses a great challenge to scientists. Krieg explains: "Inflammatory cells respond in a multitude of ways and they form complex networks. We have started to track the pathologic changes so that we can begin to develop novel treatments targetting key enzymes or proteins involved in these processes." With this he refers to rheumatoid arthritis, an autoimmune disorder, or to psoriasis. Both are treated more efficiently today because therapeutic intervention can now target a much earlier event in the chain of pathological reactions leading up to the disease. According to Krieg: "With state-of-the-art information resulting from excellent science and research, we can apply today's pharmacological agents a lot more effectively with considerably less side effects than in the past."

Elucidation of mechanisms

Another important area of science and research at the universities of the BioRiver region is centered around infectious diseases. Activities range from basic science all the way to clinical medicine and drug development. To understand these complex diseases, BioRiver research teams focus on cellular functions and differentiation,

"BioRiver scientists induce genetic modifications in mice which closely resemble human diseases."

Professor Dr. Thomas Krieg, Clinic and Polyclinic for Dermatology and Venereology at the University of Cologne, Center of Molecular Medicine

State-of-the-art technology in the BioRiver region is the source of progress in biomedical research.

and on cell-cell interactions and signals between cells and their microenvironment. It is the prime goal of these research activities to elucidate mechanisms underlying inflammatory processes, tumor development and host defense against infection. State-of-the-art technology in cellular and molecular biology, genetics, imaging, genomics and proteomics as well as in bioinformatics are in place to support this science.

One such technology pioneered by researchers at Cologne University under the direction of Klaus Rajewsky in the past ten years is targeted gene modification. Using this technique, scientists can introduce precise genetic modifications in mice, thereby inducing pathological defects resembling human disease. These genetically determined models are important tools to learn more about the disease itself and to design suitable therapies targetting the genetic defects. In collaboration with the university hospitals and regional biotech companies, such new concepts are then taken to clinical application. The goal of this combined effort is to ▸

Inflammation, Infection and Tumors

Aachen University

Collaborative Research Centers (SFBs):
542: Molecular Mechanisms of Cytokine Mediated Inflammatory Processes: Signal Transduction and Pathophysiological Consequences

University of Bonn

Collaborative Research Centers (SFBs):
284: Glycoconjugates and Contact Structures at the Cell Surface;

Research Groups (DFG-funded)
Keratinocytes – Proliferation and Differentiation in the Epidermis; Genetic Epidemiology and Medical Genetics of Complex Diseases

Research Centers
Colorectal Cancers (BMBF)

Other Major Institutions
Metastatic Spreading of Malignant Tumors: Genetic Mechanisms and Therapeutic Modulation; Forum Biomedicin

University of Cologne

Collaborative Research Centers (SFBs)
502: Molecular Aspects of Pathogenesis, Diagnostics and Therapy of M. Hodgkin and Related Diseases; 572: Commitment of Cell Arrays and Cell Type Specification; 419: Environmental problems of industrialized regions; 612: Molecular Analysis of Cardiovascular Functions and Dysfunctions (together with Düsseldorf University)

Research Groups (DFG-funded)
Cell-cell and Cell-matrix Interactions in Skin. Control of Barrier Function and Defense.

Research Centers
Center for Molecular Medicine (ZMMK); Coordination Center for Clinical Studies Cologne (KKS Köln); Dictyostelium discoideum Genome Project; German Study Group "Hodgkin Lymphoma"; Development and Clinical Evaluation of a Novel Bispecific Molecule in the Treatment of Patients with Hodgkin Lymphoma

Graduate Colleges
International Graduate School in Genetics and Functional Genomics;
Graduate Program in Molecular and Cell Biology

Competence Networks
Malignant Lymphoma; Systemic Scleroderma, Pediatric Oncology; Stem Cell Network North-Rhine Westphalia

Other Major Institutions
National Programs "Genetic and Molecular Analysis of Basement Membranes"; "Innate Immunity"

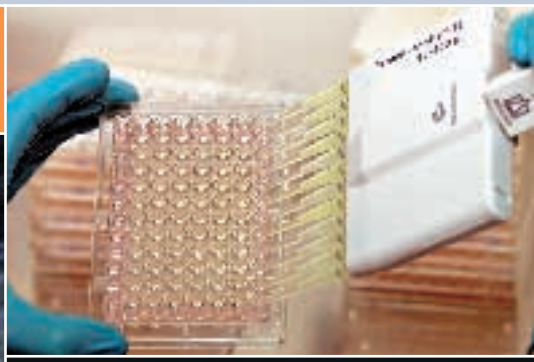
University of Düsseldorf

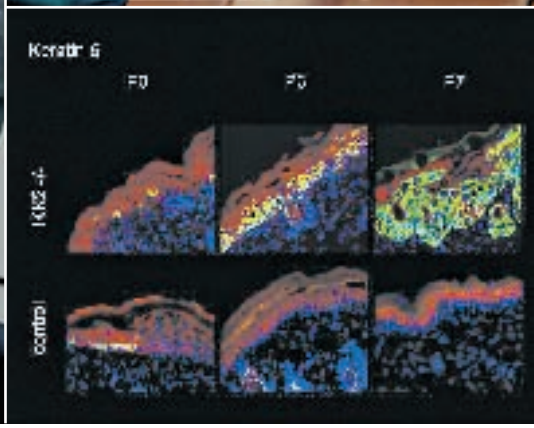
Collaborative Research Centers (SFBs)
503: Molecular and Cellular Mediators of Exogenus Noxae; 575: Experimental Hepatology; 590: Inherent and Adaptive Processes in Differentiation; 612: Molecular Analysis of Cardiovascular Functions and Dysfunctions

Research Centers (BMBF)
Diabetes Research Institute; Biological-medical Research Center: Infectiology, Cellular Communication, Cellular Proliferation

Competence Networks
Stem Cell Network North-Rhine Westphalia

Analysis of simple organisms has helped to identify genes responsible for human diseases.





improve treatment of such widespread diseases as cancer, chronic inflammation, atherosclerosis, diabetes, rheumatoid arthritis and allergy.

Focus on cellular communication and infection

To adequately address the needs of modern medicine, the Universities of Cologne and Düsseldorf have created Centers for Molecular Medicine. In Cologne, scientists address the role of cellular differentiation and the regulation of inflammation in cardiovascular disorders and chronic diseases of organs such as skin, liver, kidney or the eye. The Bio-Medical Research Center in Düsseldorf (BMFZ) focuses on cellular communication and infection. Again, research of imflammatory processes plays a critical role, which is also a theme at the Forum Biomedicine in Bonn.

Many collaborative research centers and groups

Excellence of research at these universities is further reflected by several collaborative research centers (SFBs) and research groups. The SFB 542 "Molecular mechanisms of cytokine-mediated inflammatory processes: Signaling pathways and pathophysiological consequences" at Aachen University is an example where scientists focus their work on acute and chronic inflammatory diseases in the liver and kidney and allergic reactions. This large network of scientists, led by Professor Dr. Peter Heinrich, postulates that the inflammatory reaction was optimized throughout evolution. Professor Dr. Helmut Sies in the Department for Physiological Chemistry in Düsseldorf with his group of scientists focuses on oxygen radicals and their biological activities. The SFB 503 in Düsseldorf concentrates on immune defense, immunotoxicity and chronic inflammatory disorders of the skin. These scientists hope that their research will lead to the development of novel therapeutic concepts for inflammatory diseases including atopic dermatitis and psoriasis.

Cancer represents the second most frequent cause of death in the Western world after cadiovascular diseases. As a logical consequence hematology and oncology are a major focus of research in the BioRiver region. In fact, the term cancer represents more than 250 diseases, which differ in their etiology and disease progression. Cancer is basically a form of uncontrolled cell growth resulting from combinations of genetic defects, environmental influences, such as radiation fallout or UV, and viruses. Initially, the tumor grows in one particular place, but, by the action of enzymes, can spread to the blood and lymphatic system and finally forms secondary tumors or metastases throughout the body.

Today we know that – for successful combat of cancer – we need to intervene at the earliest possible stage of the disease. In addition to standardized patient care of

cancer patients, research activities include the development of novel therapies, the optimization of diagnostic technologies, and basic research on the pathogenesis and pathophysiology of malignant neoplasms. Scientists in Cologne and Düsseldorf want to learn more about the enzymes and receptors expressed on the surface of cancer cells and responsible for the formation of both the tumor itself but also metastases. Targetting such genes might decrease tumor growth or spreading of tumor cells to other organs. Other molecularly defined approaches attempt to directly combat cancer cells. The best example is immune mediated lysis of malignant cells. Cancer cells can be recognized by the patient's immune system and killed by specialized immune cells. However, certain cancer cells have altered their surface such that they cannot be recognized anymore and they thus escape the body's immune patrol. "The aim now is to unravel such 'masking' mechanisms and thus to give the host a chance to use its own immune system to fight the cancer," says Professor Dr. Joachim Schultze from Cologne University.

Center for treatment of hematologic malignancies

Several centers of excellence have been established at different universities and research institutions within the BioRiver region. For instance, over the past 10 to 15 years a center was established in Cologne, headed by Professor Dr. Volker Diehl, which concentrates on the treatment of hematologic malignancies such as lymphoma and leukemias, which are cancers derived from blood, bone marrow or lymphoid organs. Under the direction of Diehl, researchers at this internationally recognized center have successfully cured a special type of lymphoma called Hodgkin's disease. Today, this center also hosts the head quarter of the German Competence Network on "Malignant Lymphoma". In Düsseldorf, gene therapy to fight leukemias complements the efforts on hematologic malignancies in the BioRiver region.

In addition to hematologic malignancies, malignant skin tumors such as melanoma, tumors of the liver and cancer in children are areas of intense research and development of innovative strategies to combat cancer.

Scientists in Cologne, but also in Bonn and Düsseldorf have initiated research programs concentrating on tumor immunology and immunotherapy. Specifically, they want to better understand defects of the immune system in cancer patients, and they seek to establish novel therapies based on antibodies and cancer vaccines.

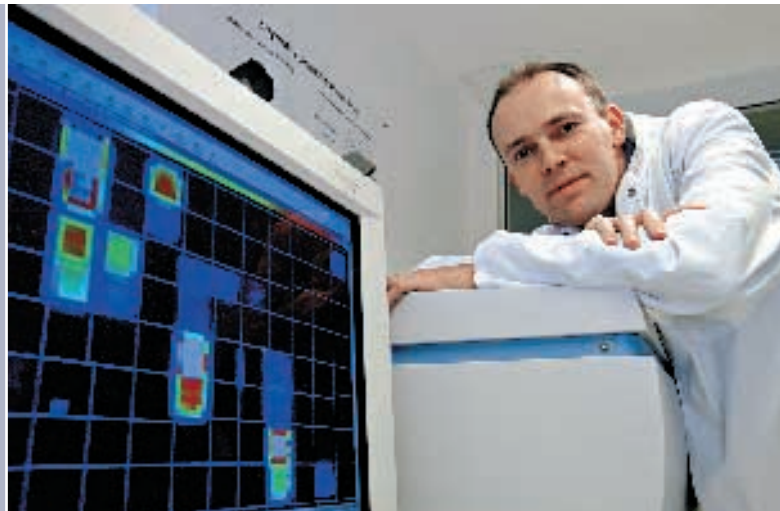
Diagnostics plays a central role to cancer treatment, and a major focus at Düsseldorf University is the development of novel and innovative molecular and cytogenetic tests to detect cancer as early as possible.

Tumor research is one of the most international disciplines in the life sciences. Expectedly, all centers at the universities in the BioRiver region maintain an extensive network of international and national collaborations to conquer cancer.

Success is achieved by interdisciplinary collaboration of experts from a variety of different fields, each contributing specialized knowledge. Professor Dr. Thomas Krieg from Cologne considers this the only way to reach the longterm goal of the BioRiver scientists and clinicians: to recognize at an early stage in the disease which treatment form is best suited for a particular patient and to tailor therapy according to the individual requirements. ■

"We want to give the host a chance to fight the cancer."

Professor Joachim Schultze, Medical Clinic I, University of Cologne



Microorganisms Produce Fine Chemicals and Pharmaceuticals

Coaches get their athletes to train hard in order to improve their performance levels and managers optimize their production processes in order to maximize profits. A similar process is involved when biotechnologists attempt to produce certain substances with the aid of microorganisms.

If the plant and livestock breeders were as successful as the microbiologists, then the problems of feeding the world would have been solved: in 1950, the first fungal strains produced just six milligrams of the antibiotic penicillin per liter during half a week – today's highly productive strains manage 60,000 milligrams – ten thousand times as much in the same period. "And this is in spite of the fact that until recently most advances have been made thanks more to elbow grease than to the little grey cells", says Professor Dr. Hermann Sahm, Director of the Institute of Biotechnology 1 (IBT) at the Research Centre Jülich, with a smile. "For scientists, this was an unsatisfactory state of affairs." Biotechnologists decided to use similar methods to those of their colleagues in cattle breeding in order to improve their fungi or bacteria: they looked for strains that were naturally more productive and optimized them either by crossing various highly productive strains or by exposing the strains to UV light or chemicals in order to create accidental mutations. The production of even more antibiotics, amino acids or vitamins became possible. Until now researchers have had a lot of success with this. "However, now these methods have reached their limits", says Sahm. "We have to get away from the 'trial and error' approach and adopt a targeted strategy instead."

In Jülich, this strategy consists of three building blocks, which Sahm describes as "genomics, proteomics, metabolomics": using the most up-to-date methods in genome and proteome research and sophisticated spectroscopic measuring procedures, the scientists first try to find out how the cells actually synthesise the product. How do cells manage to generate a vital protein building block or a highly effective antibiotic from sugar and a few nutrient salts after 20 or 30 reaction steps? And how can this sequence of reactions be made even more effective? It was known that certain genes and proteins in cells are much more active than usual during the synthesis of a product. The biotechnologists in Jülich are looking for exactly such differences in activity – not a simple task considering the thousands of hereditary factors and cell proteins that are present in even the simplest bacteria and fungi.

Making reactions more effective

The researchers use gene chips in their work. These are chips on which they arrange the required DNA strands. Since the individual strands only bond with specific components of a biological sample, biologists can quickly identify those hereditary factors that play an important part in the sequence of reactions.

"We have to adopt a targeted strategy."

Professor Dr. Hermann Sahm, Director of the Institute of Biotechnology 1 (IBT 1) and Professor Dr. Christian Wandrey, Director of the Institute of Biotechnology 2 (IBT 2) at the Research Centre Jülich

At the NMR lab at the Research Centre Jülich researchers observe the metabolism of bacteria (top). Under conditions close to those in industry, scientists at the pilot plant are testing new biotechnological processes (left).

Further elucidation of the metabolic path was made possible by labelling experiments. Here biotechnologists feed their "guinea-pigs" with, for example, glucose which they have labelled in some way, and then watch in which intermediate products this label appears again. Sahm and his team in Jülich have tested this procedure on a harmless soil bacterium, with which they wanted to produce the amino acid L-Lysine – a major component of infusion solutions for artificial nutrition.

Using the trial and error method, other scientists had already created strains that could produce L-Lysine – albeit only slowly and in small quantities. "In order to develop this metabolic path into a motorway, we used our labelling method to look for points at which the flow of reactions became congested", Sahm explains. "And we then specifically widened this bottleneck by, for example, ensuring that the bacterium produced larger quantities of a catalyst that accelerates the bottleneck reaction". The turbo-bacterium is now being used in the fermenters of Degussa, which has allowed the company to become one of the largest producers of L-Lysine in the world. One seventh of the world production – about ▸

Biotechnology Platform

Aachen University

Collaborative Research Centers (SFBs):
540: Model Based Experimental Analysis of Kinetic Phenomenon in Mulitphase Fluidic Action; 380: Asymmetric Synthesis with Chemical and Biological Methods (together with Research Centre Jülich)

Research Centers
Fraunhofer Institute of Molecular Biotechnology

Graduate Colleges
Removal of endocrin active compounds of sewage water (AGEESA)

University of Bonn

Collaborative Research Centers (SFBs)
624: Templates – From the Design of Chemical Templates to Reaction Control; 284: Glycoconjugates and Contact Structures of the Cell Surface

Research Groups (DFG-funded)
423: Genetic Epidemiology and Medical Genetics of Complex Diseases; 425: Adaptamers, Drugs, Signalling Molecules: Combinatorical Analysis of Cellular Functions and Organogenesis'

Research Centers
Life and Medical Sciences Bonn (LIMES);
Center for Molecular Biotechnology (CEMBIO)

Graduate Colleges
Analysis of Cellular Functions by Combinatoral Chemistry and Biochemistry; Functional Domains of Proteins

University of Cologne

Collaborative Research Centers (SFBs)
572: Commitment of Cell Arrays and Cell Type Specification

Research Groups (DFG-funded)
1070: Structure of Functional Modules of Energy-converting Systems in Prokaryotes

Research Centers
BRENDA – Enzyme and Metabolic Database

Graduate Colleges
Molecuar Analysis of Development Processes of Plants; Genetics of Cellular Systems; International Graduate School in Functional Genomics and Genetics; Molecular Physiology

Competence Networks (BMBF)
Functional Genomics and Proteomics;
Helmholtz-Network for Bioinformatics;

Research Centre Jülich

Research Groups (DFG-funded)
Instationary 13C Flux Analysis; Metabolic Modelling with in vivo, in vitro and in silicio Data

Research Centers
Biotechnikum

Graduate Colleges
Molecular Physiology (together with University of Düsseldorf); Methods in Asymmetric Synthesis (together with University Aachen)

Competence Networks (BMBF)
Microbial Genome Research; Microbial Proteome Research; Biocatalysis (NRW)

University of Düsseldorf

Collaborative Research Centers (SFBs)
TR1: From Procaryotes to Eucariotic Organelles

Research Groups (DFG-funded)
Analysis of Genomic Data

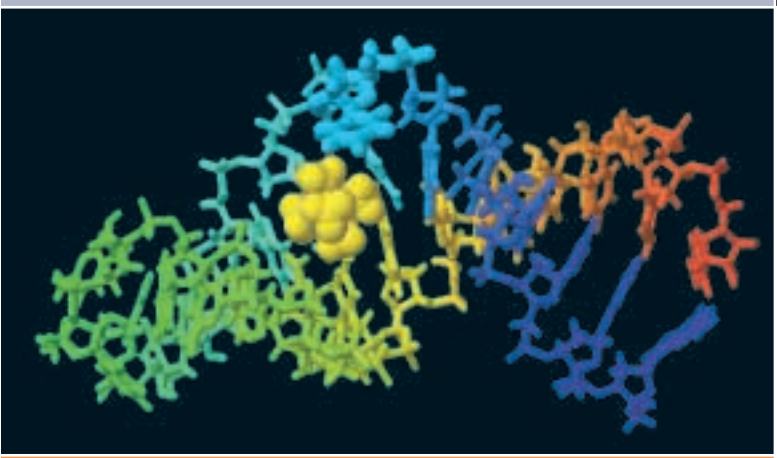
Graduate Colleges
Molecular Physiology

Competence Networks
TSE (Prion-Diseases)-Platform; Prion Diseases: Diagnostics and Therapy; VIP-GEN: Virtual Genetic Lab

Other Major Institutions
ASSICUIOIRT: Proteom of Interacting Membrane Protein (EU)

"The structural analysis of proteins and nucleic acids is becoming increasingly important for biotechnology."

Professor Dr. Detlev Riesner, Institute of Biophysics, University of Düsseldorf



Structure of a catalytic RNA as determined by nuclear magnetic resonance.

70,000 tons annually – comes from the German company alone. Sahm knows that "the same strategy can also be used to create specific, highly productive strains which produce large quantities of vitamins or antibiotics." But what does work in laboratory does not automatically work in the huge reaction vessels of industrial production facilities. To ensure that this step is successful, Sahm's team is working in cooperation with Professor Dr. Christian Wandrey, head of the Institute of Biotechnology 2 (IBT 2) in Jülich and Professor of Biotechnology at Bonn University.

At the IBT 2, Wandrey and his colleagues are trying to find the ideal conditions to spur microorganisms on to peak performance. That is no trivial task: Starting at the composition of the nutrient solution, its pH value and its temperature or the oxygen content in the fermenter atmosphere and the decision whether the billions of inhabitants prefer to be stirred, shaken or not, there are numerous parameters that can be modified. "In earlier times, it was primarily a matter of experience to find the ideal combination", explains Wandrey. "Today we use a quantitative analysis of the metabolic processes to determine the specific preferences and limitations of the respective microorganisms and to establish a process development. And yet – it does not quite work without testing. However, this testing should be carried out as intelligently as possible. For this purpose, we have developed intelligent mini-fermenters in the past few years", continues Professor Dr. Wandrey.

Studying the catalysts of cells

The close cooperation between IBT1 and 2 is one of the main sources of the Jülich biotechnologists' success. A further source is to be found only a few metres away, also in the research centre, but belonging to Düsseldorf University: the Institute of Enzymology Technology. Here, the catalysts of cells are studied. Enzymes accelerate metabolic reactions that would normally take place only very slowly. This also makes them interesting from a human perspective: enzymes in detergents get rid of stains quickly and thoroughly. The pharmaceutical industry uses enzymes in order to change antibiotics in a very targeted way to combat, for example, the resistance mechanisms of bacteria. The advantage of this is that the natural catalysts are highly effective and, what's more, extraordinarily accurate. Unlike with chemical syntheses, only the desired product is created. For many applications, however, the enzymologists are still desperately searching for a suitable biocatalyst. In view of the multitude of organisms with interesting metabolic attributes, this is a search for the proverbial needle in a haystack, but one for which Professor Dr. Jochen Büchs, a biochemical engineer from Aachen University is developing efficient methods. Together with a company, specialised in robotics, a fully automated culture system for 96 bioreactors, each as large as a finger tip, was designed. This system will provide online measurement for all individual bioreactors as an absolutey unique feature and will dramatically enhance the throughput of cultural experiments. Many enzymes that are used today, first had to be optimized for their task, as conditions in the hot soapy water of a washing machine are very different from those that exist in the cells from which the detergent enzymes were synthesized.

Detector to recognize prions early

The knowledge of the tertiary structure of a protein – also called 3D structure – is absolutely essential for the understanding of all biological functions, ranging from the metabolism and the immune system to sending specific signals through the body. Just how important the

right 3D structure is for the function of cell proteins is illustrated by the BSE epidemic and the more than 100 victims of the new variant of Creutzfeld-Jacob disease in the United Kingdom. Here it is a protein in the brain that takes on the wrong form and thereby even "infects" neighbouring proteins.

The Düsseldorf biophysicist Professor Dr. Detlev Riesner was the first researcher in Germany to work with prions – the name given to the altered proteins that lead to various diseases. He is interested above all in why the prion protein changes its 3D structure during the process of infection, thereby becoming a completely new kind of pathogen. "At the moment, we are working on a highly sensitive prion detector. At least in the laboratory we can now already detect individual prions using a sophisticated biophysical method and thus form the basis for early detection of infected cattle", Riesner explains.

Understanding the metabolic reaction

The enzyme researchers at the Research Centre Jülich are cooperating closely with biophysicists, information scientists and mathematicians in the Aachen-Bonn-Düsseldorf triangle. "The structural analysis of proteins and nucleic acids, the carriers of the hereditary information and the necessary methodological developments are becoming increasingly important for biotechnology", explains the scientist who co-founded Qiagen, one of the most successful biotech companies in Europe.
Teams in Cologne, Düsseldorf and Jülich are applying most advanced techniques of x-ray analysis and nuclear magnetic resonance to determine the 3D structure of proteins and nucleic acids to explore new catalytic activities in biotechnology and medicine. The experimental work is complemented nowadays by highly advanced computer programs. Those can sometimes predict the 3D structure by sequence alone. "This only works, though, if we have additional information and, for example, already know other enzymes with a similar function", explains Professor Dr. William Martin, plant physiologist and bioinformation scientist at Düsseldorf University and specialist in working with gene databases. The Cologne University Bioinformatics Center (CUBIC) headed by Professor Dr. Dietmar Schomburg, is one of the large-scale bioinformatics centers created by the German federal government to open up new areas of bioinformatics and to establish centers for graduate courses.

The next step in bioscience research is taken by analyzing the metabolome, i.e. the network of all metabolites in the cell, thus going beyond the interpretion of genome, protein and structural information.
"In order to better understand metabolic processes in bacteria and fungi as well as in plants or humans, and to make them useful in a biotechnological way, work has to be carried out on many different fronts", explains Riesner. It is the cooperation of the institutes and universities involved, that, during the last decade, has allowed the BioRiver region to develop into a biotechnology platform that is unique in Germany. The whole thing is like a giant jigsaw puzzle: if only one person works on it, it takes a long time to get the overall picture, which becomes recognizable only right at the end. But if a number of people are involved, each working from an different end, the players gain a much quicker overview of the parts' interconnection. ■

"Most advanced techniques help us determine 3D strucures of proteins and nucleic acids."

Professor Dr. William Martin, University of Düsseldorf

Science Shows Ethical Responsibility

Advances in the natural sciences and modern medicine raise moral questions which often lead to public controversy. In the BioRiver Region, there are specialist institutes devoted to these moral and ethical arguments.

How should we deal with the issues of genetic engineering, the use of embryonic stem cells, preimplantation diagnosis, assisted death and many other problematic areas? And what dangers for the individual and society are associated with the new technological possibilities? "A rational discussion can only be conducted on the basis of an ethical analysis", says Professor Dr. Ludger Honnefelder. He is the Chairman of the Institute for Science and Ethics e.V. (IWE) founded jointly by the Universities of Bonn and Essen and the major research facilities in Jülich (Research Centre Jülich) and Cologne-Porz (DLR) in 1993. It is supported by the State of North-Rhine Westphalia and is recognised as an Institute of the Universities of Bonn and Essen. Here, moral questions and their complex prerequisites are antithetically studied in interdisciplinary collaboration and with the help of analytical methods: Are the objectives correct? Are the methods to be used appropriate and permitted?

Since its foundation, in a series of externally funded interdisciplinary projects, the IWE has dealt with ethical and, in particular, bioethical questions and has also issued numerous specialist publications. With its "Science and Ethics Annual", already in its seventh issue, the Institute has created a forum for the scientific debate. In addition, the Institute organizes specialist conferences, colloquies, addresses and lecture series.

An adequate discussion of ethical problems is only possible with comprehensive information. However, this is widely dispersed and hard to find. Therefore, the IWE and the University of Bonn jointly founded the German Reference Center for Ethics in the Bio-Sciences (DRZE), which is supported by the Federal Ministry for Education and Research (BMBF). The DRZE collects information and literature from the whole field of bioethics, edits it up and, as far as possible, places it online. The DRZE also issues overviews of the progress of the discussion on complex questions such as cloning or preimplantation diagnosis. "We make important documents and information easily accessible to the public and thus help science, society, politics and media to form an qualified opinion," says Honnefelder, who is also Director of the DRZE. "In this way, we promote a well founded discussion of the moral and ethical questions in the life sciences."

"Rational discussion can only be conducted on the basis of an ethical analysis."

Professor Dr. Ludger Honnefelder, Chairman of the Institute of Science and Ethics e.V. (IWE), University of Bonn

Patents and Company Founders

Young branches of science are often pushed forward by young founders of companies. Many of them have in the past worked at universities. The BioRiver region offers future founders of companies the support they need.

Professor Dr. Detlev Riesner is convinced that "real innovations are brought about on the basis of research into fundamental principles. Industrial research is generally dedicated only to finding improvements in existing methods. Universities, on the other hand, can afford to open up completely new fields."Riesner knows what he is talking about: the biophysicist is one of the founders of Qiagen, a company based in Hilden near Düsseldof. With 1,500 employees worldwide, it is Germany's showcase biotech company. Qiagen came into existence only because, more than twenty years ago, a handful of scientists hit on the idea of researching more extensively into viroids that cause diseases in plants. Therefore the scientists developed a method to purify the viroid's RNA and to enrich it to a high degree of concentration, which shortly thereafter became extraordinarily important for many branches of gene technology. Today, Qiagen achieves a considerable part of its turnover by producing materials, entire kits or devices for obtaining DNA, RNA and proteins in pure form. Other companies in the Bioriver region, like RheinBiotec, Milteny, Amaxa, and others have had similar success stories. There are more than 230 life science companies in North-Rhine Westphalia. The majority of them are located in the triangle formed by the three cities Aachen, Cologne and Düsseldorf, and were founded by university members. For this and other reasons the BioRiver region became one of the three german "Bioregios", elected and particularly supported be the federal government.

When starting a company certain aspects have to be taken into account. "The scientific idea is the all-important thing – not the fact that you have worked out in advance how the accounts will look", is biophysicist Riesner's advice to young company directors. Future founders of companies, he adds, can acquire the requisite business management skills to some extent on their own, in parallel to their studies. But it is even more important to find the right partners when founding a company. Almost every higher education establishment by now offers highly refined training programs for people who are starting up a business. These include all know-how that company founders need: from the drawing up of financial plans and the acquisition of venture capital right through to personnel management. Progress on this way is expected particularly from new interdisciplinary studies. For example a combination of business and chemistry as offered in Düsseldorf – in addition to chemical science –, is not supposed to promote scientific progress in chemistry but to transfer chemistry into business.

The activities of universities and research institutions are strongly supported by the government granted initiative Bio-Gen-Tec-NRW which is managed by Hartmut Thomas and about ten employees. They are consultants for founders, spin-offs and also for the North-Rhine Westphalia department of Economy. The Bio-Gen-Tec-NRW organizes biotec-events and international contacts and promotes biotechnologies in general public.

A particularly important subject for young biotechnologists and other scientists in life sciences is protection against the theft of intellectual property. Consequently they need to learn how to conduct accurate research into a legal position before founding a new enterprise, and thus make sure that their own knowledge is adequately protected. For good reasons, patents are thought of as being the capital of a company founder. Taking all necessary precautions will help founders to find financial backers. At the colleges and universities of the BioRiver region, students can now attend entire lectures on patent rights. There are also transfer facilities that offer the opportunity of consulting patent lawyers. In the North-Rhine Westphalia university patent strategy, this is a means of ensuring that researchers can protect their discoveries.
The range of events offered for future company founders demonstrates that the BioRiver universities pofoundly promote entrepreneurial spirit. They see top-quality research into fundamental principles as the basis for industrial development.

Life Science Companies in the BioRiver Region

Companies total	approx. 230
Companies with research activites	approx. 90
Companies founded by members of the Universities and the Research Centre Jülich	approx. 60

Neuroscience

Institute of Neuropathology
University of Bonn Medical Center
Professor Dr. Otmar Wiestler
Sigmund-Freud-Straße 25
D-53105 Bonn
Phone: ++49/(0)2 28/2 87 66 02
Fax: ++49/(0)2 28/2 87 43 31
E-mail: otmar.wiestler@uni-bonn.de

Institute of Medicine (IME)
Research Centre Jülich
Professor Dr. Karl Zilles
D-52425 Jülich
Phone: ++49/(0)24 61/61 30 15
Fax: ++49/(0)24 61/61 29 90
E-mail: k.zilles@fz-juelich.de

Medical Technology, Biomaterials

Diagnostic Radiology, University Clinics
Aachen University
Professor Dr. Thomas Schmitz-Rode
Pauwelsstraße 30
D-52074 Aachen
Phone: ++49/(0)2 41/8 08 87 09
Fax: ++49/(0)2 41/8 08 24 80
E-mail: smiro@rad.rwth-aachen.de

German Wool Research Institute at
Aachen University
Professor Dr. Hartwig Höcker
Veltmanplatz 8
D-52062 Aachen
Phone: ++49/(0)2 41/4 46 90
Fax: ++49/(0)2 41/44 61 00
E-mail: hoecker@dwi.rwth-aachen.de

IZKF "BIOMAT", University Clinics
Aachen University
Professor Dr. Willi Jahnen-Dechent
Pauwelsstraße 30
D-52074 Aachen
Phone: ++49/(0)2 41/8 08 01 63
Fax: ++49/(0)2 41/8 08 25 73
E-mail: willi.jahnen@rwth-aachen.de

Inflammation, Infection and Tumors

Clinic and Policlinic of Dermatology and Venerology
University of Cologne
Professor Dr. Dr. Thomas Krieg
Joseph-Stelzmann-Straße 9
D-50931 Cologne
Phone: ++49/(0)2 21/4 78 45 12
Fax: ++49/(0)2 21/4 78 45 49
E-mail: thomas.krieg@uni-köln.de
Homepage: www.zmmk.uni-koeln.de

Immunological Laboratory of the Medical Clinic 1
University of Cologne
Professor Dr. Joachim Schultze
Joseph-Stelzman-Straße 9
D-50931 Cologne
Phone: ++49/(0)2 21/4 78 34 10
Fax: ++49/(0)02 21/4 78 67 33
E-mail: joachim.schultze@medizin.uni-koeln.de

Biotechnology Platform

Institute for Biotechnology
Research Centre Jülich
Professor Dr. Hermann Sahm
Professor Dr. Christian Wandrey
D-52425 Jülich
Phone: ++49/(0)24 61/61 32 94
Fax: ++49/(0)24 61/61 27 10
E-mail: h.sahm@fz-juelich.de

Institute of Biophysics
University of Düsseldorf
Professor Dr. Detlef Riesner
Universitätsstraße 1
D-40225 Düsseldorf
Phone: ++49/(0)2 11/81 1 48 40
Fax: ++49/(0)2 11/8 11 51 67
E-mail: riesner@biophys.uni-duesseldorf.de

Ethics

Institute for Science und Ethics e.V. (IWE);
German Reference Center for Ethics
in the Bio-Sciences (DRZE)
University of Bonn
Professor Dr. Dr. Ludger Honnefelder
Niebuhrstraße 51
D-53113 Bonn
Phone: ++49/(0)2 28/73 19 20
Fax: ++49/(0)2 28/73 19 50
E-mail: iwe@iwe.uni-bonn.de

Institute for History and Ethics of Medicine
University of Cologne
Professor Dr. Dr. Klaus Bergdolt
Joseph-Stelzmann-Straße 9
D-50931 Cologne
Phone: ++49/(0)2 21/478 52 66
Fax: ++49/(0)2 21/478 67 94
E-mail: bergdolt@rrz.uni-koeln.de

Philosophical Institute
University of Düsseldorf
Professor Dr. Dieter Birnbacher
Universitätsstraße 1
D-40225 Düsseldorf
Phone: ++49/(0)2 11/81-12 912
Fax: ++49/(0)2 11/81-15 651
E-mail: dieter.birnbacher@uni-bonn.de

Company Founding, Patents

Bio-Gen-Tec-NRW
Hartmut Thomas
Nattermannallee 1
D-50829 Cologne
Phone: ++49/(0)2 21/94 98 24 54
Fax: ++49/(0)2 21/94 98 24 44
E-mail: thomas@bio-gen-tec-nrw.de

Facts & Figures

Aachen University	
Students	29,667
Professors	414
Scientific staff members	1,930
Year of foundation	1870
Homepage	www.rwth-aachen.de

University of Bonn	
Students	38,000
Professors	538
Scientific staff members	2,143
Year of foundation	1818
Hompage	www.uni-bonn.de

University of Cologne	
Students	63,890
Professors	512
Scientific staff members	1,609
Year of foundation	1388
Homepage	www.uni-koeln.de

University of Düsseldorf	
Students	25,200
Professors	301
Scientific staff members	1,236
Year of foundation	1965
Homepage	www.uni-duesseldorf.de

Research Centre Jülich	
Professors	47
Scientific staff members	1,100
Year of foundation	1956
Homepage	www.fz-juelich.de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