



DZHK
DEUTSCHES ZENTRUM FÜR
HERZ-KREISLAUF-FORSCHUNG E.V.

DZG DEUTSCHE ZENTREN
DER GESUNDHEITSFORSCHUNG

German Centre for Cardiovascular Research

ANNUAL REPORT

2018

The DZHK is the largest research institution for cardiovascular diseases in Germany. Our goal is to promote scientific innovation and to bring it quickly into clinical application and to patient care in order to improve the prevention, diagnosis and treatment of cardiovascular diseases.

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Foreword – What was important in 2018?

Co-operations

The DZHK is now an established player in cardiovascular research and has a large number of co-operation partners. What is new is our first international collaboration with the British Heart Foundation, with whom we issued our first joint research funding programme in 2018. In addition, the DZHK gratefully received a donation for the first time: the association “Kinderherzen wollen leben e. V.” donated € 400,000 to the DZHK. This money – topped up with DZHK funds – will be used to establish a five-year endowed professorship for cardiogenetics of congenital structural heart diseases (see Chapter 10).

Real translation - from early research to the patient

At the DZHK, we want to conduct science that has an impact on patients. We want to bridge the gap between preclinical and clinical research and cross it on our own. In the year under review, we took a considerable step towards achieving this goal. In two late preclinical studies sponsored by the DZHK, the results are so promising that the interventions are being tested in first-in-man studies. One of these studies – conducted by an external research institution – has already begun and we will report on the progress next year. Another first-in-man study received a funding recommendation from the DZHK in 2018 and has begun preparations for implementation in 2020. For us, it is a great success that after only seven years of funding we are in the process of actually reducing the translational gap (see Chapters 5.1 and 6.1).

Recruitment in clinical trials: on the road to success

In the year under review, another study completed recruitment, so that two clinical projects have now successfully completed recruitment. Of course, this is only the first step, because patient follow-up is still ongoing in both studies and the evaluation of the results has not been completed. But it clearly demonstrates that recruitment in a network like the DZHK works successfully (see Chapter 6.1).

Promoting young talent

From the very beginning, we have devoted great attention to promoting young talent. We are pleased that in the year under review, we recruited two new junior research group leaders and included the first four early career and excellent physicians in our new Clinician Scientists Programme (see Chapter 7.3). This way, we support early career scientists who are of particular importance for the translation of basic research into clinical research. Science is international and so we conducted our Mentoring Programme in English for the first time in the year under review and were able to include 14 mentees from nine nations in the programme (see Chapter 7.1).

Infrastructure as a basis for comparability and sustainability

We invested a lot of time and money early on in the development of a clinical research platform so that all DZHK studies work according to the same standards and use the same infrastructure. In 2018, we established an image data management system in this central infrastructure, which was already used by two studies in 2018 (see Chapter 6.2). Image data from DZHK studies is now uploaded locally and then evaluated centrally by certified core labs.

New regulations

A centre like the DZHK needs a fixed set of rules. We adopted three sets of rules in the year under review. First, the publishing policy, initially introduced in 2012, was revised. In addition, we have adopted rules for dealing with conflicts of interest, which are largely based on the rules of the European Research Council (ERC). Finally, we have also prepared and adopted a set of rules that govern the procedure when milestones agreed in clinical trials are not met. All three regulations strengthen the DZHK.

Capacity to act - taking difficult decisions

For the first time since the DZHK was founded, we terminated projects prematurely: one preclinical project (see Chapter 1 and 5) and three clinical projects (see Chapter 6). These decisions were difficult and at the same time important. Although each early termination had very different reasons, we are proud that the democratic nature of the DZHK, and decentralised structure, is able to make such difficult decisions.

Highlights from research - our first main topic: heart failure

Heart failure leads to most hospital admissions in Germany, it's not curable and the causes and progress of the disease are very complex. Research into heart failure therefore plays a major role at the DZHK, from molecular

basics, risk factors and accompanying diseases, to clinical studies for new therapies and diagnostic procedures (see Chapter 2).

In short, it was an exciting year in which we achieved a great deal. We are looking forward to the coming years!



Thomas Eschenhagen
Chairman of the Board



Gerd Hasenfuß
Board of Directors

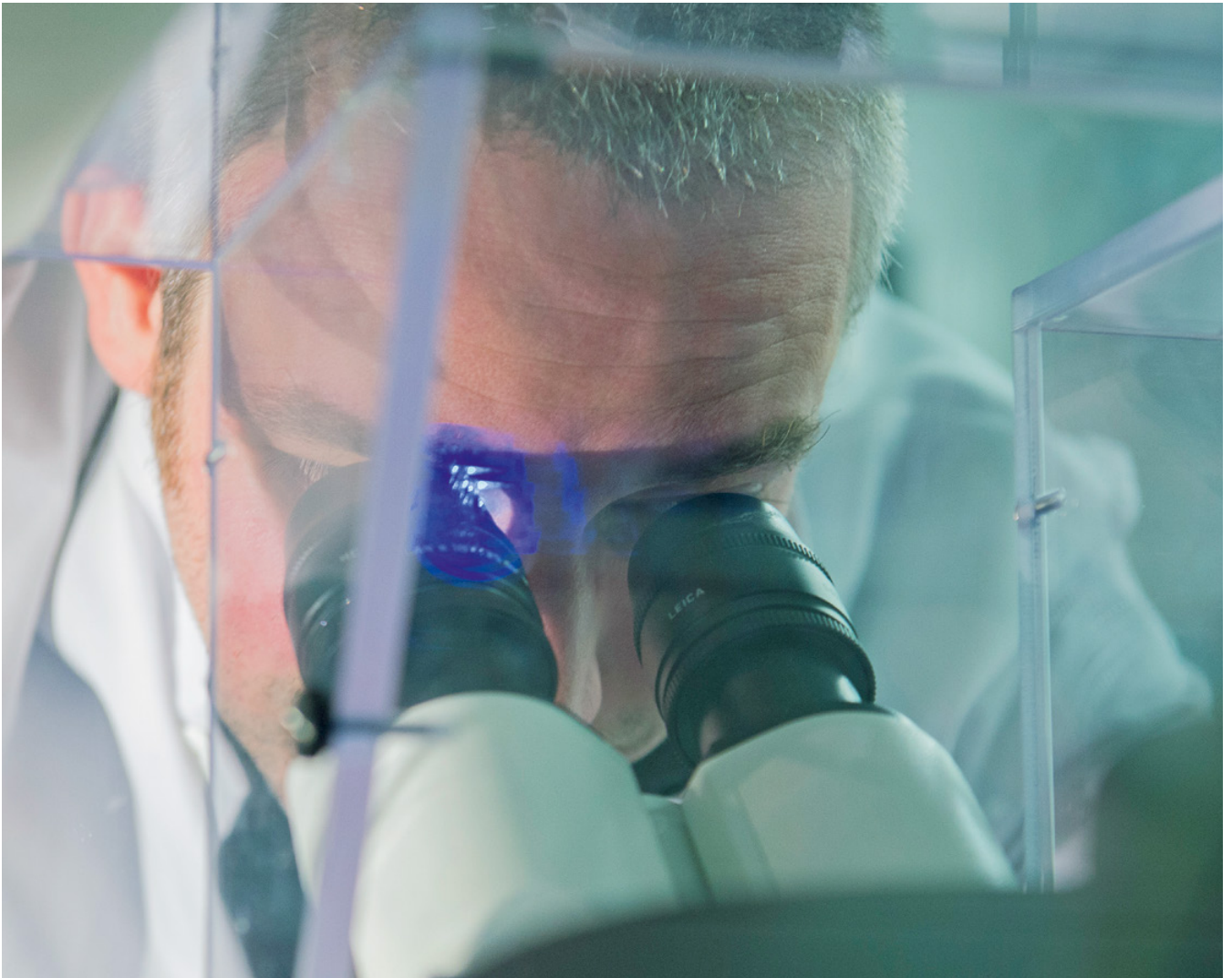


Thomas Sommer
Board of Directors



Participants of the 6th DZHK Retreat in Königstein im Taunus

The DZHK – Focus on Translation



Overcoming the hurdles of translation

Translation, i.e. the transfer of results from preclinical research into clinical practice, is the founding mission of the German Centres for Health Research (DZG) and thus also the mission of the DZHK. The critical translational hurdle lies between late preclinical research and early clinical research and practice and it is generally accepted that this knowledge transfer often does not take place.

One reason for this is that the translational expertise required is lacking in many areas. While the pre-clinician has to talk to the clinician for patient benefit, it is no longer only a question of scientific results and clinical needs, but also regulatory concerns and safety, competing principles and not least questions of intellectual property and commercialisation.

Advice on translation

Since its foundation, the DZHK has paid special attention to supporting both pre-clinical and clinical researchers in translation, and our Scientific Advisory Board has always encouraged us on this path. We launched a funding programme for clinical studies in 2012 and then developed funding for late translational projects in 2014. We have established a Translational Research Group and a Clinical Study Group.

Both Groups have the task of advising and improving projects where there is possible translational overlap. Both committees are also staffed with external expertise and we are very grateful that high-ranking scientists from Germany and abroad have accepted our invitation and are advancing the DZHK with their experience and knowledge.

Important step: Large animal model

We at the DZHK have taken major steps in translation. We are currently supporting eleven late translational research projects (see Chapter 5.1), the aim of which is to bring concepts closer to practice, e.g. by testing the results of early research in a large animal model. If this confirms the results from a small animal model or from cell culture, then a decisive step has been taken. However, these late preclinical projects are also committed to identifying potential dangers, e.g. testing the toxicity of substances.

In 2018, the DZHK prematurely terminated a translational research project for the first time. The reason for this was not the excellence of science, which is beyond question, but the fact that the first results made translation into clinical practice unlikely. This makes it clear that we take the process of translation seriously.

First trials with volunteers

The next step is the early clinical trial, of which the DZHK supports eight. As the DZHK is in its infancy, the ideas that are tested in these early clinical trials do not derive from the DZHK. Two projects are about to cross the translational bridge. One project from Rhine-Main (Development of miR-92a inhibitors for the treatment of cardiovascular disease) led to a first-in-man trial and in 2018 we recommended funding for a first-in-man trial based on a translational research project from Göttingen. This study on heart patches will probably include the first patient with severe heart failure in 2020 (see also Chapter 6).

Focusing on priorities

In the year under review, the Executive Board and the partner site speakers discussed the future focus of the DZHK in two strategy rounds. We have come to the conclusion that our original focus is still valid. We will continue to expand late preclinical and early clinical trials and invest less in guideline-relevant studies. The DZHK is a bridge between late preclinical research and early clinical research and we will continue to expand this function.

Highlights 2018

JANUARY



Announcement of the joint research funding scheme with the British Heart Foundation (page 48)

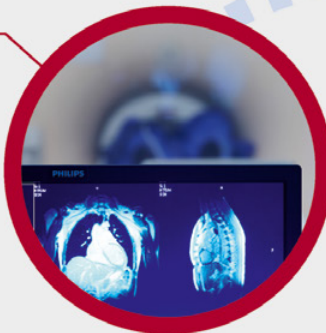
FEBRUARY

Alexander Bartelt (Munich) and Nuno Camboa (Rhine-Main) are new DZHK Junior Research Group leaders at the DZHK (page 40)



MARCH

First clinical trial connected to digital DZHK Imaging Data Management System (IDMS) (page 33)



APRIL

Internal DZHK audit: All research units of the 17 member hospitals receive the quality label "DZHK Clinical Study Unit" (page 31)



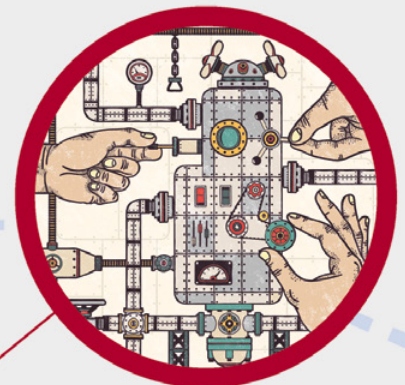
MAY

"The Heart Patient in Research" – DZHK Board member Gerd Hasenfuß at the Annual Meeting of the Honorary Representatives of the German Heart Foundation



JUNE

DZHK Symposium "Precision Medicine Summit" in Heidelberg (page 42)



SEPTEMBER

6th DZHK Retreat (annual conference), keynote speakers: Barbara Casadei (photo) and Elizabeth McNally (page 42)



OCTOBER

The METRIS-HF-DZHK18 clinical trial starts patient recruitment (page 27)



NOVEMBER

The DZHK receives a generous donation of € 400,000 from "Kinderherzen wollen leben e. V." for the establishment of a research professorship (page 49)



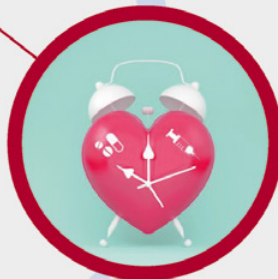
AUGUST

Two consortia including DZHK Principal Investigators receive significant funding from the Leducq Foundation for Cardiovascular Research (page 59)



JULY

"Chrono-pharmacological Targeting of the CCL2-CCR2 Axis Ameliorates Atherosclerosis" becomes DZHK Paper of the Month which is partly made possible by shared expertise support from DZHK partner sites Munich & Hamburg/Kiel/Lübeck (page 58)



DECEMBER

14 DZHK researchers are among the most cited scientists in 2018



Research Focus Heart Failure

Every tenth German over 70 lives with a chronic heart failure and is therefore massively restricted in their quality of life. The number of deaths due to heart failure has been continually decreasing since 1990, but the incidence of the disease is increasing steadily. In Germany, heart failure is the most frequent cause of inpatient hospitalisation. Telemedical care prolongs patients' lives and reduces the number of hospital stays. This is demonstrated by the TIM-HF2 study, in which numerous DZHK scientists participated. (see p. 12)

When the pumping action of the heart decreases

If the heart is no longer able to supply the body with sufficient oxygen-rich blood, doctors call this heart failure. In systolic heart failure, this is because the pumping ability of the heart is limited. In diastolic heart failure, the pumping ability is maintained, but the left ventricle is stiff and is not adequately filled with blood. In both cases the affected person suffers from shortness of breath, feels weak and is no longer able to work under pressure. Fluid accumulation in the lungs and limbs also occurs, as the blood accumulates in the veins. Heart rhythm disturbances can also occur and as heart failure worsens, it is divided into different stages.

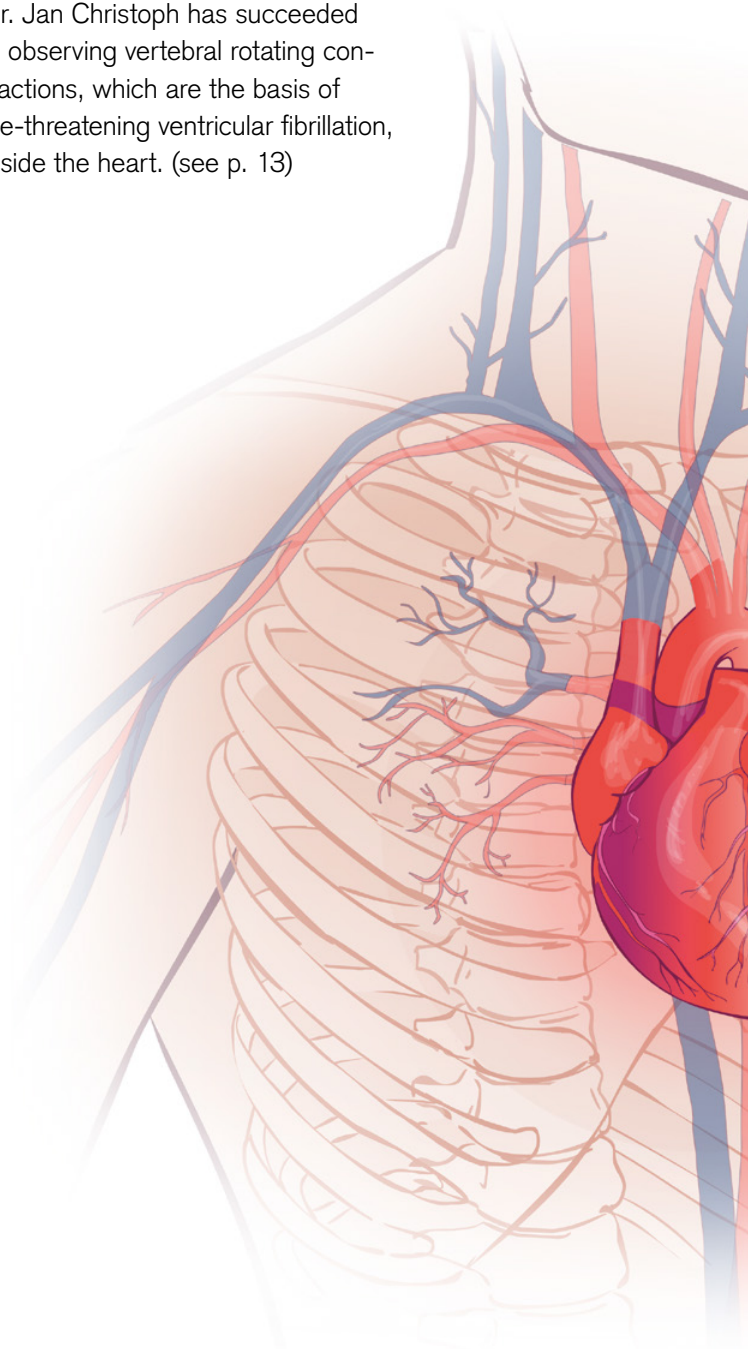
Diseases that cause heart failure

Heart failure is often the result of other diseases. Systolic heart failure is most often caused by coronary heart disease (narrowed coronary vessels) and high blood pressure. Other diseases that may cause heart failure can be congenital heart muscle diseases, heart valve defects or chronic lung diseases.

Diastolic heart failure can also have other causes, including inflammation or thickening of the heart muscle. These conditions often occur alongside high blood

pressure, diabetes, atrial fibrillation and obesity. Heart rhythm disturbances can be both the cause and a consequence of heart failure.

For the first time, DZHK researcher Dr. Jan Christoph has succeeded in observing vertebral rotating contractions, which are the basis of life-threatening ventricular fibrillation, inside the heart. (see p. 13)



Slowing progression and fighting symptoms

Even in early stages, systolic heart failure is treated with medications such as ACE inhibitors, beta-blockers and diuretics. The aim is to reduce symptoms, prevent hospital stays and improve the survival rate. However, these drugs have no effect on diastolic heart failure and there is currently no treatment available. The DZHK SPIRIT-HF study is investigating whether a proven active substance could be a new option for the treatment of this heart failure. (see p. 14)

New research suggests that people with heart failure benefit from regular physical exercise of moderate intensity. They become more resilient and are admitted to hospital less.

DZHK researcher Professor Martin Halle found out that just a few minutes of exercise a day are enough to reduce someone's cardiovascular risk. (see p. 15)

If the disease is more advanced, the implantation of a pacemaker may be necessary to prevent asynchronous contractions of the heart. It may also be necessary to implant a defibrillator or cardioverter to protect against life-threatening cardiac arrhythmias. These small devices emit electric shocks to stop the dangerous heart rhythm disturbances.

Last option: transplantation

In terminal heart failure, the heart has become so badly damaged that it is no longer able to pump sufficient oxygen-rich blood through the body, even at rest. Even without physical exertion, those affected feel shortness of breath, are weak, unable to work under pressure and bedridden. For many, heart transplantation is the only chance to survive in the long term. However, the waiting lists for transplantations are long. On average, patients wait 17 months for a donor heart.

In 2018, DZHK researchers were part of an international research team that achieved a breakthrough in the transplantation of hearts across species boundaries, the so-called xenotransplantation. (see p. 16)

“The incidence of heart failure has been increasing for years. In 2017, heart failure was the most frequent single diagnosis of patients treated as in-patients.”

Source: Heart Report 2018

Patients with Heart Failure Benefit from Telemedicine

Telemedical co-management extends the lives of patients with heart failure and reduces the number of hospital stays. This applies regardless of whether they live in rural or metropolitan areas. This is the result of the TIM-HF2 study, in which numerous DZHK scientists were involved.

The researchers examined 1,538 patients with chronic heart failure. One half received additional telemedical care, while the rest were treated conventionally. Nationwide, 113 cardiological and 87 GP facilities participated in the study.

The patients treated with telemedicine received four measuring devices: an electrocardiograph (ECG) with an additional finger clip for measuring oxygen saturation, a blood pressure monitor, a scale and a tablet with which the participants could assess their own state of health. The tablet automatically transmitted the values to the Charité Cardiovascular Telemedicine Centre. Doctors and nursing staff of the Centre evaluated the transmitted values for 24 hours a day, seven days a week. If the values deteriorated, they took appropriate measures, such as changing the medication or recommending an outpatient visit or hospitalisation.

According to the study results, such assisted patients had to spend fewer days in hospital due to unplanned admissions from heart failure: On average, it was 3.8 days per year compared to 6 days per year in the control group. In addition, the telemedical patient group showed significantly lower overall mortality compared to the control group. Of 100 heart failure patients, about 11 patients (11.3 per 100 patient years) died in one year under the regular conditions, whereas about 8 patients (7.8 per 100 patient years) died with telemedical co-management.



Heart patients cared for by telemedicine have to go to hospital less often

The study shows that telemedicine can extend lifetimes. This result was independent of whether the patient lived in a rural area with little infrastructure or in a metropolitan town or city. Telemedicine is therefore also suitable for compensating for regional differences in care between urban and rural areas and for improving the overall quality of care.

Publication: Koehler, F. et al. Efficacy of Telemedical Interventional Management in Patients with Heart Failure (TIM-HF2): a randomised, controlled, parallel-group, unmasked trial, *The Lancet* 2018. doi: 10.1016.

A New Look Inside the Heart

DZHK cardiac researchers from Göttingen have developed a new, promising ultrasound diagnosis of abnormal heart rhythms.

In Germany alone, a person dies every five minutes from sudden cardiac death caused by ventricular fibrillation, the most common single cause of death worldwide. This is also due to the fact that doctors do not yet exactly understand what happens in the heart. Until now, it has not been possible to visualise the dynamic processes in the flickering heart muscle. The DZHK scientists Dr. Jan Christoph and Professor Stefan Luther from the Max Planck Institute for Dynamics and Self-Organization and Professor Gerd Hasenfuß from the Heart Centre of the University Medical Centre Göttingen have now been able to observe vortex-like rotating contractions, which are the basis of life-threatening cardiac fibrillation, inside the heart for the first time. They use a new imaging method for this, for which already established ultrasound devices can be used. This will enable physicians to better investigate abnormal heart rhythms as well as other heart diseases such as heart failure and develop new treatment methods.

Breakthrough for diagnostics

With the new diagnostic method, the fibrillation of the heart muscle can be more accurately visualised and analysed than previously possible in patients. Treatment of ventricular fibrillation and possibly also atrial fibrillation could thus become more effective.

The researchers hope that their method will also lead to the further development of low-energy defibrillation. Currently, patients receive painful high-energy electric shocks to stop the dangerous flicker. With the new form of ultrasound diagnostics, physicians can find out how and where to apply targeted electrical impulses with lower



With the new ultrasound method, the flickering of the heart muscle can be more accurately depicted and analysed.

energy in ventricular fibrillation in order to bring the heart back into rhythm.

The researchers from Göttingen also want to make the complex excitation dynamics of atrial fibrillation visible. In future, cardiologists will be able to see where dangerous and unpredictable heart rhythms can be treated. The doctors will also be able to investigate the causes of heart failure with detailed ultrasound examinations so that they can detect the disease earlier and treat it more effectively. Luther is certain: “The deep view into the inner dynamics of the heart is a milestone in cardiac research and will have a decisive influence on the understanding and treatment of heart diseases in the future”.

Publication: Christoph, J. et al. Electromechanical Vortex Filaments During Cardiac Fibrillation, *Nature* 2018. doi: 10.1038/nature26001

New Hope for Heart Failure Patients?

The course of heart failure with preserved pump function cannot currently be controlled. Doctors can only try to alleviate the patient's symptoms. The SPIRIT-HF-DZHK8 clinical trial, which was started in 2018, is investigating whether a proven active substance can change this.

Half of all people with heart failure have preserved ejection fraction (HFpEF). In contrast to heart failure with reduced pumping function, the heart can still contract and pump well during this disease, but its relaxation phase, the diastole, is disturbed. The reason for this is that the left ventricle is so thick and stiff that it can no longer fill sufficiently with blood. As a result, too little blood rich in oxygen and nutrients enters the body during the subsequent contraction of the heart.

Patients with a thickened and stiff left ventricle often have no symptoms at first. But in the course of the disease they suffer from the same symptoms as patients with heart failure with reduced pumping function: For example, they are quickly exhausted, have fluid accumulation in the legs and abdomen, the need to urinate at night and a dry cough. "There is currently no treatment for this form of heart failure that successfully addresses the disease mechanisms", says Professor Burkert Pieske, one of the investigators at Charité - Universitätsmedizin Berlin.

Stopping harmful remodelling processes

The multi-centre SPIRIT-HF-DZHK8 study is investigating whether people with heart failure who have maintained pump function go to hospital less often and live longer if they take spironolactone. Similar positive effects of the drug are already known for heart failure with reduced pumping function. A total of 1,300 patients are expected to participate in the DZHK study.



Patients with diastolic heart failure initially have no symptoms, their performance decreases in the course of the disease.

Spironolactone influences the hormonal component of heart failure, in which too much of the hormone aldosterone is produced. This overproduction has a negative effect on the heart. The process of remodelling takes place in which functionless connective tissue cells replace important heart muscle cells. As a result, the heart is less efficient. Spironolactone can inhibit the effect of aldosterone and is thus supposed to stop the processes of heart reconstruction that weaken the heart.

Title of study: SPIRONOLACTONE IN THE TREATMENT OF HEART FAILURE (SPIRIT-HF-DZHK8)

Just a Little Exercise Reduces the Risk of Heart Disease and Diabetes

Walking rapidly for seven to eight minutes a day can alleviate the worst consequences of obesity and at best even prevent it. The risk of cardiovascular disease and diabetes is reduced by up to 20 per cent.

However, patients should carry out this minimum programme quickly in order to stress their heart considerably more because only this additional strain causes the muscles to release risk-minimising hormones. Anyone who completes a short exercise programme every day can expect significantly improved muscle metabolism, more elastic blood vessels and increased heart function after just six to eight weeks.

“All in all, the effects are comparable to those that can be achieved if a patient continuously loses 20 kilos over two years,” reports Professor Martin Halle. At the DZHK, he is researching how sport and exercise can prevent cardiovascular diseases or positively influence them.

The Munich scientist is convinced that most advice and rules for a healthy lifestyle ignore the realities of people's lives. The effect is well known: for many, jogging three times a week for 30 minutes each is simply not manageable so they don't do it at all. According to Halle, the rule of thumb that exercise must last at least 30 minutes is also a widespread misconception: “We are currently working on two major studies that will show, among other things, that significantly shorter units can really improve cardiovascular health.”

Too much weight damages the blood vessels

If the body receives more energy than it consumes, excess calories accumulate in the fatty tissue and excess sugars and fats in the liver. This alone is associated with



People who complete a short exercise programme daily, can improve their heart function in just six to eight weeks

certain health risks because those who are overweight put strain on their joints as well as the cardiovascular system. And the strained liver often leads to diabetes while inflammatory substances are produced in the blood vessels. These substances alter the blood vessels and further increase the risk of cardiovascular diseases.

As a result, overweight people are less resilient, can suffer from erectile dysfunction or develop stiffened heart muscle, which in the worst case leads to heart failure. Professor Martin Halle: “Moving helps not only to burn excess calories more easily, but also counteracts the production of harmful inflammatory factors in fatty tissue.”

Important Progress in Xenotransplantations

An international team of researchers, including scientists from the DZHK, succeeded for the first time in transplanting genetically modified pig hearts into monkeys that survived for several months.

There are too few donor organs in Germany. According to experts, this trend is to be continued in the future. That is why alternatives are needed. An interdisciplinary team of scientists has been working on xenotransplantation for two decades. The aim is to use genetically modified pig hearts to replace the monkey heart and ultimately the human heart. The researchers have now succeeded in taking a significant step forward: Baboons with transplanted, genetically modified pig hearts survived up to six and a half months. However, about 60 per cent of the animals died within two days.

Pig hearts - demanding and large

The success is essentially based on two changes. In the past, researchers have removed the pig hearts, cleared them using a specific solution and then stored them on ice until implanted in baboons. This corresponds to the common technique used for heart transplants in humans. Recently, however, scientists have discovered that extracted pig hearts are more difficult to preserve than human hearts. Now they regularly supply the organ with oxygen and a special nutrient solution after removal and during implantation. The researchers also found that implanted pig hearts grow too big for the chest of the baboon after implantation. As a result, the liver is congested and fails. With the drug Rapamycin, they were able to stop heart growth.

Genetic changes reduce rejection reaction

In collaboration with an American team, the experts have tripled the genetic make-up of the donor pigs. They hope



Baboons with transplanted, genetically modified pig hearts survived up to six and a half months

to modulate blood coagulation and suppress the violent rejection reactions that a recipient develops against organs from another animal species. In fact, after transplantation, the baboons no longer needed the immunosuppressive drugs that had to be given after transplantation of human donor organs. This is a great advantage because these drugs usually damage the kidneys of the recipients in the long term. Further advantages of xenotransplantation: the supply of donor hearts would be ensured and transplantation would be a more predictable operation.

Publication: Längin, M. et al., Consistent success in life-supporting porcine cardiac xenotransplantation, *Nature* 2018. doi: 10.1038

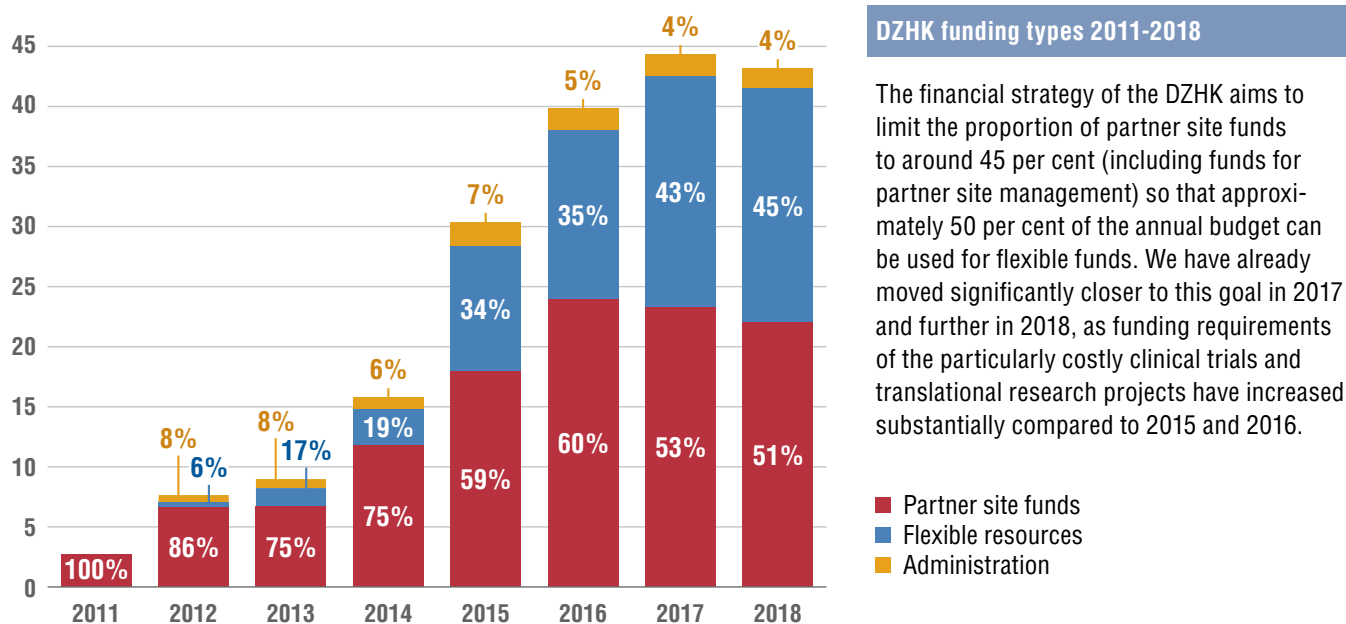
Research at our Partner Sites



Research Cluster III with the cardiological basic research laboratories at the DZHK Greifswald site

Network structures such as the DZHK depend on the excellence of their partners. Our partner sites are the basis of our success. In 2018, we financed partner site projects with approximately €21 million, which is 49 per cent of our budget. Partner site projects address a wide range of topics from basic research to clinical trials, investments and the funding of DZHK Professorships.

The aim is to strengthen the partner sites and support their scientific profile. The partner site-specific projects are selected competitively at the site. Thematically, the partner site projects are not restricted; each partner site should be deliberately free to allocate the funds in the way that is strategically appropriate for them in the long term.



DZHK funding types 2011-2018

The financial strategy of the DZHK aims to limit the proportion of partner site funds to around 45 per cent (including funds for partner site management) so that approximately 50 per cent of the annual budget can be used for flexible funds. We have already moved significantly closer to this goal in 2017 and further in 2018, as funding requirements of the particularly costly clinical trials and translational research projects have increased substantially compared to 2015 and 2016.

DZHK Idea Contest - thinking outside the box

In the summer of 2017, we announced a unique contest: Encouraged by our Scientific Advisory Board, we wanted to identify innovative, high-risk and cross-partner site projects with a 'lighthouse' character that would go beyond our established funding lines. We organised the competition openly and online. All scientists at the DZHK (Principal Investigators, DZHK Scientists or members of the Young DZHK) were invited to take part, either by submitting their own ideas or by supporting the open access proposals. 19 project proposals were submitted and evaluated by the community. At the end of the competition, five ideas were submitted to the Research Coordinating Committee and the Scientific Advisory Board for further review at the beginning of 2018.

Three projects were then able to secure start-up funding of € 150,000 each:

- Innovative approaches to precision medicine: impact of clonal hematopoiesis on cardiovascular disease, Andreas Zeiher (Rhine-Main)
- Therapeutic strategies based on bio-sensitive telomere imaging, Stephan Lehnart (Göttingen)
- Development of heart-specific adeno-associated viruses (AAVs) prototypes via genetic capsid engineering for intravenous cardiac gene delivery, Patrick Most (Heidelberg/Mannheim)

In 2019, we will decide how and if subsequent funding can be made possible after external evaluation of the projects.

DZHK Professorships



The DZHK Professors and the heads of the DZHK Junior Research Groups form the programme committee for the DZHK Retreat.

(from left to right) Stephan von Haehling, Johannes Backs, Eike Nagel, Georgios Kararigas, Reinier Boon, Tanja Zeller, Jens Fielitz, Shirin Doroudgar (Junior Research Group Leader), Tommaso Gori, Michael Joner, Christoph Knosalla, Arne Hansen, Stefan Luther, Martin Uecker; Not in the picture: Alexander Bartelt (Junior Research Group Leader), Nuno Guimarães Camboa (Junior Research Group Leader), Jeanette Erdmann, Holger Gerhardt, Lars Mägdefessel (Junior Research Group Leader), Oliver Müller, Oliver Söhnlein, Sabina Ulbricht

The DZHK is proud that in 2018 it was able to recruit two more professorships at the Greifswald and Göttingen partner sites and thus has 18 top-class professors sponsored by the DZHK. As a committee, the professors and the four DZHK Junior Research Group Leaders (see p. 40) are responsible for the programme design of the annual scientific conference (DZHK Retreat, see p. 42).

In the meetings and videoconferences of the Committee, however, other substantive issues are also discussed and brought to the attention of the Research Coordinating Committee (RCC), the strategic body of the DZHK. The professors have voting rights in the RCC and are thus involved in committee matters like funding decisions.

The DZHK Professors appointed in 2018:



In April 2018 **Sabina Ulbricht** was appointed to the DZHK-W2-Professorship for Behaviour-Based Prevention of Cardiovascular Risk Factors in the Population at the Greifswald University Hospital (DZHK partner site in Greifswald). Her scientific work focuses on the development and evaluation of

innovative intervention approaches with the aim of increasing physical activity in adults. Together with her research group, she is investigating methodological aspects of the acceptance and recording of physical activity as well as the effectiveness of psychologically based and automated interventions, in particular by incorporating modern communication technologies. The aim of her research is to contribute to the reduction of behavioural cardiovascular risk factors and thus to achieve the highest possible health-related benefit for the population.



In April 2018 **Stephan von Haehling** was granted a DZHK-W2-Professorship for Metabolic Cardiology at the Department of Cardiology and Pneumology of the University Medical Center Göttingen. Heart failure, its comorbidities and oncocardiology are the focus of the working group. The main focus is on meta-

bolic effects on the skeletal muscle, the heart muscle and the effects of tumour diseases on the cardiovascular system. Together with his team, he hopes to characterise the pathophysiology of heart failure and associated diseases with imaging, functional tests and the investigation of biomarkers. The aim is to find new treatment options, test them in clinical studies and implement them.

Achievement of milestones in 2018

- ✓ Two more DZHK Professorships filled
- ✓ 100 per cent of the partner site funds approved for 2018 have been paid out
- ✓ Proportion of female Principle Investigators further increased (see p. 65)

Targets 2019

- Decision taken on the continuation of the three projects resulting from the Idea Contest
- Endowed professorship filled (see Chapter 9, Kinderherzen wollen leben e. V.)
- Individual partner site projects supplemented by urgently needed investments
- Preparation of the evaluation in January 2020: Decision taken on new partner site projects

Preclinical Research



Preclinical research generates knowledge that provides a better understanding of the mechanisms underlying disease. Preclinical research thus also forms the basis for applied or translational research and is the starting point for innovations and future applications in patient care. Translational research will be used to specifically advance the transfer of findings from preclinical research to practical application and commercialisation.

The DZHK supports both early preclinical research projects and translational preclinical projects. In 2018, the DZHK provided € 3.6 million of its flexible and competitive funding for translational research projects as well as internal and external co-operation projects.

5.1. Translational Research Projects

The transfer of results from basic research into clinical practice is also an important topic in public discussion. Initial results from the laboratories are often promising, but frequently do not fulfil the requirements for first application in humans, so that direct translation into clinical practice is not possible. The funding of translational research projects is intended to improve these conditions.

In 2018, the DZHK provided € 1.7 million for new translational research projects.

Translational Research Projects Approved in 2018:

I CAR inhibitors for the treatment of heart attack

Duration: 2019–2020

Budget: € 233,000

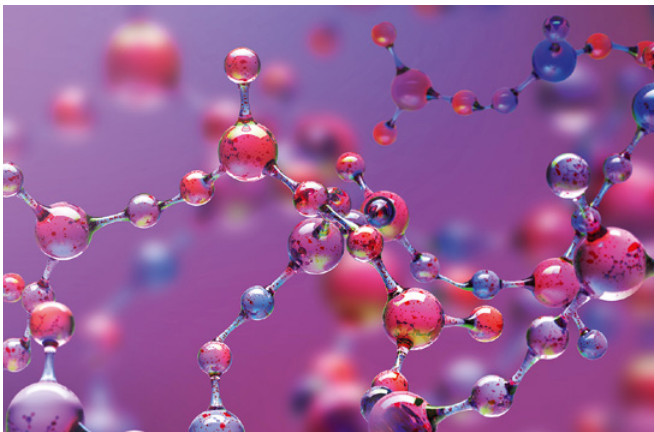
The Coxsackievirus and Adenovirus Receptor (CAR) is a cell contact protein that mediates virus uptake and is essential for early heart development. Mice lacking CAR are protected against Coxsackievirus infection and show hardly any health restrictions.

In a translational approach, we want to investigate CAR as a therapeutic target protein and develop CAR inhibitors for the treatment of heart disease. Building on our initial evaluation of different CAR inhibitors, we will focus on the production and validation of a human anti-CAR antibody. Our aim is to improve the survival of cardiomyocytes, the remodelling processes and the pumping function of the heart. This work includes investigations in the cell culture system, which will then be validated in animal models.

We are convinced that CAR is an excellent therapeutic target for heart disease based on (1) the protective effect of CAR deficiency after heart attack, (2) access to inhibitors and (3) the low level of unwanted side effects when CAR is lacking.

Participating scientists:

Michael Gotthardt, Christoph Knosalla, Volkmar Falk



Real-time MRI-guided targeted endomyocardial biopsy of radiofrequency-induced lesions in pigs

Running time: 09/2019–05/2020

Budget: € 114,933

The diagnostic benefit of catheter-assisted endocardial myocardial biopsy under fluoroscopy control is mainly limited due to sampling errors. In a proof-of-concept study in mini pig we were able to show that targeted endocardial myocardial biopsy of acute lesions under real-time MRI has a higher diagnostic accuracy than undirected biopsy under fluoroscopy control. Our goal is to further develop the targeted real-time MRI-guided myocardial biopsy into a clinically safe and fast method. The first milestone of the project will be promoted, in which the mechanical properties of a new MR-suitable bioptome in our animal model will be examined for its equivalent to a conventional biopsy with a steel bioptome. With the same procedural success rate of the new MR-compatible bioptome, the entire project can be continued with the aim of developing it into a clinically relevant procedure.

Participating scientists:

Christina Unterberg-Buchwald, Martin Uecker, Christian O. Ritter, Joachim Lotz, Jens Frahm

During the application phase, projects are closely overseen by the members of the Translational Research Group (TRG). The TRG was founded in 2014 with the mission to develop, collate and share translational expertise in the DZHK, while also advising applicants. Through close collaboration, critical steps in projects can be identified early and risks can be minimised. This close support in the application phase can, in turn, lead to longer selection procedures, which is why we have not shortened the application procedures as planned in the previous annual report. Ongoing projects are also monitored by TRG members and interim results are

intensively discussed and reviewed. In 2018, the TRG recommended for the first time to terminate a project prematurely (Late pre-clinical development of CD40-TRAF6 inhibitors TRAF-STOPS; Lutgens/Weber/Atzler). It was explicitly not about the excellence of science, which was beyond question, but because early results show characteristics of the investigated molecule which, from the TRG's point of view, make clinical application rather unlikely.

The TRG members met three times in 2018 and held a video conference.

Translational Research Projects (TRP)

Applicant/ Project Lead	Institution	Project title	Start	Budget [Euro]
Stefanie Dimmeler	Goethe University Frankfurt	Development of miR-92a inhibitors for the treatment of cardiovascular disease	01.02.2015	2,643,120
Georg Lutter	Christian-Albrecht University of Kiel	Off-pump transapical mitral valved stent implantation	01.01.2016-31.12.2017	337,290
Stefan Luther	Max-Planck-Institute for Dynamics and Self-Organization, Göttingen	Low-energy termination of ventricular fibrillation in a porcine heart failure model	01.04.2016	1,023,000
Thomas Eschenhagen, Arne Hansen	University Medical Center Hamburg-Eppendorf	IPSC-EHT transplantation for cardiac repair – towards first-in-patient	01.09.2016	1,752,032
Lucie Carrier	University Medical Center Hamburg-Eppendorf	Gene therapy for neonatal sarcomeric cardiomyopathies: towards first-in-patient	01.10.2016	446,893
Christian Schulz	Hospital of the Ludwig-Maximilians-University Munich	Generation and functional characterization of macrophage cell lines from yolk sac precursors	01.04.2017	256,655
Christian Weber Esther Lutgens Dorothee Atzler	Hospital of the Ludwig-Maximilians-University Munich	Late pre-clinical development of CD40-TRAF6 inhibitors (TRAF-STOPS)	01.07.2017	613,230
Hugo Katus	University Hospital Heidelberg	A novel inotropic/lusitropic peptide drug against decompensated chronic heart failure	01.01.2018	377,683
Wolfram-H. Zimmermann	University Medical Center Göttingen	GMP-Production of Engineered Human Myocardium for Heart Failure Repair	09.01.2018	1,824,600
Michael Gotthardt	Max Delbrück Center for Molecular Medicine in the Helmholtz Association	CAR inhibitors to treat myocardial infarction (CARTI)	01.01.2019	233,000
Christina Unterberg-Buchwald	University Medical Center Göttingen	Real-time MRI-guided targeted endomyocardial biopsy of radiofrequency ablation lesions in a porcine model	01.09.2019	114,933

5.2. Co-operation through Shared Expertise

In order to answer complex or multidisciplinary research questions, co-operation is key. It enables the exchange of knowledge, methods or materials. Often, a technical infrastructure is necessary that is not available everywhere. The DZHK provides funds for co-operation projects by means of 'Shared Expertise' in order to provide know-how or infrastructures of a DZHK partner site to scientists at other locations. In doing so, we aim to enable and strengthen cross-partner site co-operation and networking.

In 2018, 25 co-operation projects were approved using Shared Expertise (27 in 2017). These projects were funded with a total volume of € 1.6 million. 28 per cent of the applicants were members of the Young DZHK. The ten most frequently used Shared Expertise were used in 40 per cent of the co-operation projects.

The ten most frequently used Shared Expertise infrastructures in the DZHK since 2012

SE	Location	Name of Shared Expertise	Number of applied uses in 2018	Usage since 2012
SE006	Berlin	Genomics/Proteomics	1	31
SE171	Göttingen	Stem Cell Unit and Cardiomyocyte/Engineered Heart Muscle Phenotyping	3	20
SE028	Heidelberg/Mannheim	AAV Vector Platform	1	19
SE001	Berlin	Generierung und kardiovaskuläre Phänotypisierung transgener Ratten		17
SE041	Munich	OMICS-Plattform		13
SE031	Heidelberg/Mannheim	Next-Generation Sequencing Plattform		10
SE056	Rhine-Main	Vascular Proteomics		9
SE099	Greifswald	Proteome and metabolome profiling of cell cultures, biofluids and tissue specimen	3	8
SE063	Hamburg/Kiel/Lübeck	MicroRNA-Array platform		7
SE024	Hamburg/Kiel/Lübeck	EHT Screening Plattform	2	6

In last year's annual report, we stated that our goal was to make the Shared Expertise available to external and even international partners. We have postponed this idea, but will continue to consider the issue.

5.3. Preclinical Collaborations with External Partners

Co-operations with partners outside the DZHK is just as important as co-operations between member institutions. If methods or infrastructures are not available at a member institution, research co-operations with external partners can be established, which in turn contributes to the knowledge of the DZHK.

Six co-operation projects with external partners with a total volume of € 300,000 were approved in 2018 (13 in 2017). 67 per cent of the applicants were members of the Young DZHK.



Co-operations with external partners 2018

Institution	DZHK Funding
Centre of Excellence for Life Sciences gGmbH, Institute of Molecular Biology (IMB), Mainz	€ 34,200
University Hospital Erlangen, Section for Experimental Oncology and Nanomedicine	€ 22,500
Leipzig University Hospital, Clinic and Polyclinic for Gastroenterology and Rheumatology	€ 22,500
Friedrich-Alexander-University Erlangen-Nuremberg, Institute of Cellular and Molecular Physiology	€ 22,318
TU Darmstadt, Department of Computer Science	€ 17,353
University Hospital Würzburg, German Centre for Heart Failure Würzburg	€ 20,250

Achievement of milestones in 2018

- ✓ Concept developed for the use of Shared Expertise by external scientists
- ✗ Selection process for Translational Research Projects accelerated

Targets 2019

- Total funding for Translational Research Projects increased for current and future years
- Complete further Translational Research Projects successfully

Clinical Research



6.1. Clinical trials

Why do we need clinical trials?

By conducting clinical trials, we want to advance medicine and provide answers to crucial questions, such as “Is a new therapy or diagnostic procedure better than the current standard?”, “Are certain treatment strategies better than others?” or “Is a certain drug effective or does it work better than another?”. Clinical trials that are conducted with voluntary participants are a focus of DZHK research. In line with our research strategy, we support early clinical trials in which innovative therapies or diagnostic procedures are tested on humans for the first time,

as well as guideline-relevant studies whose results are incorporated into treatment guidelines and thus directly benefit the patient. The strategic focus of the DZHK in 2018 was on early clinical trials.

In 2018, 24 clinical studies were performed at the DZHK, 18 of which are wholly financed by the DZHK, two are part financed and four are associated with the DZHK (without financial support) (see table on page 28). The financial support of the DZHK's clinical trials totalled € 7.6 million in the year under review.

Recruitment completed in more studies

The CTSN-TVR-DZHK14 study completed the recruitment of 76 patients on time in the year under review. After TORCH-DZHK1, this is the second study that has completed recruitment. The study is the German arm of a trial conducted by the US Cardiothoracic Surgical Trials Network (CTSN) with a total of 400 participants. The aim is to clarify whether it is beneficial to patients to treat the often slightly damaged tricuspid valve at the same time as operating to repair a damaged mitral valve. The surgeons currently lack data for this. As a result of the study, patient guidelines could be refined.



ISAR-REACT5, which is partially financed by the DZHK, also successfully completed recruitment in 2018 – enrolling 4,018 patients. The results of the DZHK-associated CULPRIT-Shock trial, which was completed in 2017, were included in several guidelines in the year under review. (Eur Heart J 2018, 39 and Eur Heart J 2019, 40(2)).

All these studies have been in the data completion phase since recruitment was completed. This includes follow-up, data input and monitoring.

New studies on heart failure and acute coronary syndrome

Two early clinical trials started in 2018. **METRIS-HF-DZHK18** is investigating whether the diabetes drug metformin can improve the heart's pumping capacity in heart failure patients. The drug interferes with the energy metabolism of the cell and researchers hope that this can improve the ability of the heart cells to contract and pump. The study, which will involve 88 patients, is led by the Charité at the DZHK site in Berlin.

Stroke and ischaemic heart disease have a common cause: blocked blood vessels interrupting the blood and nutrient supply, resulting in severe damage to the brain and heart, respectively. The study **PRAISE-DZHK19 I DZNEB001** examines how stroke patients with elevated troponin levels can best be treated. Troponin is a diagnostic marker for a coronary artery disease requiring treatment - the so-called acute coronary syndrome. The study aims to establish a clinical algorithm to predict acute coronary syndrome or a heart attack in stroke patients. It is the first co-operation between the DZHK and the German Centre for Neurodegenerative Diseases (DZNE) in the field of clinical research. The study, with 251 patients, is also managed at the Charité in Berlin.

DZHK-financed studies (red), co-financed studies (orange) and associated studies (grey)

Acronym	Condition/Treatment/Diagnostics	Study type	Responsible PI (DZHK partner site)	Recruitment target	Enrolled*
TORCH-DZHK1	Myocardial diseases	Registry	Katus (Heidelberg/Mannheim), Hoffmann (Greifswald)	2,300	complete
TransitionCHF-DZHK2	Heart failure	Cohort	Hasenfuß, Wachter, Edelmann (Göttingen)	1,000	529
VAD-DZHK3	Severe heart failure, heart transplantation	GRS	Falk, Knosalla (Berlin), Hasenfuß, Friede (Göttingen)	200	54
TOMAHAWK-DZHK4	Cardiac arrest	GRS	Desch (Hamburg/Kiel/Lübeck), Thiele	558	276
FAIR-HF2-DZHK5	Heart failure and iron administration	GRS	Karakas (Hamburg/Kiel/Lübeck), Anker (Berlin)	1,200	245
DEDICATE-DZHK6	Aortic valve stenosis	GRS	Blankenberg, Seiffert (Hamburg/Kiel/Lübeck)	1,600	348
APPROACH-ACS-AF-DZHK7	Circulatory disorders of the heart in combination with atrial fibrillation	GRS	Wakili, Massberg (Munich)	400	288
SPIRIT-HF-DZHK8	Heart failure	GRS	Pieske, Edelmann (Berlin)	1,300	2
SMART-MI-DZHK9	Sudden cardiac death after myocardial infarction	ECS	Bauer, Käab, Massberg (Munich)	400	201
CAVA-ADHF-DZHK-10	Heart failure	ECS	Jobs (Hamburg/Kiel/Lübeck), Thiele	388	223
Ex-VAD-DZHK11	Exercise with a ventricular assist device	ECS	Edelmann, Pieske, Falk (Berlin), Halle (Munich)	66	32
Decipher HFpEF-DZHK12	Heart failure, MRI	ECS	Nagel (Rhine-Main)	170	19
CTSN-TVR-DZHK14	Mitral valve insufficiency	GRS	Falk (Berlin)	76 (in D)	complete
SCREEN-AF-DZHK15	Early detection of atrial fibrillation	GRS	Wachter, Hummers-Pradier (Göttingen)	267 (in D)	225
CLOSURE-AF- DZHK16	Atrial fibrillation	GRS	Landmesser, Boldt (Berlin), Eitel (Hamburg/Kiel/Lübeck)	1,512	96
HFpEF-stress-DZHK17	Heart failure	ECS	Schuster (Göttingen)	70	46
METRIS-HF-DZHK18	Heart failure	ECS	Doehner, Pieske (Berlin), Friede	88	2
PRAISE-DZHK19	Ischemic heart disease	ECS	Endres, Landmesser, Nolte (Berlin)	251	17
ISAR-REACT 5	Circulatory disorders of the heart	GRS	Kastrati, Schüpke (Munich)	4,000	complete
Revcept-PCI in CAD	Coronary heart disease	ECS	Kastrati, Massberg (Munich)	332	173
SFB/TR19plus#	Myocarditis	Cohort	Felix (Greifswald)	500	94
CULPRIT-Shock	Myocardial infarction with cardiogenic shock	GRS	Thiele (Lübeck/Leipzig)	706	complete
FIX-HF-5C	Heart failure	GRS	Hasenfuß (Göttingen)	160	n.d.
SORT-AF	Atrial fibrillation, Adipositas	GRS	Willems (Hamburg), Steven ((Cologne)	140	138

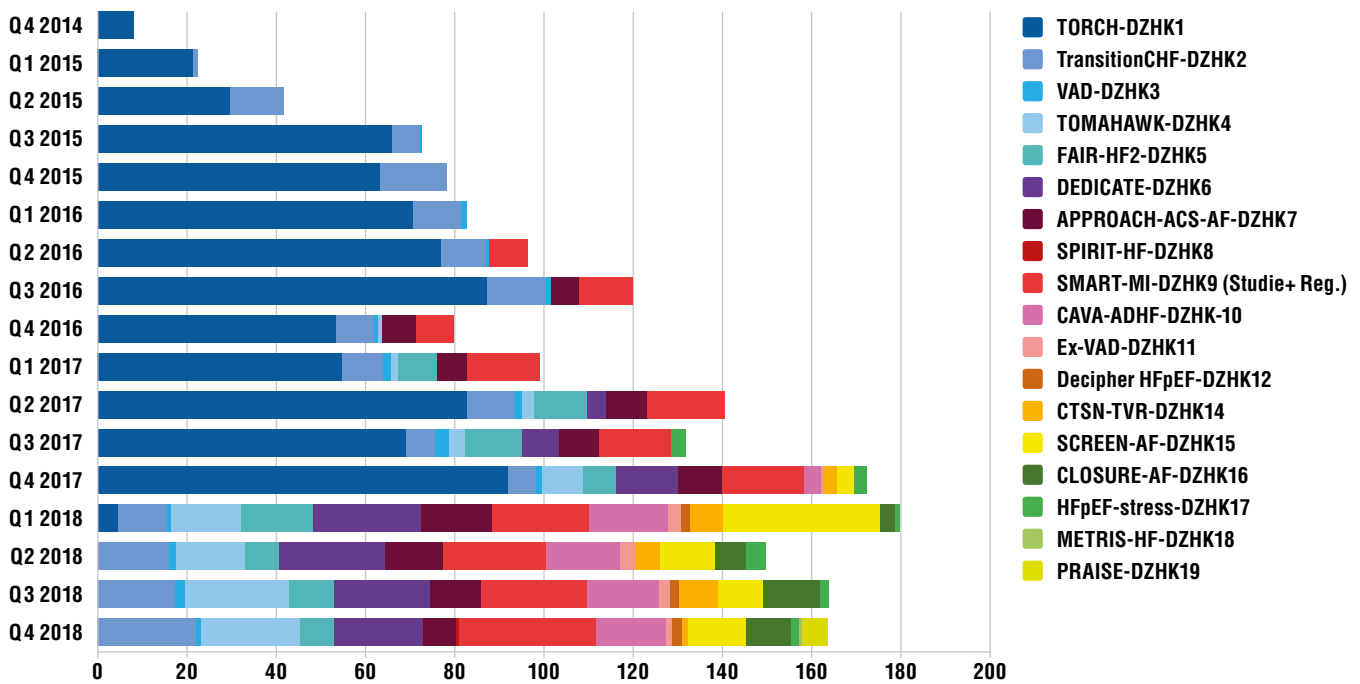
* Last update 31.12.2018

Follow-up observations of patients from the SFB TR19 at the UM Greifswald

Recruitment: challenges and achievements

Between 2015 and the end of 2018, approximately 5,480 patients were enrolled in DZHK trials (associated and competence network trials were not counted), of which 1,942 were registered in 2018 (2017: 1,677). One challenge this year was to maintain the good recruitment level of 2017, which was significantly influenced by the **TORCH-DZHK1** register (recruitment completed

in 2017). A large part of the ongoing DZHK studies are intervention studies, which are subject to randomisation. This requires more work than the inclusion of patients in a register. We are glad that, despite the discontinuation of the **TORCH** recruitments, we were able to improve the recruitment level from 2017 to 2018 thanks to the considerable improvement of the recruitment performance in a large number of DZHK studies.



Overview of recruitment in DZHK studies (monthly mean values per quarter; Updated: 31.12.2018)

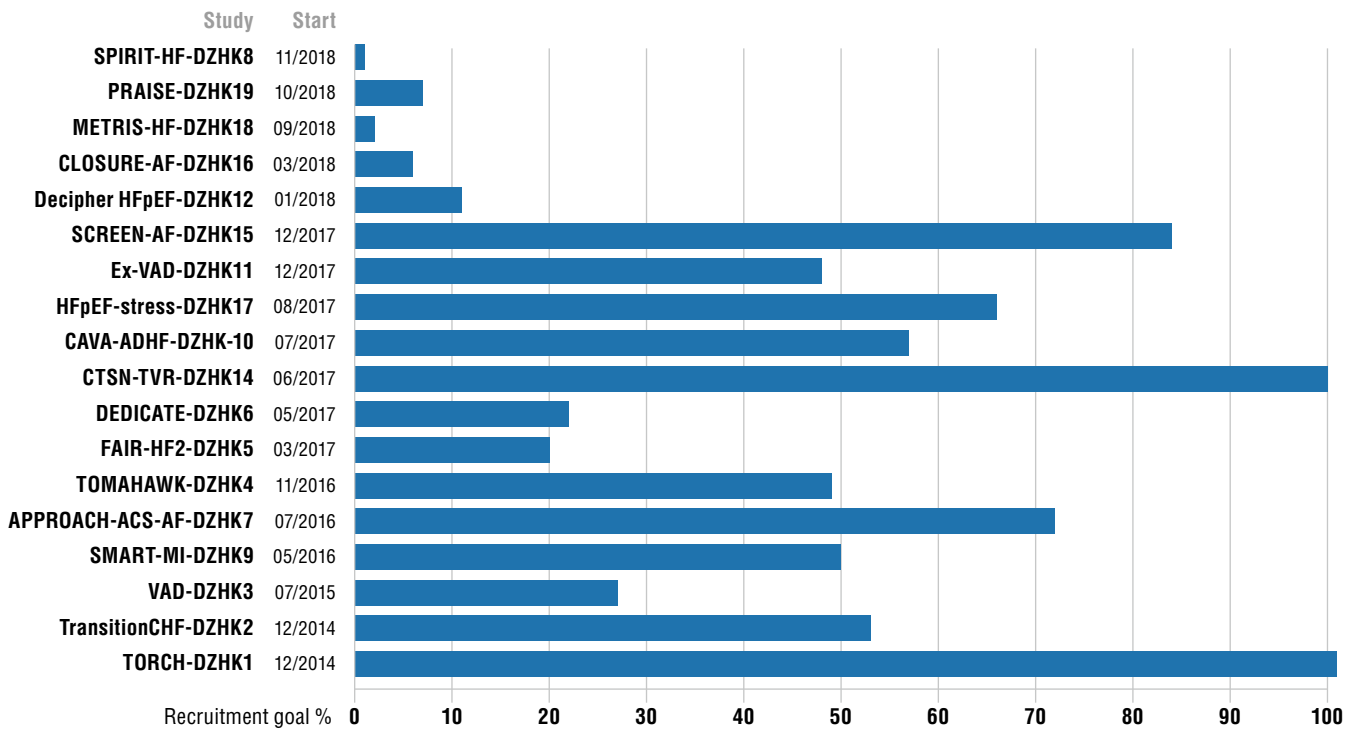
In order to compare the 17 clinical study centres of the DZHK, we developed a **recruitment score** in 2017 that reflects the recruitment performance of the study centre. The score is generated monthly and made available on the intranet together with other recruitment-relevant overviews.

The score was used to derive the budget for **clinical staff** positions at the DZHK study centres for the years 2019 and 2020. Scores were compared at the end of March 2018 and the DZHK Centre Charité Campus Virchow-Klinikum led the field. As such, it has received the largest proportion of the budget for financing clinical staff positions over the next two years.

The clinical staff support study physicians and nurses at its facilities across departments and disciplines in their work on DZHK studies.

The top three recruitment scores at the end of 2018 (31.12.2018):

- Charité - Universitätsmedizin Berlin, Campus Virchow-Klinikum: 468 Score points
- Charité - Universitätsmedizin Berlin, Campus Benjamin Franklin: 460 Score points
- University Medicine Göttingen: 449 Score points



Recruitment status of DZHK studies in per cent (Last update: 31.12.2018)

Press release March 2018

DZHK Clinical Study Units

Introducing a quality badge for DZHK Clinical Study Units



All 17 member clinics of the German Centre for Cardiovascular Research (DZHK) run a cardiovascular clinical research unit. These units host the patient examinations of the DZHK clinical trials. In an internal audit process in 2018, all research units received the “DZHK Clinical Study Unit” quality badge.

The DZHK conducts large multi-centre studies. These require standardised procedures for recruiting patients and obtaining sample material across all DZHK clinical centres.

The DZHK Clinical Study Units all consist of one to three rooms, provided by the clinics. The DZHK has equipped these rooms with standardised devices for cardiovascular diagnostics. For the DZHK biobank, standardised equipment was also purchased for the collection and storage of samples.

The internal audit examined whether all equipment financed by the DZHK was in place and operated in accordance with the DZHK regulations. Another focus was the verification of correct data entry into the central DZHK data management systems.

“The DZHK has invested major resources in building up these research units. Now we wanted to make sure they work to our satisfaction,” explains DZHK

Managing Director Joachim Krebsler. To set up rooms at 17 different clinics, was not an easy task and required considerable effort for all involved.

In addition to the technical equipment, the DZHK Clinical Study Units provide added value in many ways. “We literally provide more space to clinical cardiovascular research,” says Professor Frank Edelmann of the Berlin Charité, Campus-Virchow. The cardiologist leads several DZHK studies and knows from his own experience that clinical research can only be carried out with adequate equipment. “In the DZHK Clinical Study Units, our study staff can concentrate fully on research.”

This increases the quality of the data and the motivation of the employees, says Edelmann. This supports high-quality clinical research in the DZHK - for the benefit of cardiovascular patients.

Centres involved in clinical DZHK studies



Centres in Germany and Europe that have agreed to participate in clinical trials or enroll patients

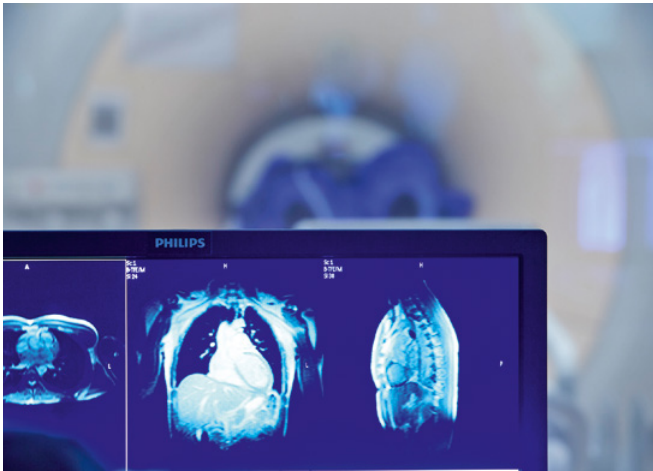
6.2. Clinical Research Platform

The clinical research platform of the DZHK is a unique academic infrastructure in Germany for carrying out multi-centre clinical studies. It has been established over the past six years and consists of various networked IT sys-

tems, as well as regulations and processes for sample and data acquisition and storage. At the end of 2018, the cross-study data of approximately 5,480 patients was available via the research platform (2017: 3,543).

Images are managed digitally

In 2018, the focus was on the further implementation of the Image Data Management System (IDMS). A total of four trials and all associated study centres now use the system and transfer files from imaging during the trials into the system. The images are evaluated by certified core labs according to harmonised standards. This contributes significantly to high data quality and data security. Images are no longer sent on CD-ROM. In 2018, 229 images were uploaded as part of the four trials. For 2019, we plan to include at least two further studies in the IDMS.



Four DZHK studies already use the image data management system

Compliance with the DSGVO

In 2018, we also focused our activities on adapting the processes and forms of the clinical research platform to the General Data Protection Regulation (GDPR), which has been in force since May 2018. As we had previously adhered to the rules of the Federal Data Protection Act, we were able to implement this process quickly and complete it in the year under review.

“100 Samples” - test project confirms high sample quality

While our efforts in the first few years focused primarily on building infrastructures and IT systems, since 2018 we have increasingly focused on evaluating and improving data quality. In 2018, we therefore launched the “100 Samples” test project. This was an internal DZHK quality control of our data and samples obtained in multi-centre studies. The project recreated how a scientist might use samples and data to investigate any given research question. The evaluation included the entire process and laboratory analysis. The tests have shown a very high quality of our samples, comparable to the quality of NAKO samples. Simple errors and mix-ups of samples were in the lower single-digit percentage range. For example, the gender of one of 105 samples was given incorrectly. The process was also very time efficient. Optimisation possibilities arose to some extent in the outgoing logistics and the shipping of the samples. The experience gained here will be incorporated into the upcoming revision of the DZHK regulations.

Project extension 2019-2023

At the end of 2018, the current project phase of the clinical research platform expired, with the extension decision pending. After an international review and a positive evaluation of the established structure in 2017, the DZHK decided to continue funding the platform. In the new funding phase 2019-2023, the focus will increasingly be on testing sample and data quality. In addition, we want to “market” the possibility for DZHK internal and external scientists to apply for the use of data and samples. Since the clinical research platform is a dynamic and growing system, we have to continually adapt and optimise processes and further increase the usability, which will also be part of the new project phase.

6.3. Secondary use of data and samples

The data and samples collected in the clinical research platform are made available to interested scientists worldwide to answer a wide range of cardiovascular research questions. The transfer of data and samples (Use & Access) is managed by usage regulations. This allows two types of use: Researchers use the data from their own trials for new questions. For these, they must

submit a usage notice to the Use & Access Committee of the DZHK, which is published on the DZHK website. If a completely new question requires data across the entire collection, an application for use must be submitted. The Use & Access Committee evaluates the applications with regard to compliance with ethical and legal standards and examines the scientific significance of the question. Finally, it submits a recommendation to the RCC.

Overview of secondary data use in projects and applications:

Name of secondary use project	Status	Scientific Lead	Description
Whole genome sequencing of patients with dilated cardiomyopathy	In progress	Hugo Katus, Benjamin Meder	Within the framework of the DZHK OMICs Plus project, selected cardiomyopathy patients are examined with genome-wide analyses. The aim is to identify new disease triggers that are important for the treatment and risk assessment of patients.
Evaluation of clinical features and long term prognosis of distinct cardiomyopathies	In progress	Hugo Katus, Benjamin Meder	Using the DZHK-TORCH data, the clinical results and biomarkers as well as primary and secondary endpoints of the different CMPs are compared with each other. Specific event frequencies and associated risk factors will be identified, which at best help to derive first therapeutic recommendations.
100 DZHK Basis biomaterial samples and phenotypes – a quality control	Completed	Thomas Eschenhagen, Matthias Nauck, Tanja Zeller	The comprehensive collection of biomaterial and related clinical data of the DZHK is tested for quality. The focus here is on the application processes for biomaterial by scientists as well as the quality of the biomaterial.
Impact of clonal hematopoiesis on cardiovascular disease	In progress	Hugo Katus, Florian Leuschner	Within the framework of the DZHK CHIP project we are investigating whether changes in the production of inflammatory cells in the bone marrow affect the progression of cardiac insufficiency.
Molecular biology of cardiomyopathies	In progress	Hugo Katus, Benjamin Meder	DZHK TORCH data and biomaterials of all subtypes are analysed and compared at the molecular level using OMICs analyses and state-of-the-art computer science to identify new treatment targets such as disease-causing mechanisms/modifiers and genome changes or specific biomarkers.

Interview: OMICs resource

Subtleties of the German genome deciphered

In 2018, the DZHK sequenced the genes of 1,200 healthy individuals from Germany. They serve as a comparative resource - not only for cardiovascular research. The processing of the raw data should be completed by mid-2019, after which the data can be used for research. We spoke with project lead Professor Heribert Schunkert from the DZHK in Munich.

Professor Schunkert, why does research need genetic data of healthy people from Germany?

For the first time, we have deciphered the subtleties of the German genome. Our data come from six different population studies in the regions around Hamburg, Heidelberg, Mainz, Munich, Kiel and Mecklenburg-Western Pomerania. Genetic data in



their entirety differ from country to country and even from region to region. With a German cohort, we can more accurately identify the differences between healthy and sick people in our country.

What exactly is to be researched?

Almost all cardiovascular diseases are multifactorial, as are most other common diseases. Multifactorial means that not a single modified gene, but many

different gene variants - in combination with lifestyle and environmental factors - lead to the disease. In so-called genome-wide association studies, the variants of sick people are compared with those of healthy people. Patterns of variations that occur more frequently in the sick than in the healthy then begin to emerge. The corresponding sites on the genome can provide indications for the disease mechanism and form the basis for new therapies. With our comparative data obtained in Germany, we call it OMICs resource, these comparisons can be made more precisely.

And what diseases are we talking about?

In cardiovascular research, we are looking for genetic patterns for risk factors such as high blood pressure and lipometabolic disorders as well as for diseases such as heart attacks, heart failure or atrial fibrillation. Cancer, diabetes, lung diseases and neurodegenerative diseases are also multifactorial and can be better analysed with the OMICs resource.

Can researchers from all these disciplines use the data?

Yes, exactly. Of course, we want to make the data available to DZHK researchers, but also to other scientists, for example from the German Centres for

Health Research. We have even received inquiries from paleogeneticists. They want to compare today's genome in Germany with that of people from the Stone Age who lived here.

Can gene data simply be left to others for use?

The use of our data is of course subject to strict rules. All researchers are legally obliged to adhere

to these rules. For example, you cannot identify individuals from their data. Sharing research data is clearly in line with the current trend, and with the OMICs resource we are taking this up. We believe that as much knowledge as possible should be gained from research data. We owe this to our patients who are waiting for new therapies.

Achievement of milestones in 2018

- ✓ At least 1,700 patients enrolled in clinical research platform in 2018
- ✓ Auditing of the 17 DZHK study centres completed
- ✓ At least 90 per cent of DZHK study centres successfully certified as "DZHK Clinical Study Unit"
- ✓ Recruitment in the DZHK partially financed ISAR-REACT5 study (n = 4,000 international study participants) successfully completed
- ✓ All DZHK centres are connected to LIMS
- ✓ Four trials are connected to the IDMS
- ✓ Use and Access processes tested and improvements started to implement
- ✗ Several data and sample usage requests received and processed

- ✗ Scientific publication submitted for clinical research platform
- ✓ Infrastructure and trials work in accordance with the GDPR
- ✗ OMIC's resource: Raw data processing completed
- ✗ OMIC's resource: first applications for use received

Targets 2019

- Recruitment in two more DZHK trials completed
- Benchmarks for clinical trials (e.g. for DZHK sample collection) developed which are recruitment-independent
- Data and sample collection: increased visibility of data and sample collection
- OMIC's resource: Data processing completed and made available for use

Supporting Young Talent



Workshop as part of the Mentoring Programme

Promoting young scientists is one of our most important investments for the future. In 2018, a total of € 4.5 million was available for training programmes, mentoring and excellence initiatives - a record sum after € 2.5 million for 2017 and € 1.5 million for 2016.

7.1. The Young DZHK - a network of young researchers

The Young DZHK is our fastest growing network, comprising of more than 1,100 young scientists. Young-DZHK members connect at the partner sites and the initiative offers the opportunity for exchange and networking across the entire DZHK. The Young DZHK

administers itself with two representatives elected at each partner site. Representatives from all partner sites make up the Young DZHK Postdoc Committee, which met three times in the year under review. This committee then sends an elected representative to various DZHK committees. Like the DZHK professors, the Young DZHK spokesperson has the right to vote in the RCC - in this way, the Young DZHK is involved in all strategic decisions. Further tasks of the Young DZHK Postdoc Committee are the organisation of the annual Young DZHK Retreat (see p. 42) with around 100 participating young scientists from all DZHK partner sites, the organisation of Young DZHK Workshops and networking with other national and international Young Scientist networks.



The Young DZHK Postdoc Committee in Königstein

These are the Young DZHK Postdoc Committee members:

Speaker: Thorsten Kessler (Munich)

Deputy speakers:

Nadya Al-Wakeel-Marquard (Berlin) und Martin Bahls (Greifswald)

Berlin: Nadya Al-Wakeel-Marquard, Djawid Hashemi

Göttingen: Aline Jatho, Norman Liaw

Greifswald: Eileen Moritz, Martin Bahls

Hamburg/Kiel/Lübeck: Anca Remes, Katharina Scherschel

Heidelberg/Mannheim: Tobias Jakobi, Elham Kayvanpour

Munich: Sebastian Clauß, Thorsten Kessler

Rhine-Main: Jiong Hu, Sven-Oliver Tröbs

7.2. Training & Mentoring

The **Training Programme** of the DZHK addresses all Young DZHK members. With this Training Programme we intend to encourage participation in scientific events and increase mobility. Travel grants are offered for participation in high-ranking congresses, external workshops, DZG-independent workshops and all DZHK-internal events such as DZHK symposia, co-financed congresses and lectures. The Visiting Scientist Programme enables short-term stays to learn new methods in laboratories in Germany and abroad. Since medical students who wish to write an experimental research thesis are

Support activities of the Training Programme for Young DZHK members in 2018 (2017):

Travel scholarships for high-ranking congresses	279 (289)
Doctoral scholarships*	33 (38)
Visiting Scientist Programmes	27 (20)
Attendance of external workshops	45 (63)
Mentoring (Call 2018 for Programme 2019/2020)	11 (14)

of particular importance for translational research, the DZHK has established a PhD scholarship programme for young researchers.

In order to enable our various international Young DZHK members to participate in the **Mentoring Programme**, the programme for the 2018/2019 edition was conducted entirely in English. This was of great interest to the members, supporting our perceived need for this English-language programme: 14 mentees from a total of nine nations were selected from 25 applicants. In addition to the actual mentoring, which focuses on discussion between mentees and mentors, the programme also includes the possibility of personal coaching and four workshops on the topics of career planning, communication and conflict management in a leadership position, work-life balance and self-presentation. We invite established leaders as role models to these workshops, who present their personal career paths to the mentees and pass on important knowledge from their point of view.

7.3. Excellence Programme

The Excellence Programme includes funding schemes for junior researchers who hold a doctorate; an overview of the grants in the reporting period is shown in the table on page 59. In the year under review, a new funding line was established. The aim of the new scheme is to provide targeted support to female scientists on their way to professorship who have children of preschool age.

Funding for non- scientific personnel and consumables for up to one year can be applied for under this funding.

In this annual report, we present scientists who have been accepted into the **Clinician Scientist Programme** and the heads of two new Junior Research Groups.

The Clinician Scientist Programme enables young physicians to conduct intensive research parallel to their

specialist training. The DZHK finances their research for up to two and a half years. The aim is to achieve specialist training and the prerequisites for a professorship at the same time. The first four DZHK Clinician Scientists were selected in 2018 and started their individual curricula. The **Junior Research Group** enables the establishment of a first independent research group and is primarily intended to recruit excellent young scientists to the DZHK.

The first DZHK Clinician Scientists



Markus Anker

Charité - Universitätsmedizin Berlin: Cardiovascular phenotyping in patients with cancer: impact of arrhythmias and altered cardiac function on prognosis.

Markus Anker investigates people with tumours, with regard to the occurrence of abnormal heart rhythms and impairment of heart function using 24-hour long-term ECG, strain echocardiography and biomarker analyses. Furthermore, he will investigate how these factors can impact on the outcome of patients. The research project is based on the assumption that different tumours, and the therapies used to treat them, are associated with cardiac dysfunction.



Inga Hemmerling

University Hospital Heidelberg: Clonal hematopoiesis and the relevance of DNMT3a in Heart Failure.

The aim of the project is to investigate the contribution of hematopoietic stem and myeloid cells to heart remodeling (wound healing) after a heart attack. It was shown

that the presence of mutations in the genes ASXL1, TET2 or DNMT3a in haematopoietic stem cells increases the risk of coronary heart disease, heart attack or stroke. The underlying pathomechanism is not yet understood. Therefore, there is great interest in investigating this and especially the age-related somatic mutation of DNA methyltransferase alpha (DNMT3a).



Leo Nicolai

Clinic of the University of Munich: The role of platelet migration in thrombosis and atherosclerosis.

Thrombocytes, also known as blood platelets, prevent bleeding by sealing off vascular injuries in seconds.

Unfortunately, this mechanism leads to life-threatening vascular occlusions during rupture of atherosclerotic plaques, which can lead to a heart attack or stroke. At the same time, it has been shown in recent years that thrombocytes also play an important role in acute and chronic inflammation and can even actively move, i.e. migrate. In his research project, Leo Nicolai is trying to understand how these different platelet functions are related in order to gain new therapeutic approaches.



Moritz von Scheidt

German Heart Centre Munich:
Identification and validation of key driver genes in atherosclerosis relevant networks.

Moritz von Scheidt's project is dedicated to the development and progression of atherosclerosis.

The focus is on coronary heart disease, where deposits in the coronary arteries lead to an undersupply of the heart muscle. The aim is to develop atherosclerosis-relevant networks and their central regulatory genes based on bioinformatic models. This is of great clinical interest in view of the establishment of new therapeutic approaches.

Junior Research Group



Alexander Bartelt

University Hospital Munich:
Nfe211-mediated proteasomal activity in heart function and cardiovascular disease.

Alexander Bartelt moved from Harvard University in Boston to the University Hospital in Munich. He is investigating mechanisms that enable the adaptation of the heart to stress situations and are therefore extremely critical for the function of the heart. Bartelt is investigating the role of the protein Nfe211 in the healthy and diseased heart, which ensures that no waste accumulates in the cells. In this way, he hopes to elucidate the mechanisms of a possible stress reaction.



Nuno Miguel Guimarães de Sá Camboa

Goethe University Frankfurt am Main:
Deciphering transcriptional networks regulated by TBX18 in cardiovascular disease.

Nuno Guimarães Camboa did research at the University of California and now has his own group at the Goethe University Frankfurt am Main. He is investigating a protein, TBX18, which occurs characteristically in three cell types of the vessels and heart, all of which are involved in the development of cardiovascular disease. Camboa hopes to learn which signalling pathways in these cells are controlled by the protein, and better understand signal transduction in cells involved in the development of serious cardiovascular diseases.

Additional Programmes

The **Postdoc Start-up Grant**, which is announced twice a year, contains funds for the generation of initial research results to enable the acquisition of a first independent major third-party funding project. The **Rotation Grant** releases physicians from clinical obligations by financing replacement personnel to carry out a research project.

Promotion of Excellence in 2018

Name	Institution	Funding Line	Title
Alexander Bartelt	University Hospital Munich	Junior Research Group	Nfe2l1-mediated proteasomal activity in heart function and cardiovascular disease
Nuno Camboa	University Hospital Frankfurt	Junior Research Group	Deciphering transcriptional networks regulated by TBX18 in cardiovascular disease
Jan Christoph	Universitätsmedizin Göttingen	Postdoc Start-up Grant	3D ultrasound-based high-resolution mapping of ventricular arrhythmias in the presence of functional and structural heterogeneity
Anne Dueck	Technical University of Munich	Postdoc Start-up Grant	LncRNA function in cardiac resident macrophages
Florian Gärtner	University Hospital Munich	Postdoc Start-up Grant	The role of platelet migration in biofilm formation and infective endocarditis
Felix Hohendanner	Charité – Universitätsmedizin Berlin	Postdoc Start-up Grant	Ca homeostasis, metabolism and impaired mechanics during heart failure with preserved ejection fraction
Tobias Jakobi	Heidelberg University Hospital	Postdoc Start-up Grant	Investigating roles of dynamic RNA editing in the endoplasmic reticulum stress response in the heart
Yosif Manavski	University Hospital Frankfurt	Postdoc Start-up Grant	Impact of endothelial cells clonal expansion during neonatal heart regeneration
Tobias Petzold	University Hospital Munich	Postdoc Start-up Grant	Role of oral FXa inhibitor treatment on platelet function and arterial thrombosis
Kerstin Wilhelm	Max Planck Institut for Heart and Lung Research	Postdoc Start-up Grant	Regulation of cardiac lymphatics in heart disease
Anna Lena Hohneck	University Hospital Mannheim	Rotation Grant	Detection of electromechanical dispersion in patients with Brugada Syndrome using phase-contrast magnet resonance imaging
Elham Kayvanpour	Heidelberg University Hospital	Rotation Grant	Investigating the role of VARS2 in idiopathic dilated cardiomyopathy
Wieland Staab	University Hospital Munich	Rotation Grant	Cardiac magnetic resonance imaging of the atria: multiparametric assessment of atrial fibrillation
Markus Anker	Charité – Universitätsmedizin Berlin	Clinician Scientist Programme	Cardiovascular phenotyping in patients with cancer: impact of arrhythmias and altered cardiac function on prognosis
Inga Hemmerling	Charité – Universitätsmedizin Berlin	Clinician Scientist Programme	Clonal hematopoiesis and the relevance of DNMT3a in Heart Failure
Leo Johannes Nicolai	University Hospital Munich	Clinician Scientist Programme	The role of platelet migration in thrombosis and atherosclerosis
Moritz von Scheidt	German Heart Centre Munich	Clinician Scientist Programme	Identification and validation of key driver genes in atherosclerosis relevant networks

Achievement of milestones in 2018

- ✓ Development of a funding line for female scientists
- ✓ First Clinician Scientists selected
- ✓ Mentoring Programme conducted in English for the first time

Targets 2019

- First grants awarded in the new scheme “Promotion of women scientists”
- Board mentoring established for Clinician Scientists

Scientific Exchange



Networking, exchange and communication across disciplines - all of these contribute significantly to the success of research. The DZHK offers various platforms and funding opportunities to support the interaction of researchers. For example, DZHK Symposia enable our members to organise one-day or several-day conferences on specific topics. The only symposium financed by the DZHK in the reporting year was the “DZHK Precision Medicine Summit on Cardiomyopathies and Heart Failure” in Heidelberg in June. The 17 project groups in the DZHK also promote internal networking with the aim of providing new inspiration and research ideas.

In 2017, we held the first DZHK Conference on Translational Medicine. This international conference will take place every two years in Berlin, with the next planned for 2019. In the year under review, we developed the programme and invited high-ranking international speakers.

The aim of the conference is to facilitate an interdisciplinary exchange on translation.

DZHK Retreat and Young DZHK Retreat

In 2018, the 6th DZHK annual scientific conference, the DZHK Retreat, took place. Over two and a half days, 250 scientists met in Königstein im Taunus. Highlights of the conference were the two outstanding keynotes on “Atrial Fibrillation: Known and Unknowns” by Barbara Casadei, President of the European Society of Cardiology, and “Genetic Modifiers of Myopathy” by Elizabeth McNally, Vice-Chairwoman of the Scientific Advisory Board of the DZHK. In order to further strengthen the exchange with the other German Centers for Health Research (see p. 45), we included a DZG session in the conference programme. Melanie Börries, junior research group leader at the German Cancer Consortium (DKTK),

Martin Hrabě de Angelis, board spokesperson at the German Center for Diabetes Research (DZD), and Werner Seeger, board chairman at the German Center for Lung Research (DZL), presented their research priorities and discussed possible ways to work with the DZHK.



Melanie Börries (DKTK), Werner Seeger (DZL) and Martin Hrabě de Angelis (DZD) with DZHK board member Gerd Hasenfuß (left), Thomas Eschenhagen (right) and the chairman of the programme committee Tanja Zeller (front)

The Young DZHK Retreat in Königstein, which preceded the main event, offered thirty extra places this year, due to increased demand. Almost 100 young scientists from all partner sites presented their research with posters and lectures.



Poster presentation at the DZHK Retreat

The organisers attracted three high-ranking guest speakers to the meeting: Katey Rayner from the University of Ottawa, Linda van Laake from the University Medical Center Utrecht and Florian Leuschner from the University Hospital Heidelberg. The best presentations and the best poster were chosen at the main retreat. The winners of the Young Investigator Awards 2018 were:

Lectures

- **Wesley Abplanalp** (Frankfurt): Single-cell RNA-sequencing defines monocyte clusters in patients with mutations leading to clonal hematopoiesis: implications for prognosis of ischemic heart disease
- **Christoph Hofmann** (Heidelberg): Translational regulation determines the acute cardiac response to ischemia/reperfusion
- **Eric Schoger** (Göttingen): CRISPRa mediated in vivo activation of endogenous gene expression in the postnatal mammalian heart

Poster

- **Lucas Bacmeister** (Hamburg): A close up on murine pressure-volume-analysis under beta-adrenergic stimulation: positive end-expiratory airway-pressure, hypertonic saline injection and endystolic pressure-spikes



DZHK Board of Directors with the winners of the Young DZHK Retreat 2018: Christoph Hofmann (2nd from left), Wesley Abplanalp (3rd from left), Eric Schoger (3rd from right). Not on the picture: Lucas Bacmeister

Co-financed congresses at DZHK member institutions

The DZHK may financially support meetings at member institutions, if the aims fall within the DZHK's remit. As such, a number of conferences and symposia were co-financed by the DZHK in 2018:

Title	Date and place	Organisers
10 years of GWAS - Looking back – looking forward	12.01.2018 Lübeck	Jeanette Erdmann (Hamburg/Kiel/Lübeck)
Cardiovascular Imaging 2018 – Consolidating the basics and imaging the future	16.-17.02.2018 Frankfurt	Eike Nagel, Andreas Zeiher (Rhine-Main)
Workshop on Preclinical Drug Development – organized by German Society for Pharmacology (DGP)/ Safety Pharmacology Society (SPS)/ DZHK	26.02.2018 Göttingen	Wolfram-H. Zimmermann (Göttingen)
16 th Dutch-German Joint Meeting of the Molecular Cardiology Groups	15.-17.03.2018 Amsterdam	Reinier Boon (Rhine-Main)
Pro- and Reprogramming the heart: A Göttingen DZHK meeting on cardiac developmental and reprogramming tools	03.-04.09.2018 Göttingen	Katrin Streckfuß-Bömeke, Laura Zelarayan (Göttingen)
The Heart by Numbers: Integrating Theory, Computation and Experiment to Advance Cardiology	04.-07.09.2018 Berlin	Martin Falcke (Berlin)
Clinical Psychocardiology – Where do we stand today?	14.09.2018 Göttingen	Christoph Herrmann-Lingen, Tim Meyer (Göttingen)
Expert Meeting on strategic recruitment of patients with (nearly) asymptomatic heart failure (NYHA class I)	20.-21.09.2018 Göttingen	Gerd Hasenfuß (Göttingen)
Bridging silos. Mobile technology-enhanced TeamCare as a holistic approach to care for somatic, psychological, and behavioral needs of cardiac patients	25.-27.10.2018 Göttingen	Christoph Herrmann-Lingen (Göttingen)
Joint meeting: ESC Working Group on Coronary Pathophysiology and Microcirculation and DZHK	26.11.2018 Berlin	Vera Regitz-Zagrosek (Berlin)
Subclinical Cardiovascular and Metabolic Changes across the life span – from childhood to later life	03.-04.12.2018 Berlin	Marcus Dörr (Greifswald)

Achievement of milestones in 2018

- ✓ Planning and organisation of the 2nd DZHK Conference
- ✓ Number of participants for Young DZHK Retreat increased
- ✗ At least two DZHK Symposia held

Targets 2019

- Interactive formats introduced for the Retreat
- DZHK Symposia open for joint implementation with the other DZGs

Joint Activities of the German Centres for Health Research (DZG)

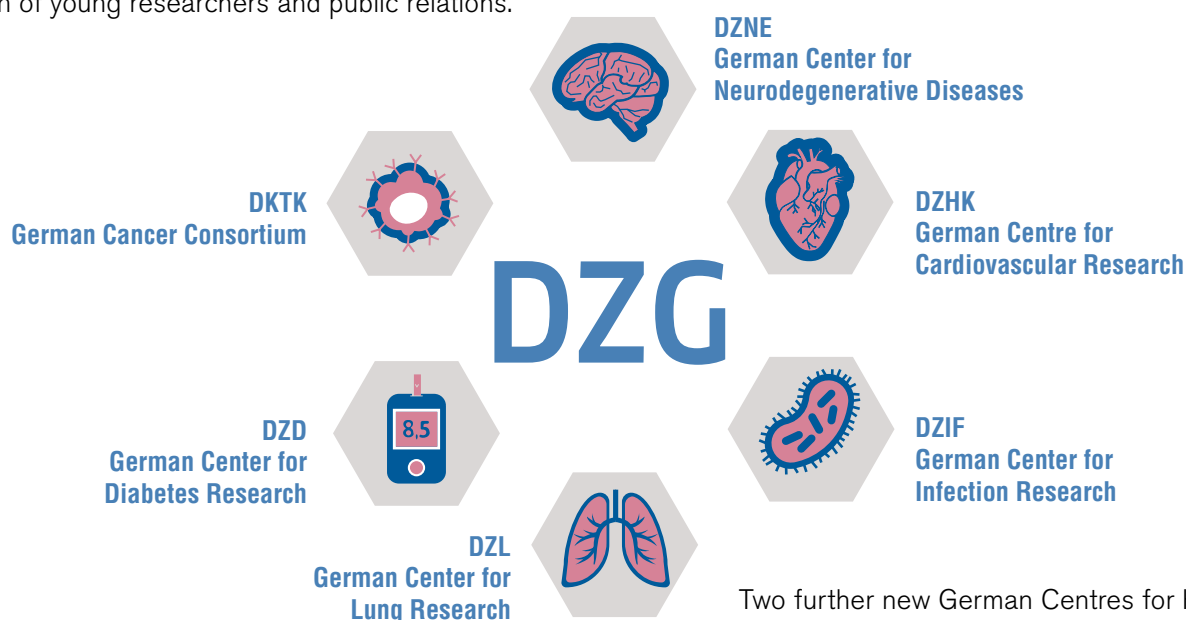


Poster exhibition at the day of the DZG in Lübeck

The DZHK is one of the six German Centres for Health Research (DZG) founded between 2009 and 2012 on the initiative of the Federal Ministry of Education and

Research (BMBF). Each Centre brings together the expertise of top-class scientists from all over Germany in a field known as 'widespread diseases'.

Although each DZG has a specific health research focus, there are many overlaps and synergies that can be identified and exploited through active co-operation. Some specific projects are already being implemented in cross-DZG working groups covering the topics of prevention, IT and artificial intelligence, biobanking and data management, global health, promotion of young researchers and public relations.



For example, two workshops for young DZG scientists were held in 2018 (“Planning and designing a good clinical study”, organised by the DZHK in Berlin, and “Planning and design of biosample collections”, organised by the DZIF in Munich). The joint research magazine “SYNERGIE - Forschung für Gesundheit” (SYNERGY - Research for Health) was also published as part of public relations work. In addition, a DZG exhibition stand was sent to Boston for the annual conference of the German Academic International Network (GAIN).

In the regular discussion forums of the DZG board members, strategic and political framework conditions are discussed and concerns - primarily addressed to the funding institutions of the centres - are resolved. In 2018, the implementation of the recommendations of the German Council of Science and Humanities from 2017 was a central topic.

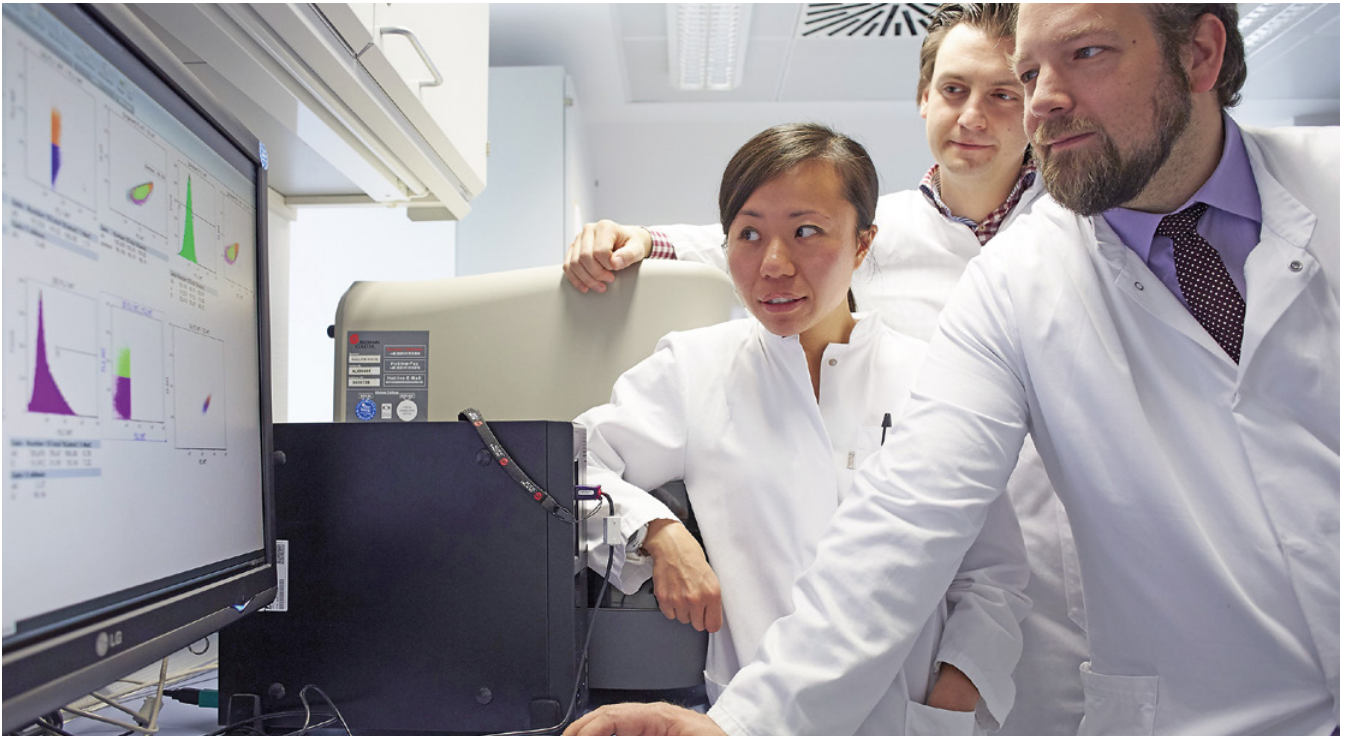
Two further new German Centres for Health Research are currently planned:

A centre for child and youth health and a centre for mental health. The foundation of these centres were announced in September 2018.



Joint DZG booth at the GAIN Annual Meeting in Boston

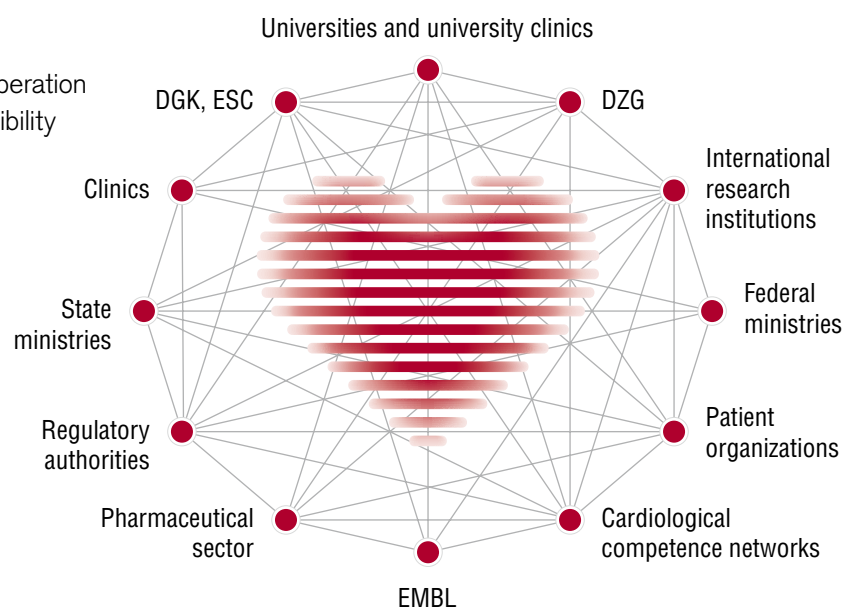
National and International Co-operations



Co-operative network

Co-operation is important in science. Co-operation enhances knowledge, opportunities and visibility and is a sign of the success of the DZHK.

Investments in the DZHK flow into the efficient overall network of translational research.



British Heart Foundation

In January 2018, the DZHK announced the first joint research funding programme with the British Heart Foundation (BHF). The BHF is one of the largest independent funders of cardiovascular research worldwide. We have thus launched a programme that promotes research projects across international borders and addresses new and important global issues relating to cardiovascular diseases. Over a period of at least three years, there will be an annual call for proposals in which up to € 4 million (€ 2 million provided per partner) will be made available per funding round. The aim is to fund one or two research projects per call, supporting innovative projects that cover a broad range of disciplines - from biochemistry and medicine to data science and artificial intelligence - and show added value through international cooperation.

At the end of the first application period in June 2018, the BHF and DZHK had received 12 applications. In an external evaluation process, the projects were evaluated by international experts. The successful projects of the first round were announced in spring 2019.

<https://www.bhf.org.uk/>

German Heart Foundation

The German Heart Foundation (DHS) is the leading organisation in Germany for the education and counselling of heart patients. Many DZHK cardiologists are members of the Foundation's scientific advisory board and hold voluntary online consultation hours. Since the DZHK intends to include patient representatives in its decision-making bodies in the future, we can benefit from the Foundation's experience in this field. In the medium term, we also plan to make the DHS target group, i.e. cardiovascular patients, more aware of research and to interest them in participating in our clinical studies. As part of this, DZHK board member Gerd Hasenfuß was invited to the annual meeting of DHS volunteers in Mainz in

May to give a lecture on "The heart patient in research". Central to the presentation was the importance of the ongoing clinical studies at the DZHK and how patients can benefit from them.

<https://www.herzstiftung.de/>

German Cardiac Society e.V. (DGK)

The DZHK has worked closely with the German Cardiac Society (DGK), Europe's largest specialist cardiology society, from its inception. Since 2013, the DZHK and the DGK have been jointly delivering the "Basics of Cardio-



Thomas Eschenhagen, Chairman of the Board of the DZHK and Conference President of the 84th Annual Conference of the DGK

vascular Research" programme for early career scientists. Three workshops are organised each year. If an individual early career scientist participates in at least seven of a total of 13 workshops, they receive a training certificate. In 2018, one workshop was held in Mannheim and two workshops in Berlin:

- Formalia and Soft Skills (4. April 2018)
- Going in Vivo – Animal Models (13. June 2018)
- CA²⁺ and Arrhythmia (12. October 2018)

Thomas Eschenhagen, Chairman of the Board of Directors of the DZHK, was president of the 84th annual conference of the DGK, which had the motto "From basic research to high-performance medicine". In addition, three scientific meetings were organised at the DGK conference: one meeting called "Current Focal Points of Cardiology in the Focus of the DZHK" as well as two joint Young DZHK and Young DGK meetings.

<https://dgk.org/>

Kinderherzen wollen leben e. V.

The non-profit, voluntary association "Kinderherzen wollen leben" (Children's hearts want to live), based in Neumünster, made a generous donation of € 400,000 to the DZHK in 2018. With this donation, the association enabled the establishment of a five-year professorship (W2) for "Cardiogenetics of Congenital Structural Heart Diseases". The DZHK will transfer the donation to its member institution, the Christian-Albrechts-Universität zu Kiel (CAU), for defined research and supplement it with another publicly-financed DZHK project. Kinderherzen wollen leben e.V. has set itself the goal of promoting research that serves to improve the long-term prognosis of children with congenital heart conditions. The association was founded 19 years ago by parents whose children were treated in the Kiel Children's Heart Center. With the integration of the professorship into the nationwide networked activities of the DZHK and into the DZHK partner site Hamburg/Kiel/Lübeck, the DZHK strengt-

ens its commitment to paediatric heart research. The research activities are supported by the structures of the Competence Network Congenital Heart Defects and the data and samples from the National Register are used. The professorship was announced in August with appointment planned for 2019.

<https://www.kinderherzen-wollen-leben.de/>

Cardiological Competence Networks

Since 2015, the DZHK has supported the cardiological competence networks for congenital heart defects (KNAHF), atrial fibrillation (AFNET) and cardiac insufficiency (KNHI). As a result of a lengthy discussion on the strategic orientation and fit of the competence networks with the DZHK, it was decided in the year under review to support AFNET for the years 2019–2022 in the form of phase-out funding, totaling up to € 0.52 million for the scientific co-ordination of ongoing studies. For the KNAHF, it was decided to fund the Registry for Congenital Heart Defects until the end of 2019 to allow time for an external evaluation. The funding of the Competence Network KNHI ended at the end of 2018.

Competence Network for Congenital Heart Defects

Since 2015, the DZHK has been funding the infrastructure of the Competence Network for Congenital Heart Defects (KNAHF) with around € 1 million per year, thus enabling clinical, basic and healthcare research projects in the field of congenital heart conditions and cardiovascular diseases in children. The National Registry for Congenital Heart Defects (NRAHF) is the core of the research network supported by the cardiological societies DGPK, DGK and DGTHG. The worldwide unique database supports multi-centre international research with data from over 55,000 patients. The biobank comprises biomaterials from around 8,000 sample donors. The network ensures compliance with applicable ethical guidelines and ensures the quality, verifiability and re-usability of data and samples.

Advances in prenatal diagnostics, paediatric cardiology and cardiac surgery have significantly reduced the increased mortality caused by congenital heart conditions. More than 90 percent of young patients now reach adulthood. This brings new challenges into focus. Achievements in the field of artificial intelligence (AI) are also helping us to cope with these challenges. Two first international AI studies at the KNAHF confirm this: deep learning algorithms - i.e. self-adaptive, calculation processes in machine learning that can be adapted without external help - facilitate the identification of health risks in congenital heart conditions. An AI research platform is currently under construction at the KNAHF. And with ATROPOS, an international mortality register has been established to investigate the causes of sudden cardiac death.

In order to improve the quality of life of people born with cardiovascular diseases, we need better prevention, diagnostics and therapy strategies. The KNAHF, which is funded by the German Heart Foundation, the Fördergemeinschaft Deutsche Kinderherzzentren e. V. and the EMAH Foundation Karla Völlm, remains the ideal platform for solving this problem.

 <https://www.kompetenznetz-ahf.de/>

Atrial Fibrillation Network

The Atrial Fibrillation Network e.V. (AFNET) is an academic research organisation with the aim of improving the lives of people with cardiovascular diseases. At AFNET, scientists and physicians from clinics and practices work together to research new treatment methods, especially for atrial fibrillation. To this end, AFNET conducts science-initiated clinical trials and registries at national and international levels.

The international clinical studies EAST - AFNET 4 (early rhythm-preserving treatment; NCT01288352) and NOAH - AFNET 6 (anticoagulation in atrial radio-frequency episodes; NCT02618577), in which AFNET

has overall responsibility as a sponsor, and the nationwide patient registry AFNET-EORP (treatment of atrial fibrillation in Germany), now called AFNET 2 Register after a name change, were further supported by the DZHK in 2018. Measures to increase patient recruitment, the support of a study-specific biobank and parts of the AFNET infrastructure, in particular the project management in the Münster office, were financed.

The EAST - AFNET 4 study is in the follow-up phase and will be supported until 2020. The NOAH - AFNET 6 study, for which patient recruitment will still take several years, will receive funding until 2022. The AFNET-EORP Register is nearing completion and will be funded in 2019.

The results of the AXAFA - AFNET 5 study (anticoagulation during catheter ablation; NCT02227550), which was funded by the DZHK and completed between 2015 and 2018, were published in March 2018 (DOI: 10.1093/eurheartj/ehy176).

In addition to its own studies, AFNET is also involved in DZHK studies as a partner. In the CLOSURE-AF-DZHK16 study (atrial ear closure in atrial fibrillation) started in 2018, AFNET is involved in project management and staffing the study committees.

In addition, AFNET carries out further clinical studies in which it acts as a sponsor and is also involved in national and international studies and projects.

 <http://www.kompetenznetz-vorhofflammern.de>

Competence Network Heart Failure

The Competence Network Heart Failure (KNHI), a nationwide alliance for research into heart failure, has set itself the goal of improving prevention, early detection and therapy. The research provides insights into the mechanisms of heart failure and possible therapies. The aim is

to integrate the findings into medical care and thereby further improve the treatment of people with heart failure.

As part of the KNHI, the DZHK has funded five studies in recent years, which were initiated 10-15 years ago - the long-term follow-ups ran until the end of 2018. Observation over such a long period of time provides a unique opportunity to better assess the long-term course of a disease and the effects of appropriate therapy. By the end of 2018, approximately 3,050 visits had been carried out and the five sponsored studies had been completed. As part of the KNHI studies, a comprehensive biomaterial bank was also established containing samples from almost 16,000 patients. These are also available for future research questions.

In addition, the KNHI itself is involved as a study centre in two DZHK studies. Since 2017 the KNHI has been involved in the recruitment to the Transition-CHF-DZHK 2 study with the aim to include 70 patients - in CAVA-ADHF-DZHK 10 the recruitment started in 2018.

In order to achieve a direct improvement in patient care, the KNHI has expanded its heart failure nurse training. Furthermore, a nationwide curriculum for further training in heart failure MFA is being developed in consultation with the DGK and the Heart Failure Units Certification Committee. In future, this will ensure that this occupational group receives further training at a high level, thus helping to strengthen outpatient care for heart failure patients.

 <http://knhi.de/>

Achievement of milestones in 2018

- ✓ Decision taken on the further promotion of the competence networks
- ✓ DZHK-BHF cooperation announced

Targets 2019

- Two issues of the DZG magazine "SYNERGIE. Research for Health"
- Funding programme with the BHF extended to include the Dutch Heart Foundation and second call published
- Coordinated lobbying with the German Heart Foundation and the German Society of Cardiology started

The DZHK in Public



Communication with study patients and the general public

One focus of our public relations in 2018 was to better inform patients about the goals of clinical trials in the DZHK, and how patients can contribute to advance medical care by participating in clinical trials. At the beginning of the year, we organised a workshop to determine the needs of our study physicians. The aim of the workshop was to find out what questions study patients ask their physicians, and what information we should give them about the DZHK and their individual study. As a result, we have started producing our first video for study patients, to answer these questions and help study physicians better inform their patients.

In addition, we have created an informative patient brochure tailored to that audience, with 2,000 copies distributed all over Germany. The brochure can be handed out to patients by the study staff before, during and after the consent consultation and displayed in the waiting areas of Clinical Study Units. It explains in an easily understandable way what the DZHK is and what it wants to achieve with its clinical research.

On our website we have launched a new section on “Heart Diseases” for patients and the general public, which contains easy-to-understand information on the clinical conditions researched at the DZHK as well as general tips on the prevention of cardiovascular diseases.

The clinical research platform of the DZHK has continued to grow in recent years. For all individuals working with the clinical research platform, at the DZHK and beyond, we have started to design a three-minute explanatory video. It is intended to give a brief overview of the structure and the most important components and will also help recruiting personnel to get a better understanding of the subject. Completion has been scheduled for 2019.

In 2018, the public relations resources were significantly occupied by coordinating the editor-in-chief and the project management roles for the magazine "SYNERGIE. Research for Health", which was launched by the German Centres for Health Research (DZG). The magazine presents up-to-date medical research in an engaging way. The plan is to publish the joint magazine twice a year. The first issue was released at the beginning of 2019.

Press and multimedia

With 22 press releases, we remained at a similar level of media engagement in 2018 as in the previous year. We were able to improve the response to our English press releases to 4 clippings per release. We believe this is due to the consistent posting of reports on international platforms such as "Research in Germany" and distribution via social media, in particular Twitter.

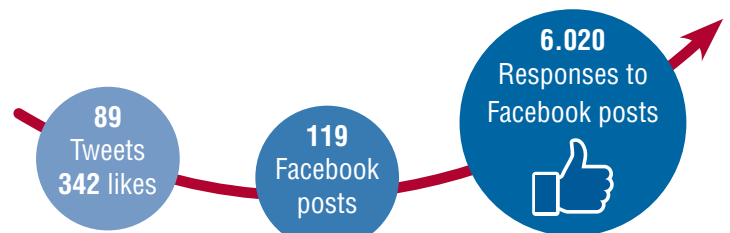
In 2018, we also launched a new publication series, "DZHK IMPULS", in which the perspectives of DZHK scientists on various topics related to cardiovascular research are published. In the first issue, Professor Frank Edelmann and Dr. Tobias Trippel from the Charité in Berlin described how junior researchers in clinical research could be better supported and which instruments are already available at the DZHK. Further issues will be published at intervals on relevant topics.



First edition of "DZHK IMPULS"

Social media channels

On social media, we were able to further increase our activity and response rates in 2018. We used these channels to announce research successes and awards of our members, to publish event information and to draw attention to calls for applications of the DZHK. Our Twitter followers more than doubled and on Facebook the DZHK page had 1,145 followers at the end of the year.



ELEVATING SCIENCE - Five floors for science. YouTube series of the DZHK:

- Why does research often not reach the patient? (2016) With Professor Thomas Eschenhagen
- Clinical trials - new career paths for young scientists. (2016) With Professor Frank Edelmann
- The DZHK - What patients really need. (2017) With Professor Stefanie Dimmeler
- Prospective instead of retrospective - How patients benefit from prospective studies. (2017) With Professor Karl Wegscheider

New 2018 with Professor Martin Halle:



Exercise:
The key to lifelong health



Views of all Elevating Science videos

until
the end
of 2018:
4,553



*Diabetes drug helps with heart failure:
The most shared post on the DZHK Facebook page*

Events

For several years now, the DZHK has been presenting itself at the annual conferences of the German Cardiac Society (4-7 April 2018 in Mannheim) and the German Society for Internal Medicine (14-17 April 2018 in Mannheim) with an exhibition booth together with the Cardio-logical Competence Networks.

During the BMBF Health Day "Hand on your Heart" in Bonn (19 June 2018), the DZHK was also represented with a booth where one of our experts explained the walk-in heart to the interested public.

Achievement of milestones in 2018

- ✗ Soft relaunch of the website
- ✗ First DZHK patient video prepared for our study participants
- ✓ DZHK patient flyer created for our study participants
- ✗ Video created to explain the clinical research platform to users
- ✓ Increased response to English-language press releases

Targets 2019

- Website relaunch completed
- DZHK patient video for study participants published
- Explanation video for users of the clinical research platform published
- First and second issue of DZG magazine published
- DZHK Instagram account set up

Success Indicators for Translational Research



Indicators for the success of translation

Indicator	Definition	2018 (2017)
Short- and mid-term indicators		
1. "Physician Scientists"	Share of scientifically active (licensed) physicians of 1,590 scientists registered at the DZHK	51% (49%)
2. Cooperations between locations	a. Number of Shared Expertise projects (year)	25 (27)
	b. Number of publications with at least two DZHK authors from different	143 (115)
	c. Number of ongoing large multicentre projects (recruiting DZHK studies and TRPs) (31.12.) involving multiple DZHK partner sites	19 (15)
	d. Number of co-operative project groups (31.12.)	17 (17)
	e. Number of Visiting Scientist stays at other DZHK partner sites (year)	12 (8)
3. Communication with regulatory authorities	Consulting appointments (e.g. PEI, BfArM) in the context of recruiting DZHK studies, TRP and partner site projects (year)	4 (1)
4. Cooperation with industry	Cooperation with partners from industry within the framework of recruiting DZHK studies, TRP and partner site projects (31.12.)	18 (13)

Success indicators for translation

Indicator	Definition	2018 (2017)
Short- and mid-term indicators		
5. Cooperative structures in clinical research	a. Type (quality) of cooperative structures (31.12.)	Clinical research platform (data storage, Trusted Third Party, laboratory information management system, image data management system and ethics project, use & access), stem cell registry, OMICs resource
	b. Amount (Quantity)	
	- Patients included in ZDM (31.12.)	5,635 (3,543)
	- SOPs (31.12.)	23 (21)
	- Data and biomaterial usage applications/notifications (year)	1/2 (0/4)
	- Approved usage applications and notifications (year)	1/2 (0/1)
6. High-ranking publications	All publications with DZHK affiliation with impact factor > 10	123 (113)
7. Preclinical projects and clinical trials	a. Number of Translational Research Projects and recruiting DZHK studies (31.12.)	29 (23)
	b. Publications from Translational Research Projects and DZHK clinical studies	11 (13)
Long-term success criteria		
8. Revised medical guidelines	Number of guidelines changed as a result of DZHK trials and competence network trials (total)	1
9. New therapeutic and diagnostic principles	Number of new therapeutic and diagnostic principles developed in DZHK projects and entering clinical application (total)	0
10. Patients treated according to new therapeutic or diagnostic principles	Number of patients who have been enrolled according to new, by DZHK researchers developed, therapeutic, or diagnostic principles (overall) (measurability is questionable)	0

Remarks on the table:

- *Definition of DZHK studies: from competitive/flexible means; predominantly or fully DZHK-financed; study uses the infrastructure for clinical studies of the DZHK*
- *All indicators refer exclusively to projects financed from DZHK funds; no indicator refers to otherwise financed research by DZHK member institutions. Because they are easier to record, indicators 2a, 2c, 2e, 5, 7 and 8 refer exclusively to the competitive/flexible DZHK funds and not to DZHK location projects.*
- *The values for indicators 3, 4 and 7b come from a query to all PI.*

Scientific Publications and Awards



Publications in professional journals are an important factor for the success of scientific research. Publications do not only report new scientific findings and breakthroughs to the research community and the public. Scientific publications provide authors with national and international visibility and thus contribute to networking among scientists.

From its inception, the DZHK has had a code of conduct for publications, which was replaced in 2018 by a comprehensive set of publication rules drawn up jointly by various committees. The publishing policy regulates the naming of the DZHK ("Affiliation") in the relevant publications and contains recommendations on the subject of authorships based on international standards. In 2018, publications with a DZHK affiliation increased once more.

A list of the publications can be found on the Internet:

📄 <https://dzhk.de/en/research/publications/publications-2018/>

Publications 2018	Amount 2018	2017
Total publications	1,132	986
First authorship of a DZHK PI	63	46
Last authorship of a DZHK PI	300	272
First authorship of a Young DZHK member	273	196
First authorship DZHK Scientist	106	104
Last authorship DZHK Scientist	275	204
Publications involving several locations	143	115
Publications published in:		
Nature Publishing Group	35	30
Cell Press	8	5
NEJM, Lancet, JAMA	9	10
Circulation, Circ Res, EHJ, JCI, JACC	68	66
Science	3	2

Paper of the Month 2018

The DZHK Board of Directors selects a Paper of the Month each month, which is then announced in the DZHK newsletter and published on the DZHK website.

January

Hu, J. (Klinikum der Johann Wolfgang Goethe-Universität) et al.: **Inhibition of soluble epoxide hydrolase prevents diabetic retinopathy.** *Nature*. DZHK locations involved: [Rhine Main](#), [Heidelberg/Mannheim](#)

February

Puntmann, V. O. (Klinikum der Johann Wolfgang Goethe-Universität) et al.: **Native T1 and ECV of Noninfarcted Myocardium and Outcome in Patients With Coronary Artery Disease.** *Journal of the American College of Cardiology*. DZHK locations involved: [Rhine Main](#), [Berlin](#)

March

Vion, A. C. (Max-Delbrück-Centrum für Molekulare Medizin Berlin) et al.: **Primary cilia sensitize endothelial cells to BMP and prevent excessive vascular regression.** *The Journal of Cell Biology*. DZHK location involved: [Berlin](#)

April

Christoph, J. (Max-Planck-Institut für Dynamik und Selbstorganisation) et al.: **Electromechanical vortex filaments during cardiac fibrillation.** *Nature*. DZHK location involved: [Göttingen](#)

May

Li, D. Y. (Klinikum rechts der Isar, TU München) et al.: **H19 Induces Abdominal Aortic Aneurysm Development and Progression.** *Circulation*. DZHK locations involved: [Munich](#), [Rhine Main](#)

June

Tóth, A. D. (Universitätsklinikum Heidelberg) et al.: **Inflammation leads through PGE/EP3 signaling to HDAC5/MEF2-**

dependent transcription in cardiac myocytes. *EMBO Molecular Medicine*. DZHK location involved: [Heidelberg/Mannheim](#)

July

Winter, C. (Klinikum der Universität München): **Chrono-pharmacological Targeting of the CCL2-CCR2 Axis Ameliorates Atherosclerosis.** *Cell Metabolism*. DZHK locations involved: [Munich](#), [Hamburg/Kiel/Lübeck](#)

August

Kröll-Schon, S. (Universitätsmedizin Mainz) et al.: **Crucial role for Nox2 and sleep deprivation in aircraft noise-induced vascular and cerebral oxidative stress, inflammation, and gene regulation.** *European Heart Journal*. DZHK location involved: [Rhine Main](#)

September

Koehler, F. (Charité – Universitätsmedizin Berlin) et al.: **Efficacy of telemedical interventional management in patients with heart failure (TIM-HF2): a randomised, controlled, parallel-group, unmasked trial.** DZHK locations involved: [Berlin](#), [Hamburg/Kiel/Lübeck](#)

October

Meyer, A. (Deutsches Herzzentrum Berlin) et al.: **Machine learning for real-time prediction of complications in critical care: a retrospective study.** *The Lancet. Respiratory medicine*. DZHK location involved: [Berlin](#)

November

Mohamed, B. A. (Universitätsmedizin Göttingen) et al.: **Sarcoplasmic reticulum calcium leak contributes to arrhythmia but not to heart failure progression.** *Science Translational Medicine*. DZHK location involved: [Göttingen](#)

December

Bartolomaeus, H. (Max-Delbrück-Centrum für Molekulare Medizin Berlin) et al.: **The Short-Chain Fatty Acid Propionate Protects from Hypertensive Cardiovascular Damage.** *Circulation*. DZHK locations involved: [Berlin](#), [Greifswald](#)



DZHK Scientist Dirk Sibbing receives the Award of the German Heart Research Foundation



DZHK Scientist Katrin Streckfuß-Bömeke received the Franz-Maximilian-Groedel Research Award of the DGK which is endowed with €5,000

Prizes, Grants, Personalia 2018 (selection)

Name	Prize/Funding
Bartelt, Alexander (Munich)	Friedmund Neumann Award 2018 of the Schering Foundation
Cuello, Friederike (Hamburg/Kiel/Lübeck)	DFG-Funding (€ 243,300)
Dechend, Ralf (Berlin) und Müller, Dominik N. (Berlin)	Franz-Gross-Science Award of the German Hypertension Society
Doroudgar, Shirin (Heidelberg/Mannheim)	Science Award of the Universitätsmedizin Göttingen
Frahm, Jens (Göttingen)	European Inventor Award 2018 for rapid MRI in medical diagnostics
Furlong, Eileen (Heidelberg/Mannheim)	Advanced Grant of the European Research Councils (ERC)
Erdmann, Jeanette (Hamburg/Kiel/Lübeck) Joner, Michael und Schunkert, Heribert (Munich)	Members of the new translational project PlaQOmics, which is founded by the Leducq Foundation for Cardiovascular Research with \$ 6 million for 5 years
Hübner, Norbert (Berlin)	Advanced Grant of the European Research Council (ERC)
Kastrati, Adnan (Munich)	Else-Kröner-Memorial-Stipend (€ 220,000)

Name	Prize/Funding
Kessler, Thorsten (Munich)	Research Grant of the Corona Foundation (€ 998,300)
Leuschner, Florian (Heidelberg/Mannheim)	Heisenberg Professorship for immunocardiology at the Medical Faculty Heidelberg
Moretti, Alessandra (Munich)	Advanced Grant of the European Research Council (ERC)
Müller, Dominik N. (Berlin)	Björn Folkow Award of the European Society of Hypertension (ESH)
Sager, Hendrik (Munich)	Else Kröner Excellence Stipend (€ 300,000)
Schell, Richard (Heidelberg/Mannheim)	Research Grant of the members and sponsors of the Dresden Heart Day 2018
Scholl, Ute (Berlin)	Franz Volhard Prize 2018 of the German Society for Nephrology
Schwaninger, Markus Hamburg/Kiel/Lübeck)	Synergy Grant of the European Research Councils (ERC)
Sibbing, Dirk (Munich)	Wilhelm P. Winterstein Award of the German Heart Foundation
Söhnlein, Oliver und Massberg, Steffen (Munich)	Partner of a Consortium, which receives a funding of \$ 6 million from the Leducq Foundation for Cardiovascular Research for atherosclerosis research
Thierfelder, Nikolaus (Munich)	Dr. Rusche Resarch Project Award of € 60,000 of the German Heart Research Foundation
Weber, Christian (Munich)	€ 12 million funding in 4 years by DFG for Collaborative Research Centre 1123 (SFB 1123)
Wilck, Nicola (Berlin)	Theodor Frerichs Award 2018 of the German Society for Internal Medicine
Zeller, Tanja und Blankenberg, Stefan (Hamburg/Kiel/Lübeck)	Research Grant of the EU Horizon 2020 Project "euCanSHare" (€ 553,205)

Finances and Staff



Finances of the DZHK

In 2018, the DZHK had around €41 million in funding and a carryover from 2017 of €10.6 million (2016: €13.8 million). Of this, a total of €43.2 million was spent in the year under review (2017: €44.1 million). The spendings in 2018 were therefore slightly below the prior year.

In general, partners called on funds at an earlier stage and on a more regular basis this year. In total, the spendings were higher than originally in the 2018 business plan, so this was compensated by continuing the reduction of the positive fund balance carried over from previous years (Selbstbewirtschaftungsmittel) that had started in 2017, to the order of around €2.3 million. €8.3 million was not spent in 2018 and will be carried over to 2019. In relative terms, the spend vs new funds (the annual budget excluding carryovers from previous years) was 74 per cent in 2015, 97 per cent in 2016, 108 per cent in 2017 and 105 per cent in 2018.

The DZHK is reducing its positive fund balance over the course of many years in consultation with the Commission of Funding Authorities (Kommission der Zuwendungsgeber). These funds were built up mainly in the years 2015 and 2016. A considerable proportion of the remaining balance has been approved for clinical trials, but will be allocated after a justifiable delay due to reasons such as slow recruiting of patients for the trials. For ethical reasons, it is not generally possible to discontinue the delayed studies or to reduce the funds not requested in a calendar year under these circumstances. These funds are ultimately well-founded reserves for clinical trials.

However, even though there is a gradual funding source due to the positive fund balance, the DZHK will still need regular increases in its total funds.

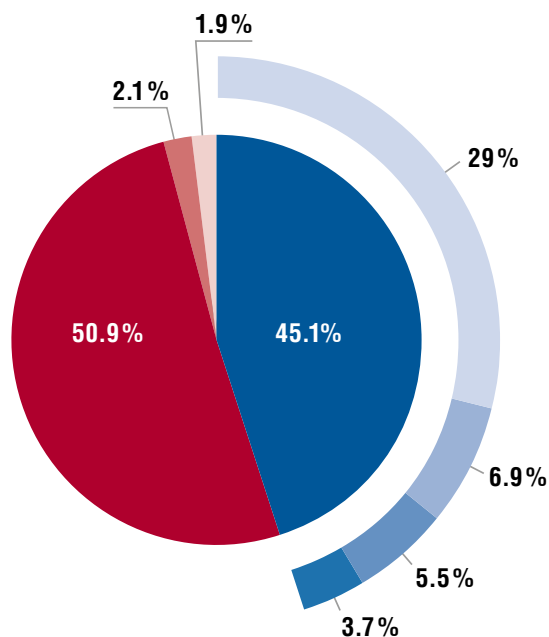
The DZHK urgently needs regular annual growth of three per cent, which is standard for other non-university research institutions in Germany. In view of high collective wage agreements and rising material costs, the budget, which has remained unchanged since 2015, has been 'outgrown', necessitating reductions in personnel and scientific output. The DZHK is optimistic that its funding bodies will agree in 2019, and beyond, to grant the same regular funding growth as the other large non-university research organisations, alongside the other German Centres for Health Research.

At the end of 2018, the German Bundestag imposed a suspension of funds on Helmholtz Centres. The aim is to persuade every Centre to reduce their positive fund balance in 2019. Since the DZHK budget is paid out via the Max Delbrück Center for Molecular Medicine, the block also applies to the DZHK. A reduction of our positive fund balance - the reserves for delayed patient recruitment in clinical trials - would cause a financial disaster for the

DZHK. In 2019, the successful handling of the suspension of funds will therefore represent the greatest financial challenge for the DZHK, in addition to lobbying for regular growth.

The funds spent in 2018 in the amount of € 43.2 million were broken down as follows:

- **Partner site funds:** € 22.0 million
- **Flexible funds:** € 19.5 million
(including clinical research: € 12.6 million, preclinical research: € 3.0 million, training programme: € 2.4 million and external funding: € 1.6 million (including competence networks: € 1.3 million and co-operation with external partners: € 300,000))
- **Membership fees:** € 900,000
(contributions for the 2019 main office budget, which amounts to € 1.2 million; the remaining amount was not spent until 2019)
- **Funding management department:** € 800,000

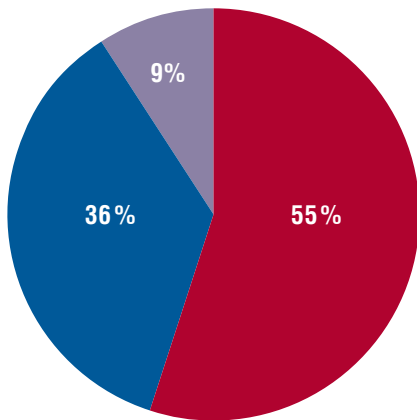


Allocation of spent DZHK funds 2018 by expenditure areas

- **Partner site funds** (2017: 52.6%)
- **Flexible funds** (2017: 43.2%)
- **Funding management department** (2017: 1.7%)
- **Membership fees** (2017: 2.5%)

Flexible funds are made up of

- **Clinical Research**
- **Preclinical Research**
- **Promotion of young talent**
- **External**



Budget of the DZHK main office

The budget of the main office of the DZHK e. V., financed from membership fees, amounted to € 1.14 million in 2018 (2017: € 1.05 million). This budget was fully financed by membership fees.

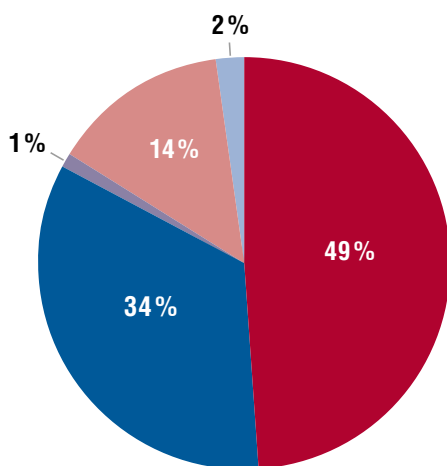
Of this amount, € 1.05 million (2017: € 1.02 million) was spent - other income amounted to € 12,500. The use of the surplus (€ 102,000) will be decided by the DZHK

Staff expenditures, material expenses and investments

- **Staff costs:** €24 million
- **Material expenses:** € 15.4 million
- **Investments:** €3.8 million

General Assembly in September 2019. A surplus of around € 100,000 from the 2017 financial year was not carried over to 2018, but was set aside for the planned relocation of the office in 2019.

Schomerus & Partner Berlin (tax consultants, lawyers, auditors) was commissioned to prepare the annual financial statements of the association.



Staff expenditures, material expenses, and investments of the main office

- **Staff costs: €0.64 million**
(2017: €0.57 million)
- **Material expenses: €0.24 million**
(2017: €0.23 million)
- **Investments: €8,000**
(2017: €10,000)
- **Public relations: €0.17 million**
(2017: €0.19 million)
- **Contributions (TMF e. V.): €20,000**
(2017: €20,000)

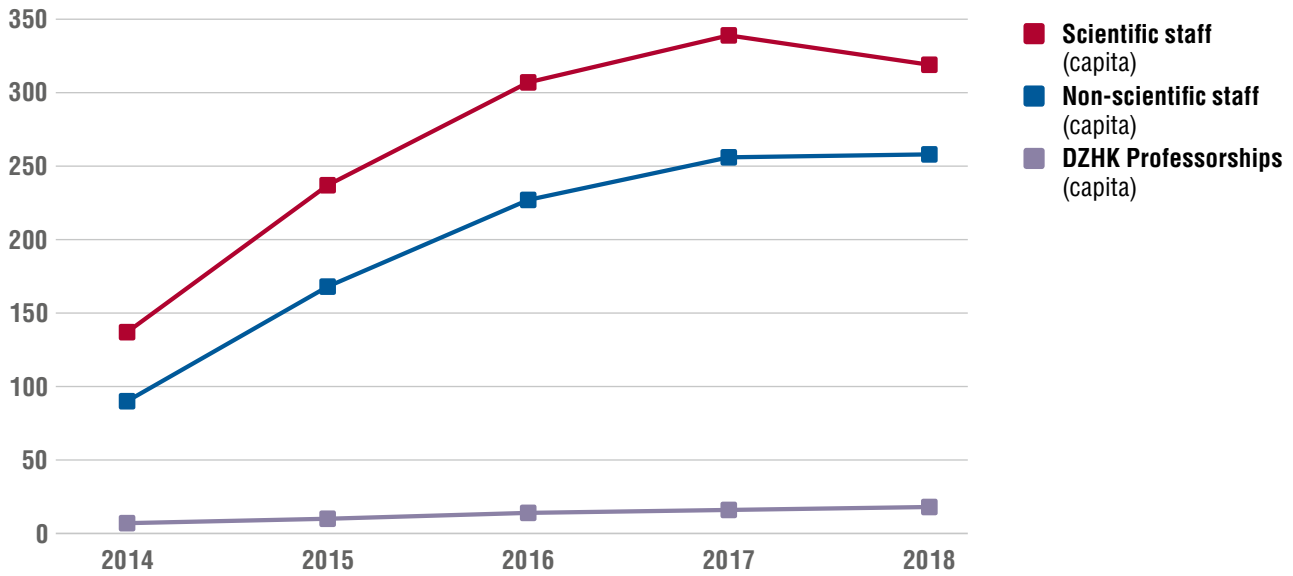
Staff

As of 31 December 2018, 432.73 (2017: 431.13) full-time equivalents (FTE) and 595 (2017: 612) persons or “heads” were financed from DZHK funds. These also included 15 employees at the DZHK office, 12 employees in the funding management department and 22 employees in the competence networks.

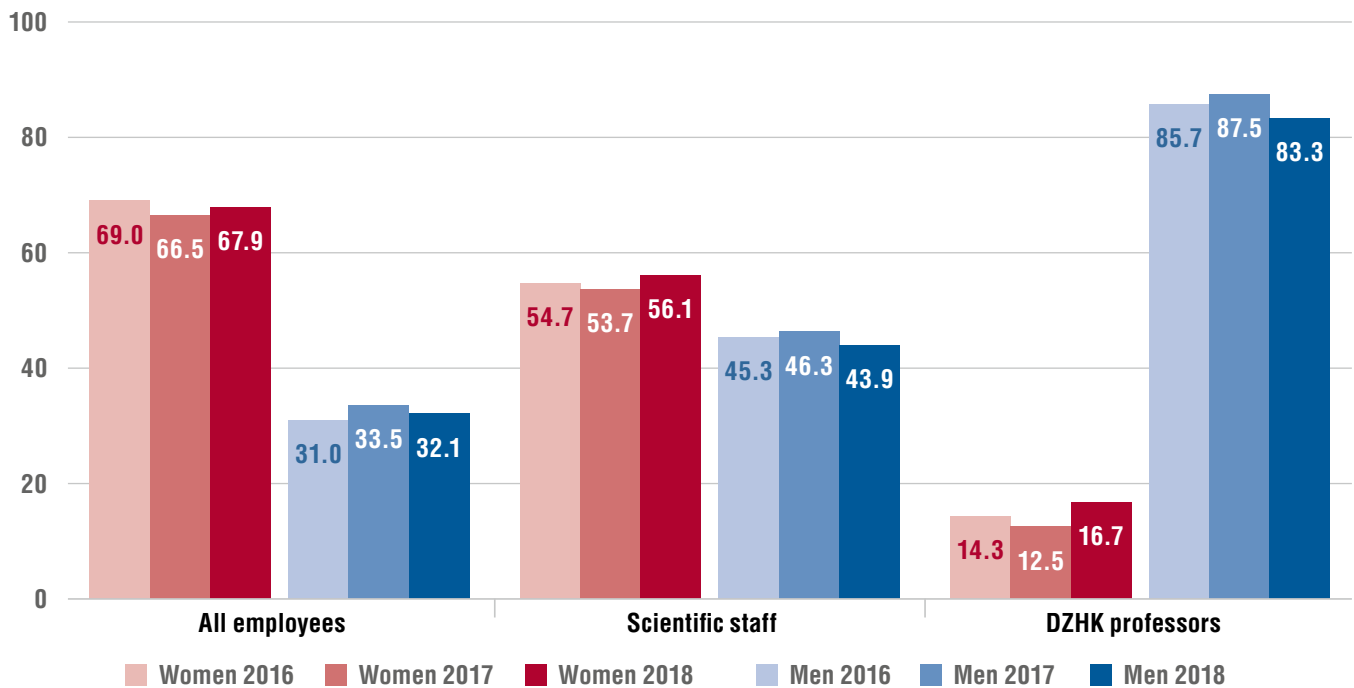
Number of staff financed by the DZHK 2015-2018

	2015	2016	2017	2018
Number of employees (as of 31 December) FTE	286.5	403.58	431.13	432.73
Number of employees (as of 31 December) capita	415	532	612	595
thereof male	130	165	205	191
thereof female	285	367	407	404
Number of scientific staff (FTE)	154.39	220.76	237.23	240.36
Number of scientific employees (capita)	237	307	339	319
thereof male	98	139	157	140
thereof female	139	168	182	179
Number of non-scientific employees (FTE)	122.11	168.82	179.50	176.19
Number of non-scientific employees (capita)	168	227	256	258
thereof male	26	27	36	41
thereof female	142	200	220	217
Number of DZHK professorships (FTE)	10	14	14.40	16.18
Number of DZHK professorships (capita)	10	14	16	18
thereof male	8	12	14	15
thereof female	2	2	2	3

Development of DZHK employees 2014-2018



Gender distribution in the DZHK in per cent – 2016-2018 comparison



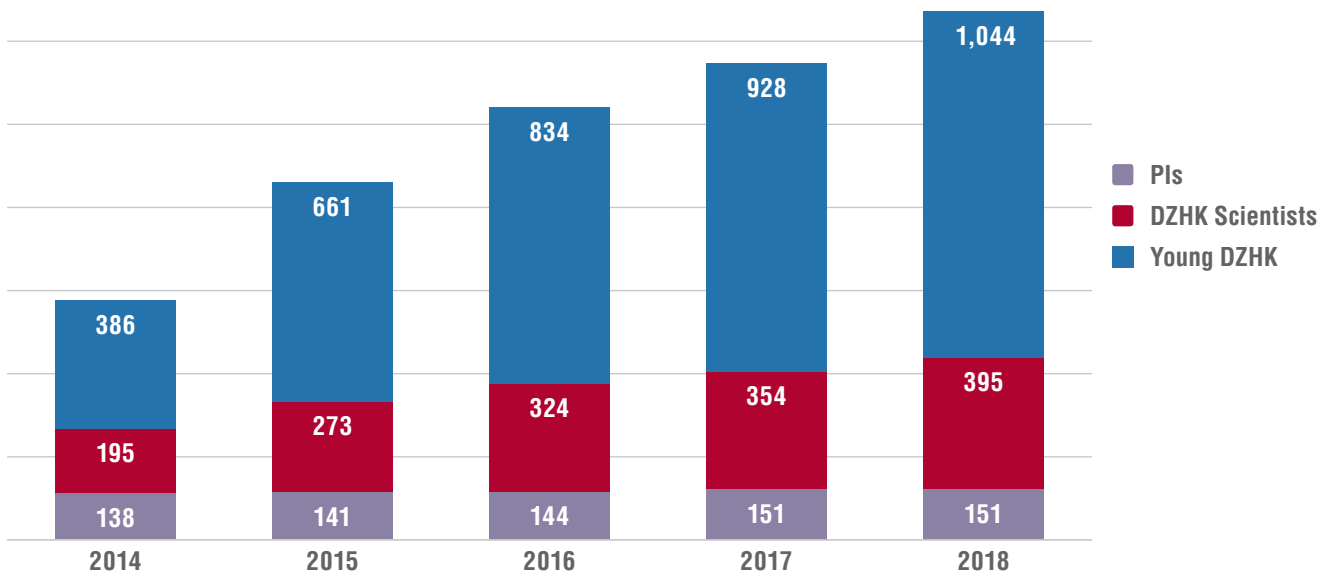
Principal Investigators, DZHK Scientists, Young DZHK Members

Principal Investigators (PIs) are of central importance for the DZHK. In most cases, the PIs are not financed by the DZHK, but contribute their ideas and expertise to the co-operation and the DZHK committees and thus significantly contribute to the success of the DZHK. In the year under review, the DZHK had an unchanged 151 PIs. These are nominated by the partner sites and confirmed by the general assembly. Each partner site has a maximum of 20 PI positions. There are additional

positions for each DZHK professorship, which are established at the partner site from DZHK funds.

In order to assign those scientists who are not PIs to the DZHK, there are two statuses that must be applied for: "Member of the Young DZHK" and "DZHK Scientist". Pre-requisites are a defined commitment to the DZHK and the possibility of assignment to a DZHK PI working at a partner site. In the year under review, the DZHK had 395 DZHK Scientists (2017: 354) and 1044 Young DZHK members (2016: 928).

Development PIs, DZHK Scientists and Young DZHK 2014-2018



The **share of physicians** in these status groups is as follows for 2018:

- Young DZHK: **47.7%**, (71.7% men and 28.3% women)
- DZHK Scientists: **54.2%**, (81.8% men and 18.2% women)
- PIs: **62.9%**, (83% men and 17% women)

Facts and Figures

Administration

DZHK administration

The employees of the main office, the funding management department and the seven partner site management units together form the scientific administration of the DZHK. The co-operation was further intensified in 2018 by 32 weekly video conferences and five face-to-face meetings at the DZHK sites or main office, among other things. In 2018 the focus of the joint work was on the preparation of the new partner site projects for 2019/2020, in addition to the exchange on the current DZHK funding procedures and all administrative processes from application to reporting.

Main office

In 2018, 15 employees (12.55 FTE as of 31.12.2018) worked in the main office, including the managing director. The office mainly supports the Board of Directors of the association to co-ordinate the scientific co-operation in the DZHK.

During the reporting period, these included:

- Organisation of the regular calls for proposals and the selection and evaluation procedures in the three areas of preclinical research, clinical research and promotion of young scientists
- Organisation of the Mentoring Programme
- Organisation of the Young DZHK Retreat and the DZHK Retreat
- Preparation of the 2nd DZHK Conference on Translational Medicine
- Co-ordination of the joint call with the British Heart Foundation
- Controlling of the outflow of funds together with the funding management department and the location management
- Organisation, preparation and follow-up of all committee meetings
- Press and public relations work as well as internal communications of the DZHK



Employees of the DZHK's main office and funding management department

Funding management department

The funding management department (FMM) as part of the Max Delbrück Centre for Molecular Medicine in the Helmholtz Association (MDC) is entrusted with the administrative implementation of the funding to the DZHK partner institutions and external co-operation partners. It is responsible for the review of grant applications on their compliance with grant legislation as well as to inspect the use made of the funds in accordance with the DZHK provisions and the conditions of grant use of the German Federal Ministry of Education and Research (BMBF). In addition, the FMM prepares controlling reports for the association's Board of Directors and the executive management, the association's committees and the site management in order to support them in their effective management of funds.

In the reporting year 2018, the FMM was responsible for transferring the grant funds for project funding to 28 of the 32 partner institutions of the DZHK. The five partner institutions to which the FMM does not forward any funds are: Robert Koch Institute (since it is a government research facility), University of Göttingen (funding only goes to the University Medical Centre Göttingen, which is itself a member), University of Heidelberg (funding to the University Hospital Heidelberg, which is itself a member), Max Planck Institute for Experimental Medicine Göttingen (so far no funding), Max Delbrück Center for Molecular Medicine Berlin-Buch (no transfer of funds). In addition, grants will be forwarded to 29 external co-operation partners in 2018 (2017: 41), including the funding of three competence networks. A total of 560 ongoing projects were funded in 2018 (2017: 617). The total number of DZHK projects to date is 1,240.

As of 31.12.2018, the FMM had 10.3 FTEs (12 heads). One position in the area of finance/contract preparation

was filled on 15.02.2019. The total of 13 FMM staff positions are distributed among the following tasks: management, scientific review, application and proof of use review, controlling, administration and contract management.

Partner site management

As a rule, the seven de-centralised site management units in 2018 included a scientist (site manager) and an administrator, both funded by the DZHK with a full time position. The partner site managers form the interfaces between scientific projects, partner site's executive board, third-party funding administrations, human resources, deaneries of the research offices, legal departments, the DZHK main office and FMM. They coordinate all activities at the partner site, organise site retreats, PI meetings and co-ordinate the work of the executive board as well as the application and reporting system. In addition, they conduct de-centralised financial controlling for their partner site. Together with the office and the FMM, they also develop procedures and processes in the DZHK.



Site managements are the interface between the researchers at the site, the DZHK main office and the funding management department

Facts and Figures

Partner Sites



MDC – Max Delbrück Centre for Molecular Medicine in the Helmholtz Association

DZHK Partner site Berlin

Partner site spokesperson: Holger Gerhardt, Max Delbrück Center for Molecular Medicine in the Helmholtz Association

Deputy spokesperson:

Burkert Pieske, Director at University Medical Centre, Division of Cardiology, Charité – Universitätsmedizin Berlin

Site management: Carola Schubert (site manager), Mariam Abou-Saleh (site administrator), Charité – Universitätsmedizin Berlin

Partner institutions at the DZHK location Berlin

Max Delbrück Center for Molecular Medicine in the Helmholtz Association (MDC); German Heart Centre Berlin (DHZB); Federal Republic of Germany, represented by the Federal Ministry of Health, represented by the Robert Koch Institute (RKI); the German Institute of Human Nutrition Potsdam-Rehbrücke (DIfE)

Research Focus at the DZHK

The Berlin site is focussing on research into vascular diseases as well as the development and therapy of heart failure. At the Charité, clinical and translational research is carried out primarily in the fields of HFpEF and HFrEF, vascular diseases, metabolism and systems biology with an additional focus on gender aspects in clinical practice, research, teaching and the promotion of young scientists. Research at the MDC focuses on genomics, vascular biology, molecular cardiology, myocardial function and transgenic animal models. The DHZB focuses on surgery for heart failure, transplantation and assist systems as well as cardiovascular diseases in children. The partner institutions RKI and DIfE (located in the federal state of Brandenburg) facilitate epidemiological studies in large cohorts on factors such as nutrition and metabolism and their effects on the development, manifestation and prevention of cardiovascular diseases.

The study centres for currently seven clinical studies are located in Berlin, which all recruit patients and have also initiated study centres at other locations. In addition, the clinical facilities of the Berlin partner institutions are also successfully recruiting into nine DZHK and DZHK-associated trials.

The first Berlin DZHK partner site retreat took place in October 2018. The event gave primarily young scientists the opportunity to present their projects and discuss them with experienced colleagues. In November 2018, a joint meeting was held with the ESC working group on “Coronary Pathophysiology and Microcirculation”, at which representatives of the ESC and representatives of the DZHK Berlin location presented projects and research strategies and discussed priorities and possible new strategies.



DZHK Site Meeting in April 2019

DZHK Partner site Göttingen

Partner site spokesperson: Wolfram-H. Zimmermann, Director of the Institute for Pharmacology at the University Medical Centre Göttingen

Deputy spokesperson: Eberhard Bodenschatz, Director of the Max Planck Institute for Dynamics and Self-Organisation

Site management: Axel Kaul (site manager), Uschi Hübner (scientific project manager), [since 03/2019 Vanessa Kruse], Sylvia Vann (site administrator), University Medical Centre Göttingen

Partner institutions at the DZHK location Göttingen

Georg August University Göttingen; University Medical Centre Göttingen (UMG); Max Planck Institute for Biophysical Chemistry, Max Planck Institute for Dynamics and Self-Organisation; Max Planck Institute for Experimental Medicine; German Primate Centre

Research Focus at the DZHK

The main focus of the DZHK Göttingen site is heart failure research with the topics “Mechanisms of the transition from clinically asymptomatic heart muscle weakness to symptomatic heart failure” and “Heart regeneration in heart failure”. At the Göttingen location, the focus is on infrastructure funding through eleven partner site projects and three DZHK Professorships in 2018 (Luther, von Haehling, Uecker). With Professor Stefan von Haehling, the DZHK Professorship for Metabolic Cardiology was successfully filled. A further appointment to a DZHK Professorship in genome editing (call for proposals 2019) is planned. Three clinical trials and two translational research projects are currently being coordinated by the DZHK in Göttingen. Another clinical study and two translational research projects have been recommended for funding and are scheduled to start in 2019.

In 2018, the co-operation with the DZNE was further developed in Göttingen with the focus on “Heart and Brain” research. In order to strengthen this DZG research focus, the construction of a research building called “Heart and Brain Centre Göttingen (HBCG)” will start in 2019. It is funded by the federal and state governments. The successful acquisition of the Cluster of Excellence “Multiscale Bioimaging: from Molecular Motors to Networks of Excitable Cells” with an organ-related focus on “Heart and Brain” will also strengthen basic and translational research and interdisciplinary research for patients in the sense of the overarching DZG mission. In addition, the acquisition of Professor Rabea Hinkel as W3 Professor for Laboratory Animal Science at the German Primate Centre will strengthen late translational research in Göttingen and for the DZHK.



University Medicine Greifswald

DZHK Partner site Greifswald

Partner site spokesperson: Stephan B. Felix, Director of the Department of Internal Medicine at University Medical Centre Greifswald

Deputy spokesperson: Marcus Dörr, University Medical Centre Greifswald

Site management: Stefan Groß (site manager), Susanne Franck (site administrator), University Medical Centre Greifswald

Partner institutions at the DZHK location Greifswald

University Medical Centre Greifswald

Research Focus at the DZHK

Special expertise of the Greifswald partner site is in conducting population-based epidemiological and clinical studies with comprehensive cardiovascular phenotyping,

research on the prevention of systolic/diastolic heart failure or dilative cardiomyopathy, high-throughput multi OMICs analyses, telemedicine, biobanking and data management/analysis in large patient cohorts.

In 2018 the partner site projects from the first funding phase (2011-2018) were completed. Further publications from these projects are currently being published. Furthermore, in the second half of 2018, the new cross-institute collaborative project structure was established for the start of the new funding phase in 2019, with the focus on “heart failure prevention and therapy, immunological mechanisms in heart failure, molecular mechanisms of heart failure and cardiac cachexia”. The two DZHK Professorships “Molecular Cardiology” (since 04/2017 Professor Jens Fielitz) and “Cardiovascular Prevention” (since 04/2018 Professor Sabina Ulbricht) are also integrated into this new project structure.

In 2018, the University Medical Centre Greifswald participated as a study centre in the clinical DZHK studies TORCH, TransitionCHF, TOMAHAWK, SMART-MI, APPROACH-ACS, FAIR-HF2, CLOSURE-AF, CAVA-ADHF and SPIRIT-HF. Recruitment for TORCH was completed at the beginning of 2018, so that the one-year follow-up will still take place there. The ESC-EORP Cardiomyopathies Registry has included approximately 90 subjects since 2015 and further myocarditis patients are expected to be enrolled in 2019. In the field of clinical research, Greifswald has set up the Trusted Third Party of the Central Data Management (joint project together with the Göttingen site and the main office in Berlin). In addition, the site is responsible for patient management in the TORCH study. Furthermore, the DZHK basic and trial biobanking as well as the Laboratory Information Management System of the DZHK is operated in Greifswald.



Participants of the site retreat

DZHK Partner site Hamburg/Kiel/Lübeck

Partner site spokesperson: Thomas Eschenhagen, Director of the Institute for Experimental Pharmacology and Toxicology at University Hospital Hamburg-Eppendorf (as of January 2019: Norbert Frey, Kiel)

Deputy spokesperson: Norbert Frey, Director of the Cardiology and Angiology Clinic at University Hospital Schleswig-Holstein (as of January 2019: Heimo Ehmke, Hamburg) und Jeanette Erdmann, Lübeck)

Site management: Doreen Stimpel (site manager), Monika Glimsche (site administrator), University Hospital Hamburg-Eppendorf

Partner institutions at the DZHK location Hamburg/ Kiel/Lübeck

University Hospital Hamburg-Eppendorf, Christian Albrecht University Kiel, University of Lübeck, Asklepios Klinik St. Georg

Research Focus at the DZHK

The scientific focus at the partner site is on the identification of genetic risk factors and biomarkers of cardiovascular diseases, stem cells and tissue engineering as well as on mechanisms and therapies of congenital and acquired heart muscle diseases.

Four DZHK-funded clinical trials (DEDICATE and FAIR-HF2 in Hamburg, as well as TOMAHAWK and CAVA-ADHF in Lübeck) are conducted at the site, all of which are currently in the recruitment phase.

In addition, two preclinical projects of the Translational Research Projects funding line (both projects at the UKE) are working on innovative therapeutic approaches with a prospect for clinical application (gene and heart muscle replacement therapy). The site is involved in a variety of co-operations through Shared Expertise and with external partners and has gained one of the most frequently used Shared Expertise in the DZHK with the AAV Vector Platform in Kiel.

In 2018, the DZHK received a donation of € 400,000 from the Neumünster-based non-profit association "Kinderherzen wollen leben". The donation and other DZHK site funds will finance a five-year endowed professorship (W2) for cardiogenetics of congenital structural heart disease at the Kiel Children's Heart Centre. The professorship has already been advertised and the appointment is planned for 2019. A constant focus at the site is on regular internal communication, networking and scientific exchange among local researchers and with external experts. A series of internal seminars in Hamburg, Kiel and Lübeck takes place every three months to ensure collaboration and foster exchange. In June 2018, the annual site retreat was again carried out with great success and was very well attended with more than 80 scientists.



University Medical Centre Mannheim

DZHK Partner site Heidelberg/Mannheim

Partner site spokesperson: Hugo A. Katus, Medical Director of the Department of internal Medicine III of the Heidelberg University Hospital (as of July 2019: Johannes Backs, Heidelberg)

Deputy spokesperson: Thomas Wieland, University Hospital Mannheim (as of July 2019: together with Patrick Most, Heidelberg)

Site management: Tanja Weis (site manager), Annabell Skarabis (scientific project manager), Ines Schneider (site administrator, since April 2019: Denise Kampffmeyer), Heidelberg University Hospital

Partner institutions at the DZHK location Heidelberg/ Mannheim

Heidelberg University; University Hospital Heidelberg; University Hospital Mannheim; German Cancer Research Centre (DKFZ); European Molecular Biology Laboratory (EMBL)

Research Focus at the DZHK

The scientific focus of the Heidelberg/Mannheim partner

site is the investigation of genetic and inflammatory cardiomyopathies and arrhythmias in integrative and translational approaches. Genetic, epigenetic and electrophysiological methods, imaging diagnostics, ps-iPS cells and model systems from cellular systems to zebrafish, mouse, rat and human-relevant pig models are used for the functional analysis of molecular signalling pathways and the identification of new diagnostic and therapeutic target structures. Methodological platforms (e.g. next-generation sequencing, zebrafish platform, large animal platform, ps-IPS platform) and a state-of-the-art biobank with fully automated sample processing and storage are available for DZHK projects. The translational pipeline has already identified several genetic loci and variants, epigenetically modified candidate genes, miRNAs and other potential targets, which will then be functionally investigated for their diagnostic and therapeutic potential. Committed to the DZHK, the Heidelberg/Mannheim site is involved in a wide variety of clinical and preclinical research.

In 2018, the partner site successfully recruited for 10 clinical studies and further study participations were prepared. In the area of preclinical research, a total of nine collaborations were conducted with Shared Expertise (SE) or external partners. In 2018, Heidelberg/Mannheim offered a total of 27 SEs. In the Excellence Programme a Postdoc Start-up Grant, a Clinician Scientist Project and two Rotation Grants could be secured. In addition, the Junior Research Group was positively evaluated by Shirin Doroudgar during the reporting period and will continue to be promoted. To promote scientific exchange and networking, various lectures were supported and the DZHK Symposium "Precision Medicine Summit on Cardiomyopathies & Heart failure" was held. In May 2018, the third and largest local site retreat took place, focusing on scientific strategy and the promotion of young scientists. The newly established Heisenberg Professorship for Immunocardiology (W3), which Professor Florian Leuschner took up in Heidelberg, should also be highlighted as a structural success for the site.



Participants of the "Munich Heart Alliance" Meeting 2018

DZHK Partner site Munich

Partner site spokesperson: Stefan Engelhardt, Director of the Institute for Pharmacology and Toxicology of the Technical University of Munich

Deputy spokesperson: Christian Weber, Director of the Institute for Prophylaxis and Epidemiology of Cardiovascular Diseases at Ludwig Maximilian University Munich

Site management: Sandra Rauser (site manager), Martina Michel (site administrator), Technical University of Munich

Partner institutions at the DZHK location Munich

Technical University of Munich (TUM); Hospital of Ludwig Maximilian University of Munich (KUM); Ludwig –Maximilian University Munich (LMU); German Heart Centre Munich (DHM); Klinikum rechts der Isar (MRI); Helmholtz Centre Munich – German Research Centre for Health and the Environment (HMGU); Max Planck Institute for Biochemistry (MPI)

Research Focus at the DZHK

The DZHK partner site in Munich (called "Munich Heart Alliance" (MHA)) focuses on research into molecular mechanisms of cardiovascular diseases that are yet unknown, the development of new therapeutic approaches based on these mechanisms, and their translation into clinical studies.

In the field of clinical research, Munich with its three cardiology university hospitals has participated in 17 of the 22 clinical trials sponsored by the DZHK. Also, the study centres of four trials are located in Munich. Under the direction of the Frankfurt and Heidelberg site, Munich participated in the idea competition "First-milestone projects" at the DHM and MRI as part of preclinical research. The Review Panel for the DZHK Excellence Funding has awarded three proposals for post-doc start-up funding and two proposals for the Clinician Scientist Programme to young Munich scientists. The DZHK Junior Research Group, headed by Dr. Alexander Bartelt, began its work at the KUM.

In addition to the primary DZHK activities, the Munich scientists were also very successful in obtaining additional funding. Dr. Thorsten Kessler raised almost € 1 million from the Corona Foundation as part of the "Junior Research Group for Cardiovascular Diseases" programme. Professor Alessandra Moretti was awarded an ERC Advanced Grant, Professor Heribert Schunkert was awarded a co-operation project in the second ERA-CVD Call and the SFB 1123 "Atherosclerosis" (spokesperson: Professor Christian Weber) received funding for another four years. In addition, Professor Michael Joner, Professor Steffen Massberg and Professor Oliver Söhnlein each raised € 6 million for two consortia within the transatlantic Leducq network.

At the 2nd Young DZHK Meeting in Munich, Dr. Sebastian Clauß was elected as Deputy Young DZHK Speaker Munich, and the 13th and 14th meetings of the MHA took place in February and July 2018.



Goethe University Frankfurt

DZHK Partner site Rhine-Main

Partner site spokesperson: Andreas Zeiher, Director of the Cardiology Department of the University Hospital Frankfurt

Deputy spokesperson: Stefanie Dimmeler, Director of the Institute for Cardiovascular Regeneration of the University Hospital Frankfurt

Site management: Katharina Schulenburg (site manager), Linda Sulzmann (site administrator), University Hospital Frankfurt

Partner institutions at the DZHK location Rhine-Main

Goethe University Frankfurt; Max Planck Institute for Heart and Lung Research, Bad Nauheim; Kerckhoff-Klinik, Bad Nauheim; Johannes Gutenberg University Mainz

Research Focus at the DZHK

The focus of the DZHK Rhine-Main site is on the identification of epigenetic signatures and mediators of cardiovascular diseases in order to use them either as biomarkers or as potential targets for the repair and regeneration of vessels and cardiac muscle tissue.

In Frankfurt am Main, the mechanism by which AntimiRs mediate cardioprotective effects against miR-92a was further deciphered. This work accompanies the clinical development of AntimiR-92a, which is currently being tested in two phase I studies in humans. In addition, central new metabolic and epigenetic regulatory principles have been discovered that regulate vascular growth and remodelling. Dr. Nuno Camba was recruited as a new international junior scientist for a Junior Research Group of the DZHK. In Mainz, the Myovasc trial was successfully completed with a total of 3,289 participants. A precision proteome profiling platform was also established in Mainz. Scientific highlights include research into a Nox2-dependent mechanism that shows damage to blood vessels caused by aircraft noise. In addition, it has been possible to identify new genetic variants that contribute to the occurrence of cardiac arrhythmias. At the Kerckhoff-Klinik, 16,500 patients were enrolled in the biomarker registry. The MPI in Bad Nauheim showed a critical role of the cation channel Piezo1 and the heterotrimeric G proteins Gq/11 in vascular inflammation. Important breakthroughs were achieved in the investigation of the heterogeneity of cardiac progenitor cells and the function of Myh10 for the remodeling of the extracellular matrix.

In the field of clinical research, the Rhine-Main site successfully recruited for six DZHK trials (Transition-CHF, TOMAHAWK, CAVA-ADHF, DEDICATE, CLOSURE-AF and DECIPHER) during the reporting period. One study is in the follow-up phase (TORCH), three further studies (CTSN-TVR, Screen-AF and PRAISE) are in preparation.

Acronyms

AFNET	Arterial Fibrillation Competence Network	KNHI	Competence Network for Heart Failure
BHF	British Heart Foundation	LIMS	Laboratory Information and Management System
BMBF	Federal Ministry of Education and Research	LMU	Ludwig –Maximilian University Munich
CSG	Clinical Study Group	MDC	Max Delbrück Center for Molecular Medicine
DGK	German Cardiac Society	MHA	Munich Heart Alliance (DZHK site Munich)
DHM	German Heart Centre Munich	MPI	Max Planck Institute
DHS	German Heart Foundation	PI	Principal Investigator
DHZB	German Heart Centre Berlin	RCC	Research Coordinating Committee
DiFe	German Institute of Human Nutrition	RKI	Robert Koch Institute
DKFZ	German Cancer Research Centre	SE	Shared Expertise
DKTK	German Cancer Consortium	SOP	Standard Operating Procedure
DZD	German Center for Diabetes Research	TRG	Translational Research Group
DZG	German Centers for Health Research	TRP	Translational Research Project
DZHK	German Centre for Cardiovascular Research	TUM	Technical University Munich
DZIF	German Center for Infection Research	UMG	University Medical Centre Göttingen
DZL	German Center for Lung Research	VZÄ	Full-time equivalent
DZNE	German Center for Neurodegenerative Diseases	ZDM	Central data management
ECS	Early clinical study	✓	Target achieved
EMBL	European Molecular Biology Laboratory Heidelberg	✓	In progress
ERA-CVD	European Research Area Network on Cardiovascular Diseases	✗	Goal not reached
ERC	European Research Council		
ESC	European Society of Cardiology		
FMM	Funding Management Department		
HD/MA	Heidelberg/Mannheim (DZHK site)		
GAIN	German Academic International Network		
GRS	Guideline-relevant study		
IDMS	Image Data Management System		
KNAH	Competence Network for Congenital Heart Defects		

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