




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

DZG DEUTSCHE ZENTREN
DER GESUNDHEITSFORSCHUNG

German Centre for Cardiovascular Research

ANNUAL REPORT

2019



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

When we look back at 2019, the past year seems a very different time: We are now in the middle of the corona pandemic, our work, our everyday life, and our leisure time have changed significantly. Our colleagues in the clinics see patients with a previously unknown disease. They want to understand and shed some light on this disease, and they are looking for ways to help the sick in the best possible way - almost overnight, a new field of research was created.

Therefore, we would like to use this report, which primarily summarises 2019, to present research projects and the results of early Covid-19 research at the DZHK.

Gerd Hasenfuß's time as a DZHK board member ended in 2019 and as someone who has been with us since our very inception, we look even further back in time to thank him for his valuable work. For seven years, the cardiologist from Göttingen brought the view of the experienced clinician to the board. We are glad that he will remain with the DZHK as a researcher and physician. He was succeeded on January 1, 2020, by Steffen Massberg from the Munich University Hospital, whom we warmly welcome to the Board of Directors.

We look back on the busy and successful year 2019 at the DZHK. We want to thank all those who supported us on this path for their commitment and their continued work with us.

September 2020



Thomas Eschenhagen
Spokesperson of the
Board of Directors



Steffen Massberg
Board of Directors



Thomas Sommer
Board of Directors

Special: Covid-19

2020 has been shaped by the corona pandemic at the DZHK - both in our everyday work and in research. We would therefore like to take this opportunity to outline the status of pandemic-related activities at the DZHK until the end of August 2020.

Cardiovascular patients are particularly affected by the pandemic, which is why many DZHK research groups have temporarily focused on such topics. Due to the Federal Ministry of Education and Research's generous regulations for the reallocation of funds and staff, we have been able to react quickly and without complications.

BASIC RESEARCH

Groups from basic research have, among other things, addressed the question of the extent to which SARS-CoV-2 attacks cells and tissue of the cardiovascular system. They also investigated how the ACE2 receptor is expressed in these tissues and whether there are differences in patients with heart disease. It was shown that the ACE2 receptor is expressed in heart muscle cells, especially in patients with heart disease (Nicin et al., *Eur Heart J.* 2020 May). In addition, it was observed in a subanalysis that higher levels of ACE2 can be found in heart muscle cells of patients treated with ACE inhibitors. The influence of ACE inhibitors and angiotensin receptor blockers on the expression of the SARS-CoV-2 receptor ACE2 is currently being clarified in further larger observational clinical studies (Wild et al., *JMCC* 2020). In the laboratory, a collaboration between the Rhine Main, Hamburg/Kiel/Lübeck, and Munich sites also demonstrated that heart muscle cells or tissue can be infected with SARS-CoV-2 in vitro (Bojkova et al., *Cardiovascular Research* in press). Whether this is also the case in patients is not yet clear.

CLINICAL RESEARCH

Small and large clinical studies were started at the DZHK partner sites, which primarily investigated the extent to which the cardiovascular system of Covid-19 patients is involved in the disease. For example, a group from the Rhine Main site found signs of inflammation of the heart muscle in 80 percent of recovered corona patients, even those with only mild courses of the disease (Puntmann et al., *JAMA Cardiol.* 2020 Jul). Other groups showed viral material in the heart of deceased patients (Lindner et al., *JAMA Cardiol.* 2020 Jul) and in biopsy material of patients with heart muscle inflammation after surviving Covid-19 (Escher et al., *ESC Heart Fail.* 2020 Jun; Wenzel et al., *Cardiovasc Res.* 2020 Aug).

€800,000 FOR THREE CLINICAL STUDIES

With unprecedented speed, the DZHK awarded funds for clinical studies and supports three studies with a total of approx. €800,000. These studies investigate whether discontinuing ACE inhibitors has an effect on the course of the disease (ACEI-COVID-19, Massberg), whether blood thinners can prevent the frequently occurring thromboses in corona patients (COVID-PREVENT, Landmesser) and whether smartwatches are suitable for monitoring corona patients at home (MR SPOC, Sinner). In addition, five DZHK research groups (out of a total of 14 funded groups) were awarded a grant for Covid-19 research by the German Heart Foundation.

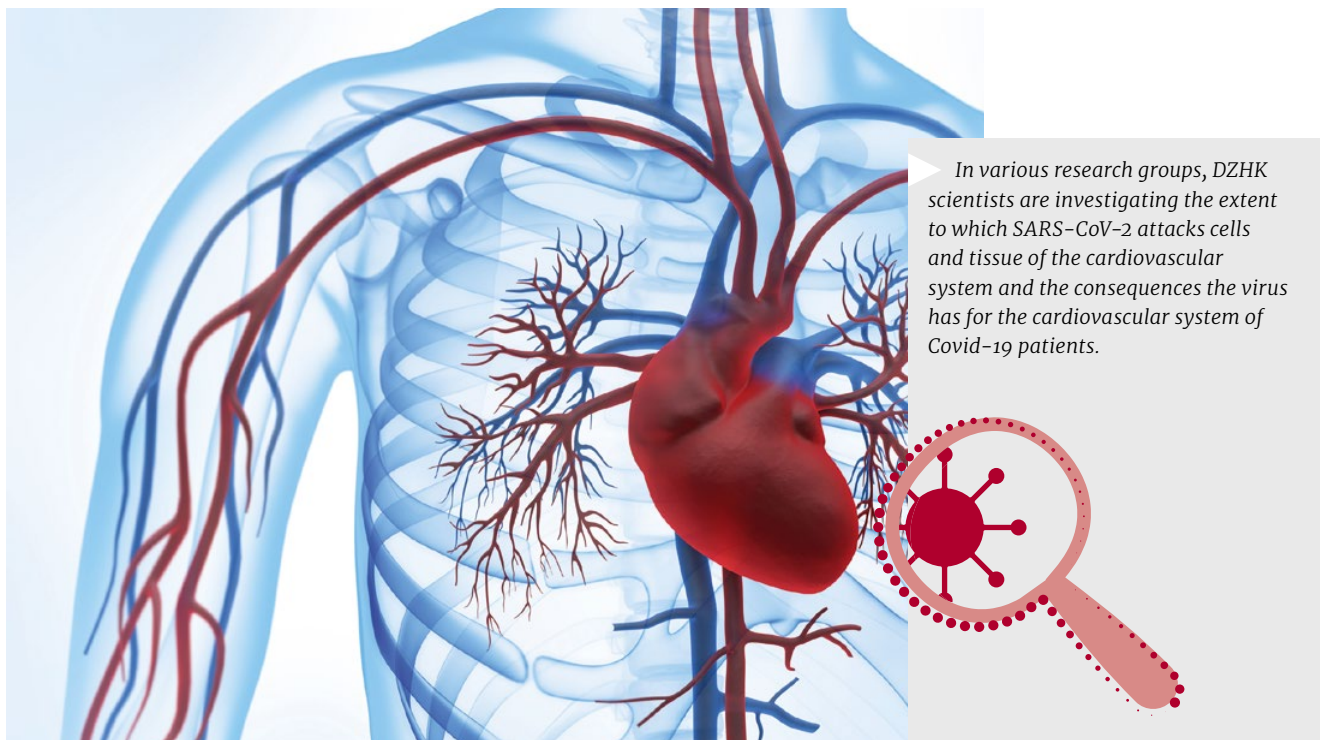
DATA PLATFORM OF THE NETWORK UNIVERSITY MEDICINE

The "Network University Medicine" (NUM), which was established by the BMBF, is to bring together research on Covid-19

nationwide. One goal of the network is to create a uniform data platform for clinical study data. The DZHK is making its clinical research platform available for a transitional period of eight months until the final NUM platform is completed. To this end, complex processes have been underway since June 2020 to adapt the DZHK's clinical research platform for Covid-19 research in order to be operational by the end of September 2020. The DZHK is using the concentrated know-how of its employees in the decentralized areas of its clinical infrastructure for this cooperation.

COMMUNICATION IN PANDEMIC TIMES

In order to bring together all information, we have created a Corona Blog. It reports on studies and research results. The Frequently Asked Questions (FAQs) for heart patients on our website had high page views and was linked to from the German Cardiac Society, among others. DZHK scientists also prepared reviews to inform scientists and clinicians about COVID-19 (Kessler & Schunkert, Herz 2020; Böhm & Zeiher, Clin Res Cardiol. 2020 May).





The DZHK – Focus on Translation



The German Centre for Cardiovascular Research was founded with the aim of harnessing discoveries from basic research for medical practice. This path is filled with complexities and therefore requires strategic considerations and the targeted support of existing weak spots in translation.

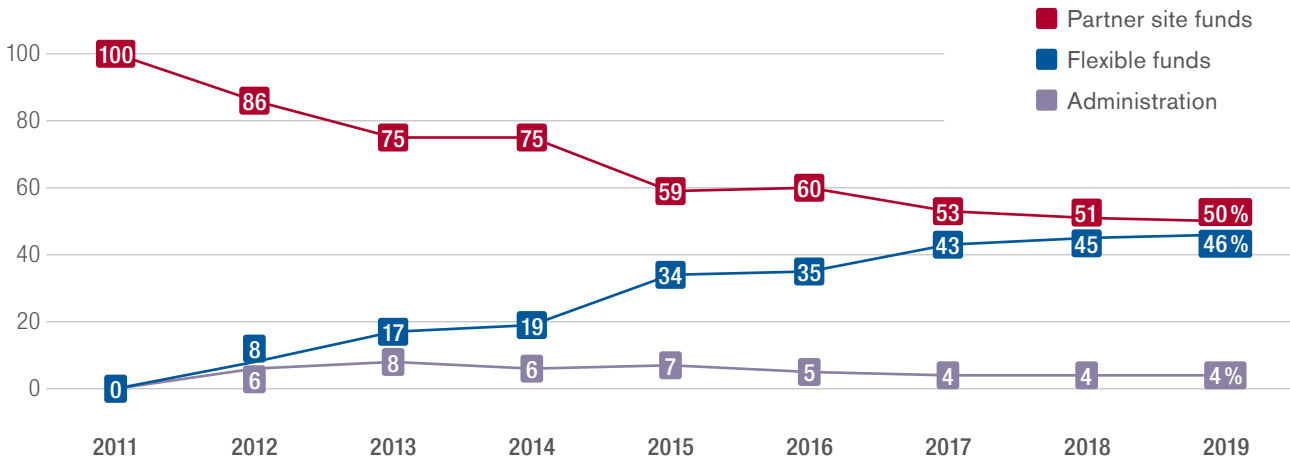
The basis for successful translation is high-quality basic research. Only if new mechanisms of cardiovascular diseases are discovered can they be further developed for the treatment of patients. The DZHK therefore brings together experts from all disciplines relevant to cardiovascular diseases from all over Germany. A special feature is the close cooperation between clinically active physicians and

laboratory researchers. Together they identify promising approaches from research and consider strategies for their translation.

IDENTIFY TRANSLATIONAL WEAKNESSES

In our view, the weak points of translation in the field of cardiovascular research are especially the late preclinical phase and the early clinical phase – i.e. the transition of a new method or active substance from the laboratory to the human body. We have therefore set up separate funding programmes for these areas, for which all scientists registered with the DZHK can apply. In this way, we want to ensure that the best and most promising ideas are given a chance.

DZHK FUNDING 2011–2019



FLEXIBLE ALLOCATION OF FUNDS

Research funding for projects is awarded through internal competition. This also includes the support of young researchers and the scientific exchange. Unusual for a research institution, in 2019, we spent almost half of our annual budget of €43 million as so-called flexible funds, i.e. the DZHK researchers must apply internally. With this scale of flexible funding, we were able to achieve a strategic goal that we have been working towards continuously for years.

LAST STEP BEFORE THE CLINIC

This year we were able to complete five of our Translational Research Projects (TRP) (see page 29-33). We are excited that a new minimally invasive technology for the replacement of a mitral valve received European approval at the beginning of the year. The valve was developed at our Hamburg/Kiel/Lübeck site as part of a Translational Research Project completed in 2017 and is now in clinical use. A TRP at the Göttingen site forms the basis for an early clinical study approved in the year under review. In this study, artificial heart tissue produced in the laboratory is used for the first time in patients with severe heart failure.

SUSTAINABLE USE OF DATA

For us, translation also means making the best possible use of the data and samples from our clinical studies, which are collected at great expense. We are now beginning to reap the rewards. Our data platform now contains clinical data, biosamples and image data from around 7,600 study participants. We make this data available to the scientific community worldwide. We have already received the first applications for use. We are breaking new ground in the process of publication and use and the associated issues, such as data protection and intellectual property, and in the year under review we have worked hard to develop clear, functioning regulations (see page 40). These must prove their value in the coming years.

CONSTANTLY CHALLENGING OURSELVES

Are we on the right track? What do the individual partner sites contribute to the success of translational research? We asked these questions in preparing the internal review of the DZHK in 2020. We used the preparation phase for the review to engage in intensive discussions across locations and research topics, to look back and to sharpen our strategy for the future. We will present the results in the next report.

Highlights and Publications 2019

The DZHK fosters scientific exchange at the 2nd Conference on Translational Medicine in Berlin. (page 50)

JANUARY



The SCREEN AF-DZHK15 clinical trial for the early detection of atrial fibrillation at home using a rhythm patch completed recruitment. (page 38)

MARCH



MAY



Together with the German Society of Cardiology, the DZHK is organising the translational symposium "Genome Editing" in Berlin. (page 51)

FEBRUARY



European cardiologists want to work together to solve urgent problems in cardiovascular medicine: Launch of the collaboration between DZHK and British Heart Foundation (BHF). In October 2019, the Dutch Heart Foundation (Hartstichting) joined this collaboration. (page 54)

APRIL



JUNE



Detect heart attacks faster and more reliably: An international team of researchers led by DZHK scientists at the Hamburg/Kiel/Lübeck partner site has developed a risk calculator based on a highly sensitive troponin test. (page 13)



Marc-Phillip Hitz from the Hamburg/Kiel/Lübeck partner site accepts the DZHK Endowed Professorship for Cardiogenetics of Congenital Structural Heart Diseases, financed by a donation from the non-profit organisation "Kinderherzen wollen leben e.V." (page 24)

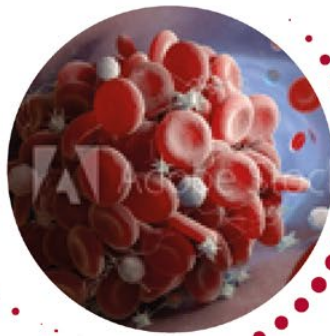
New DZHK office space: DZHK Head Office Management and the Funding Management Department move into a new office near Potsdamer Platz in Berlin. (page 66)



JULY

NOVEMBER

DZHK ISAR-REACT 5 trial delivers surprising results: the anticoagulant drug ticagrelor is superior in the treatment of heart attacks compared with prasugrel. (page 15)



SEPTEMBER

AUGUST

The third joint presentation of all DZGs takes place in San Francisco at GAIN (German Academic International Network), which is the largest networking event outside Europe for careers in science in Germany. (page 53)



OCTOBER

Basic research: Launch of Germany's largest research programme on genetic decoding at DZHK partner site Hamburg/Kiel/Lübeck for a better understanding of the causes of cardiovascular diseases. (page 19)



DECEMBER

No medical progress can be achieved without the support and participation of patients in clinical trials: a new video explains what participation in a clinical trial means. (page 57)



RESEARCH NEWS

Focus clinical research: the selected news are examples of the research approaches DZHK scientists are pursuing to progress in clinical studies.

Non-invasive view into the heart

The non-invasive measurement of blood flow to the heart using magnetic resonance imaging (MRI) is as safe and effective as cardiac catheterization. This was the result of an international study published in the New England Journal of Medicine and headed by researchers from DZHK partner site Rhine Main.

For patients with chest pain and stable coronary heart disease (CHD), therapy depends primarily on how constricted the arteries that support the heart are (coronary arteries). This is often determined using an invasive procedure called cardiac catheterization. If necessary, the pressure in the coronary arteries is also measured. The combination of these methods is currently the recognised standard for making therapy decisions. Cardiovascular magnetic resonance imaging (MRI) is an alternative for directly measuring the blood flow in the myocardium.

EXAMINATION WITHOUT RADIATION

In contrast to cardiac catheterization, MRI is non-invasive, works without ionising radiation, can be done in 40 minutes and delivers direct measurements of the blood flow to the heart. The team headed by Professor Eike Nagel, Director of the Institute for Experimental and Translational Cardio Vascular Imaging at Goethe University was able to demonstrate that MRI measurements are as safe to guide decision-making as the currently used invasive procedure. Within the international MR-INFORM study, they examined 918 patients with an indication for cardiac catheterization to see if decision-making by an MRI scan led to the same results as the current invasive method.



Same result, but gentler on the patient: The MRI examination records the blood flow in the heart muscle just as well as the catheter examination with CT.

The MRI is equivalent to the catheter examination with CT. “The results for the patients are just as good, but an examination by MRI has many advantages: the procedure takes about 40 minutes, patients merely receive a small cannula in their arm and are not subject to radiation”, resumes Prof. Nagel. The physician hopes that the less invasive method will now be used as a first choice, reducing the need for cardiac catheterizations.

In contrast to the United Kingdom, where an MRI examination of the heart is paid for by the National Health Insurance (NHS), reimbursement is often difficult in Germany and usually has to be negotiated individually. Nagel also hopes that the study will contribute to the recognition of gentle diagnostics and improve care.

Publication: Nagel, E. et al.: *Magnetic Resonance Perfusion or Fractional Flow Reserve in Coronary Disease*, *N Engl J Med* 2019;380:2418–28.

Heart attack diagnosis in one hour

Patients with a suspected heart attack can hope for a faster and more precise diagnosis: Thanks to the new "Compass MI" risk calculator, which is also available online, cardiologists can now estimate earlier and more accurately than before whether or not someone is having a heart attack.

The diagnostic aid, developed by an international team at the DZHK Hamburg partner site, is based on new tests which can detect even very low troponin levels. Troponin is a protein complex that only occurs in the heart muscle and enters the bloodstream when the muscle cells are damaged. With the help of the measured troponin values and the exact time between measurements, the treating physicians can now calculate the probability that the patient will have an acute heart attack.

The difference to the conventional test is that the deciding factor is no longer one fixed limit value for the troponin concentration in the blood, but how the troponin measurement changes over time. "We have broken up the concept of diagnosing acute heart attack as written in the medical guidelines," says Prof. Dr. Stefan Blankenberg, Medical Director of the University Heart and Vascular Center at the University Hospital Hamburg-Eppendorf.

In clinical practice, this means that if the ECG (electrocardiogram) does not provide clear signs of a heart attack when an acute heart attack is suspected, doctors can still confirm the diagnosis within about one hour and then initiate the necessary therapy. Patients can sometimes wait up to twelve hours before the doctors can reliably diagnose or exclude a heart attack.

The development of the conventional blood test, which decades ago changed the practice of heart attack diagnostics worldwide, goes back to the Heidelberg-based DZHK scientist Prof. Hugo Katus. He discovered troponin as a biomarker that indicates a heart attack.



With highly sensitive blood tests, doctors can arrive at a reliable diagnosis within an hour if an acute heart attack is suspected, even if the ECG does not provide clear signs.

GLOBAL STUDY WITH 22,000 PATIENTS

Together with international colleagues, the Hamburg scientists have published the new concept in the renowned medical journal "New England Journal of Medicine". It is based on the evaluation of data from more than 22,000 patients from 13 countries worldwide.

Publication: Neumann, J. et al.: *Application of High-Sensitivity Troponin in Suspected Myocardial Infarction*. N Engl J Med 2019; 380:2529-2540

➔ "MI-Compass" risk calculator at <https://compass-mi.com>

Risk gene influences the effect of aspirin

After inserting a stent, patients receive blood-thinning medication, including aspirin, to prevent their blood vessel from closing again. Some people do not seem to respond to aspirin. A gene variant appears to inhibit the effect of aspirin.

In acute coronary syndrome, coronary arteries are severely constricted or even completely blocked. They are reopened with the help of a catheter, and a stent is inserted. Patients receive medication to prevent the platelets from clumping together and re-closing the vessel or stent. Aspirin and so-called adenosine diphosphate (ADP) receptor antagonists, mostly clopidogrel, are routinely prescribed.

1,800 patients to determine whether the gene variant is present and how their blood platelets react to aspirin. The results were compared with register data to determine whether the patients had a new vascular blockage or heart attack after stent insertion.

A WELL-KNOWN EFFECT

GUCY1A3 is known to cardiologists because it carries the information for a protein that plays a central role in inhibiting platelet aggregation. What is new is that GUCY1A3 also influences the response to aspirin.

Neither aspirin nor clopidogrel are guaranteed to work in every patient. Clopidogrel also has a gene variant that can make it ineffective - but this variant was not present in the people investigated. It's statistically unlikely that someone would have both gene variants. Further investigations will now clarify whether the effects of the aspirin risk gene can be counteracted by prescribing a stronger ADP receptor antagonist instead of clopidogrel, for example ticagrelor or prasugrel.

Publication: Kessler, T. et al.: *Association of the coronary artery disease risk gene GUCY1A3 with ischaemic events after coronary intervention.* Cardiovasc Res. 2019 Feb 14

First author Thorsten Kessler received the Prevention Prize of the German Society for Internal Medicine for this contribution.

DZHK researchers at the Munich partner site have found that the risk gene GUCY1A3 reduces aspirin's anticoagulant effect. It makes further blood vessel narrowing or even death from a heart attack more likely. To this end, the researchers have examined blood samples from almost



The risk gene GUCY1A3 reduces the anti-clotting effect of aspirin.

Prasugrel proves superior in heart attacks

After a heart attack or unstable angina pectoris, antiplatelet treatment with prasugrel is better for patients than ticagrelor. This is the unexpected result of the ISAR-REACT 5 trial led by DZHK partner site Munich.

After one year, fewer heart attacks, strokes and deaths occurred in the group who received prasugrel, compared to those who received ticagrelor. "Also the risk for bleeding was not increased with prasugrel," says principal investigator Professor Stefanie Schüpke of the German Heart Center Munich, which is located at the Technical University Munich (TUM). "This is very good news for our patients." Based on previous studies on the pre-treatment of a certain form of heart attack, the scientists had expected that ticagrelor would outperform prasugrel.

Both drugs are among the platelet inhibitors prescribed by doctors for acute coronary syndrome (ACS). Acute coronary syndrome is a generic term for serious circulatory disorders of the heart muscle. These include heart attacks and unstable angina pectoris. For both, there is a pressing, constricting pain in the chest area, but there are no other criteria for a heart attack.

Platelet inhibitors are designed to prevent the blood platelets from clumping together and forming blood clots again in the damaged coronary vessels. So far, the treatment guidelines of the European Society of Cardiology recommend prasugrel and ticagrelor equally. "We didn't know which of the two drugs was better, because the direct comparison was missing in a sufficiently large ACS population for over a year," explains DZHK researcher Stefanie Schüpke. The results of the ISAR-REACT 5 study now close this gap. Twenty three centres in Germany and Italy participated in the study, a total of 4,018 patients with ACS were examined.



Platelet inhibitors such as prasugrel are designed to prevent blood platelets from clumping together and forming new blood clots in the damaged coronary arteries.

RELEVANCE OF THE STUDY FOR PRACTICE

The study solves the dilemma of which drug to prescribe to millions of patients who suffer from ACS annually in Germany and allows treatment to be personalised. It complements the practice of first confirming the diagnosis of ACS using cardiac catheters, thus minimises patients receiving drugs that they do not need. In addition, the data support the safety of a reduced prasugrel dose in patients with an increased risk of bleeding.

Publication: Schüpke, S. et al.: *Ticagrelor or Prasugrel in Patients with Acute Coronary Syndromes*. *N Engl J Med*. 2019 Sep 1

Who needs an implanted defibrillator?

Who benefits from an implantable defibrillator, and who does not? This question can be answered for the first time with the help of a digital biomarker, as demonstrated in a large European study with the participation of scientists from Munich and Göttingen.

Sudden cardiac death comes quickly and unexpectedly. It is usually triggered by malignant cardiac arrhythmias that occur suddenly. Hearts with low pumping capacity are more susceptible to this. Doctors, therefore, use an implantable cardioverter defibrillator (ICD) in these patients as a preventive measure. It detects life-threatening arrhythmias and then emits a current surge that brings the heart back into rhythm.

However, most patients with heart failure do not suffer from severe rhythm disorders, and the device is not required for them. Implanting the device also has considerable side effects – from infections or deliver a shock when it is not needed. However, it has not been possible to predict which patients will benefit from an ICD.

With a computer-based ECG method called Periodic Repolarization Dynamics (PRD), researchers can now calculate this. The ECG shows the effect of the stress nerve on the heart muscle, which causes the damaged heart to lose its rhythm. In previous studies, the researchers were able to show that increased PRD is associated with an increased tendency to malignant arrhythmias and sudden cardiac death.

INTERNATIONAL STUDY PROVES PREDICTIVE POWER

The EU-CERT-ICD study now supports the hypothesis that PRD is also suitable for filtering out who benefits from an implantable defibrillator. 44 centres in 15 countries participated in the large European project involving 1,371 patients. The trial demonstrated that an ICD reduced



Using a computer-based ECG method, researchers can calculate which patients will benefit from an implanted mini defibrillator.

mortality most in patients with increased PRD, while defibrillator implantation was of much less benefit to patients with lower PRD.

Many patients could thus be spared unnecessary surgery and the side effects associated with ICD therapy. An additional advantage is that it is a rather simple, ECG-based procedure that is non-invasive and therefore gentle on patients. The researchers, therefore, expect that it will soon become part of clinical routine.

Publication: Bauer, A. et al.: *Prediction of mortality benefit based on periodic repolarisation dynamics in patients undergoing prophylactic implantation of a defibrillator: a prospective, controlled, multicentre cohort study.* The Lancet, September 01, 2019

PUBLICATIONS AND PRICES

Publications in renowned scientific journals, prizes, awards, and the successful acquisition of funding are proof of scientific performance. In 2019, the number of publications with DZHK affiliation, i.e., naming the DZHK, rose to 1,139. The number of publications with an impact factor > 10 rose to 135, continuing the positive trend of recent years. DZHK scientists also received numerous prizes and awards in 2019 and raised high levels of funding.

Check out our website for a complete list of publications:

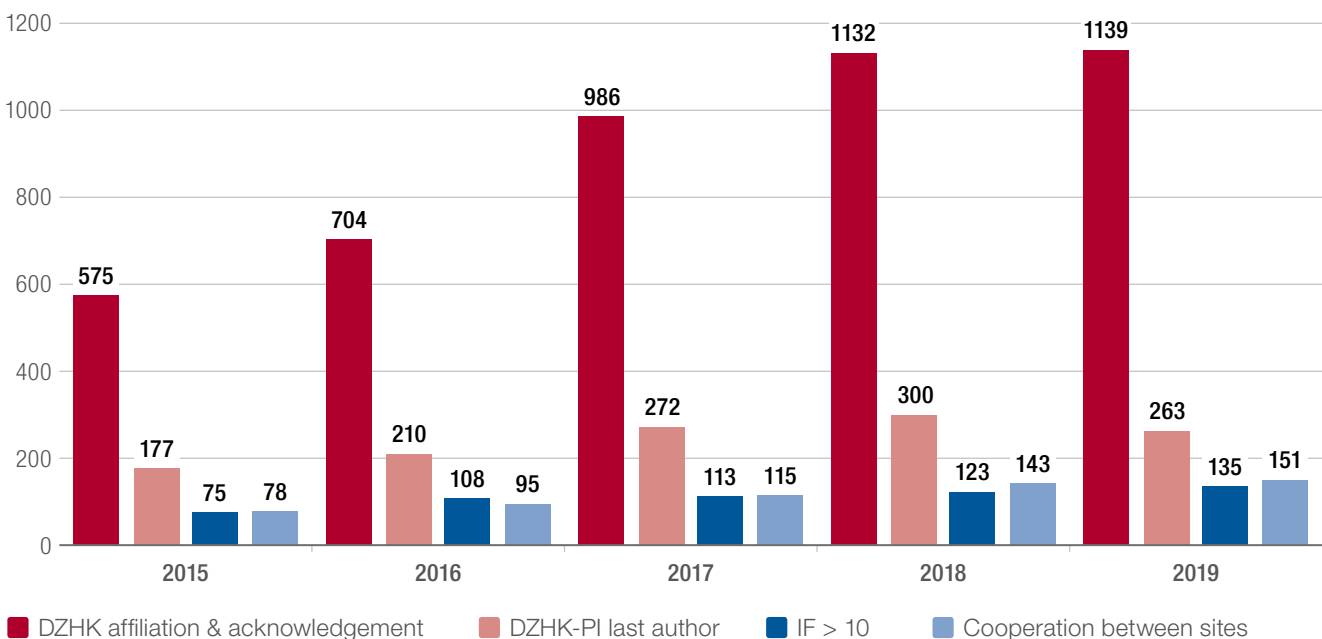
<https://dzhk.de/forschung/publikationen/publikationen-2019/>

PUBLICATIONS

	Amount 2019	2018
Total publications	1,139	1,132
First authorship of a DZHK PI	55	63
Last authorship of a DZHK PI	263	300
First authorship of a Young DZHK member	249	273
First authorship DZHK Scientist	97	106
Last authorship DZHK Scientist	239	275
Publications involving several DZHK sites	151	115

Publications published in:


Nature Publishing Group	30	35
Cell Press	8	8
NEJM, Lancet, JAMA	10	9
Circulation, Circ Res, EHJ, JCI, JACC	84	68
Science	3	3
Total (Impact Factor > 10)	135	123






PAPER OF THE MONTH 2019


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

 = DZHK sites involved


JANUARY

Weckbach, L. (University Hospital of LMU Munich) et al.: **Midkine drives cardiac inflammation by promoting neutrophil trafficking and NETosis in myocarditis.** Journal of Experimental Medicine.  Munich


FEBRUARY

Yin, C. (University Hospital of LMU Munich) et al.: **ApoE attenuates unresolvable inflammation by complex formation with activated C1q.** Nature Medicine.  Munich


MARCH

Fregin, B. (University Medicine Greifswald) et al.: **High-throughput single-cell rheology in complex samples by dynamic real-time deformability cytometry.** Nature Communications.  Greifswald


APRIL

Münzel, T. (University Medical Center of the Johannes Gutenberg University Mainz) et al.: **Cardiovascular disease burden from ambient air pollution in Europe reassessed using novel hazard ratio functions.** European Heart Journal.  Rhine Main


MAY

Söhnlein, O. (University Hospital of LMU Munich) et al.: **Externalized histone H4 orchestrates chronic inflammation by inducing lytic cell death.** Nature.  München, Hamburg/Kiel/Lübeck


JUNE

Heesch, S. van (Max Delbrück Center for Molecular Medicine) et al.: **The Translational Landscape of the Human Heart.** Cell.  Berlin, Göttingen


JULY

Nagel, E. (Goethe University Frankfurt) et al.: **Magnetic Resonance Perfusion or Fractional Flow Reserve in Coronary Disease.** The New England Journal of Medicine.  Rhine Main, Berlin


AUGUST

Neumann, J. T. (University Medical Center Hamburg-Eppendorf, UKE) et al.: **Application of High-Sensitivity Troponin in Suspected Myocardial Infarction.** The New England Journal of Medicine.  Hamburg/Kiel/Lübeck, Heidelberg/Mannheim, Rhine Main, Berlin, Munich


SEPTEMBER

Grund, A. (University Medical Centre Mannheim) et al.: **TIP30 counteracts cardiac hypertrophy and failure by inhibiting translational elongation.** EMBO Molecular Medicine.  Heidelberg/Mannheim


OCTOBER

Frank, D. (University Medical Center Schleswig-Holstein, UKSH) et al.: **Cardiac alpha-Actin (ACTC1) Gene Mutation Causes Atrial-Septal Defects Associated With Late-Onset Dilated Cardiomyopathy.** Circulation. Genomic and precision medicine.  Hamburg/Kiel/Lübeck, Göttingen

NOVEMBER

Schüpke, S. (German Heart Centre Munich) et al.: **Ticagrelor or Prasugrel in Patients with Acute Coronary Syndromes.** New England Journal of Medicine.  Göttingen

DECEMBER

Blankenberg, S. (University Medical Center Hamburg-Eppendorf, UKE) et al.: **Application of non-HDL cholesterol for population-based cardiovascular risk stratification: results from the Multinational Cardiovascular Risk Consortium.** The Lancet.  Hamburg/Kiel/Lübeck, Berlin



PRIZES, GRANTS, PERSONALIA

Editors' picks

Alexander Bartelt

(Munich)

Starting Grant of the European Research Council (ERC)
(€1.5 million)

Stefan Blankenberg and Tanja Zeller

(Hamburg/Kiel/Lübeck)

Research grant from the Kühne Foundation for genetic decoding (€12.5 million)

Reinier Boon

(Rhine Main)

Basic Science Outstanding Achievement Award of the European Society of Cardiology (ESC)

Reinier Boon and Oliver Müller

(Rhine Main, Hamburg/Kiel/Lübeck)

Research funding from the EU Research Framework Programme "Horizon 2020" (€1.4 and 1.1 million)

Stefanie Dimmeler

(Rhine Main)

Honorary Award 2019 – Lecture on Basis Science of the German Cardiac Society (DGK)

Stefanie Dimmeler and Stefan Engelhardt

(Munich, Rhine Main)

DFG funding for a collaborative research centre
(€11 million)

Norbert Hübner

(Berlin)

Research funding of the Chan Zuckerberg Initiative
(€4 million)

Mahir Karakas

(Hamburg/Kiel/Lübeck)

Research funding of the Adrenomed AG (€2.4 million)

Hugo A. Katus

(Heidelberg/Mannheim)

Gold Medal of the European Society of Cardiology (ESC)

Ulrich Kintscher

(Berlin)

Franz-Gross-Wissenschaftspreis of the Deutsche Hochdruckliga e.V.

Marc Lemoine and Maksymilian Prondzynski

(Hamburg/Kiel/Lübeck)

Wilhelm P. Winterstein-Preis 2019 of the German Heart Foundation e.V.



At the 125th Congress of the German Society for Internal Medicine, Dr. Carolin Lerchenmüller receives the Prevention Prize of around €10,000.

Carolin Lerchenmüller

(Heidelberg/Mannheim)

Prevention Prize of the German Society for Internal Medicine (DGIM) and the German Foundation for Internal Medicine (DSIM)

Steffen Massberg

(Munich)

Advanced Grant of the European Research Council (ERC)

Victoria Mauz

(Heidelberg/Mannheim)

Otto-Hess-Promotionspreis 2019 of the German Cardiac Society (DGK)

Benjamin Meder

(Heidelberg/Mannheim)

Excellence scholarship of the Else Kröner-Fresenius Foundation (€260.000)

Belal A. Mohamed

(Göttingen)

Franz Maximilian Groedel Research Award 2019 of the German Cardiac Society (DGK)

Johannes Neumann

(Hamburg/Kiel/Lübeck)

August Wilhelm und Lieselotte Becht Research Award of the Deutsche Stiftung für Herzforschung



Promotion of young researchers in patient-oriented cardiovascular research: Johannes Neumann (2nd from right) receives the August Wilhelm and Lieselotte Becht Research Prize of the DGK, with a value of €15,000.

Michael Potente

(Rhine Main)

Arthur-Weber Prize 2019 of the German Cardiac Society (DGK)

Vera Regitz-Zagrosek

(Berlin)

First Class Federal Cross of Merit

Sonja Schrepfer

(Hamburg/Kiel/Lübeck)

Galenus-von-Pergamon Prize

Heribert Schunkert

(Munich)

Franz-Loogen Prize 2019

Oliver Söhnlein

(Munich)

Albert-Fraenkel Prize 2019 of the German Cardiac Society (DGK)

Teresa Trenkwalder

(Munich)

Hans-Blömer-Young Investigator Award for Clinical Cardiovascular Research of the German Cardiac Society (DGK)

Christian Weber

(Munich)

Member of the Leopoldina - National Academy of Sciences

Nicola Wilck

(Berlin)

Starting Grant of the European Research Council (ERC) (€1.5 million)



Research at our Partner Sites



The DZHK performs research in 32 partner institutions spread over seven locations nationwide. The partner institutions include university hospitals and universities as well as centres of the Helmholtz Association, Leibniz and Max Planck Institutes, and a departmental research institute. Each partner site has its own research focus.

More than 1,800 scientists worked in cardiovascular research in approximately 60 scientific on-site projects that have been approved in 2019 and 2020. With €20.8 million, the DZHK invested around 48 percent of its funds in partner site projects. The partner sites mostly decide which projects are financed with DZHK funds. According to the principle of "strengthening strengths", they can thus sharpen their scientific profile in the long term. As a rule, these are projects in which basic research is conducted and which are suitable for further development in the sense of applied and patient-oriented research.

Besides, large-scale equipment is purchased from partner site funds, DZHK professorships, and clinical studies are financed to a small extent. Urgently needed investments to support individual site projects included fluorescence, confocal and live-cell imaging microscopes for molecular biological investigations, mobile and stationary echo devices for clinical and preclinical investigations, PCR devices and sequencers for genetic testing, and components to improve the performance of bioinformatics infrastructures for processing large volumes of data, such as those required for the analysis of OMICs data.

The partner sites developed projects in the year under review and prepared the selection for funding approval for 2021–2025. Also, the second half of 2019 was marked by intensive preparations for the internal evaluation of the DZHK and the individual sites, which was due in January 2020. (more on page 9).



MAIN FOCUS OF THE RESEARCH SITES

Research focus Berlin: The focus at this site lies on pathomechanisms that lead to progressive heart failure and maladaptation of the vascular system. The aim is to accelerate translation through innovative diagnostic technologies and treatment strategies. A further focus is on digital health, big data, and computer-aided modelling in the treatment of diseases. Berlin is also dedicated to gender differences in heart disease.

Research focus Göttingen: The Göttingen site focuses on how heart failure develops from asymptomatic to symptomatic form. Further key areas are the regeneration of the heart with artificial heart tissue, the visualisation of cardiac arrhythmias with physical methods, cardio-oncology, and the merging of cardiovascular research and neuroscience in the "Heart and Brain Center Göttingen (HBCG)".

Research focus Greifswald: Greifswald focuses on developing novel non-pharmacological interventions for the prevention and treatment of DCM and other forms

of heart failure. Another focus is investigating molecular mechanisms of heart failure progression and cardiac cachexia, emphasizing the role of immune and inflammatory processes.

Research focus Hamburg/Kiel/Lübeck: The site aims to improve the diagnosis and therapy of ischemically and genetically caused heart muscle diseases to prevent the progression of heart failure. The researchers are looking for target genes and biomarkers of cardiovascular diseases and want to decode the molecular processes that lead to cardiac remodeling processes. One focus is the regeneration of the heart muscle using heart tissue cultivated in the laboratory.

Research focus Heidelberg/Mannheim: The site engages in research into cardiac arrhythmias and cardiomyopathies. The projects range from the investigation of genetic and epigenetic causes and mechanisms to the deciphering of molecular signaling pathways and interactions. Also, scientists work on translational research approaches for innovative molecular diagnostics and therapy of cardiomyopathies, arrhythmias, and heart failure. The goal is to understand the complexity of each patient's disease and develop diagnostics and therapies towards individualised precision cardiology.

Research focus Munich: The main focus lies in investigating molecular mechanisms of cardiovascular diseases and the development of new therapies based on these mechanisms. The entire medical translation chain, from basic research to experimental studies, from the examination of clinical samples to the conduct of clinical trials, is covered.

Research focus Rhine Main: This partner site focuses on research into heart failure, coronary heart disease, and acute coronary syndrome. Scientists develop imaging methods for the diagnosis and therapy to monitor the heart and the vascular system. The use of artificial intelligence makes it possible to better understand cardiovascular diseases based on complex molecular signatures and find new approaches for diagnosis and therapy.



DZHK professors and junior research group leaders at the DZHK Retreat in Potsdam in September 2019.

DZHK PROFESSORSHIPS

The DZHK Professorships are meant to strengthen the strategic orientation of the DZHK partner sites. In 2019, the DZHK announced and filled an endowed professorship at the Hamburg/Kiel/Lübeck partner site for the first time. The DZHK is financing a total of 18 professors from the partner site funds. Together with the four DZHK

Junior Group Leaders, they are mainly responsible for the scientific concept of the DZHK Retreat, the annual scientific conference of the DZHK. Furthermore, together with the leaders of the Junior Research Groups, they have joint voting rights in the Research Coordinating Committee (RCC), the strategic decision-making body of the DZHK.

"Genetic research in Germany needs to catch up considerably: The DZHK endowed professorship, which the non-profit organisation 'Kinderherzen wollen leben' sponsors with its donation, is, therefore, a valuable investment. My goal is to gain a much more precise understanding of heart development mechanisms, including heart malformation, not only to help children with congenital heart defects. Research into genetic causes can open a door for therapies for acquired heart diseases."

Marc-Phillip Hitz



Marc-Phillip Hitz received the call for a DZHK W2 endowed professorship for cardiogenetics of congenital structural heart diseases at the Medical Faculty of the Christian-Albrechts-University of Kiel (CAU). For the first time, a DZHK Professorship is substantially financed by a donation from the non-profit association "Kinderherzen wollen leben" e.V. donated to the DZHK e.V. Partner site funds from the DZHK site Hamburg/Kiel/Lübeck will supplement the endowed professorship. Congenital heart defects

are among the most common birth defects in children, and many of those affected need medical care throughout their lives. Marc-Phillip Hitz, a specialist in human genetics and paediatrics, became the first professor of the genetics of congenital heart defects in Germany in 2019. The main focus of his work is on researching the genetic causes of congenital heart defects in the developing heart. To understand the causes, the paediatric cardiologist in Kiel emphasises close interdisciplinary cooperation.

Goals achieved in 2019?



- ✓ Endowed professorship filled
- ✓ Individual partner site projects supplemented by urgently needed investments
- ✓ Preparation of the assessment in January 2020: Decision on new partner site projects taken

Targets 2020



- ↗ Administrative application and approval of the approx. 100 partner site projects for the years 2021–2025
- ↗ Share of women DZHK PI's increased in the years 2021–2025



Preclinical Research



By preclinical research, we refer to research that precedes patient-oriented research. Open and independent preclinical research leads to a better understanding of the biology underlying diseases or functional disorders. This knowledge can, in turn, function as a basis for disease-oriented research.

In 2019, the DZHK provided €5.7 million of its flexible and competitive funding for preclinical research. The preclinical area includes Translational Research Projects (TRP) and collaborative projects using shared expertise and collaborations with external partners.

TRANSLATIONAL RESEARCH PROJECTS

Basic research results are of high value but are usually not suitable for direct transfer into clinical application. With the funding of Translational Research Projects, the DZHK supports researchers who want to further develop their ideas

and results from basic research for innovative diagnostic and therapeutic methods. In the long run, patients will benefit from the outcome. Prerequisite for funding is a clear route to a therapeutic or diagnostic application. The members of the Translational Research Group (TRG) advise the scientists during the application phase and also support them in the implementation of the projects.

The funding for Translational Research Projects was first announced in 2014. Up to 2018, the DZHK funded 12 projects with approximately €10.1 million. In 2019, three further projects to a total of €1.8 million received a funding recommendation. In the coming year, the TRG will increasingly focus on the question of how we at the DZHK can identify even more research topics that have the potential for a TRP.



Translational Research Projects with funding recommendation in 2019

Hit-to-lead development of CaMKII-HDAC4 inhibitory compounds to treat heart failure (project 1: Identification of potent hits)

Duration: 2019–2020

Budget: €553,635

Participating scientists:

Johannes Backs (*Heidelberg/Mannheim*), Bert Klebl (*Lead Discovery Center Dortmund*), Wolfram-H. Zimmermann (*Göttingen*), Matthias Dewenter, Marco Hagenmüller, Hugo A. Katus (*Heidelberg/Mannheim*)

The two proteins calcium/calmodulin-dependent protein kinase II (CaMKII) and histone deacetylase 4 (HDAC4) are formed in the heart. These play essential roles in maintaining the heart's function, but also in the development of diseases. When the heart becomes diseased, these two proteins bind together. When the binding was inhibited in mice by genetic intervention, the team observed a protective effect against heart failure.

In a first high-throughput screening method, which allows the testing of large amounts of chemical compounds, the scientists found inhibitors that prevent the two proteins from binding together. Furthermore, they were also able to demonstrate this inhibition in cells and observe functional effects. These results suggest that the inhibition of the interaction of CaMKII and HDAC4 is a promising therapeutic target.

Together with experts from the Lead Discovery Center in Dortmund, the project group would like to identify more targets for these inhibitors in this project with the help of a second high-throughput search procedure. Promising candidates from this and earlier investigations will then be characterised using a cascade of different functional analyses to determine whether they are suitable for further drug development.

Detection of plaque vulnerability with a novel hybrid intravascular NIRF-IVUS imaging system

Duration: 2020–2023

The project will start in spring 2020.

Budget: €756,119

Participating scientists:

Michael Joner, Vasilis Ntziachristos (*both Munich*)

Atherosclerosis is a chronic inflammation of the vessel wall. Unstable atherosclerotic plaques can rupture and pose a risk of cardiovascular events such as heart attack or stroke. Despite the progress in cardiovascular imaging techniques, there is no imaging method to distinguish stable from unstable plaques.

This project aims to develop a hybrid system for use in medical routine, in which vascular ultrasound and near-infrared fluorescence are coupled. With the hybrid system, molecular parameters of the inflammation can be recorded, and at the same time, the degree of permeability of unstable plaques can be determined. This technology should make it possible to identify patients at risk for further cardiovascular events and intervene early with suitable therapy. The tasks of this translational project include the reduction of the catheter size for hybrid imaging, a preclinical proof-of-concept, investigations on the safety of the technology, and finally, the development of a prototype for clinical studies.

Local miR-29b inhibition using drug eluting balloons to block abdominal aortic aneurysm progression

Duration: 2019–2021

Budget: €486,080

Participating scientists:

Lars Maegdefessel (*Munich*), Reinier Boon, Stefanie Dimmeler (*Rhine Main*)






An abdominal aortic aneurysm, which is a vascular “ballooning” of the aorta in the abdomen, is caused by a weak vascular wall. If an aneurysm ruptures, it's often fatal. The standard therapy is an open or catheter-based surgical procedure to insert vascular supports, so-called stents. It requires rapid intervention and is associated with intensive follow-up and a high long-term complication rate. Among other factors, a micro-ribonucleic acid, miR-29b, is involved in the damage to the vessel wall. Micro-ribonucleic acids are attractive targets for therapeutic approaches. In previous investigations in animal and cell culture models, the team was able to show that inhibitors directed against miR-29b can prevent the development of vascular sacculation.

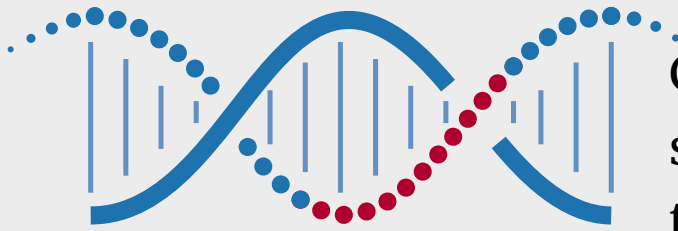
In this project, the feasibility and safety of genetically modified mini-pigs, which serve as animal models for atherosclerosis and advanced vascular diseases, will be investigated. The inhibitor will be delivered directly to the damaged vascular wall via a drug-eluting balloon catheter. This will provide evidence for a possible therapy to limit the progression of aneurysms and reduce the risk of their acute rupture.



Translational Research Projects since 2015

 These projects were completed in 2019 (more on pages 29–33)

Project title	Project lead	Budget	Duration
 Development of miR-92a inhibitors for the treatment of cardiovascular disease	Dimmeler (Rhine Main)	€2,458,430	2015–2019
Off-pump transapical mitral valved stent implantation	Lutter (Hamburg/Kiel/Lübeck)	€337,290	2016–2017
 Low-energy termination of ventricular fibrillation in a porcine heart failure model	Luther (Göttingen)	€1,023,000	2016–2019
IPSC-EHT transplantation for cardiac repair – towards first-in-patient	Eschenhagen, Hansen (Hamburg/Kiel/Lübeck)	€1,746,314	2016–2022
 Gene therapy for neonatal sarcomeric cardiomyopathies: towards first-in-patient	Carrier (Hamburg/Kiel/Lübeck)	€451,794	2016–2019
 Generation and functional characterization of macrophage cell lines from yolk sac precursors	Schulz (Munich)	€248,932	2017–2019
Late pre-clinical development of CD40-TRAF 6 inhibitors	Weber, Lutgens, Atzler (Munich)	€396,944	2017–2019
In-vivo characterization of the chemokine-receptor CXCR4 for the detection of inflammation in atherosclerotic plaques by PET/MR	Schwaiger (Munich)	€28,140	2017
 Novel inotropic/lusitropic biologics against decompensated chronic heart failure	Most, Katus (Heidelberg/Mannheim)	€472,896	2018–2019
GMP-production of engineered human myocardium for heart failure repair	Zimmermann (Göttingen)	€2,657,936	2018–2020
CAR inhibitors to treat myocardial infarction	Gotthardt (Berlin)	€232,681	2019–2021
Local miR-29b inhibition using drug eluting balloons to block abdominal aortic aneurysm progression	Maegdefessel (Munich)	€486,080	2019–2021
Real-time MRI-guided targeted endomyocardial biopsy of radiofrequency ablation lesions in a porcine model	Unterberg-Buchwald (Göttingen)	€853,003	2019–2023
Hit-to-lead development of CaMKII-HDAC4 inhibitory compounds to treat heart failure (project I: Identification of potent hits)	Backs (Heidelberg/Mannheim)	€507,041	2019–2020
Detection of plaque vulnerability with a novel hybrid intravascular NIRF-IVUS imaging system	Joner (Munich)	€756,119	2020–2023
rAAV.MRTF-A-based vascular gene therapy in chronic hindlimb ischemia	Kupatt (Munich)	€1,243,600	undergoing compliance check with funding legislation




Gene therapy for neonatal sarcomeric cardiomyopathies: towards first-in-patient

In newborns, mutations in the MYBPC3 gene encode the cardiac myosin-binding protein C (cMyBP-C), which causes cardiomyopathy. Within the first year of life, this heart muscle disease may turn to systolic heart failure or even lead to death. A heart transplant is the only treatment. In homozygous Mybpc3 knock-in mice, an animal model that mimics human neonatal cardiomyopathy, Mybpc3 gene therapy can prevent cardiomyopathy. As a first important step towards clinical application, the scientists wanted to transfer their results to a large animal model – the pig.

The mutation of the MYBPC3 gene using somatic cell nuclear transfer and embryo transfer impaired the viability of nuclear transfer fetuses and also of newborn piglets massive. Instead, the scientists introduced the mutation organ-specifically using the CRISPR/Cas-9 technique in

transgenic pigs. In parallel, MYBPC3-gene therapy has shown encouraging results with heart muscle cells derived from pluripotent stem cells of humans with cardiomyopathy.

In both Europe and the USA, a patent for "Gene-therapy vectors for treating cardiomyopathy" has been issued. The DiNAQOR company was founded, which develops MYBPC3 gene therapy for patients with severe forms of cardiomyopathy. Professor Carrier and her colleagues are involved in preclinical studies testing MYBPC3 constructs in human induced pluripotent stem cell-derived cardiomyocytes and engineered heart tissues.

 *Gene therapy for neonatal sarcomeric cardiomyopathies: towards first-in-patient*



Duration

2016 to 2019



Budget

452,000



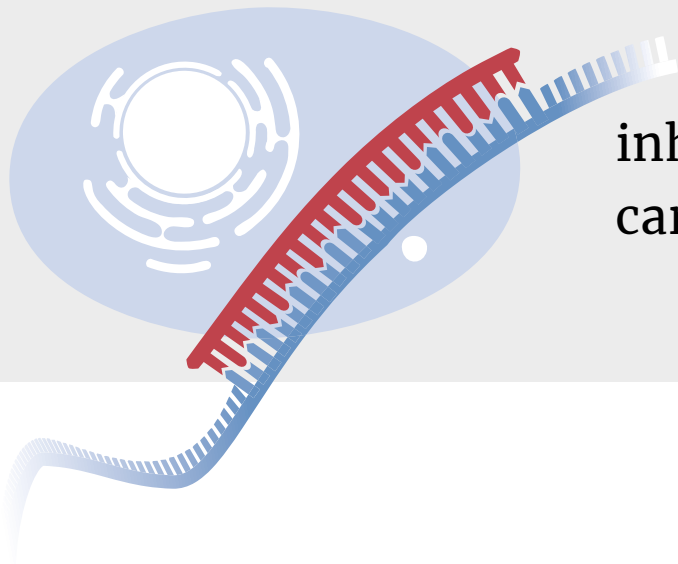
Participating scientists

- Lucie Carrier
Hamburg/Kiel/Lübeck



Partner in the DZHK

- Guilia Mearini
Hamburg/Kiel/Lübeck
- Angelika Schnieke
- Christian Kupatt
- Rabea Hinkel
- Eckhard Wolf
Munich




Development of miR-92a inhibitors for the treatment of cardiovascular disease

MicroRNAs (miRNAs) are short RNA strands that do not contain information for the construction of proteins (non-coding) but have a control function for protein synthesis. MicroRNA-92a (miR-92a) is an ischemia-regulated miRNA whose expression is upregulated under pathophysiological conditions. It represents an interesting target structure for developing new therapeutics to treat heart attack and atherosclerosis patients or wound healing disorders.

Preliminary work has shown that heart function after a heart attack improves when miR-92a is inhibited. The project aimed to test the inhibitor's safety and to optimise it for use in humans. To this end, scientists have modified the inhibitors' composition and carried out pharmacological and toxicological studies.

These preclinical studies, necessary for clinical application, were completed in 2019. It was shown that the inhibitor miRNA-92a, also called "anitmiR-92a", has no toxic effects in various species and in in vitro studies at therapeutically relevant doses.

As a result, the researchers were able to conduct two phase I studies that demonstrated the safety of antimiR-92a in healthy people. Now the next steps in clinical testing can be taken. The scientists are currently planning phase II trials in which the inhibitor will be used and tested in heart attack patients.

 *Development of miR-92a inhibitors for the treatment of cardiovascular disease*



Duration

2015 to 2019



Budget

2.5 Million



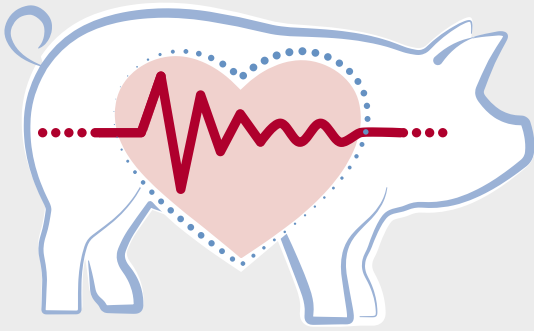
Participating scientists

- Stefanie Dimmeler
 - Andreas Zeiher
 - Angelika Bonauer
 - Ariane Fischer
- Rhine Main



Partner in the DZHK


- Christian Kupatt
 - Rabea Hinkel
- Munich



Low-energy termination of ventricular fibrillation in a porcine heart failure model

Malignant ventricular tachyarrhythmias are life-threatening cardiac arrhythmias, which currently only high-energy electric shocks can end. Alternatives are urgently needed because this treatment is painful, causes side effects such as tissue damage, and worsens the long-term outcome. In previous studies, the researchers have shown that Low-Energy Anti-Fibrillation Pacing (LEAP) needs 80 to 90 percent less energy than conventional defibrillation to stop these arrhythmias. An essential step on the way to a first-in-human study is the proof of concept in a clinically relevant large animal model. The researchers succeeded in doing this with a pig model for heart failure where the low-energy defibrillation could stop ventricular fibrillation.

A prerequisite for the development and translation of low-energy defibrillation is a fundamental understanding of the dynamic, spatio-temporal processes that are at the root of cardiac arrhythmias. A new imaging technique developed within the framework of this project made this possible. This technique allows for the first time 4D imaging of intramural, electro-mechanical rotors and thus opens up a previously unseen view of arrhythmia mechanisms and the development of new therapies. Currently, Luther and his colleagues develop low-energy defibrillation for clinical application in humans, where the next step is the proof of integration into existing technology platforms.

 *Low-energy termination of ventricular fibrillation in a porcine heart failure model*



Duration

2016 to 2019



Budget

1.0 Million



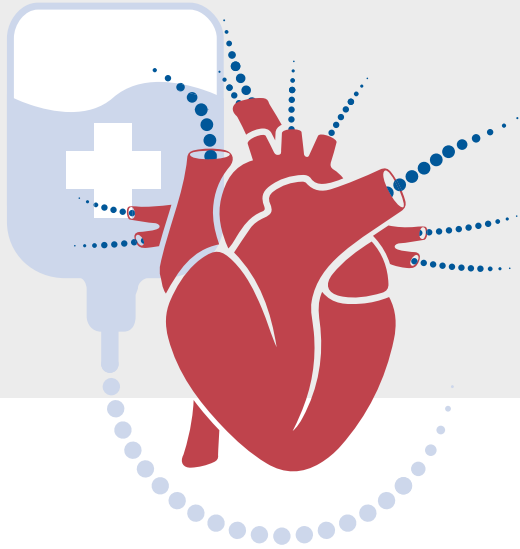
Participating scientists

- Stephan Luther
Göttingen



Partner in the DZHK

- Christian Kupatt
Munich




Novel inotropic/lusitropic biologics against decompensated chronic heart failure

Cardiac decompensation is a life-threatening complication of chronic heart failure. In most cases, it requires intensive medical care. Many patients die from it, and the drugs currently used to support cardiac performance have serious adverse effects. Better therapies that strengthen the heart muscle and prolong life are therefore urgently needed.

During research into the molecular functioning of the human heart muscle, scientists discovered the protein S100A1. It regulates calcium metabolism and calcium-dependent processes in heart muscle cells and increases the pumping power of the heart. Further investigations into the structure-function relationship of the heart protein S100A1 made it possible to develop an intravenous form of therapy:

a short synthetic peptide (S100A1ct) that can penetrate cells and increase the heart's pumping power. In numerous clinically relevant animal models, the researchers were able to show that the peptide exerts its cardiac-enhancing effect safely and without complications. The peptide also protects against arrhythmia, making it superior to current drugs such as catecholamines.

Building on this, the researchers have developed a bio-industrial and clinically relevant proof of concept for the peptide drug, an essential step for its clinical translation into a first-in-human clinical trial. These studies were successful and qualified the peptide drug for subsequent preclinical tests funded by the BMBF. They also established a strategic development partnership with a global biopharmaceutical company to optimise the peptide drug for clinical trials.

 *Novel inotropic/lusitropic biologics against decompensated chronic heart failure*



Duration

2018 to 2019



Budget

473,000



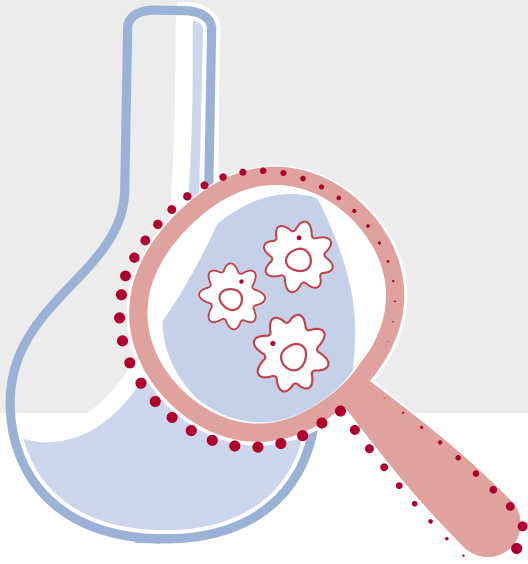
Participating scientists

- Hugo Katus
 - Patrick Most
- Heidelberg/Mannheim



Partner in the DZHK

- none



Generation and functional characterisation of macrophage cell lines from yolk sac precursors

Macrophages play a central role in defense reactions of the innate immune system and cardiovascular, inflammatory processes. Existing macrophage cell lines originate predominantly from peripheral mononuclear blood cells or leukaemia cells. However, in cardiovascular and other tissues, macrophages are derived from embryonic progenitor cells from the yolk sac. In this project, macrophage cell lines were generated from bone marrow and embryonic progenitor cells of mice to enable further cell biological and molecular analyses of tissue macrophages.

The researchers showed that macrophages of different origins have significantly different immunobiological functions. In particular, they could differentiate pro-inflammatory and anti-inflammatory properties. The results open up new starting points for macrophage-directed therapeutic strategies. The single findings are currently tested in cardiovascular tissue in vivo in a mouse model. Next, the researchers want to use immune cell lines to characterise new aspects of cell biological processes, such as the metabolism of macrophages and the effects of CHIP (clonal haematopoiesis of indeterminate potential) mutations. They are also working on strategies to achieve the survival of human macrophages under culture conditions.



Generation and functional characterization of macrophage cell lines from yolk sac precursors



Duration

2017 to 2019



Budget

249,000



Participating scientists

- Christian Schulz
Munich



Partner in the DZHK

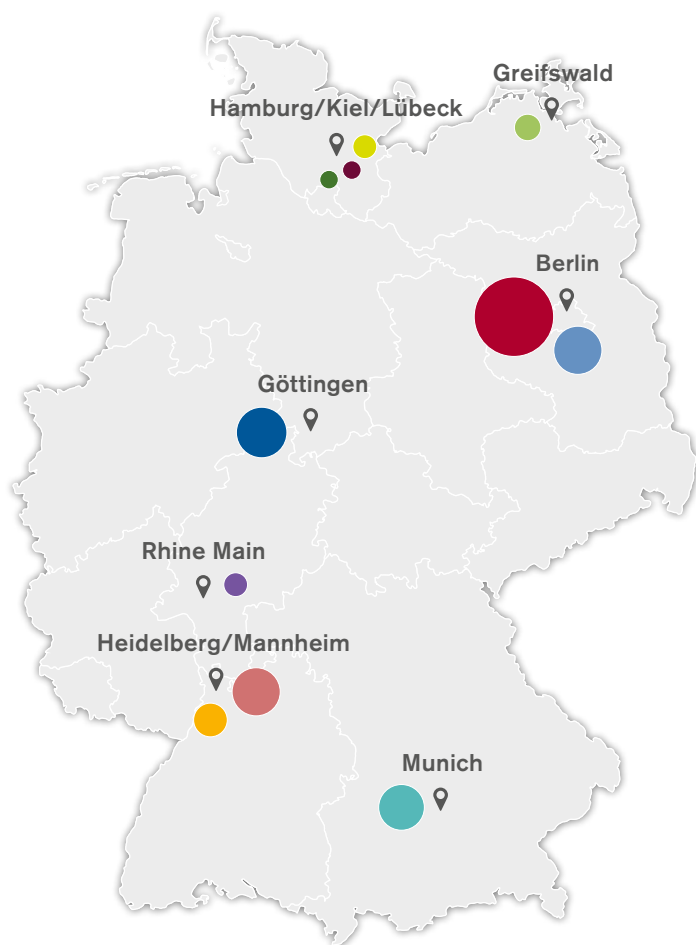
- none

SHARED EXPERTISE

Not all methods or expertise are available at all research institutions. The Shared Expertise programme promotes smaller collaborations between two locations, with one of the partners offering so-called Shared Expertise. The Shared Expertise offer makes the latest methods, infrastructure, or specialist knowledge available to scientists at other DZHK partner sites. The expertise offered should be more than just a marketplace of available infrastructures. Projects are planned together; all participating scientists contribute ideas, knowledge, and time. The individual sites independently organise an internal selection process for the projects.

In 2019, we funded 37 collaborative projects using Shared Expertise with €2.1 million. Forty-three percent of the applications involved Young DZHK members. As in previous years, there was strong demand for key technologies. Shared Expertise was also in demand in 43 percent of the projects and is one of the most frequently used services (see the following overview).

Methods and infrastructure can also be used by national and international scientists who are not registered with the DZHK. However, they cannot apply for the costs from the DZHK.



The most frequently used shared expertise at the DZHK (since 2012)

Shared Expertise	Description (Use since 2012 Requested use in 2019)
SE006	Genomics/Proteomics (33 2)
SE171	Stem cell unit (21 1)
SE028	AAV vector platform (20 1)
SE001	Generation of transgenic rats (19 2)
SE041	OMICS platform (14 1)
SE031	Next-generation sequencing platform (12 2)
SE099	Proteome and metabolome profiling (10 2)
SE056	Vascular proteomics (9 -)
SE161	AAV vector design and production (9 4)
SE024	EHT screening platform (7 1)
SE063	MicroRNA array platform (7 -)

EXTERNAL PARTNERS

Not all methods or infrastructures requested are available at the member institutions of the DZHK. A tool called "Cooperation with external partners" supports flexible cooperation with national partners outside the DZHK. In 2019, the DZHK funded five cooperation projects with external partners to the amount of €270,000.

COOPERATION WITH EXTERNAL PARTNERS

Institution	DZHK Funding
University Hospital Düsseldorf, Institute for Transplantation Diagnostics and Cell Therapeutics	€39,880
The Leibniz Institute on Aging – Fritz Lipmann Institute, Jena	€37,600
University Hospital Düsseldorf, Clinic for Vascular and Endovascular Surgery	€21,600
Essen University Hospital, Clinic for cardiology and angiology	€23,920
University Clinic Essen, Institute of Experimental Immunology & Imaging	€15,443



IDEAS COMPETITION

PROJECTS REACHED A CRITICAL MILESTONE IN 2019

To support brave and creative ideas and exploit the potential outside established funding lines, all DZHK researchers were able to participate in an ideas competition in the summer of 2017. It was based on the motto "think outside the box". Three selected projects from a total of 19 submitted ideas received "first milestone funding" with start-up financing of €150,000 each. At the end of 2019, all of them successfully reached their first critical milestone and submitted follow-up applications for further funding of up to €1 million each over four years. The Research Coordinating Committee (RCC) will decide on further funding in spring 2020.

Goals achieved in 2019?



- ✓ Total funding for Translational Research Projects increased for current and future years
- ✓ Further Translational Research projects completed
- A decision was taken on continuing the projects from the ideas competition

Targets 2020



- ↗ Development of a concept to promote the results of the DZHK Translational Research Projects
- ↗ Decision on continuation of the projects resulting from the ideas competition
- ↗ New TRG members joined



Clinical Research

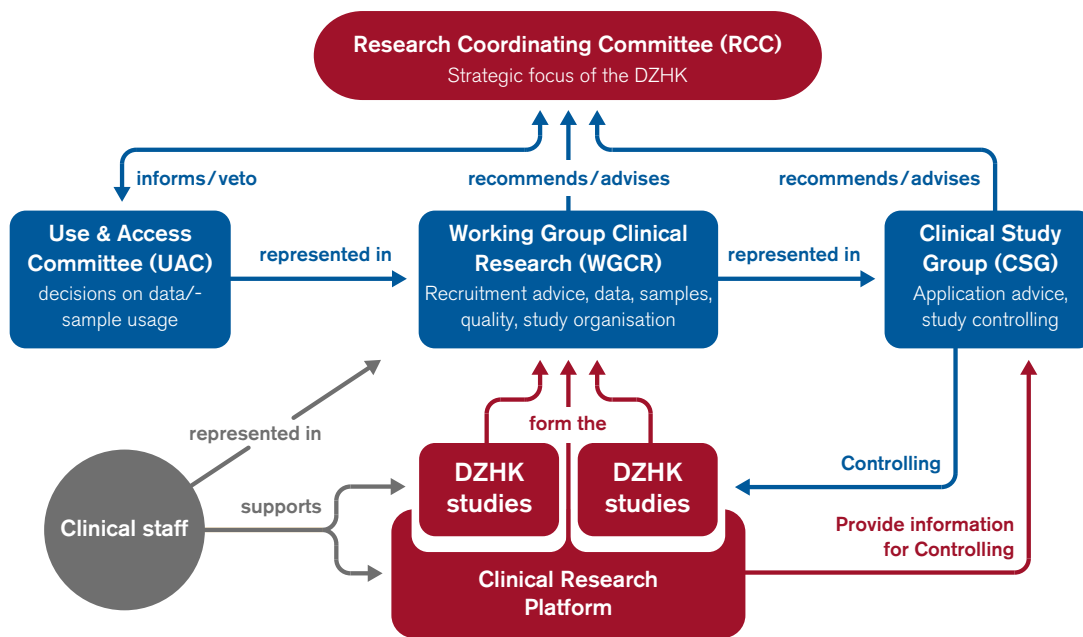


Clinical studies are a focal point in the research strategy of the DZHK. Following our research strategy, we support early clinical studies that test an innovative therapy or diagnostic procedure on humans for the first time. A further focus is on guideline-relevant studies. Their results are incorporated into treatment guidelines and thus directly benefit patients.

The DZHK has set itself the goal of closing gaps in the translation chain. Early clinical studies play a unique role here, which is why we have increased our funding for these studies. They prepare the ground for new innovative treatment approaches and increasingly build on our preclinical research. In a Translational Research Project by Wolfram-Hubertus Zimmermann from the Göttingen partner site, a production chain for artificial heart tissue was developed. This artificial heart tissue is now being used in the clinical study BioVAT for the first time in humans.

The strategic importance of clinical research at the DZHK is evidenced by the fact that different groups and committees are involved in brainstorming, decision-making, and governance (see figure page 37). This procedure ensures that only studies that conform to the strategic goals of the DZHK are funded and that the DZHK community supports the studies. The latter has a direct effect on the motivation for recruitment.

For quality assurance, we began subjecting our study centres to a second audit process at the end of 2019. Study centres that meet all criteria will receive the quality seal "DZHK Clinical Study Unit". Two sites have already been evaluated by the end of 2019. All further audit dates are planned for the first quarter of 2020.



Overview of the cooperation in the governance of clinical research at the DZHK

CLINICAL STUDIES

In 2019, the DZHK had 20 ongoing clinical studies, 15 of them financed by DZHK, two partially funded and three associated (non-material funding without DZHK funding), see table page 38. Financial support for the clinical studies of the DZHK amounted to approximately €6.9 million in the reporting year.

FURTHER STUDIES HAVE COMPLETED RECRUITMENT

From 2015 to the end of 2019, DZHK studies enrolled 7,645 patients (excluding associated and competence network studies), 2,160 of them in 2019 (2018: 1,942). Since four trials were completed in the reporting year, the number of recruits at some participating study centres decreased (see figure page 38).

The aim was to complete recruitment for two further DZHK trials in 2019. A total of four studies completed patient enrolment in the reporting period.

The **TOMAHAWK-DZHK4** study (guideline-relevant) compares the effects of immediate coronary angiography, i.e., a special X-ray examination to make blood vessels visible, to delayed intervention in survivors of cardiac arrest.

The study **CAVA-ADHF-DZHK10** (early clinical study) examines the hospital suitability of an ultrasound examination of the inferior vena cava in acute decompensated heart failure, which is the most common reason for hospital treatment in over 65-year-olds in Germany. The Hamburg/Kiel/Lübeck site controls both studies. Patient tracking, i.e., follow-up within the study, will continue until 2020.

The technology-based early clinical study **HFpEF-stress-DZHK17** (Göttingen) also completed recruitment and is now in the evaluation phase. The intention is to show whether the newly developed real-time CMR technology is suitable for early and reliable diagnosis of diastolic heart failure in which the left ventricle can't fill fully with blood.

The international study **SCREEN AF-DZHK15** (guideline-relevant), which is co-managed by the Göttingen site, aims to improve the early detection of atrial fibrillation with a rhythm patch that is applied to the chest.

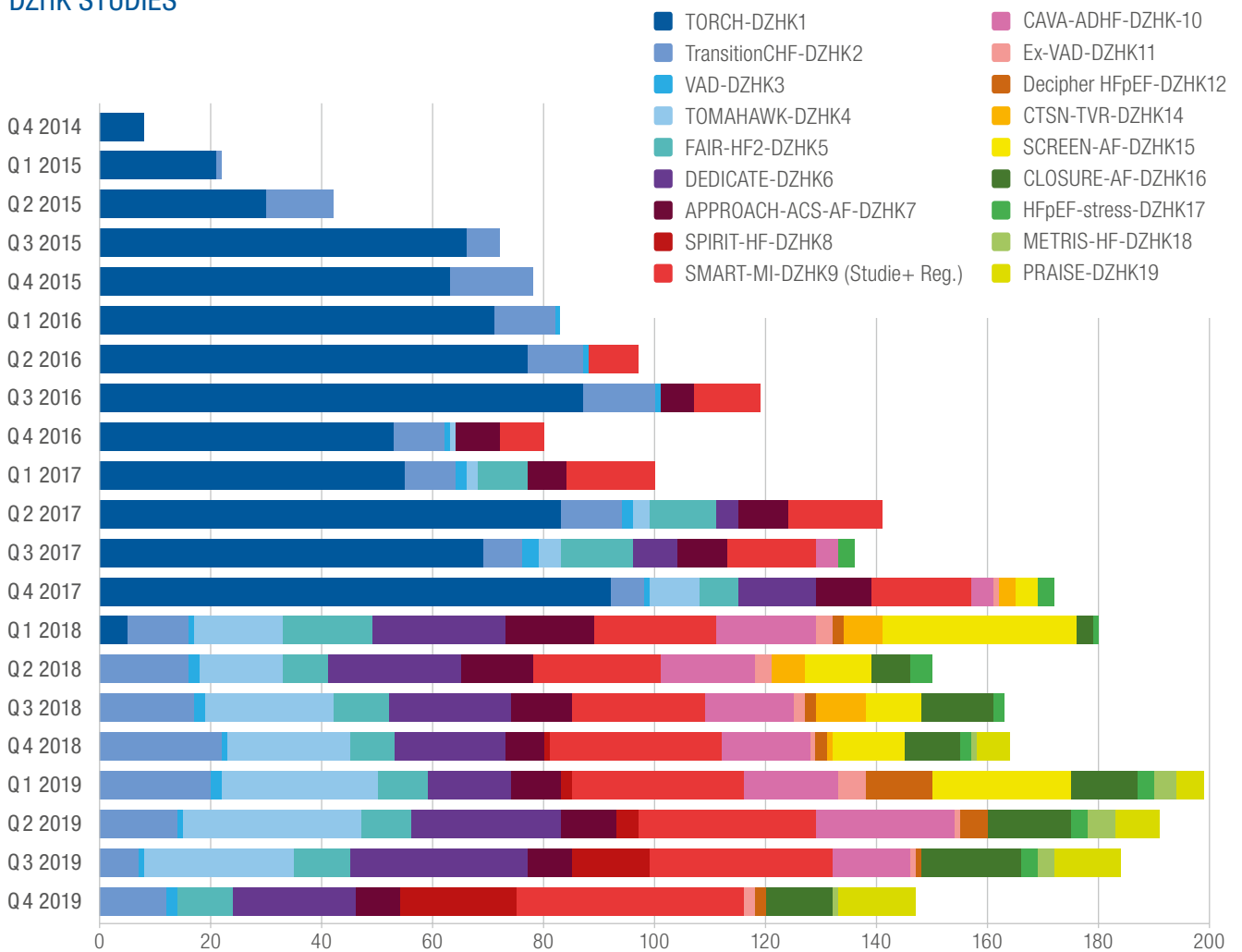
NEW STUDIES

In 2019 the preparation for the register **TORCH-Plus-DZHK21** started, as a continuation of TORCH DZHK1. The TORCH DZHK1 registry, developed 2014–2017, is a unique collection of patient data and biosamples from 2,300 people with non-ischemic heart muscle diseases. One of the aims of TORCH-Plus-DZHK21 is to collect sufficient data on less common myocardial disorders and enable longer follow-ups.

Preparations for the **BioVAT-HF-DZHK20** study were also completed mainly in the year under review, and the project began in mid-2019. The study investigates the conditions under which engineered heart tissue can be safely used in the treatment of patients with end-stage heart failure, a condition known as terminal heart failure.

Patient recruitment for both studies starts in 2020.

OVERVIEW: RECRUITED PATIENTS DZHK STUDIES



Monthly averages per quarter; as of 31.12.19

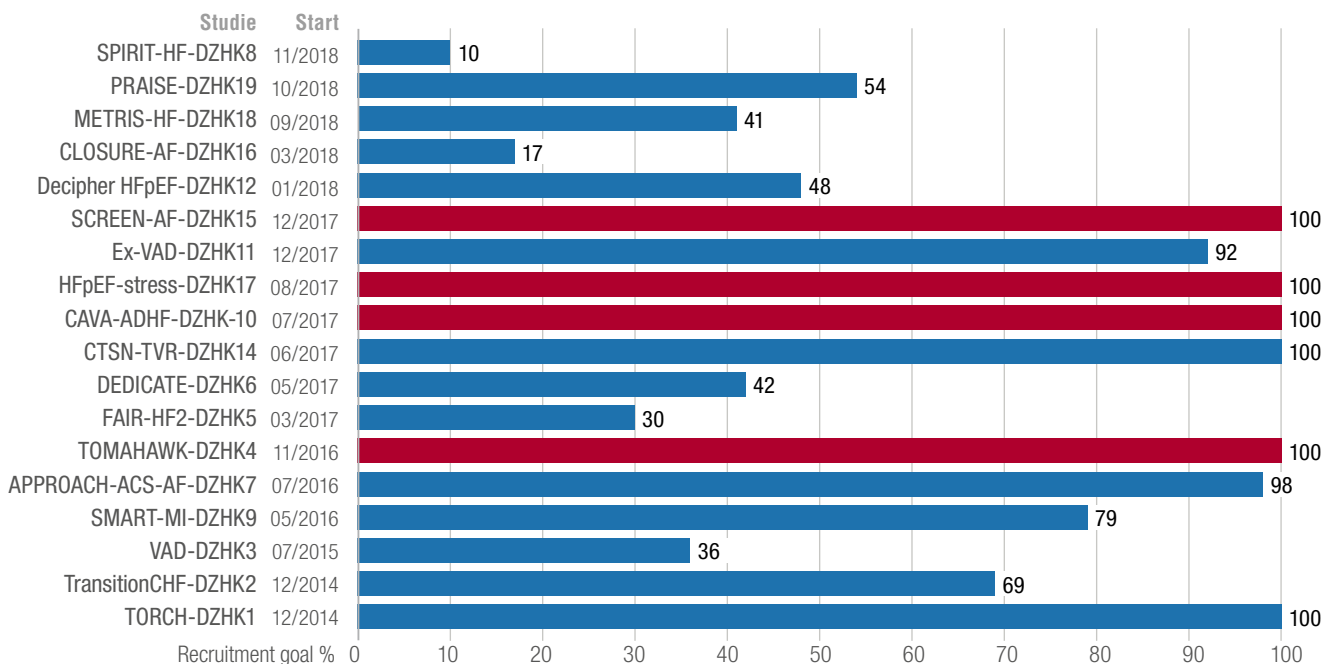
STUDIES AT THE DZHK

Acronym	Condition/ Treatment/ Diagnostics	Study- type	Responsible PI (DZHK partner site)	Recruitment target	Enrolled*
DZHK studies					
TORCH-DZHK1	Myocardial diseases	Registry	Katus (Heidelberg/Mannheim), Hoffmann (Greifswald)	2,300	complete
TransitionCHF-DZHK2	Heart failure	Cohort	Hasenfuß, Wachter, Edelmann (Göttingen)	1,000	686
VAD-DZHK3	Severe heart failure, heart transplantation	GRS	Falk, Knosalla (Berlin), Hasenfuß, Friede (Göttingen)	200	71
TOMAHAWK-DZHK4	Cardiac arrest	GRS	Desch (Hamburg/Kiel/Lübeck), Thiele	558	complete
FAIR-HF2-DZHK5	Heart failure and iron administration	GRS	Karakas (Hamburg/Kiel/Lübeck), Anker (Berlin)	1,200	361
DEDICATE-DZHK6	Aortic valve stenosis	GRS	Blankenberg, Seiffert (Hamburg/Kiel/Lübeck)	1,600	635
APPROACH-ACS-AF-DZHK7	Circulatory disorders of the heart in combination with atrial fibrillation	GRS	Wakili, Massberg (Munich)	400	393
SPIRIT-HF-DZHK8	Heart failure	GRS	Pieske, Edelmann (Berlin)	1,300	124
SMART-MI-DZHK9	Sudden cardiac death after myocardial infarction	ECS	Bauer, Kääb, Massberg (Munich)	400	315
CAVA-ADHF-DZHK10	Heart failure	ECS	Jobs (Hamburg/Kiel/Lübeck), Thiele	388	complete
Ex-VAD-DZHK11	Exercise with a ventricular assist device	ECS	Edelmann, Pieske, Falk (Berlin), Halle (Munich)	66	61
Decipher HFpEF-DZHK12	Heart failure, MRi	ECS	Nagel (Rhine Main)	185	81
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)	complete
CLOSURE-AF-DZHK16	Atrial fibrillation	GRS	Landmesser, Boldt (Berlin), Eitel (Hamburg/Kiel/Lübeck)	1,512	271
HFpEF-stress-DZHK17	Heart failure	ECS	Schuster (Göttingen)	70	complete
METRIS-HF-DZHK18	Heart failure	ECS	Doehner, Pieske (Berlin), Friede (Göttingen)	88	36
PRAISE-DZHK19	Ischemic heart disease	ECS	Endres, Landmesser, Nolte (Berlin)	251	135
BioVAT-HF-DZHK20	Severe heart failure	ECS	Zimmermann (Göttingen)	Recruitment in preparation	
TORCH-Plus-DZHK21	Myocardial diseases	Registry	Meder (Heidelberg/Mannheim)	Recruitment in preparation	
Partially-funded studies					
ISAR-REACT 5	Circulatory disorders of the heart	GRS	Kastrati, Schüpke (Munich)	4,000	complete
Revacept-PCI in CAD	Coronary heart disease	ECS	Kastrati, Massberg (Munich)	332	316
DZHK-associated studies (without DZHK funding)					
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	complete
SORT-AF	Heart failure, Adipositas	GRS	Willems (Hamburg/Kiel/Lübeck), Steven (Köln)	140	complete

* Last update 31.12.2019

[#] Follow up observations of patients from the SFB TR19 at the UM Greifswald

OVERVIEW: PATIENT RECRUITMENT IN DZHK STUDIES



Figures in percent (as of 31.12.2019)

■ These studies have completed recruitment in 2019

CLINICAL RESEARCH PLATFORM

The DZHK collects data and biosamples and makes them available to researchers worldwide. All studies fully financed by the DZHK commit themselves to use the Clinical Research Platform. It is used for the uniform collection of patient data and samples and allows further research to be carried out, beyond the initial study objective. A valuable collection of cardiovascular data and samples has thus developed. The essential concern of the DZHK is to obtain the highest possible benefit for medical research, especially cardiovascular research, from the data and samples.

The reviewed year expanded and networked the platform and focused on checking the quality of samples and data.

EXPANSION AND NETWORKING ADVANCED

The Clinical Research Platform is continuously expanded, updated, and supplemented. One of the challenges is the adaptation to different data protection and ethical principles. It applies in particular to the international recruitment of patients and the associated study-specific adjustments.

In addition to expanding the existing structure, a focus in 2019 was on the beginning networking of the Clinical Research Platform with other research platforms. It included cooperation with the German Centres for Health Research (DZG) in the Biobanking/Data Management working group. Secondly, the DZHK played a significant role in applying for a National Research Data Infrastructure (NFDI), which the DZG submitted to the German Research Foundation under the leadership of the German Center for Diabetes Research (DZD) together with the Medical Informatics Initiative. The aim is to establish a national research platform in Germany that enables the joint use of data from different data pools.

PARTICIPATING CENTRES



Centres that have already actively recruited or are anticipating recruitment

CLINICAL INDICATORS AS A QUALITY TOOL

Having focused our attention in recent years primarily on increasing recruitment figures, the year under review also addressed the quality of the data we collect. After all, the scientific questions of a study can only be answered satisfactorily with high-quality data. Clinical indicators were developed in 2019 to improve the completeness and quality of the recorded clinical data and the biobanking and image data. They originate from the IT systems of the Clinical Research Platform. The test phase ran until the end of 2019. The key figures enable us to assess the quality of the work of a study or study centre. Until now, their performance could only be evaluated based on quantitative success in patient recruitment.

Clinical Research Platform – more than data and samples

All study centres are required to use the Clinical Research Platform. It consists of IT infrastructure, processes, rules, and services for clinical studies.

- ▶ **Data and biosamples:** are recorded uniformly. Decentralised biobank (samples stored in the facilities), central storage of sample data in the Laboratory Information Management System (LIMS) | Partner site Greifswald
- ▶ **Data management:** central storage of clinical data | Partner site Göttingen
- ▶ **Ethics and data protection concept:** regulates what may be done with the data and samples.
- ▶ **Trusteeship:** pseudonymisation of the personal identifying data | Partner site Greifswald
- ▶ **Transfer Office:** publishes clinical data as well as biomaterial and image data following the usage regulations
- ▶ **Image Data Management System (BDMS):** evaluation of image data according to uniform criteria, central storage | Partner site Berlin, Munich, Rhine Main (Frankfurt)
- ▶ **IT infrastructure:** interaction between the fiduciary body, transfer office and the software systems for clinical data, BDMS and LIMS

CENTRAL, DIGITAL AND UNIFORM: ACQUISITION OF ECG DATA

In many places in Germany, ECG data are currently still being recorded digitally or on paper using various devices. There is a need for standardisation to obtain comparable data. For this purpose, an ECG expert group was established at the DZHK. The aim is to standardise the ECG data collected in the course of studies (data collection, data storage) so that they can be integrated into the image data management system of the Clinical Research Platform. The Working Group Clinical Research (WGCR) initiated this step. The working group was founded three years ago to promote patient inclusion in DZHK studies and ensure quality standards in the collected data and processes.

DZHK DATA AND SAMPLE COLLECTIONS

The data and biospecimen collected by the Clinical Research Platform form the "DZHK Data and Sample Collections". This collection is continuously growing. At the end of 2019, our database comprised 2,530 data and biospecimen; we expect this number to double next year. We make the data and biospecimens in our collection available to interested scientists worldwide to answer questions in cardiovascular research and beyond. The Use & Access Committee evaluates the applications concerning scientific relevance and ethical aspects and recommends their use to the RCC and the Board of Directors.

In the future, secondary use projects will initially be funded once by the DZHK, and we have begun to draw up new funding guidelines for this purpose. To make the collection more accessible to scientists, we have created a separate menu item on the website, which contains tools for the initial review of the collected data and biospecimens and guides users through the application procedure. To increase the number of applications for use outside the DZHK, we intend to promote the collection more in 2020. Furthermore, an amendment to the usage regulations is planned to make the procedure even more transparent.

APPLICATIONS FOR USE 2019

Home-based screening for early detection of atrial fibrillation in primary care patients aged 75 years and older: the SCREEN-AF randomized trial

Submission/year: 2019

Status: Project realisation

Scientific lead: Wachter, Hummers

This research project aims to analyse whether BNP and NT-pro BNP are suitable markers to identify high-risk patients who would benefit most from prolonged ECG monitoring. The aim is to establish a simple and cost-effective screening method in daily clinical routine to reduce the burden of cerebral ischemia-induced by undiagnosed atrial fibrillation.

Insulin growth factor binding protein (IGFBP) 5, a potential biomarker in heart disease

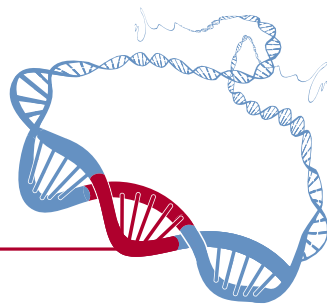
Submission/year: 2019

Status: Use and Access Evaluation

Scientific lead: Hasenfuss, Zelarayan

Insulin growth factor binding proteins (IGFBPs) are increasingly recognised as important factors in understanding the pathogenesis and severity of pathological conditions. In our study, we focused on the potential role of IGFBP5 as a cardiac and disease-specific novel biomarker for the development of heart failure. Also, they investigated whether IGFBP5 can distinguish stage-specific heart disease.

OMICS- RESOURCE



VALUABLE GENE DATA FOR IMPROVED THERAPIES

The genes of 1,200 healthy individuals from Germany were sequenced. They serve as a comparative resource to more precisely determine the differences between healthy and sick people in Germany – not only for cardiovascular research. The raw data processing – i.e., the preparation for scientific analysis – was completed in 2019. The data can now be used for research, and scientists can apply for it through the OMICs Use and Access Committee (ORC). An essential step to increase and facilitate access to the data was the publication of the first dataset of the DZHKomics resource in a publicly accessible genome browser, i.e., an interactive website providing an overview to genome sequence data.

Goals achieved in 2019?



- ✓ Recruitment in two further DZHK studies completed
- ✓ Recruitment independent benchmarks for clinical studies (e.g., for DZHK collection) developed
- Data and sample collections: visibility of data and sample collections increased
- ✓ OMICs Resource: Data processing completed and ready for use

Targets 2020



- ↗ Recruitment of three additional DZHK studies completed
- ↗ Focus on data completeness, and quality deepened
- ↗ DZHK audits 2.0 carried out at all qualifying study centres
- ↗ Data and sample collections: increased scope and visibility of data and sample collection
- ↗ Marketing goal for OMIC's resource: Receive usage request



Supporting Young Talent



The DZHK contributes to young scientists' training with specific programmes for early career scientists. Projects with a total volume of €1.8 million were recommended for funding in the Excellence Programme in 2019. Together with the training programme and mentoring, we have reserved a total of €2.7 million for promoting young talent.

YOUNG DZHK

The Young DZHK is the fastest-growing DZHK network. More than 1,200 people are now organised in the Young-DZHK and form a strong, dynamic, and interdisciplinary network of basic researchers and clinical scientists from all member institutions.

The Young DZHK is actively involved in shaping the future of the DZHK: The partner sites appoint representatives to the DZHK Postdoc Committee, which has a voice in important DZHK committees. Within the Young DZHK, junior researchers can take advantage of various funding

opportunities. These include laboratory exchanges and travel grants and support for their first independent research project, for example, through the postdoc start-up funding or the Clinician Scientist Programme. The Promotion of Women Scientists funding line was awarded for the first time in 2019 (more on page 47-48).

For the sixth time, the members of the Young DZHK met at the Young DZHK Retreat for scientific and personal exchange (more on page 51). The event with about 100 participants is organized by the DZHK Postdoc Committee and takes place annually in the run-up to the DZHK Retreat. In addition, network meetings, workshops and lectures were held at the partner sites and international



Around 100 young scientists attended the Young DZHK retreat in Potsdam.

networking promoted. Thus, there are good contacts to other Young Investigator networks in the USA and Europe.

POSTDOC COMMITTEE MEMBERS

Each partner site appoints two representatives to this committee. The speakers have voting rights in the Research Coordinating Committee (RCC), which is responsible for the scientific strategy of the DZHK.

Speaker: Nadya Al-Wakeel-Marquard

Deputy speakers: Tobias Jakobi, Norman Liaw

Berlin: Nadya Al-Wakeel-Marquard, Djawid Hashemi

Göttingen: Aline Jatho, Norman Liaw

Greifswald: Martin Bahls, Eileen Moritz

Hamburg/Kiel/Lübeck: Tobias Reinberger, Anca Remes

Heidelberg/Mannheim: Maarten van den Hoogenhof, Tobias Jakobi

Munich: Sebastian Clauß, Anne Dueck

Rhine Main: Jiong Hu, Sven-Oliver Tröbs

TRAINING & MENTORING

Young upcoming scientists need networks, exchange, personal skills, and financial freedom to do research. The training and mentoring programme of the DZHK offers all this to the members of the Young DZHK. They can apply for travel grants to attend professional congresses, workshops, and all DZHK-internal events such as DZHK symposia, co-financed congresses, and lectures. The programme aims to promote advanced scientific training and networking among young scientists across locations and DZGs. The "Visiting Scientist" mobility programme



Mentoring Alumni at the DZHK Retreat 2019 in Potsdam.

supports Young DZHK members in learning new methods and techniques in laboratories in Germany and abroad during short-term stays.

Medical doctoral students make an essential contribution to advancing translational research. The DZHK therefore awards doctoral scholarships every year. In 2019, 47 young doctors were able to devote themselves full-time to their research.

In addition to building professional competence, soft skills play an essential role in professional success. This is where the DZHK mentoring programme comes in. In 2019 and 2020, eleven mentees will have the opportunity to exchange information with their self-selected mentors regularly. In addition, they will be able to train and develop their leadership skills in personal coaching sessions and four workshops on career planning, work-life balance, self-presentation, networking and third-party fundraising, communication, and conflict management.

SUPPORT ACTIVITIES TRAINING AND MENTORING

	Amount 2019	2018
Travel scholarships for high-ranking congresses	301	279
Doctoral scholarships*	47	33
Visiting Scientist Programme	19	27
Attendance of external workshops	84	45
Mentoring (Call 2019 for Programme 2020/2021)	13	11

* incl. Partner site-financed doctoral scholarships

EXCELLENCE PROGRAMME

The DZHK supports talented, post-doctoral young professionals on their way to scientific independence with various funding schemes within the Excellence Programme (overview of projects in the Excellence Programme on page 49).

NEW FUNDING LINE FOR WOMEN ON THE WAY TO PROFESSORSHIP

To support women, the DZHK introduced a new funding scheme in 2019. The Promotion of Women Scientists programme supports female scientists with pre-school children to continue their research on their way to a professorship. DZHK initiated this programme because women often take on more responsibility in childcare during a period that coincides with the critical time of establishing independent research groups between the postdoc phase and professorship. For the first time, three female scientists received funds for non-scientific staff and consumables of up to €63,000 for up to one year (see interview page 47).

PRACTICE AND RESEARCH FOR BETTER THERAPIES

The Clinician Scientist Programme offers further support in achieving the prerequisites for a professorship and in making it easier for doctors to undertake research at the same time. In 2019, two new young physicians with doctorates received support. The programme enables them to conduct intensive research parallel to their specialist training. The DZHK finances up to two and a half years of research. In 2019, mentoring by a Board of Directors member was established. Gerd Hasenfuß accompanies the Clinician Scientists through intensive exchanges, i.e., at the DGK's annual meeting and video conferences.

As part of the DZHK Rotation Grant, a one-year leave of absence from patient care is financed. Four young doctors received the Rotation Grant of the DZHK in 2019 and can now devote one year to research in a DZHK project.

In the year under review, 17 research projects by postdocs were also approved under the Excellence Programme. The Postdoc Start-up Grant helps them generate initial research data and prepare further funding to apply for their research projects from third-party funding.



Female Empowerment – Promotion of Women Scientists

A couple of questions to three young female scientists supported by the new funding line to reconcile research and family.

Why did you start a career in science?

Yvonne Döring: I developed an interest in science and biology at school. I could have imagined studying psychology, but in the end, I decided to study life sciences. I am fascinated by understanding connections and recognising mechanisms that interlock.

Do you feel that as a woman, you have to prove yourself more than your male colleagues in research?

Carolin Lerchenmüller: Individually – yes. But I think the question is relevant to women in science in general. There are excellent studies that demonstrate, for example, that women receive less recognition – including citations – for equal publication achievements. Among other things, this also means that women need longer before they can raise their first relevant research funds. These data reveal that women often have to work harder to compete.

How do you perceive the role of women in science today? And what else must change?

Carolin Lerchenmüller: Women play a vital role in science. Generally speaking, diversity in organisations is a marker for innovation and productivity, and the composition of teams also influences the topics being researched. And although more than half of all students in the life sciences are women, the number of female managers is still stagnating. A generational effect cannot explain this discrepancy; time alone will not resolve this problem. Active measures are needed, such as programmes for the advancement of women, representation of women on review boards, and in functions in professional societies, as well as measures against implicit bias and gender-based discrimination.

Why did you take part in the DZHK's women empowerment programme?

Anna Szymborska-Mell: My supervisor and I came up with an exciting research idea, but it was clear that we needed additional resources since I was already involved in another project. The Excellence Grant enabled us to hire a technician who could execute the lion's share of the time-consuming laboratory work. The one year grant gave us enough time to deliver valuable data and open up several research avenues for the future. I also believe that it was an excellent way to increase my visibility and make a step towards becoming an independent leader.

How can you imagine your everyday life between research and family?

Yvonne Döring: It is undoubtedly a challenge to combine family and research without missing out on any part of it. But it is a challenge that you face anew every day. It sounds simple, but proper planning helps enormously. And you should be able to make compromises and give up on getting everything done perfectly. That helps to avoid going crazy.

What advice do you have for the future generation of girls and women considering a career in science?

Anna Szymborska-Mell: I would advise them the same thing I would recommend boys and men – go for it! It can be tough, but it is a gratifying career. I'd tell them not to waste their mental energy on worrying whether the system is perfect or whether the competition is fair. Instead – focus on becoming the best scientist you can be, ask questions that you genuinely find interesting, and find good mentors and collaborators that will support you and that you can learn from. Have kids and family if and when you want them, learn from your failures and make sure to celebrate your successes.

Anna Szymborska-Mell

Max Delbrück Center for Molecular Medicine in the Helmholtz Association



"The scholarship enabled me to take an important step towards becoming an independent leader."

The study aims to gain a better understanding of the mechanisms of vascular development. All blood vessels in the human body are lined with a single layer of cells. They adhere tightly to one another through dedicated protein complexes. When new vessels are formed, the strength of these contacts is carefully balanced to allow cells to move past each other, while keeping the vessels sealed to prevent bleeding. Using advanced proteomic techniques and the zebrafish embryo as a model, the team identifies which proteins act at the cell contacts during consecutive stages of vascular development.

Carolin Lerchenmüller

University Hospital Heidelberg



"The number of female executives is stagnating – time alone will not solve this problem. Active measures are therefore needed."

Yvonne Döring

Ludwig-Maximilians-University of Munich



"It is a challenge to combine family and research. Good planning helps enormously."

The funded study intends to answer whether physical endurance sports can influence cardiac regeneration in the aged heart. The loss of heart muscle cells is a basis for the development of heart failure, as the heart has only a limited ability to compensate for dead heart muscle cells by generating new cells. Furthermore, the study aims to understand the underlying mechanisms of cardiac regeneration and whether these can be used preventively or therapeutically.

The study, which Yvonne Döring is conducting with funds from the Promotion of Women Scientists programme, investigates what functions the enzyme PCSK9 has outside the liver. PCSK9 reduces the breakdown of cholesterol in the liver. In therapy, PCSK9 inhibitors are used to lower cholesterol levels: Antibodies block the enzyme, increasing the availability of LDL receptors in the liver, which means that more cholesterol can be broken down. PCSK9 may interact outside the liver but also with other molecules in the body.

Goals achieved in 2019?



- ✓ First grants Promotion of Women Scientists awarded
- ✓ Clinician Scientists receive mentoring by members of the Board of Directors

Targets 2020



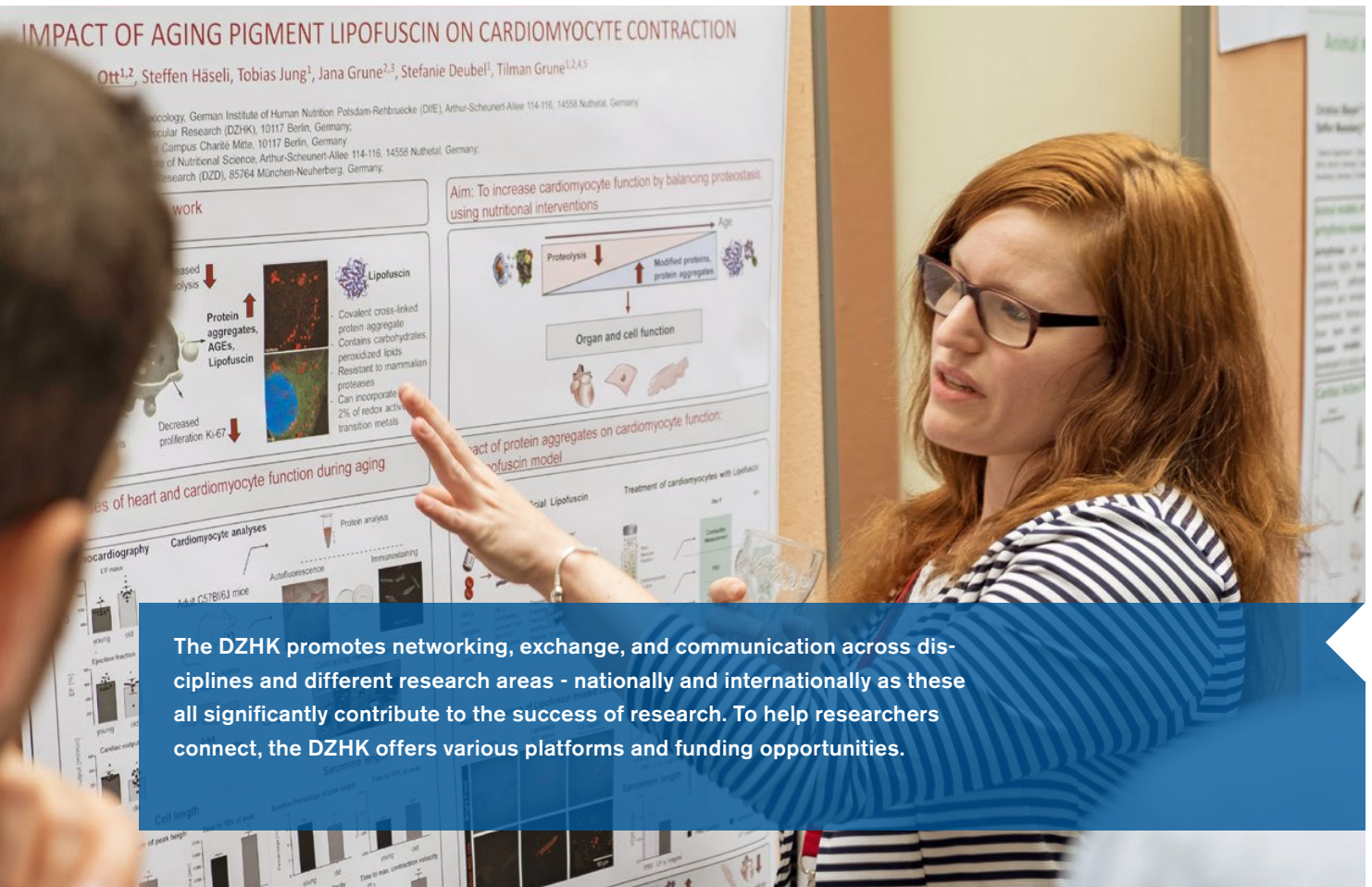
- ↗ Promotion of Women Scientists funding line further developed and extended
- ↗ Maximum funding amounts of DZHK Excellence Programme increased

PROJECTS IN THE EXCELLENCE PROGRAMME

Name	Institution	Funding Line	Title
Dario Bongiovanni	University Hospital Munich	Clinician Scientist Programme	Reticulated platelet biology in patients with coronary artery disease
Henry Nording	University of Lübeck	Clinician Scientist Programme	Mechanisms and clinical relevance of angiogenesis modulation through the platelet C5a receptor
Wesley Abplanalp	University Hospital Frankfurt	Postdoc Start-up Grant	Role of circulating monocytes in heart failure subjects with mutations driving clinical haematopoiesis
Sofia Iris Bibli	University Hospital Frankfurt	Postdoc Start-up Grant	Metabolic reprogramming in age endothelial cells
Sören Brandenburg	Universitätsmedizin Göttingen	Postdoc Start-up Grant	Mitochondrial redox stress and maladaptive Ca ²⁺ release unit remodelling as therapeutic targets in atrial fibrillation
Sebastian Cremer	University Hospital Frankfurt	Postdoc Start-up Grant	Relevance and mechanistic role of hematopoietic KMD6A mutations in Ischemic Heart Failure
Yvonne Döring	University Hospital Munich	Postdoc Start-up Grant	Role of ChemR23 on macrophages in perivascular adipose tissue in atherosclerosis
Xuemin Gong	Heidelberg University Hospital	Postdoc Start-up Grant	ATGL cardiomyopathy: From mechanism to a new epigenetic therapy approach
Jana Grune	Charité – Universitätsmedizin Berlin	Postdoc Start-up Grant	B-cell mediated autoimmunity in pulmonary hypertension associated to left heart disease
Sebastiaan van Heesch	Max Delbrück Center for Molecular Medicine Berlin	Postdoc Start-up Grant	Deciphering the role of novel mitochondrial microproteins in the human heart
Maarten van den Hoogenhof	Heidelberg University Hospital	Postdoc Start-up Grant	Gender-dependent disease severity in RBM20-cardiomyopathy - is there a role for Camk1δ?
Jessica Kornherr	Rechts der Isar Hospital	Postdoc Start-up Grant	Human-mouse chimera for characterisation of human cardiac progenitors during embryonic development
Marc Lemoine	University Medical Center Hamburg-Eppendorf	Postdoc Start-up Grant	Maturing hiPSC-cardiomyocytes: the role of CSQ2 in automaticity and arrhythmia
Silvia Mas-Peiro	University Hospital Frankfurt	Postdoc Start-up Grant	Impact of DNMT3A and TET2 mutations on immune-inflammatory pathways in pts undergoing TAVI for aortic stenosis
Sören Meyer	Heidelberg University Hospital	Postdoc Start-up Grant	The role of FAM129B in monocytes during myocardial infarction
Oliver Otto	Greifswald University Hospital	Postdoc Start-up Grant	Viscoelastic properties of peripheral blood cells as label-free biomarker for immune cell activation
Joachim Pircher	University Hospital Munich	Postdoc Start-up Grant	Effects of antimicrobial peptides on blood coagulation and venous thrombosis
Felizia Voß	Max Delbrück Center for Molecular Medicine Berlin	Postdoc Start-up Grant	Adapting intercellular communication to improve cardiac function and the response to hypoxia
Felix Wiedmann	Heidelberg University Hospital	Postdoc Start-up Grant	Characterizing the role of adenosine-to-inosine RNA editing in atrial cardiomyopathy
Yvonne Döring	Ludwig Maximilian University of Munich	Promotion of Women Scientists	Establishing a new interplay between PCSK9 and chemokine receptors in chronic vascular inflammation
Carolin Lerchenmüller	Heidelberg University Hospital	Promotion of Women Scientists	Exercise-induced cardiomyogenesis in the aged mammalian heart
Anna Szymborska-Mell	Max Delbrück Center for Molecular Medicine Berlin	Promotion of Women Scientists	Dynamics of endothelial cadhesome in growing blood vessels
Christophe Arendt	Goethe University Frankfurt	Rotation Grant	Validation of myocardial perfusion analysis for detection of regional ischemia in an experimental pig model
Nicolai Bogert	Heidelberg University Hospital	Rotation Grant	ITGA3 knockout attenuates pathological remodelling and fibrosis upon myocardial infarction
Markus Heckmann	Heidelberg University Hospital	Rotation Grant	Cardiac midkine, a diet dependent cytokine as a regulator in cancer induced cardiac cachexia
Badder Kattih	Goethe University Frankfurt	Rotation Grant	Impact of a skeletal muscle derived myokine on right ventricular failure and pulmonary hypertension



Scientific Exchange



The DZHK promotes networking, exchange, and communication across disciplines and different research areas - nationally and internationally as these all significantly contribute to the success of research. To help researchers connect, the DZHK offers various platforms and funding opportunities.

2ND DZHK CONFERENCE ON TRANSLATIONAL MEDICINE

How does research reach the patient? Scientists and doctors of all disciplines around the world are asking this question. In particular, widespread diseases such as dementia, cardiovascular diseases, or cancer are major challenges in an ageing society. Under the motto "Paving the way to new therapies", the DZHK organised the 2nd DZHK Conference on Translational Medicine in Berlin on 9 and 10 January 2019 with around 150 participants.

Translation is a challenge in all areas of medicine. The conference, therefore, not only focused on cardiovascular research but also presented examples of successful translation from different medical disciplines such as oncology, neurology, and infectious diseases, as well as the contribution of stem cell technologies, CRISPR/Cas, and artificial intelligence in translational research. Since the topic is interdisciplinary, holding the next conference together with other German Centres of Health Research is being considered.



280 scientists met for the DZHK retreat in Potsdam

DZHK RETREAT AND YOUNG DZHK RETREAT

In 2019 the annual scientific conference of the DZHK took place for the seventh time: From 12 to 14 September, around 280 scientists met for the DZHK Retreat at Lake Templin in Potsdam. The annual retreat is the largest networking event of the DZHK.

Highlights of the meeting were the keynote lectures "Pathogenesis and treatment of genetic cardiomyopathies" by Leslie Leinwand, Scientific Director of the BioFrontiers Institute at the University of Colorado, and "Integrative high-throughput modeling to understand the mechanisms of atrial fibrillation" by Calum MacRae, Vice Chairman for Scientific Innovation at Brigham and Women's Hospital and Associate Professor at Harvard Medical School.

This year's new format were the Flash Talks, in which participants presented the Papers of the Months 2018 and selected abstracts. To promote intergenerational scientific exchange, several Young DZHK researchers also had the opportunity to present their research to the broader audience at the main event in selected Highlight Talks.

Almost 100 young scientists from all DZHK sites took part in the preceding 6th Young-DZHK Retreat with lectures, posters, or five-minute Rapid Fire Talks. The DZHK Postdoc Committee was able to recruit Aldons Jake Lusi

from the University of California ("Genetic and metabolic interactions in diastolic dysfunction") and Ingo Hilgendorf from the University of Freiburg ("Macrophages in atherosclerosis – sick of eating") as guest speakers.

SYMPOSIA IN BERLIN, GÖTTINGEN, GREIFSWALD AND WÜRZBURG

In 2019, the DZHK held four internal symposia, in which more than 400 scientists participated. The DZHK provides funds for symposia and for inviting high-ranking scientists to give lectures at smaller local events called DZHK Lectures or, co-financed, at larger conferences.

For the second time, DZHK scientists organised a symposium together with the German Society of Cardiology. "Genome Editing – The hope and hype" took place in Berlin in February, hosted by Friederike Cuello from the Hamburg/Kiel/Lübeck site.

In May, the symposium "Heart and Brain Diseases: Integrative Research across Scales" took place in Göttingen, jointly organized with the German Centre for Neurodegenerative Diseases, under the direction of Wolfram-H. Zimmermann from the Göttingen site.

The "DZHI/DZHK Joint Symposium: Heart Failure Interfaces" was held in Würzburg in July. It was jointly organized by the DZHK partner site in Heidelberg/Mannheim and the German Center for Heart Failure (DZHI) at the University Hospital of Würzburg, under the direction of Johannes Backs and Marco Hagenmüller.

The Greifswald and Berlin sites organised a symposium on the topic of prevention of cardiovascular diseases. "Current Aspects of Translational Cardiovascular Disease Prevention with Exercise" was held in Greifswald in September 2019 and organized by Nicolle Kränkel (Berlin), Marcus Dörr, and Martin Bahls (both Greifswald).

SYMPOSIA AND CO-FINANCED CONGRESSES



If events take place at member institutions that fall within the DZHK's subject area, the DZHK offers the possibility to support the meetings financially.

Title	Date and Place	Host
17 th Dutch-German Joint Meeting of the Molecular Cardiology Working Groups	14–16 March 2019 Göttingen	Wolfram-H. Zimmermann Susanne Lutz (Göttingen)
50 Years of Excitable Media: From Theory to Applications	30 June – 2 July 2019 Göttingen	Stefan Luther (Göttingen)
International know-how transfer workshop on patient recruitment into large-scale cohort studies by the example of TransitionCHF	19–20 September 2019 Göttingen	Anja Sandek (Göttingen)
15 th Congress International Xenotransplantation Association	10–13 October Munich	Eckhard Wolf (Munich)
Annual meeting of the German Society for Microcirculation and Vascular Biology	25–27 October Heidelberg	Markus Hecker (Heidelberg/Mannheim)

Goals achieved in 2019?



- Interactive formats for the retreat introduced
- ✓ DZHK Symposia open for joint implementation with the other DZG

Targets 2020



- Interactive formats for the retreat introduced

Cooperations



The DZHK actively contributes to networking in medical research. It cooperates closely with the other German Centres of Health Research (DZG) – for example, in research infrastructures, communication, and promotion of young scientists. It also maintains intensive cooperation with cardiology partners in Germany and abroad.

COOPERATION WITH THE DZG

Although each DZG has a specific health science focus, overlaps and synergies are identified and used through active cooperation. Cross-DZG working groups implement particular projects in prevention, IT and artificial intelligence, biobanking and data management, global health, promotion of young scientists, regulatory issues, and public relations. For example, in 2019, a workshop for DZG junior scientists was held ("Nature Masterclasses: Workshop in Scientific Writing and Publishing", organized by the German Center for Diabetes Research). As part of the public relations work, the first two issues of the DZG's joint research magazine "SYNERGIE. Forschen für Gesundheit" were published. The DZHK functioned as a project lead. The DZG again travelled to the German

Academic International Network (GAIN) annual conference in San Francisco and maintained a joint exhibition. Also, the six DZGs, together with the consortia of the Medical Informatics Initiative and with considerable effort, prepared an application for a National Research Data Infrastructure (NFDI).



Shared booth of the DZG at the annual conference of the German Academic International Network (GAIN) in San Francisco.

The DZG discussion forums of the DZG board members, which take place regularly, primarily discuss strategic and political issues, and address questions that are directed at the centres' funding bodies. In 2019, a central topic was preparing the internal reviews of all DZGs planned for the years 2020–2022.

Two new German Centres for Health Research are in the planning process: a Centre for Child and Youth Health and a Centre for Mental Health. The call for both centres will be issued in 2020.



Participants of the DZG workshop “Nature Masterclasses: Workshop in Scientific Writing and Publishing”

NATIONAL AND INTERNATIONAL COOPERATIONS

The growing complexity of scientific challenges makes it necessary to combine competencies and connect scientists. The DZHK maintains close partnerships with cardiological partners in Germany and abroad, such as in funding issues and workshops for young scientists.

BRITISH HEART FOUNDATION AND DUTCH HEART FOUNDATION

In 2018, together with the British Heart Foundation (BHF), we announced a funding programme for the first time to use cardiovascular research resources across borders and generate synergies. Out of ten applications, two projects were awarded funding and started in September 2019, each receiving €1 million for three or four years.

The Dutch Heart Foundation (Hartstichting) also participated in a second call for proposals in October 2019. British, Dutch, and German (DZHK) researchers could apply for funding in bi- or trilateral teams. The BHF and the DZHK each provided €2 million, the Dutch Heart Foundation provided €1 million. The decision will be made in spring 2020.

Project 1:

“Genetic discovery-based targeting of the vascular interface in atherosclerosis”



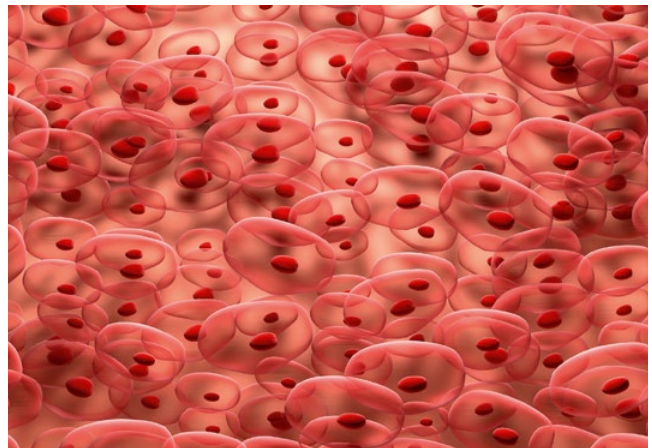
The researchers want to find out which genes are responsible for higher risk of heart attack and the underlying mechanism.

German partners: Jeanette Erdmann (coordinator), University of Lübeck | Heribert Schunkert, German Heart Centre Munich | Christian Weber, Ludwig-Maximilians-University of Munich

British partners: Hugh Watkins (coordinator), University of Oxford | Shu Ye, University of Leicester | John Danesh, University of Cambridge

Project 2:

“Spatially resolved cellular and molecular drivers of cardiac remodeling in healthy and failing human hearts”



Heart failure causes heart cells to change. The team hopes to use new cutting-edge technologies to analyse thousands of individual cells and find out how different parts of the healthy heart are composed and what changes occur in diseased hearts.

German partners: Norbert Hübner (coordinator), Max Delbrück Center for Molecular Medicine (MDC) | Thomas Eschenhagen, University Medical Center Hamburg-Eppendorf | Nikolaus Rajewsky, Max Delbrück Center for Molecular Medicine (MDC) and Berlin Institute for Medical Systems Biology (BIMSB)

British partners: Michela Nosedà (coordinator), Imperial College London, National Heart and Lung Institute | Sarah Teichmann, Wellcome Trust Sanger Institute | Stuart Cook, Imperial College London, National Heart and Lung Institute

OTHER COOPERATION PARTNERS

CARDIOLOGICAL COMPETENCE NETWORKS

The Cardiological Competence Networks conduct valuable work in the collaborative research of cardiac diseases. Therefore, the DZHK has been funding selected studies and structures of the Cardiological Competence Networks since 2015. Key areas are guideline-relevant studies in the field of heart failure and atrial fibrillation and funding for the National Registry for Congenital Heart Defects. Financing of the Competence Network Heart Failure ended in 2019; the other two networks will receive funding up to and including 2021. In 2019, the funding amounted to €1.04 million.

GERMAN HEART FOUNDATION

The German Heart Foundation offers patients information on all questions concerning cardiovascular diseases. A large number of the leading DZHK scientists are

honorary members of the Scientific Advisory Board of the German Heart Foundation. They are on hand to answer patients' questions with expert advice. To explore further possibilities for cooperation, the board members and employees of both offices met for a discussion in Berlin.

The DZHK participated in the Heart Weeks 2019 with a dossier and an expert interview on

➤ “Sudden Cardiac Death: Understanding Causes, Recognizing Harbingers and Developing Effective Therapies”.

GERMAN CARDIAC SOCIETY

The DZHK has worked closely with the German Cardiac Society (DGK), the largest cardiological specialist society in Europe, right from the start. Leading representatives of the two institutions met in Düsseldorf to discuss joint strategies for positioning cardiovascular research in Germany.

Since 2013, the DZHK and DGK have been jointly running the young scientists' funding programme "Fundamentals of Cardiovascular Research". Three workshops are organised each year as part of the programme. By participating in at least seven of a total of 13 workshops, the young scientists receive a certificate of advanced training.

Goals achieved in 2019?



- ✓ Two issues of the DZG magazine "SYNERGIE. Research for Health" published
- ✓ Joint funding programme with the BHF extends to the Dutch Heart Foundation and second call for proposals opened
- Coordinated lobbying with the German Heart Foundation and the German Cardiac Society started

Targets 2020



- A decision on BHF-DHF-DZHK projects taken
- DZG-overlapping meeting with NAKO Gesundheitsstudie on joint usage applications
- Joint DZG utilization regulation developed

Public Relations



In 2019, the focus of our public relations activities shifted to audiovisual communication and social media. We produced two YouTube videos supporting clinical research. One is an explanatory video on our clinical research platform. It addresses medical staff who work with our systems and increasingly come from centres that otherwise have little to do with the DZHK.

We have also created a video for study participants. As these are mainly senior and vulnerable cardiovascular patients, this video works with emotional messages and is easy to understand. The video should help build trust in the DZHK among study participants and supports the study staff in providing information.

NEW INSTAGRAM CHANNEL DZHK_OFFICIAL

The DZHK performed very well on social media. We increased our number of followers on Twitter to 731 (2018: 446) and on Facebook to 1,648 (2018: 1,145). In the engagement segment, one of the essential social media key performance indicators, our Facebook values increased significantly compared to the previous year. Users commented, liked, shared, and clicked on DZHK posts more frequently.

In the spring, we set up an Instagram channel that, in addition to Facebook, primarily reaches a younger target group (on Facebook, our fans are between 45 and 65+, on Instagram 25 to 44 years old). By the end of the year, the Instagram account had already reached 434 subscribers and a high engagement rate.

INFORMATION ON CARDIOVASCULAR DISEASES ATTRACTS VISITORS TO THE DZHK WEBSITE

When analyzing the website www.dzhk.de, it was remarkable how extraordinarily successful pages on cardiovascular diseases performed that were created in 2018. The page on sudden cardiac death was accessed 365 times in 2018; in 2019, it was already 16,910 hits. It makes the site the most frequently visited page of the DZHK in 2019, which indicates a great need for health information from reputable sources in the population. We will, therefore, continue to expand this area.

Compared to the previous year, we were able to increase the monthly user numbers of the entire website by 2.5 (11/2018: 5,746, 11/2019: 14,925). The increase is mainly due to excellent rankings in search engines (especially Google). Contents of the DZHK are listed among the top 3 search results. That applies not only for search terms related to general clinical pictures in the cardiovascular field but also for more specific search terms in the research field. For many search terms with a high search volume (e.g., "sudden cardiac death"), Google lists the corresponding DZHK page as a top search result.

At the end of the year, we were able to complete the website's soft relaunch, which mainly involved structural adjustments. The presentation of our now 20 clinical studies has been completely renewed and made more attractive.

In September, we presented the DZHK at the Health Day for BMBF employees in Berlin. Young cardiologists from

the Berlin partner site explained a walk-in heart and provided information on cardiovascular diseases and the latest research approaches.

The public relations department also accompanied two important events of the DZHK with communication and marketing measures: the 2nd Conference for Translational Medicine in January and the inauguration of the office in Potsdamer Straße in November.



In the year under review, the first two issues of the DZG's joint research magazine "SYNERGIE. Forsuchen für Gesundheit" were published, with the DZHK acting as the project manager.

Goals 2019 achieved?



- ✓ Website relaunch finished
- ✓ DZHK patient video for study participants released
- ✓ Explanatory video published for users of the Clinical Research Platform
- ✓ The first and second issue of the DZG magazine published
- ✓ DZHK Instagram account established

Targets 2020



- ↗ DZHK partner programme launched
- ↗ DZHK Podcast initiated
- ↗ Web platform "service4studies" started (together with clinical group)
- ↗ Two further issues of the DZG magazine "SYNERGIE. Research for Health" published



Success Indicators for Translational Research



SHORT- AND MID-TERM INDICATORS

Indicator	Definition	2019	2018
1. "Physician Scientists"	Share of scientifically active (licensed) physicians of 1,605 scientists registered at the DZHK	52.5%	51%
2. Cooperations between DZHK sites	a. Number of Shared Expertise projects (year)	37	25
	b. Number of publications with at least two DZHK authors from different sites	151	143
	c. Number of ongoing large multicentre projects (recruiting DZHK studies and TRPs) (31.12.) involving multiple DZHK partner sites	15	19
	d. Number of Visiting Scientist stays at other DZHK partner sites (year)	4	12
3. Communication with regulatory authorities	Consulting appointments (e.g. PEI, BfArM) in the context of recruiting DZHK studies, TRP and partner site projects (year)	6	4
4. Cooperations with industry	Cooperations with partners from industry within the framework of recruiting DZHK studies, TRP and partner site projects (31.12.2019)	18	18

SUCCESS INDICATORS FOR TRANSLATIONAL RESEARCH

Indikator	Definition	2019	2018
5. Cooperative structures in clinical research	a. Type (quality) of cooperative structures (31.12.2019)	Clinical Research Platform (data storage, Trusted Third Party, LIMS, BDMS and ethics project, Use & Access), stem cell registry, OMICs resource	
	b. Amount (Quantity)		
	• Patients included in Clinical Research Platform (31.12.2019)	7,645	5,635
	• SOPs (31.12.2019)	23	23
	• Data and biospecimen usage applications/notifications (year)	2/8	1/2
	• Approved usage applications and notifications (year)	2/5	1/2
6. High-ranking publications	All publications with DZHK affiliation with impact factor > 10	135	123
7. Preclinical projects and clinical trials	a. Number of Translational Research Projects and recruiting DZHK studies (31.12.2019)	26	29
	b. Publications from Translational Research Projects and DZHK clinical studies	40	11

LONG-TERM SUCCESS CRITERIA

Indicator	Definition	2019	2018
8. Revised medical guidelines	Number of guidelines changed as a result of DZHK trials and Competence Network Trials (total)	1	1
9. New therapeutic and diagnostic principles	Number of new therapeutic and diagnostic principles developed in DZHK projects and entering clinical application (total)	0	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	0

Remarks on the table:

Definition of DZHK studies: from competitive/flexible funds; 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 partner site projects.

The values for indicators 3, 4 and 7b come from a query to all PIs.

..... Facts and Figures



FINANCES AND STAFF

In the reporting year 2019, the DZHK had annual funds of approximately €40.8 million and a carryover from 2018 of €8.3 million (2017: €10.6 million). Of this amount, funds totalling €43.3 million were spent (2018: €43.2 million).

The allocation of funds in 2019 was thus slightly higher than in the previous year. The partners called up funds at an earlier stage and on a regular basis. In total, more funds were requested than initially planned in the 2019 business plan, so that the reduction of our positive balance, which began in 2017, was around €2.45 million.

Accumulated funds amounting to €5.8 million were not spent and were carried over into 2020. In relative terms, the outflow of funds in relation to the respective new funds

(annual budget without carryovers from previous years) was 97 percent in 2016, 108 percent in 2017, 105 percent in 2018, and around 106 percent in 2019.

The DZHK is reducing its reserve balance over 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 the slow recruiting of patients for the trials. It is not generally possible for ethical reasons to discontinue the delayed studies or reduce the funds not requested in a calendar year under these circumstances. These funds are ultimately well-founded reserves for clinical trials.

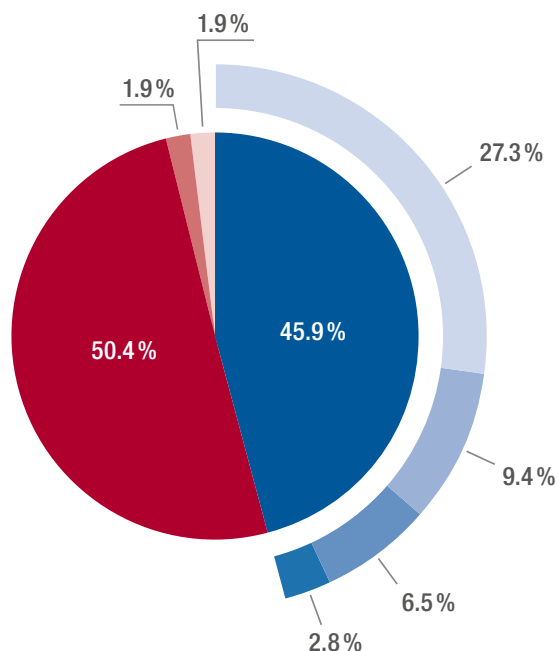
The year 2019 was very much affected by the budget freeze for the Helmholtz Association of German Research Centers (HGF), decided by the German Bundestag's Budget Committee. The budget freeze affects the DZHK via the Max Delbrück Center for Molecular Medicine

(MDC). The budget release was dependent on spending 75 percent of the budget and all positive fund balance early in the year. Intensive communication with the partner sites and third-party funding departments lead to the result that funds were called up earlier and more regularly. On 26th September 2019, the Budget Committee of the German Bundestag gave its approval for the release of the funds blocked for 2019. The agreed budget freeze will continue to apply to the DZHK to the same extent in 2020.

The funds spent in 2019 amounting to €43.3 million were broken down as follows:

- **Partner site funds:** €21.8 million
- **Flexible funds:** €19.9 million (including clinical research €11.8 million, preclinical research €4.0 million, Young DZHK €2.8 million and external funding €1.2 million [including competence networks €1.04 million and cooperation with external partners €161,000])
- **Membership fees:** €0.8 million (contributions for the 2019 main office budget, which amounts to €1.16 million; the remaining amount will not be spent until 2020)
- **Funding management department:** €21.8 million

On 17th September 2019, the German Centres of Health Research (DZG) received a message from the BMBF about a 3 percent increase in budget starting 2021, similar to the increase agreed for the members of the new Pact for Research and Innovation. The DZGs are required to use part of this funding for strategic and cross-centre cooperation projects.



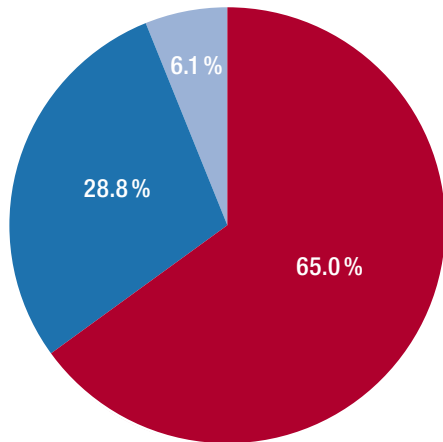
ALLOCATION OF SPENT DZHK FUNDS 2018 BY EXPENDITURE AREAS

- Partner site funds (2018: 50.9%)
- Flexible funds (2018: 45.3%)
- Funding management department (2018: 1.8%)
- Membership fees (2018: 2.0%)

Flexible funds are made up of

- Clinical research
- Preclinical research
- Promotion of young talent
- External

Figures in percent: Totals may differ from 100 percent due to rounding of individual share values.



STAFF EXPENDITURES, MATERIAL EXPENSES AND INVESTMENTS

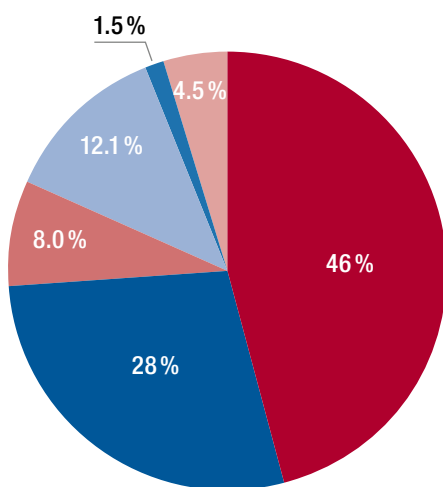
- Staff costs: €28.1 million
- Material expenses: €12.5 million
- Investments: €2.6 million

BUDGET OF THE DZHK MAIN OFFICE

The budget of the main office of the DZHK e. V., financed from membership fees, amounted to €1.17 million in 2019 (2018: €1.14 million). This budget was fully financed by membership fees. Of this amount, €1.34 million (2018: €1.05 million) was spent – other income amounted to €9,097. The result is a deficit of €158,590.

To cover the gap, the reserves from 2016 and 2017 were released as agreed. It still leaves a surplus of €38,536 which will be offset against the membership fees for 2022.

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



STAFF EXPENDITURE, MATERIAL EXPENSES, AND INVESTMENTS OF THE MAIN OFFICE

- Staff costs: €0.62 million (2018: €0.64 million)
- Material expenses: €0.37 million (2018: €0.24 million)
- Investments: €0.11 million (2018: €8.000)
- Public relations: €0.16 million (2018: €0.17 million)
- Membership fees (TMF e.V.): €20,000 (2018: €20,000)
- Rent deposit: €60,000

Figures in percent: Totals may differ from 100 percent due to rounding of individual share values.

STAFF

As of 31 December 2019, 408.71 (2018: 432.73) full-time equivalents (FTE) or 515 (2018: 595) individuals or "heads" were financed from DZHK funds.

This number includes 15 employees of the DZHK main office, 11 employees of the funding management department, and 18 employees in the competence networks.

NUMBER OF STAFF FINANCED BY DZHK 2017–2019

At the request of the BMBF, the human resources reporting system was changed in 2019 to compare the total number of employees with previous years.

	2017	2018	2019
Number of employees (as of 31 December 2019) (FTE)	403.58	432.73	408.71
Number of employees (as of 31 December 2019) (capita)	612	595	515
thereof male	205	191	174
thereof female	407	404	341
Number of scientists and physicians (FTE)	–	–	226.55*
Number of scientists and physicians (capita)	–	–	308*
thereof male	–	–	139
thereof female	–	–	169
These include:			
DZHK Professorships and Junior Research Group Leader (FTE)	–	–	19.81
DZHK Professorships and Junior Research Group Leader (FTE) (capita)	–	–	22
thereof male	–	–	18
thereof female	–	–	4
Senior Scientists und Postdocs (FTE)	–	–	161.73
Senior Scientists und Postdocs (capita)	–	–	212
thereof male	–	–	84
thereof female	–	–	128
PhD students (FTE)	–	–	45.01
PhD students (capita)	–	–	74
thereof male	–	–	37
thereof female	–	–	37
Non-scientific staff and others (FTE)	–	–	116.6*
Non-scientific staff and others (capita)	–	–	163*
thereof male	–	–	22
thereof female	–	–	141

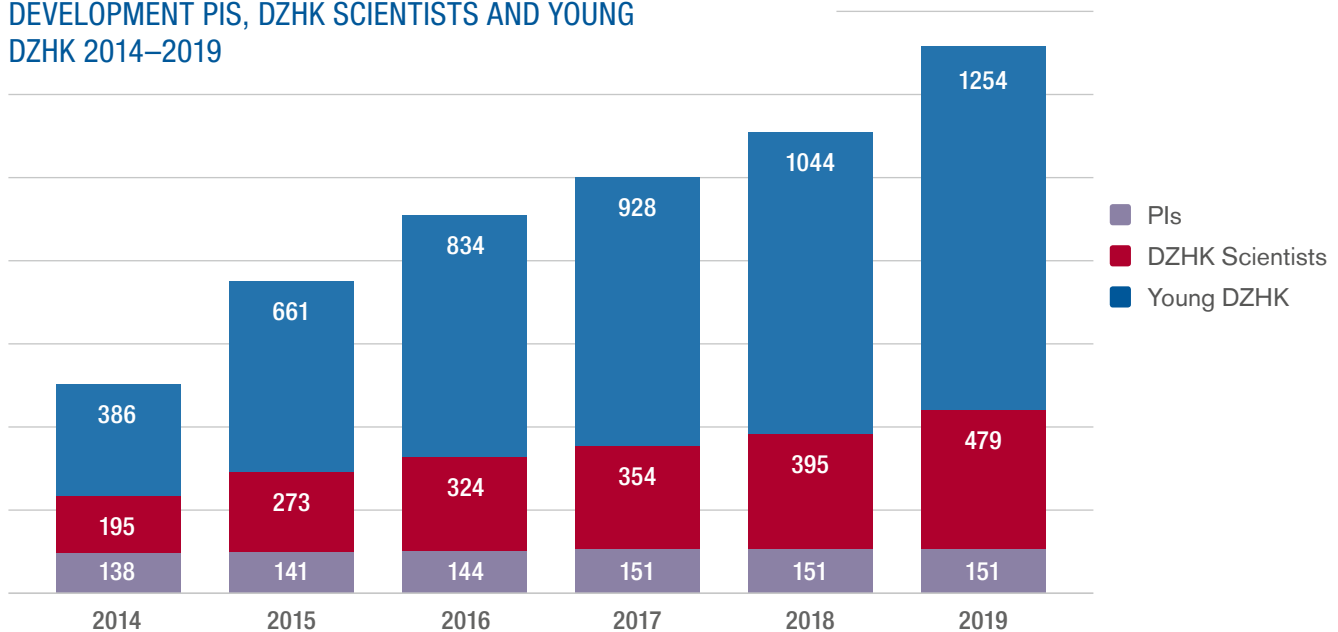
* without employees DZHK main office, FMM and competence networks

PRINCIPAL INVESTIGATORS, DZHK SCIENTISTS, YOUNG DZHK MEMBERS

In addition to the scientists financed by the DZHK, Principal Investigators (PI) play an essential role in the DZHK. In most cases, the PIs are not funded by the DZHK. Still, they contribute their ideas and expertise to the DZHK committees, thus making a significant contribution to the success of the DZHK. In the year under review, the DZHK had an unchanged number of 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, with

additional posts for each DZHK professorship established at the partner site using DZHK funds. To assign those scientists who are not PIs of the DZHK, there are two statuses: "Member of Young DZHK" and "DZHK Scientist". Potential candidates must apply to both groups. Prerequisites are a defined commitment to the DZHK and the possibility of an assignment to a DZHK-PI working at a partner institution. In the reporting year, the DZHK had 479 DZHK scientists (2018: 395) and 1,254 Young DZHK members (2018: 1,044) in addition to the PIs.

DEVELOPMENT PIS, DZHK SCIENTISTS AND YOUNG DZHK 2014–2019



DZHK ADMINISTRATION

The DZHK head office employees, the funding management department (FMM), and the seven partner sites together form the science management of the DZHK. The proven close cooperation between the association management and FMM has been simplified by moving to new shared premises in July 2019. The new office is still located in Berlin. The independence of FMM as a department of the Max Delbrück Center for Molecular Medicine in the Helmholtz Association (MDC) in the approval and review of DZHK projects will be maintained. The partner site management acts as a decentralized branch office of the association management and is located at each of the seven partner sites.

The employees will continue the intensive cooperation in 2019. In addition to the exchange of information on the current DZHK funding procedures and all administrative procedures from application to reporting, one focus in 2019 was preparing the international review, which takes place in January 2020.

DZHK HEAD OFFICE

In the year under review, 15 employees (11.38 FTE as of 31.12.2019), including the managing director, were employed at the DZHK Head Office. Together with the Board of Directors of the DZHK, the Head Office led by Joachim Krebsler (Managing Director since the foundation of the DZHK in 2012) is responsible for the strategic planning of the cooperative research, for the allocation of funds available in the coming years and press and public relations.

In addition to the classic tasks of a head office, the DZHK management sets strong strategic focus. It includes the supervision of a mentoring programme and a unique harmonised clinical infrastructure in Germany with central data storage, ethics guidelines, use and access management, and an image database. Also, it coordinates the regular invitation to tender for 12 funding guidelines and associated review procedures.

In 2019, the following tasks were of particular relevance:

- Preparation of the international review in January 2020
- Application together with all DZG for a National Research Data Infrastructure
- Preparation of the move to a joint office with the funding management department including an inauguration ceremony
- Support of the association's Board of Directors in the coordination of scientific cooperations in the DZHK
- Organisation of regular calls for proposals and selection and evaluation procedures in the three areas of preclinical research, clinical research and promotion of young scientists
- Organisation of the mentoring programme
- Organization of the annual conference (DZHK Retreat and Young-DZHK Retreat)
- Controlling the funds together with the funding management department and the partner site management
- Organisation, preparation, and follow-up of committee meetings
- Reporting obligations in the form of an annual report and publication summaries
- Internal and external communication

FUNDING MANAGEMENT DEPARTMENT

As part of the Max Delbrück Center for Molecular Medicine in the Helmholtz Association (MDC), the Funding Management Department (FMM) is responsible for the administrative implementation of funding to the DZHK partner institutions and external cooperation partners. The MDC is responsible for reviewing applications for funding and verifying the use of funds according to the regulations of the DZHK and the Federal Ministry of Education and Research (BMBF).

In addition, the FMM prepares controlling reports for the Board of Directors and the partner sites to support them in effectively managing their funds. In the 2019 reporting year, the FMM was responsible for forwarding the funds for project funding to 28 of the 32 partner institutions of the DZHK. It also passed on grants to 24 external cooperation partners in 2019 (2018: 29), including the funding of two competence networks.

An example: The DZHK e. V. has 28 members. Additionally, there are 4 Max Planck Institutes and the office of the DZHK e. V. as recipients of funds. The four partner institutions to which the MDC does not forward funds are RKI (because it is a departmental research institution), University of Heidelberg (funding received by Heidelberg University Hospital, which is itself a member), Max Planck Institute for Experimental Medicine Göttingen (no funding to date), Max Delbrück Center (no forwarding of funds).

The DZHK funded a total of 514 ongoing projects in the reporting year (2018: 560). The total number of projects funded to date is 1,411.

The FMM counted 10.08 FTE (11 capita) as of 31.12.2019. One controller and one administrator position in the finance department and the position of a student assistant were unfilled. The FMM's staff has the following tasks: management, scientific review, review of applications and proof of use, controlling, secretary, and contract management.

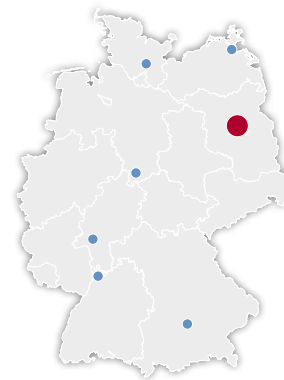
PARTNER SITE MANAGEMENT

The partner site managers coordinate the seven DZHK partner sites' activities and are also decentralized employees of the DZHK management headquarters. In 2019, the DZHK provided funds for the site management within the project funding for one full-time position for a scientist acting as a site manager and one full-time position for an administrator. The site management units form the interfaces between scientific projects, partner site speakers, third-party funding administrations, human resources departments, research deaneries, legal departments, DZHK main office, and FMM. They coordinate all on-site activities, organize site retreats, PI meetings, and coordinate the work of the site executive board and the application and reporting system. Also, they carry out decentralized financial controlling for their partner site. Together with the DZHK headquarters and FMM, they also develop procedures and processes at the DZHK.

..... Partner Sites



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

Partner site management

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

Partner institutions at the DZHK partner site Berlin

Charité – Universitätsmedizin 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 research activities of the Berlin DZHK focus on the understanding of risk factors and mechanisms across diseases leading to progressive heart failure and vascular maladjustments. The goal is to accelerate the translation towards innovative diagnostics, prevention, and treatment of cardiovascular diseases. To this end, DZHK scientists benefit from an outstanding research landscape, which includes the five partner institutions and strong inter-institutional networks that significantly promote both

cardiological and interdisciplinary research approaches. The two research institutes, BIH (Berlin Institute of Health) and ECRC (Experimental and Clinical Research Center) - jointly operated by Charité and MDC - specialise in translational research and enable the use of novel interdisciplinary and systems medicine approaches. The expertise of Charité and DHZB in the field of clinical and surgical cardiology is also an excellent basis for the seven DZHK-funded clinical studies currently coordinated at the site. Two more studies are currently in the approval phase.

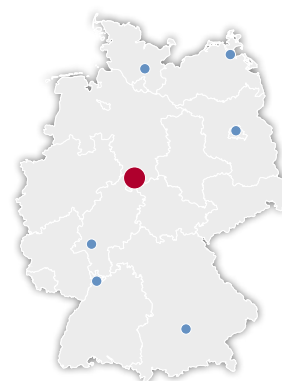
Furthermore, the DHZB is one of the leading European centres for cardiovascular medicine and heart transplantation, and it has two state-of-the-art hybrid surgical units for the simultaneous performance of cardiac and other surgical interventions. The MDC provides various technology platforms focusing on imaging, OMICs and data analysis, disease models, and high-throughput technologies, enabling outstanding innovative research approaches. Additionally, RKI and DIfE provide access to large cohorts and enable DZHK scientists to conduct epidemiological studies.

In November 2019, the second Berlin DZHK partner site retreat took place with over 100 participants and was received very well.

The four grants acquired in the DZHK Excellence Program, as well as the start of the TRP project "CAR inhibitors to Treat Myocardial Infarction (CARTI)" and the BHF Partnership research grant "Spatially resolved cellular and molecular drivers of cardiac remodelling in healthy and failing human hearts" are also noteworthy.



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
Rabea Hinkel, Professor for Laboratory Animal Science at the German Primate Centre, Leibniz Institute for Primate Research (DPZ)

Partner site management

Axel Kaul (partner site manager), Vanessa Kruse (scientific project manager), Annette Kuhring and Sylvia Vann (partner site administrator), since 10/2019 Marie-Christin Ernst (assistance), University Medical Centre Göttingen

Partner institutions at the DZHK partner site Göttingen

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

RESEARCH FOCUS AT THE DZHK

The main focus of the DZHK Göttingen partner site is heart failure research with the topics "Mechanisms of transition from clinically asymptomatic heart muscle

weakness to symptomatic heart failure" and "Heart regeneration in heart failure". A particular area of interest is the translation of new diagnostic (e.g., real-time MRI) and therapeutic (e.g., cardiac patches) procedures into clinical application.

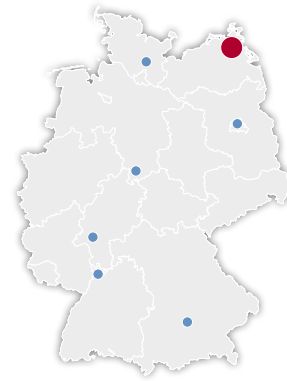
At the Göttingen site, the focus is on infrastructure support via eleven partner site projects and three DZHK professorships (Luther, von Haehling, Uecker) with the participation of four institutions. To strengthen the translation of innovative genome editing methods into clinical application, a fourth DZHK professorship for genome editing focusing on human genetic mutation diagnostics will be filled in 2020. The DZHK Göttingen is currently coordinating four clinical studies and two translational research projects. One translational research project was completed in 2019. DZHK scientists completed the preclinical validation of the heart patch approach in 2019 as a basis for the clinical BioVAT-HF study, which will start in 2020.

The link between "heart and brain" research was deepened in 2019 and will be further strengthened by the Heart and Brain Center Göttingen (HBCG), a research building funded by the German federal and state governments.

At the DZHK General Assembly 2019, Professor Wolfram-Hubertus Zimmermann (UMG) was confirmed as the partner site's DZHK spokesperson. He will be supported by Professor Eberhard Bodenschatz (MPI-DS) and Professor Rabea Hinkel (DPZ) as deputy spokespersons. Thus, the DZHK partner site Göttingen is represented externally by representatives of three of the four participating institutions at the Göttingen site.



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 and Jens Fielitz, University Medical Centre Greifswald

Partner site management

Stefan Groß (partner site manager), Susanne Franck (on parental leave)/ Kornelia Sadewasser (partner site administrator), University Medical Centre Greifswald

Partner institutions at the DZHK partner site Greifswald

University Medical Centre Greifswald

RESEARCH FOCUS AT THE DZHK

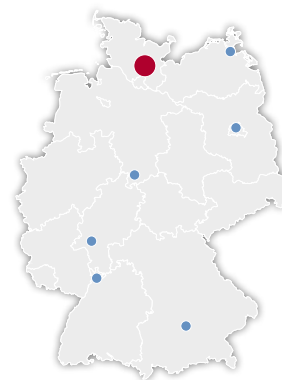
Special expertise of the Greifswald partner site includes population-based epidemiological and clinical studies with comprehensive cardiovascular phenotyping and research on the prevention of systolic/diastolic heart failure or dilated cardiomyopathy, high-throughput multi-OMICs analyses, e-health, biobanking, and data management and analysis of large patient cohorts.

In 2019, the partner site projects of the new funding period 2019-2020 were started with the cross-institutional collaborative project structure focusing on "heart failure" with the three pillars 1. Translational approach of heart failure prevention and therapy, 2. Immunological mechanisms in heart failure, 3. 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 integrated into this project structure.

In 2019 the University Medical Center Greifswald recruited for the clinical DZHK studies Transition-CHF, CAVA-ADHF, TOMAHAWK/ TOMAHAWK-Register, SPIRIT-HF, FAIR HF2, APPROACH-ACS, SMART-MI, Closure-AF, and PRAISE. Recruitment in TOMAHAWK and CAVA-ADHF was completed during the year.

In clinical research, the trust office of the Central Data Management (joint project together with the Göttingen site and the office in Berlin) has been established in Greifswald. Also, Greifswald operates the central LIMS system. Besides this, the Greifswald partner site coordinates the DZHK basic and study biobanking.

DZHK PARTNER SITE HAMBURG/KIEL/LÜBECK



Partner site spokesperson

Norbert Frey, Director of the Cardiology and Angiology Clinic at University Hospital Schleswig-Holstein (Kiel)

Deputy spokesperson

Heimo Ehmke, Director of the Institute for Cellular and Integrative Physiology at the University Hospital Hamburg-Eppendorf and Jeanette Erdmann, Director of the Institute for Cardiogenetics at the University Medical Center Schleswig-Holstein (Lübeck)

Partner site management

Doreen Stimpel (partner site manager), Monika Glimsche (partner site administrator), University Hospital Hamburg-Eppendorf

Partner institutions at the DZHK partner site 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 DZHK partner site is identifying 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.

In clinical research, four fully funded clinical studies (DEDICATE and FAIR-HF2 in Hamburg and TOMAHAWK

and CAVA-ADHF in Lübeck) are conducted at the site, all of which were in the recruitment phase in 2019.

Within the funding line Translational Research Projects, two preclinical projects deal with innovative therapeutic approaches focusing on clinical application (gene and heart muscle replacement therapy, both at UKE).

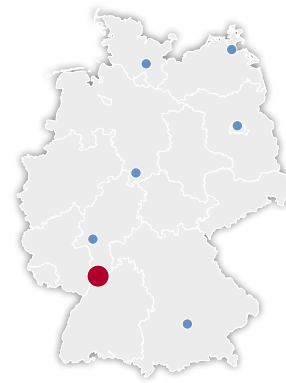
In two international projects in cooperation with the BHF, research is being conducted on the development of coronary heart disease (in Lübeck) and heart failure (in Hamburg). The Hamburg/Kiel/Lübeck site is involved in a variety of collaborations through Shared Expertise as well as with external partners. It offers three of the ten most frequently used DZHK Shared Expertise offerings.

In 2018, the DZHK received €400,000 from the Neumünster-based non-profit organisation "Kinderherzen wollen leben". The donation and other DZHK site funds will finance a five-year endowed professorship (W2) for cardiogenetics of congenital structural heart diseases at the Children's Heart Center Kiel, which was successfully filled in 2019.

A constant focus at this partner site is on regular internal communication, networking, and scientific exchange among local researchers and external experts. For example, a series of internal seminars are held every three months, alternating between Hamburg, Kiel, and Lübeck. In June 2019, the annual site retreat was again a great success.



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 (until 7/2019), Johannes Backs, Director of the Institute for Experimental Cardiology, University Hospital Heidelberg (starting 7/2019)

Deputy spokesperson

Thomas Wieland, University Hospital Mannheim (until 7/2019), Jörg Heineke, University Hospital Mannheim and Patrick Most, Department of Internal Medicine III, University Hospital Heidelberg (starting 7/2019)

Partner site management

Tanja Weis (partner site manager), Annabell Skarabis (scientific project manager), Ines Schneider (partner site administrator, until 4/2019), Denise Kampffmeyer (partner site administrator, starting 4/2019)

Partner institutions at the DZHK partner site

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

At the Heidelberg/Mannheim partner site, the scientific research focuses on genetic and inflammatory cardiomyopathies and arrhythmias in integrative and translational approaches.

Scientists use 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) 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. DZHK scientists have identified several genetic loci and variants, epigenetically modified candidate genes, miRNAs, and other potential targets within the translational pipeline. They will be functionally tested for their diagnostic and therapeutic potential.

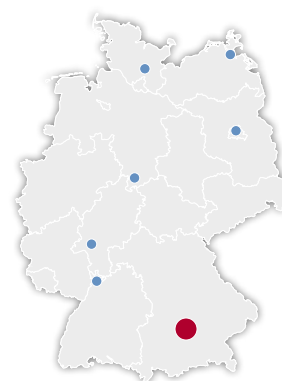
At the DZHK, the Heidelberg/Mannheim site is involved in clinical and preclinical research in various ways: The site is recruiting for almost all DZHK studies and, with the TORCH-Plus registry, has brought a further clinical project into the DZHK starting on January 1, 2020. In the recruitment score, Heidelberg and Mannheim ranked second and fourth place, respectively. In preclinical research, a total of nine collaborations were carried out with Shared Expertise (SE) or external partners. In the reporting year 2019, Heidelberg/Mannheim site offered a total of 33 SE's.

Our researchers received three Postdoctoral Start-up Grants, one Women Scientist Project, and two Rotation Grants within the Excellence Program. Furthermore, Shirin Doroudgar's Junior Research Group was extended by one year in the reporting period after a positive evaluation. The DZHI-DZHK symposium "Heart Failure Interfaces" took place in July 2019 to foster scientific exchange and networking.

In June 2019, the fourth and largest to-date local site retreat took place, focusing on scientific strategy and young researchers' promotion. As a structural success for the Heidelberg/Mannheim site, the new W3 professorship for RNA Biology at the Institute of Experimental Cardiology is of note.



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 of Munich

Partner site management

Sandra Rauser (partner site manager), Martina Michel (partner site administrator), Technical University of Munich

Partner institutions at the DZHK partner site Munich

Technical University of Munich (TUM); Hospital of Ludwig Maximilian University of Munich (KUM); Ludwig Maximilian University of 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 scientific focus at the Munich DZHK partner site ("Munich Heart Alliance", MHA) is the identification of new therapeutic targets and the development of optimised and innovative procedures for treating cardiovascular diseases and their translation into clinical studies.

With the harmonisation of ethics applications, Central Image Data Management, and the recruitment of patients in DZHK studies, Munich participates in several DZHK clinical initiatives. The results from the ISAR-REACT5 study (which was partially funded by the DZHK) were recommended for inclusion in medical guidelines.

In preclinical research, the TR projects of Professor Maegdefessel and Professor Joner were approved for funding. Professor Schunkert (DHM) and Professor Weber (KUM) received funding from the DZHK cooperation with the British Heart Foundation (BHF), under the leadership of Professor Erdmann (Lübeck). Within the Shared Expertise (SE) projects, a total of eleven new cooperation applications were approved. Five other locations use Munich SEs, Munich cooperates with six SEs from other sites.

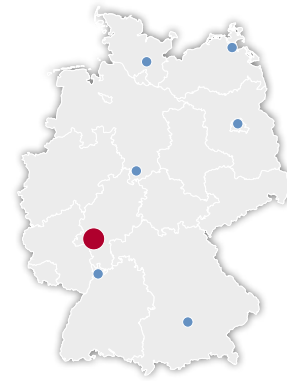
The Review Panel for the DZHK Excellence Promotion awarded one application each for the Clinician Scientist Programme and the Promotion of Women Scientists to Munich junior scientists and three applications for post-doctoral start-up funding. Professor Maegdefessel's Junior Research Group was positively evaluated and will continue to be funded. The measures in the training program and the Clinical Studies Training Programme continued to be actively used.

At the 4th Munich Young DZHK Meeting, Dr Anne Dueck was elected to succeed Dr Thorsten Kessler as the Young DZHK spokesperson for Munich. In February and July, the 15th and 16th Meeting of the MHA took place.

A Transregio SFB successfully acquired by Professor Engelhardt (TUM) and Professor Dimmeler (Rhine Main) strengthens the cardiovascular network between the two locations. At the KUM, Professor Massberg and Professor Bartelt received an ERC Advanced and Starting Grant, respectively. Dr Clauß (KUM) raised almost € 1 million in the funding program "Junior Research Group Cardiovascular Diseases" at the Corona Foundation and received approval for an ERA-CVD project. Professor Weber was accepted into the National Academy of Sciences Leopoldina.



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

Partner site management

Katharina Schulenburg (partner site manager), Linda Sulzmann (partner site administrator), University Hospital Frankfurt

Partner institutions at the DZHK partner site

Rhine Main

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

RESEARCH FOCUS AT THE DZHK

The focus of the DZHK Rhine Main site is to identify 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 heart muscle tissue. Clinical programs aim to develop imaging tools for diagnosis and therapy monitoring of the heart and elucidate myovascular interactions in cardiovascular diseases.

In the Excellence Program, four postdoctoral and two rotation grants for physicians were obtained. The first Young DZHK Retreat of the partner site took place in October.

In clinical research, our scientists gained new insights into diagnostic MRI examinations in angina pectoris (NEJM 2019). In research on clonal hematopoiesis, significant progress was made (EHJ 2019; Hematologica 2019), showing that mutations in hematopoietic stem cells lead to the expansion of the mutated cells, contributes to a poor prognosis in patients with heart failure (JAMA Cardiology 2019). The project for special statistical evaluation of data from the German Aortic Valve Registry (GARY) confirmed low mortality rates after TAVI or SAVR interventions in low-risk patients (EHJ 2019). Furthermore, the molecular effects of e-cigarette consumption concerning oxidative stress and vascular dysfunction were investigated and successfully published (EHJ 2019).

Samples from patients with rare diseases (Kerckhoff Clinic), CMR examinations, and fibroscans (Mainz) were added to the biomarker registries.

In clinical research, Rhine Main successfully recruited for ten DZHK intervention studies and one study in the follow-up phase during the reporting period.

ACRONYMS

ACS	Acute coronary syndrome	ERC	European Research Council
ADP	Adenosine diphosphate	ESC	European Society of Cardiology
BHF	British Heart Foundation	EU	European Union
BIH	Berlin Institute of Health	FMM	Funding Management Department
BIMSB	Berlin Institute for Medical Systems Biology	FTE	Full-time equivalents
BMBF	Federal Ministry of Education and Research	GAIN	German Academic International Network
CaMKII	Calcium/calmodulin-dependent protein kinase II	GRS	Guideline-relevant study
CAU	Christian-Albrechts-University of Kiel	HBCG	Heart and Brain Center Göttingen
CHIP	Clonal hematopoiesis of indeterminate potential	HDAC4	Histone deacetylase 4
CSG	Clinical Study Group	HD/MA	Heidelberg/Mannheim (DZHK partner site)
CT	Computer tomography	HGF	Helmholtz Association of German Research Centres
DCM	Dilatative cardiomyopathy	HMGU	Helmholtz Centre Munich – German Research Centre for Health and the Environment
DGIM	German Society for Internal Medicine	ICD	Implantable cardioverter defibrillator (mini defibrillator)
DGK	German Cardiac Society	IGFBP	Insulin growth factor binding proteins
DFG	German Research Foundation	IDMS	Image Data Management System
DHF	Dutch Heart Foundation	IF	Impact factor
DHM	German Heart Centre Munich	IT	Information technology
DHZB	German Heart Centre Berlin	KHK	Coronary heart disease
DIfE	German Institute of Human Nutrition	KUM	Hospital of Ludwig Maximilian University of Munich
DKFZ	German Cancer Research Centre	LEAP	Low-energy anti-fibrillation pacing
DPZ	German Primate Centre, Leibniz Institute for Primate Research	LIMS	Laboratory Information and Management System
DSIM	German Foundation for Internal Medicine	LMU	Ludwig –Maximilian University Munich
DZD	German Center for Diabetes Research	MDC	Max Delbrück Center for Molecular Medicine
DZG	German Centers for Health Research	MHA	Munich Heart Alliance
DZHI	Comprehensive Heart Failure Center Wuerzburg	miRNA	MicroRNA
DZHK	German Centre for Cardiovascular Research	miR-92a	MicroRNA-92a
ECRC	Experimental and Clinical Research Center	MPIB	Max Planck Institute of Biochemistry
ECS	Early clinical study	MPIDS	Max-Planck-Institute for Dynamics and Self-Organization
EKG	Electrocardiogram		
EMBL	The European Molecular Biology Laboratory		
ERA-CVD	European Research Area Network on Cardiovascular Diseases		

ACRONYMS

MRI	Klinikum rechts der Isar
MRT	Magnetic resonance tomography
NFDI	National Research Data Infrastructure
NHS	National Health Service
NUM	University Medicine Network
OP	Operating room
ORC	OMICs Use and Access Committee
PCR	Polymerase chain reaction
PI	Principal Investigator
PRD	Periodic Repolarization Dynamics
RCC	Research Coordinating Committee
RKI	Robert Koch Institute
SE	Shared Expertise
SOP	Standard Operating Procedure
StM	Site Management
TRG	Translational Research Group
TRP	Translational Research Project
TUM	Technical University Munich
U&AC	Use & Access Committee
UKE	University Hospital Hamburg-Eppendorf
UMG	University Medical Centre Göttingen
WGCR	Working Group Clinical Research
✓	Goal achieved
↻	In progress
—	Goal not reached

IMPRINT

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German Centre for Cardiovascular Research (DZHK)

Potsdamer Str. 58, 10785 Berlin

Ph. +49 30 3465529-01

Email: info@dzhk.de

Board of Directors: Thomas Eschenhagen, Steffen Massberg, Thomas Sommer

Managing Director: Joachim Krebsler

Editorial team: Cordula Baums (MasterMedia GmbH), Sarah Mempel, Sandra Petzold, Christine Vollgraf

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DZHK

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

German Centre for Cardiovascular Research e.V. (DZHK)

Potsdamer Str. 58, 10785 Berlin

Phone: +49 30 3465529-01

www.dzhk.de

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