A great success: ‘IdeenExpo’ visitors enjoy REBIRTH Inside

SCIENCE
Small livers on a big scale

FUNDING
Help for the ageing heart

ZEBRAFISH
Visit from Toronto
New therapeutic approach for diastolic heart failure

In diastolic heart failure, the wall of this organ thickens and becomes too rigid, so that the heart can neither properly relax nor properly fill. REBIRTH scientists working with a mouse model have discovered a new approach to treating this condition: cardiac function improved when they inhibited a particular long non-coding RNA (IncRNA) called Meg3. This IncRNA is relatively abundant in the connective-tissue cells of the heart. It regulates the level of metalloproteinases in this organ; these play a key role in the stiffening and thickening processes (fibrosis). When the researchers had silenced Meg3, fibrosis took place to a lesser extent. The aim is to develop this therapeutic approach to the point where it can be applied in patients.

Publication

New biomarkers for hiPSCs

Cardiac muscle cells produced from human induced pluripotent stem cells (hiPSCs) have potential for use in individualized tissue transplants. These cells need to be pure and well characterized. REBIRTH researchers investigated glycoproteins and N-glycans on the surface of hiPSCs, cardiac precursor cells and cardiac cells. They succeeded in identifying a number of possible new biomarkers for hiPSCs and cardiac muscle cells.

Publication

Modified macrophages prove easy to produce

Stable expression of therapeutic transgenes in induced pluripotent stem cells (iPS cells), and in progeny derived therefrom, form the basis of innovative blood cell replacement therapies. During the differentiation of human iPS cell lines into blood cells, REBIRTH researchers generated and evaluated various expression technologies. A combination of hiPS cell technology with either lentiviral vector technology or designer nuclelease-based genome editing allows the generation of transgenic IPS cell-derived macrophages with stable transgene expression, which may be beneficial in novel cellular and gene replacement therapies.

Publication

Developing a bio-artificial lung – gas exchange possible via patient’s breathing

REBIRTH researchers are working on the development of a bio-artificial lung (BA) as a therapeutic strategy offering an alternative to lung transplants. Using a mock circulation loop, they have now investigated intracorporeal implantation with the BA positioned at the upper lobe of the lung. In simulation under various clinical conditions, the scientists tested the gas exchange performance of three different oxygenators. They were, for the first time, able to show that an intracorporeal BA allows sufficient levels of gas exchange via the patient’s breathing, without damaging the gas-exchange hollow fibres in the oxygenators.

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A great success: ‘IdeenExpo’ visitors enjoy REBIRTH Inside

No sooner, it seemed, had the ‘IdeenExpo’ opened its doors than a queue formed in front of the cell-shaped tents of the 1,000 square metre REBIRTH Inside display. The line did not shorten until the early evening, and this pattern was repeated on each of the next eight days. Between 10 and 18 June 2017, some 20,000 pupils, teachers, parents and other curious visitors went on a time journey to the year 2050 and marvelled at the medicine of tomorrow. With great dedication, enthusiasm and stamina, REBIRTH researchers – including professors, post-docs, doctoral and other students, and school-leavers doing a Research Gap Year (FWJ) – guided the visitors round the five tents. They explained how widespread health problems such as heart attack and acute liver failure could be treated in the future, thanks to current research within the REBIRTH Cluster of Excellence, and what is already possible. “This exhibit is really engrossing,” says Maja R. who, with her two children, came to the REBIRTH display on the first Saturday. “It’s fascinating to learn first-hand about what modern medicine is making possible.” Her children were particularly taken with the ‘Heroes of Research’, who informed youngsters about possible career paths in medical research.

Get on your bike: in the ‘REBIRTH Active’ area, young people experienced – in a hands-on (and feet-on!) way – how they can add years to their lives. They learned how regular endurance sport such as cycling can help them maintain and improve their biological age – and, therefore, their health.
In the ‘Gene Taxi’, student and former Research Gap Year participant Annabell Wähner asks the pupils about cells and genes and explains how scientists can take viruses that have been rendered harmless and use them to smuggle genes into cells – thus transforming the body’s cells into induced pluripotent stem cells (iPS cells).

In the Future Clinic, researchers ‘disposed of’ various diseases in an oversized bin, while Research Gap Year participant Mareille Posner – after a brief introduction – provided visitors with an inside look at an operating theatre.

Professor Axel Haverich, coordinator of the REBIRTH Cluster of Excellence, outlines to Lower Saxony’s Prime Minister Stephan Weil and his cabinet how his team is enhancing the Organ Care System (OCS) and the ‘artificial lung’. The OCS allows donor organs to be transported at body temperature and the lungs to be treated outside the body.
Bloody Popcorn Machine:

Above: Professor Haverich explains to Lower Saxony’s Minister for Science, Gabriele Heinen-Kljajić, how researchers can make blood from skin cells.

Right: Doctoral student Katrin Haake outlines to Hauke Jagau, the President of Region Hannover, how she can produce blood cells from iPS cells using a bioreactor.
The Heart Reactor: REBIRTH research group leader Dr Nico Lachmann describes how REBIRTH engineers heart tissue. His audience: Ursula von der Leyen, Germany’s Minister for Defence and herself a graduate of Hannover Medical School (MHH), and Volker Schmidt, who chairs the Supervisory Board of organizers ‘IdeenExpo’ GmbH.

Prime Minister Weil was so impressed by the REBIRTH exhibit that he reiterated his impromptu recommendation to his colleague Brigitte Zypries, Federal Minister for Economic Affairs and Energy, that she include the display on her ‘IdeenExpo’ tour.

IdeenExpo 2017

Over 360,000 visitors came to marvel at science and technology, try out the 650 or so hands-on interactive exhibits, and attend more than 700 workshops. Over nine days, and on an area exceeding 100,000 square metres, 250 exhibitors highlighted the diversity of STEM careers. This year’s ‘IdeenExpo’ was the sixth in all, and it was the fifth time that the REBIRTH Cluster of Excellence had had a presence there.

REBIRTH Inside: Concept and Realisation

Concept: Hannes Malte Mahler, Franz Betz and design agency neuwaerts
Organisation and realisation: design agency neuwaerts
Production and construction: AT-Promotion GmbH
All thanks to REBIRTH: successful collaboration between two quite different realms of science

Michael Ott

Investigators from two different REBIRTH units recently published their joint findings on the use of functionalized drugs. These two research groups are Functionalized Polymers and Regenerative Agents (led by Professor Andreas Kirschning of the University of Hannover’s Institute of Organic Chemistry (OCI), and Hepatic Cell Transplantation and Genetic Manipulation (headed by Professor Michael Ott within the Department of Gastroenterology, Hepatology and Endocrinology).

The key question: how can drugs be modified so that they do not exert their therapeutic action until they are right where they are needed – as opposed to everywhere in the body? The scientists at OCI, Katja Seidel and Liang-Liang Wang, are working with complex chemical compounds that break down into their constituent parts under the influence of heat. They consist of various components: SPION (an iron oxide nanocarrier), thermosensitive chemical linkers, and the active ingredient itself. “If the drug, which may be a highly potent chemotherapeutic agent – a toxin – bonds with the SPION component, then this drug, for the time being at least, is deactivated,” says Professor Kirschning. “When the nanostructured drug, which can be guided by a magnet, has reached the tumour, we could heat up the SPION core (which contains iron) by specifically applying a magnetic field in the tumour region; this technique is known as hyperthermia. This would cause the complex to disintegrate and the drug to be released only in the vicinity of the tumour – meaning it would exert its effect only where it needs to.”

It was here that the MHH researchers came in. Dr Asha Balakrishnan (of Professor Ott’s work group) – who has, for some years now, been involved in developing new therapies for liver cancer – was immediately taken with the idea. She conducted numerous experiments both in cell culture and using a mouse model, and was indeed able to substantiate the predicted mode of action. The tumours stop growing following treatment with the complexes derived from organic chemistry – without other organs being damaged by the ‘smuggled in’ substances.

This successful demonstration of the mode of action of thermosensitive linkers marks only the beginning of extensive collaboration between the two units, says Professor Ott: “Targeted local release of active ingredients, such as hormones or growth factors, would be beneficial to many applications in regenerative medicine, and would both improve the action of drugs at the target site and reduce side-effects for the body as a whole.”

“Looking back, the REBIRTH interdisciplinary research alliance was the vital catalyst in our collaboration,” the two co-leaders of this research project affirm. They agree that: “Without the platform that is the Cluster of Excellence, we may well never have found out about the other work group’s activities at all.”

Publications
“It’s like a miracle”

Cardiologists at MHH publish three studies on peripartum cardiomyopathy (PPCM)

Bianca W. laughs and jokes with her two-year-old son Tim. “It still feels like a miracle,” she says. Following the birth of her daughter Ronja in April 2013, doctors had advised her against getting pregnant again. During her pregnancy back then, she had suffered a life-threatening heart condition called peripartum cardiomyopathy (PPCM), which is a pregnancy-related weakness of the heart muscle.

Bianca W. lives in the German town of Bad Oeynhausen. The cardiac centre there lost no time in referring her to the Department of Cardiology and Angiology at Hannover Medical School (MHH), Europe’s largest centre for PPCM. When she became pregnant once more, the MHH-based cardiologists joined forces with the practice-based physicians treating her where she lived to ensure close monitoring of her condition. “PPCM is a rare disease that can be managed well in most cases,” comments the Department’s director Professor Johann Bauersachs, “but subsequent pregnancies are associated with high risks and necessitate the best attention possible within centres of expertise. The mother-to-be requires close ongoing support from an interdisciplinary team of cardiologists, obstetrics professionals and neonatologists – both in pregnancy and during and after childbirth – and needs a carefully tailored treatment plan.”

Three studies lent weight to findings

Professor Bauersachs and Professor Denise Hilfiker-Kleiner (of the REBIRTH unit on Endogenous Regeneration Mechanisms of the Heart) have now lent weight to their findings with three scientific publications in the prestigious European Heart Journal.

Bromocriptine improves treatment

In this multicentre study the physicians demonstrated that,
when bromocriptine is used to augment the standard therapy for heart failure, it improved treatment outcomes for PPCM. Bromocriptine inhibits the release of the breast-feeding hormone prolactin. "A cleavage product of prolactin appears to be a crucial factor in PPCM. Bromocriptine therapy prevents this factor being formed," explains Professor Hilfiker-Kleiner. And Professor Bauersachs adds: "This study shows that, in combination with the medication for heart failure, bromocriptine aids recovery from PPCM. In most cases, concomitant treatment with bromocriptine lasting seven days is sufficient to reduce both mortality and heart transplant rates, and to promote the heart’s full recovery." The study included 63 women with PPCM at 12 centres in Germany.

PPCM: the risk associated with another pregnancy

In a further study, the cardiologists were able to prove that, for mothers who had developed PPCM during a previous pregnancy, the risk associated with getting pregnant again very much depends on how successfully the PPCM had been treated. Here, too, it was evident that – where there was complementary administration of bromocriptine immediately after birth – the outcome of PPCM treatment was better. This means that, for these women, the risk of suffering heart failure if they have another pregnancy was reduced. "One of our study’s findings is that, for patients with severely compromised cardiac function who become pregnant once more, the risk is higher that the condition of their heart will worsen. However, we also found that, in patients who are given bromocriptine immediately after childbirth, cardiac health was less likely to continue to deteriorate," says Professor Hilfiker-Kleiner. This investigation, involving 34 mothers, was carried out by the MHH physicians in collaboration with colleagues at two teaching hospitals in South Africa and Scotland.

PPCM is a worldwide problem

In the third study, an international research consortium discovered, with reference to the worldwide PPCM register, that this condition occurs worldwide in women with various ethnic backgrounds, irrespective of marked differences in socioeconomic status. For this investigation, the team had access to data for 411 women from 43 countries. “The majority of PPCM cases worldwide are diagnosed after childbirth, and most of the women affected have severe heart failure,” says Professor Bauersachs.

About this publication

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NEW SCIENTIFIC FINDINGS

Scientists put together a comprehensive atlas of blood formation

Every day, the body produces billions of new blood cells; it needs to, as many of these cells have a lifespan of only a few days or weeks. Researchers at Hannover Medical School (MHH) have now created the first comprehensive ‘atlas’ to map a special class of molecules crucial to this process. These are the non-coding ribonucleic acids, of which there are some 40,000. They control a wide range of very different processes in the cells – including which genes are transcribed, when and how often.

“Our atlas enhances our understanding not only of how blood cells form, but also of how blood diseases develop. It is also possible to predict the course of disease in leukaemia patients more accurately, allowing more personalized therapy,” says Dr Jan-Henning Klusmann, an associate REBIRTH member within MHH’s Department of Paediatric Haematology and Oncology. This atlas can be viewed online at www.leukemia-research.de (under the heading ‘Inc-Scape’). The underlying study was published by Dr Klusmann’s team in the journal Nature Communications. Its lead authors are Dr Dr Adrian Schwarzer (from MHH’s Institute of Experimental Haematology and the School’s Department of Haematology, Haemostaseology, Oncology and Stem Cell Transplantation) and Stephan Emmrich (formerly of MHH’s Department of Paediatric Haematology and Oncology, now based at the University of Rochester, New York).

The blood contains different types of cells: platelets (which, strictly, are cell fragments), red and white blood cells. Their maturation in the bone marrow depends on complex – and, thus far, poorly understood – interplay between non-coding RNAs and other molecules in the cell. The researchers’ analysis enabled them to assign functions to many of these non-coding RNAs. For example, they found non-coding RNAs that are important in the maturation of granulocytes (a type of white blood cell and hence part of the immune system). “Our aim is to use this atlas to help us determine the cause of leukaemia in individual patients and, on this basis, make recommendations on treatment,” Dr Klusmann says.

Publication
Understanding brain function is one of the primary concerns of our modern society – the reason for this being social changes such as stress or sleep problems, ageing of the population and the associated greater prevalence of neurological and psychiatric illness. It is therefore extremely important to improve our awareness of the origin and mechanisms of the neurological and psychiatric disorders that are a major financial burden on our society. Many of these conditions, such as depression, addictions, autism, schizophrenia, stroke, epilepsy, Alzheimer’s and Parkinson’s disease arise from impairment of communication between individual nerve cells – interaction that takes place at highly specialized intercellular contacts, the synapses.

In this study we investigated the interaction between serotonin receptors and the extracellular matrix (ECM), which coats the neurons like a mesh and has a protective and stabilizing effect. Using high-resolution imaging in conjunction with electrophysiological and biophysical methods, we were able to elucidate the role of serotonin receptor 5-HT7 in controlling ECM-mediated processes in the brain. We were able to show that activation of the 5-HT7 receptor initiates local remodelling of the ECM. This results in long-term im-
stem cells in our bone marrow keep us supplied with new blood cells and immune cells. If they malfunction – due to a hereditary disease or leukaemia, say – transplantation of bone marrow cells is usually the only treatment option. To prevent a patient’s immune system from rejecting these transplanted stem cells, however, it must be suppressed. This unfortunately, makes it easy for bacteria and viruses to cause complications, which they frequently do – from rejection of the donor organ to life-threatening illness. Scientists at TWINCORE and the German Cancer Research Center (DKFZ) have now joined forces to explore the influence that viral infections have on transplant success. They have been assisted by Dawn Lin of the Walter und Eliza Hall Institute in Melbourne who, with support from the REBIRTH Cluster of Excellence, completed a three-month period of research at the TWINCORE facility in 2015. The investigators recently published their findings in *Cell Reports*.

Rather than look at donors’ health at the moment of donation – which is checked anyway – this study examined the

"For stem cell donors, background checks as to infection history need to be tightened."

"The mechanisms may also be relevant for myocardial cells

The mechanisms we have discovered by which the ECM is remodelled in patients with heart failure – so that new therapeutic strategies can potentially be devised to prevent the progression of heart failure.

Publication
NEW SCIENTIFIC FINDINGS

Long-term effect of viral infections (that have already subsided) on the properties of bone marrow cells. The researchers’ particular focus was on those stem cells that are the least differentiated and live the longest. Known as long-term stem cells, these cells are dormant (‘quiescent’) under normal conditions and divide only very rarely. They are activated only in especially critical situations (e.g. the presence of major inflammatory stimuli), where the type I interferon that is secreted ‘wakes’ the cells.

Since type I interferon is formed primarily as a defence response to viral infection, the researchers investigated the activation of stem cells during infection by different viruses. They showed that not every viral infection that triggers interferon secretion automatically activates the quiescent bone marrow stem cells – but when this does occur, it is a big factor in the success of transplantation. This is because “the function of cells activated [by a virus] is considerably impaired: they are no longer as well-balanced or reliable in the way they differentiate,” says Dr Christoph Hirche, who used to be a scientist at TWINCORE’s Institute of Experimental Infection Research and is now based at the Heidelberg Institute for Stem Cell Technology and Experimental Medicine (HI-STEM). The bone marrow cells’ function remains compromised even several weeks post-infection. “We now know that, for stem cell donors, background checks as to infection history need to be tightened,” stressed Professor Ulrich Kalinke, director of the above-mentioned TWINCORE institute.

**Publication**

Small livers on a big scale

Scientists are seeking intently for authentic liver cell models to help them research and develop new pharmaceuticals. Investigators from the REBIRTH unit on Translational Hepatology and Stem Cell Biology, led by Professor Tobias Cantz, have now succeeded in generating liver organoids in suspension culture. Dr Malte Sgodda, the study’s lead author, outlines the production process. “We start by growing pluripotent stem cells in conventional two-dimensional (2D) culture and differentiating them into liver precursor cells. Then we transfer these cells into an Erlenmeyer flask, in which they form three-dimensional (3D) liver cell aggregates.” He continues: “This process is highly superior to 2D culture conditions in terms, for example, of being able to draw conclusions – based on these organoids – about liver metabolism following paracetamol poisoning, the most frequent cause of drug-induced liver failure.”

Professor Cantz adds: “This is a paradigm shift that represents a real breakthrough for our research group. Cultures of this nature will now enable us to explore much more subtle malfunctions in disease-specific stem cell systems.” Previously, these cell aggregates contained only the liver cells – the hepatocytes – themselves. The next step for the scientists is to add other types of cells, allowing them to generate more complex organoids with bile ducts and vascular systems.

In developing their scalable 3D suspension system, the researchers were ably supported by Dr Robert Zweigerdt (of REBIRTH’s Mass Production of Pluripotent Stem Cells unit). Professor Michael Ott (from REBIRTH’s unit on Hepatic Cell Transplantation and Genetic Manipulation) and Dr Amar Deep Sharma (a member of the Cluster’s miRNA in Liver Regeneration unit) also contributed their expertise in cell culture of pluripotent liver precursor cells.

Publication
Visit from Toronto

Professor Brent Derry of The Hospital for Sick Children & University of Toronto, Canada, is currently visiting REBIRTH: he is spending a sabbatical research period working with the Cluster’s unit on Zebrafish Cardiovascular Developmental Genetics. Professor Derry is here to collaborate with this group’s leader, Professor Salim Seyfried, on a research project relating to haemorrhagic stroke. Back in Toronto, Derry works with the nematode *C. elegans*, but here in Germany he is familiarizing himself with the zebrafish as an animal model. “I very much like working here in Germany. The German research scene values basic research much more than is the case in Canada. It’s a fact that many medical conditions are cured thanks to this fundamental research,” says Derry. “In particular, our rare-disease model could be a point of entry into a stroke model.”

The two researchers have been working together since 2015 within European Research Area Network (ERA-Net) CCMCURE, which is investigating a group of rare vascular disorders termed cerebral cavernous malformation (CCM). CCM, a rare condition affecting only one in 5,000 people, is characterized by lesions in the blood vessels of the brain, which are frequently prone to leakage and cause haemorrhaging and strokes. As yet, no active agents are available to treat it, so the aim of this joint research is to find a suitable drug.

In conjunction with collaborator Professor Jens von Kries of the Leibniz Institute für molekulare Pharmakologie (FMP) in Berlin, and in Toronto, the research team carried out high-throughput screening using nematodes, involving more than 5,000 drugs approved by the U.S. Food and Drug Administration (FDA). The investigators have just completed their first exhaustive pharmacological screening for promising compounds. They are now writing up their findings for publication, but this much can be disclosed: the international team was able to identify a few potential candidates. One of the candidate compounds has been successfully tested in a preclinical mouse model. In addition they also wish to explore the relevant signalling pathway in the endothelial cells in order to understand how this abnormal change affecting the blood vessels comes about. “When we know more about how vascular lesions form in this rare disease, we can also directly apply this knowledge to other medical conditions – of the cardiovascular system, for example,” comments Professor Seyfried. “Direct interaction with Brent is proving highly constructive and fruitful! We’re continually developing new ideas on this project.”

In addition to the above-mentioned researchers, Professor Peter Roy of the University of Toronto (Canada) and Professor Elisabeth Tournier-Lasserve of Paris Diderot University (France) are also involved in the ERA-NET consortium project designated CCMCURE.
Help for the ageing heart

The elderly are more likely to suffer from cardiac insufficiency and heart failure than younger people. However, too little is known about how the heart changes as we age. These processes are now being addressed in two new research projects, designated EXPERT and LIPCAR-HF, which are being coordinated by Professor Thomas Thum. He heads Hannover Medical School’s (MHH) Institute of Molecular and Translational Therapeutic Strategies, which is part of the Integrated Research and Treatment Centre Transplantation (IFB-Tx) and is incorporated into the REBIRTH Cluster of Excellence. These projects are being funded under a programme called ‘European Research Area Network on Cardiovascular Diseases’.

The EXPERT project

Under this project, researchers from six countries are seeking new strategies for age-appropriate diagnosis, prognosis and treatment of cardiovascular diseases. They postulate that ribonucleic acids called non-coding RNAs will play a key role here. “These ribonucleic acids regulate cell and tissue functions, and may prove to be valuable markers for both diagnostic and prognostic purposes, as well as targets for new drugs,” says Professor Thum. Junior research group leader Dr Christian Bär is coordinating the part of the EXPERT study that is being carried out at MHH. This project is being funded to the tune of about 1.4 million euros in total over a three-year period. Of this, MHH will be receiving around 300,000 euros from Germany’s Federal Ministry of Education and Research (BMBF).

The LIPCAR-HF project

Within the LIPCAR-HF project, investigators from five partner institutions are aiming to get the ribonucleic acid LIPCAR established as a new biomarker for diagnosing cardiac insufficiency and for predicting how the condition will progress in patients who already have it. Professor Thum is jointly coordinating LIPCAR-HF with scientists from the French Institut national de la santé et de la recherche médical in Paris. Overall, some 820,000 euros in funding has been earmarked for the project, with MHH to obtain 300,000 euros of this from the BMBF.
Strengthening cooperation with Ukraine

Since 2009, the REBIRTH unit on Cell Protection Technology, based at the University of Hannover’s (LUH) Institute of Multiphase Processes (IMP), has been cooperating closely with different research and educational institutions in Ukraine. Scientists from both countries are collaborating, inter alia, on biomedical image processing, three-dimensional (3D) printing technology, cryopreservation of blood and blood components, development of cryopreservation protocols for long-term storage of cells and tissues, and novel bioactive coatings on magnesium implants.

From May to August 2017, with funding from the LUH’s IP@Leibniz programme, visiting scientist Mr Dmytro Tarusin (Institute for Problems of Cryobiology and Cryomedicine, IPC&C) (left) developed a protocol for fabrication of collagen-hydroxyapatite scaffolds with mesenchymal stromal cells (MSCs) for bone tissue engineering. He also confirmed the biocompatibility of these scaffolds with amnion-derived MSCs. Mr Tarusin was supervised by Mr Vitalii Mutsenko (right), a participant on the Ph.D. programme in Regenerative Sciences, and Dr Oleksandr Gryshkov of the REBIRTH unit on Cell Protection Technology.

In 2016, for example, Dr Maksim Tymkovych from the Department for Biomedical Engineering of the Kharkiv National University of Radio Electronics designed and validated software for 3D reconstruction of alginate hydrogels with encapsulated stem cells. Due to their properties, these gels may have multiple benefits: protecting of cells from ice propagation and recrystallization during cryopreservation; protection of cells from shear stress upon their expansion in a bioreactor; and controlled differentiation of induced pluripotent stem cells.
In cryopreservation of cells, mechanical and osmotic stress occurs during the freeze/thaw cycle. This may have an adverse effect on the cells and their DNA. Also in 2016, Lena Raush, a student of the Department for Biomedical Engineering of the Kharkiv National University of Radio Electronics, has developed novel imaging software for the purpose of analyzing fluorescent images resulting from what are known as comet assays (or single-cell electrophoresis) more accurately. She used this software to assess DNA damage in cells frozen using different cryopreservation strategies within a network project. This network project was funded by the German Federal Federal Ministry for Economic Affairs and Energy’s (BMWi) Central Innovation Programme for SMEs (ZIM).
In the 2016 financial year, Hannover Medical School (MHH) generated a net profit of 8.2 million euros. After five straight years with negative year-end earnings, this is one of the best financial results in MHH’s history. “I’m delighted that joint measures by the federal state and the School have enabled MHH to consolidate its finances and get back into the black,” said Lower Saxony’s Minister for Science and Culture, Gabriele Heinen-Kljajić. She also stressed that “at the same time, with a special fund earmarked for a new building, we are ensuring that the School remains a high-performance centre for research-focused patient care.”

Professor Christopher Baum, MHH’s president, is especially proud that “we were able to consolidate MHH without resorting to job cuts. The MHH2020 structural plan, jointly developed in 2015 and 2016 with the Senate and the University Council in consultation with the Ministry of Science, proved effective.” With this plan, MHH also demonstrated the importance of further raising its research profile, and of excellence in teaching as part of the university’s core mission. Baum emphasized: “This shows that our position as completely future-proof extends to MHH’s function as a business enterprise.”

In 2016, MHH treated more patients than ever before. “Within the Presidium, our top management body, we are aware how much the workload has increased across all our operations.”

From left: At a press conference announcing the annual results: Andrea Aulkemeyer, Gabriele Heinen-Kljajić, Professor Christopher Baum and Dr Andreas Tecklenburg.
areas of activity. We are grateful to all our employees for their hard work and dedication," added Dr Andreas Tecklenburg, Vice President responsible for the Division of Patient Care.

Commenting on these results, Dr Tilman Fabian, managing director of the REBIRTH Cluster of Excellence, says: “This also sends out an encouraging signal to the REBIRTH Cluster of Excellence. Only if it is well-placed in the face of competition can our university pursue, or enhance, new structures and measures that we need to succeed within the highly competitive context of the Excellence Strategy.”
Of biological experimentation and mathematical modelling

As in previous years, a Research Week has been held in 2017. The dates were 24–28 July, and the place was the LifeScience Lab Hannover at the School Biology Centre, a municipal facility. The focus this time round was on the interdisciplinary field that is systems biology, which looks at metabolic processes in organisms and their predictability. For example, predictions allow conclusions to be drawn regarding the side effects of drugs. During the Research Week, the participating upper-secondary-level pupils worked in teams and explored the metabolism of a model organism, *Escherichia coli*. They mathematically analysed lab data on enzyme activity and growth, and learned how to factor the outcome into a computer simulation. They proposed hypotheses concerning the processes involved, and tested their predictions by means of further experiments.

Teacher Hendrika van Waveren, who organized the Research Week, was ably assisted in supervising the youngsters by Nora Siefert and Mareille Posner. Siefert took part in the 2015 Research Week after which, with the project she developed during the event, she entered ‘Jugend forscht’, a nationwide competition for young researchers; this winter semester will see her commence studies at the German Cancer Research Center (DKFZ) in Heidelberg. Posner completed a research gap year (FWJ) within the REBIRTH unit on *Translational Hepatology and Stem Cell Biology* at the end of August 2017 and is starting a biology degree in Hannover in the autumn. Her verdict on the week? “The Research Week was great fun and it was evident just how much organization goes into it. All credit to REBIRTH for providing the framework for the event and for valuable input. The week is a fantastic way of encouraging school pupils who are keen on the STEM subjects.”

This year’s Research Week received particular support from the ‘Joachim Herz Stiftung’ foundation – which jointly developed the system biology project week with Göttingen-based XLAB – and the LifeScience Lab Hannover at the city’s School Biology Centre, in collaboration with the Faculty of Natural Sciences at the University of Hannover (LUH) and the REBIRTH Cluster of Excellence.
News from Ph.D. programme

Examination June 2017

Dr Daniela Pelz, coordinator of Ph.D. programme

On 23 June 2017, the 100th final examination in the Ph.D. programme on Regenerative Sciences was announced with a real fanfare: Alexandra Kuhn had just finished introducing her Ph.D. project when the fire alarm sounded. To the accompaniment of this ear-splitting din, the doctoral candidate, her examiners and the audience left the lecture theatre and the building. While the fire brigade drew up and fire-fighters dismounted wearing breathing apparatus, the group relocated to the Hans Borst Centre to continue the exam. Fortunately, it proved to be a false alarm, so that the graduation ceremony was able to take place in Lecture Theatre H as planned. We’d like to congratulate all of the graduates on this special day and wish them all the very best for their future endeavours.

- **Fanziska Geis** (Dr. rer. nat.) *Analysis of Retroviral Vector-Host Interactions in Induced Pluripotent Stem Cells to Improve Retroviral Gene Transfer*, Supervisor: Professor Axel Schambach, Institute of Experimental Haematology, Hannover Medical School (MHH)
- **Miriam Hetzel** (Dr. rer. Nat.) *Hematopoietic Cell Based Gene Therapy Strategies for Hereditary Pulmonary Alveolar Proteinosis*, Supervisor: Professor Thomas Moritz, Institute of Experimental Haematology, Hannover Medical School (MHH)
- **Alexandra Kuhn** (Dr. rer. nat.) *Safety-improved Gene Therapy Approach Utilizing TALEN Technology and Suicide Genes*, Supervisor: Professor Thomas Moritz, Institute of Experimental Haematology, Hannover Medical School (MHH)
- **Skadi Lau** (Dr. rer. nat.) *Strategies for the Generation of Fully Autologous Tissue-engineered Fibrin-based Vascular Grafts Resembling Three-layered Natural Arteries*, Supervisors: PD Dr Ulrike Böer and Professor Mathias Wilhelmi, both Department of Cardiothoracic, Transplantation and Vascular Surgery (HTTG), Hannover Medical School (MHH)
- **Eva Maria Mall** (Dr. rer. nat.) *Genetic Knockout of Foxg1 in Murine Pluripotent Stem Cells and Evaluation of its Functionality via Neuronal Differentiation In Vitro*, Supervisor: Professor Heiner Niemann, Institute of Farm Animal Genetics, Friedrich Löffler Institute (FLI), Mariensee
- **Maria-Teresa Piccoli** (Dr. rer. nat.) *Identification of Long Noncoding RNA Targets for the Treatment of Cardiac Fibrosis and Diastolic Dysfunction in Heart Failure*, Supervisor: Professor Thomas Thum, Institute of Molecular and Translational Therapeutic Strategies (IMTTS), Hannover Medical School (MHH)
- **Miao Zhang** (PhD) *Towards Dry Preservation of Mammalian Cells*, Supervisor: Professor Willem F. Wolkers, Institute of Multiphase Processes (IMP), University of Hannover (LUH)
What are you working on and why?
During their terminal stages, many diseases lead to organ failure and, even though treatment options may have improved, the organ often has to be replaced. However, there just aren’t enough transplantable donor organs to meet this demand.

One way of redressing this situation is to transplant organs from other species into humans.

In our research group at the Institute of Farm Animal Genetics, we’re working on making it possible to transplant pig organs into people. Our aim is to generate a pig whose organs are ‘invisible’ to the human immune system, thus giving us a universal donor. Our approach involves specifically modifying pig DNA, enabling us to modulate the cells’ epitopes responsible for the rejection response.

Why did you decide to enrol in the Ph.D programme in Regenerative Sciences?
In my view, the Ph.D. programme in Regenerative Sciences offers a unique opportunity to obtain a doctorate within an environment where research intersects with highly topical issues, and where interaction with other specialist fields is writ large. When combined with the interdisciplinary seminars and tutorials, for me it’s the ideal mix if you’re a young scientist seeking to equip yourself for the future.

And for me personally, as a vet, the programme is a great chance to broaden my expertise by exploring the human-medicine perspective.

What do you like about science? Did you always want to become a scientist?
When I was little I wanted to be a pilot. At upper secondary school, however, I made the choice to study veterinary medicine. The decision to follow a career path with an academic/scientific focus was one I made during my studies, during a research visit to Cornell University in the USA. What I find especially fascinating about science is that it provides you with new challenges every single day – which means it never gets boring!

What is your favourite quotation?
My favourite quotation comes from a German-language satirical radio drama series called Stenkelfeld, originally broadcast by NDR 2. This particular section, from the third episode, is called ‘The Mushroom Advisory Service’ and answers the question ‘How can I tell if a mushroom is poisonous?’

It’s actually pretty easy. For the mushroom picker, even a cursory look through the electron microscope will show them the tell-tale chain of reverse-spiralling nucleic acids with valent cytochlorinated sulfonamides and a striking octopolar molecular structure, which tells them in no uncertain terms: “Leave well alone!”

Ph.D. programme
Regenerative Sciences
Who is Who

Hendrik Sake (26) from Germany, REBIRTH Unit 9.1 Large Animal Models