



**DZHK**  
Deutsches Zentrum für  
Herz-Kreislauf-Forschung



DEUTSCHE ZENTREN DER  
GESUNDHEITSFORSCHUNG

# German Centre for Cardiovascular Research

ANNUAL REPORT

2022



**The DZHK is the largest research institution for cardiovascular diseases in Germany.**

Our goal is to promote scientific innovations and bring them rapidly into clinical application and therefore into patient care, in order to improve prevention, diagnosis and treatment of cardiovascular diseases.

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# ..... Foreword

In the first year after the pandemic, the focus at the DZHK was on networking and collaboration – in addition to the now-established online formats, we are again using face-to-face meetings for this purpose. One highlight was our 10<sup>th</sup> anniversary, which we celebrated together with three other German Centers for Health Research (DZG) in May 2022 in Berlin with many guests. In September, we met again with great enthusiasm for the first time in two years for our annual DZHK Retreat in Potsdam, where we also discussed new topics, such as the gender career gap in cardiovascular research. The retreat and the Young DZHK Retreat are the most important networking events in the DZHK, which will be pursued in the coming years.

Translation can be more successful if we use the entire network and pool resources. That is why we announced the DZHK Innovation Clusters for the first time this year. In this way, we support larger collaborative projects on urgent topics in cardiovascular research with national and international impact. The subjects were mutually identified in advance with the partner sites, whereas the first round resulted in the investigation of nucleic acid therapies and the heart-brain axis.

The collaboration between the DZGs is also now well established. For the first time, cross-DZG projects have been announced in which scientists from different disciplines will work closely together on the key topics relevant to many diseases, such as "gene and cell therapy" and "the microbiome." A joint virtual DZG office has professionalized the coordination of the collaboration.

In the reporting year, we finally started preparing for an important event for the DZHK – the external evaluation at the beginning of 2024. Detailed reviews and strategic considerations will help us position ourselves even better for the future challenges of translational cardiovascular research.

Our Board of Directors and management team would like to thank everyone who has done outstanding work for the DZHK over the past year.



**Stefanie Dimmeler**  
Spokesperson of the Board  
of Directors



**Steffen Massberg**  
Board of Directors



**Thomas Sommer**  
Board of Directors



**Katharina Eulenburg**  
Managing Director

# 10 Years of DZHK: We Celebrated our Birthday!!

“The  
centers  
are  
pacesetters  
in health  
research.”



Federal  
Research  
Minister Bettina  
Stark-Watzinger

## PACESETTERS IN HEALTH RESEARCH

Four of six DZGs celebrated their 10th birthday in May 2022 with a grand ceremony in Berlin: The German Consortium for Translational Cancer Research (DKTK), the German Center for Cardiovascular Research (DZHK), the German Center for Lung Research (DZL) and the German Center for Infection Research (DZIF).



DZIF scientist  
and virologist  
Christian Drosten (l.)  
from Berlin's Charité was  
a guest on stage and  
later at the  
get-together.

Around 200  
guests were present  
at the two-hour ceremony  
and the following celebra-  
tion in Berlin's Radial-  
system on the banks of  
the Spree River.



In a boardroom  
discussion, they talked  
about promoting spin-offs  
and getting industry part-  
ners earlier on board: Stefanie  
Dimmeler, Spokesperson of the  
DZHK Board of Directors and  
Dirk Busch, DZIF Board of  
Directors.



DEUTSCHE ZENTREN DER  
GESUNDHEITSFORSCHUNG

“The Corona pandemic has shown how important it is to bring research results into clinical practice in a quick and interdisciplinary way.”



Hessian Minister of Science  
Angela Dorn

Click here for the anniversary celebration with photos, films, and a follow-up report:  
[deutschezentren.de/en/10-years-of-dzg/](https://deutschezentren.de/en/10-years-of-dzg/)

BioNTech co-founder and chief medical officer  
Özlem Türeci



Prominent guests from science and politics congratulated on the 10<sup>th</sup> anniversary.



Former Federal Minister of Research  
Annette Schavan

**2017**

First international cooperation with the British Heart Foundation and Hartstichting

**2015**

Launch of the first two Junior Research Groups

**2013**

Launch of the Clinical Research Platform

**2014**

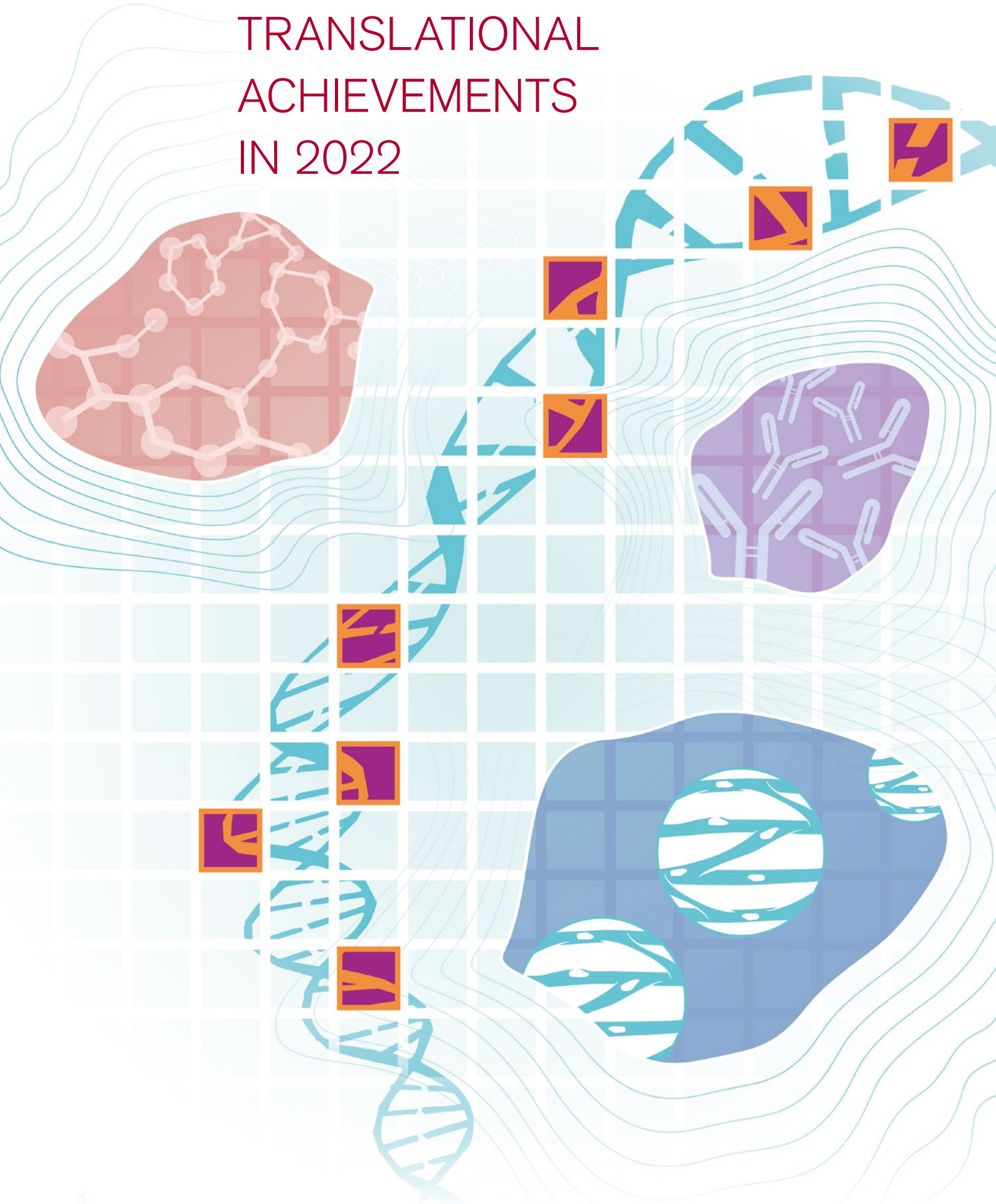
First clinical trials include patients

**2012**

Start of the DZHK Biobanks



# TRANSLATIONAL ACHIEVEMENTS IN 2022





## MYOCARDIAL DISEASE

When heart cells  
no longer "listen"

What do heart muscle cells need to be healthy and functional? Obviously, a well-performing "communication". At the cellular level, communication means the exchange of molecules and messenger substances. A research team from Frankfurt has investigated the impaired communication in the diseased heart.

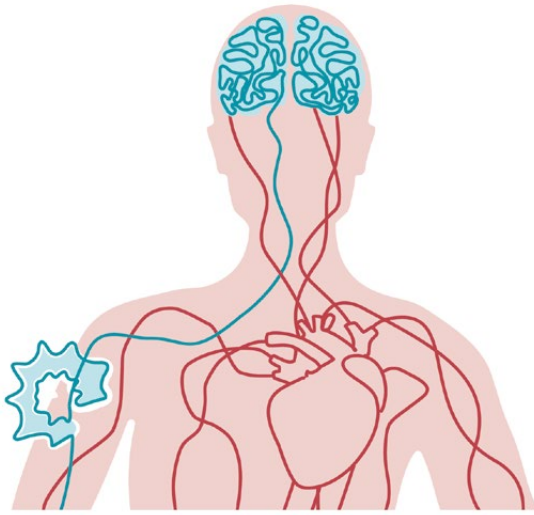
Heart tissue consists of different cell types. These can be distinguished by single-cell sequencing because they activate – meaning they express – distinct genes. First, the scientists assigned the respective cells to heart tissue-typical cell types, such as cardiac muscle cells, connective tissue cells, endothelial cells (lining the blood vessels), and immune cells. They further determined the expression of additional genes for each cell type and compared these with a data set from healthy heart tissue.

The researchers noticed cardiac muscle cells in the diseased heart communicate significantly less with other cell types. In particular, the gene for the receptor EPHB1 was only expressed to a very low degree in diseased heart cells, i.e., it had virtually stopped working. However, cardiac muscle cells communicate with endothelial cells via this receptor. The researchers hypothesize that the cardiac muscle cells no longer "hear" what the endothelial cells "have to say," which doesn't suit them. An external regulation of the newly discovered mechanism could contribute to a therapy targeting the diseased heart muscle.

Partner site project | FKZ: 81Z0200104  
Project lead | Andreas Zeiher (Rhine-Main)

📌 A human cell atlas of the pressure-induced hypertrophic heart. *Nature Cardiovascular Research*, 14 February 2022

Nature  
Cardiovascular  
Research



## ATHEROSCLEROSIS

# Blood vessels communicate with the brain

Blood vessels become inflamed when plaques build up in arteries (atherosclerosis). The wall of arteries has three components: an outer, middle, and inner layer. Plaques are found on the inside. Nerve cords do not traverse them. Whether the peripheral nervous system comes into contact with blood vessels in atherosclerosis has not been investigated yet.

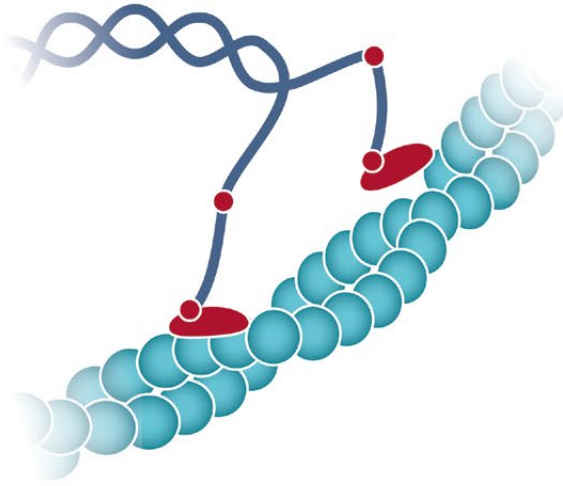
A DZHK team from the Munich site discovered that molecular sensors called receptors play a central role. They are located on the outer wall of the vessels and can detect plaques. By identifying messenger inflammation substances, they can detect where the vessels are inflamed. The receptors then send electrical signals down the nerve pathways to the brain. The brain processes the signals and returns a stress signal to the inflamed blood vessel. This process negatively affects inflammation, and atherosclerosis worsens.

DZHK researchers from the Munich partner site have described this process for the first time in the journal "Nature." When the electrical connection of diseased arteries to the brain was cut in mice, atherosclerosis was less pronounced than in controls. The findings could potentially develop a causal therapy for atherosclerosis.

Partner site project | FKZ: 81Z0600202  
Project lead | Christian Weber (Munich)

📌 Neuroimmune cardiovascular interfaces control atherosclerosis. *Nature*, 27 April 2022





## DILATED CARDIOMYOPATHY

When the heart weakens, the molecular motors are revved up

It's a paradox: In patients with a specific form of heart failure, dilated cardiomyopathy (DCM), the molecular motors in the heart muscle cells are chemically altered to produce more power. This is what researchers from the DZHK partner site in Heidelberg have discovered.

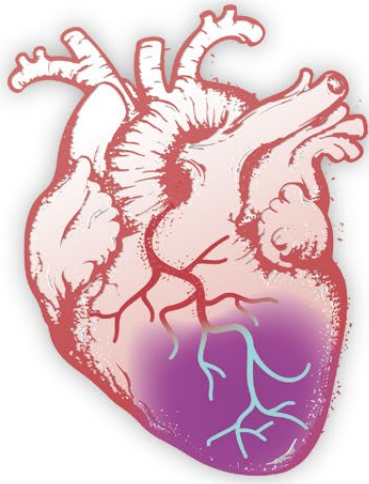
As molecular motors, myosins ensure uniform contraction of the heart muscle cells. By changing their shape, they shift certain cytoskeleton elements, the actin filaments, against each other: the heart muscle cell contracts. Chemical modifications of these proteins are an essential regulatory mechanism for cardiac muscle cells to respond to changes in stress. So-called phosphorylations, the binding of additional phosphate groups to the protein, have a positive effect on the contraction force of the cells and provide a force boost during more substantial stress.

In DCM patients, a small protein of the contraction apparatus, the essential myosin light chain (ELC), was equipped with additional phosphate groups. The enzyme NIMA-associated kinase 9 (NEK9) was responsible for this. It is found in high amounts in the human left heart muscle, binds to the ELC protein, and regulates phosphorylation. According to the researchers, the regulatory mechanism could be used for drug therapy in heart failure by supporting cardiac function via increased ELC phosphorylation.

Partner site project | FKZ: 81Z0500102  
Project lead | Benjamin Meder (Heidelberg/Mannheim)

📌 NIMA-related kinase 9 regulates the phosphorylation of the essential myosin light chain in the heart. *Nature Communications*, 20 October 2022

Nature  
Communications



## HEART ATTACK

# Reducing sequelae after a heart attack

A DZHK research team at the University Medical Center of the Johannes Gutenberg University Mainz has discovered a new signaling pathway of the coagulation system that controls scar formation after a heart attack. If this signaling pathway could be inhibited, heart attacks could heal with less subsequent damage.

If the blocked coronary vessel is not opened immediately after a heart attack, heart tissue dies. As the body "works to clean up" the spot, inflammatory cells migrate into the area, and scar tissue forms. The processes can spread to the peripheral areas of the infarct and even to more distant regions of the heart. This can lead to a particularly severe form of ischemic heart failure.

In the tissue of patients with severe ischemic heart failure, the researchers found an increased number of proteins involved in coagulation and fibrosis processes, which also occur in acute infarction. Monocytes played a role in signal transduction of the inflammatory processes. When the researchers blocked specific receptors of the monocytes, less growth factor TGF- $\alpha$ 1 was formed, consequently leading to less excessive fibrosis. This resulted in better cardiac performance and less mortality in the mouse model.

A long-known anticoagulant drug called NAPc2 can inhibit the newly found signaling pathway and would thus be a drug candidate to treat or even prevent chronic ischemic heart failure.

Promotion of Women Scientists

Project lead

Postdoc Start-up Grant

Project lead

FKZ: 81X3210106

Susanne Karbach (Rhine-Main)

FKZ: 81X3210105

Michael Molitor (Rhine-Main)

📌 Targeting myeloid cell coagulation signaling blocks MAP kinase/TGF- $\beta$ 1-driven fibrotic remodeling in ischemic heart failure. *J Clin Invest*, 22 December 2022

The Journal  
Of Clinical  
Investigation

## PERSONALIZED THERAPY


## Many different gene variants in dilated cardiomyopathy

Cardiomyopathies are not uniform diseases – different genetic defects weaken the heart muscles of the respective patients. This was reported in "Science" by an international consortium in which DZHK researchers from Berlin played a significant role.

The consortium studied 880,000 individual cells from 61 diseased hearts and 18 healthy reference hearts. The researchers focused on hereditary dilated cardiomyopathy (DCM). This is a form of heart failure that leads to heart transplantation in severe cases. They found that different mutations in different proteins led to various functional disorders of the heart. For example, in some forms, the composition of subtypes of connective tissue cells changes. In another form, which is associated with arrhythmias, heart muscle cells are lost and replaced by fat and connective tissue cells.

The scientists analyzed the vast amounts of data using bioinformatic methods. An AI algorithm can thus predict with high probability which mutation is involved in each case based on the specific gene patterns in the different cell types. The long-term goal of this research is a personalized therapy that is tailored to the distinct gene mutation – and would thus be more effective and have fewer side effects.

DZHK-BHF-Project | FKZ: 81X2100155  
Project lead | Norbert Hübner (Berlin)

 Pathogenic variants damage cell composition and single cell transcription in cardiomyopathies.  
*Science*, 5 August 2022





## REGENERATION OF THE HEART

# Exercise promotes new cardiomyocyte formation in older mice

Physical activity boosts the formation of new heart muscle cells (cardiomyogenesis) in older hearts – at least in mice. This was found by a research team from the DZHK partner site in Heidelberg/Mannheim. Mammals' hearts can only regenerate heart muscle cells to a minimal extent. In old age, this regenerative capacity decreases further, and at the same time, the risk of cardiovascular diseases increases.

The researchers have already shown that continuous exercise effectively stimulates cardiomyogenesis in younger mice; now they have investigated these findings in older specimens as well. To do this, they had the animals "exercise" in a running wheel and determined the new formation of heart muscle cells using imaging, histological, and genetic techniques. They compared the results with a "sedentary" control group and a group of younger animals.

The calculated number of heart muscle cells increased by 2.3 percent annually in the "exercising" group of older mice and not at all in the "sedentary" control group. A procedure study with young animals showed that they achieved an annual rate of 7.5 percent of new heart muscle cells through exercise, compared to 1.63 percent in the "sedentary" group. Molecular analyses revealed that the RCAN1.4 gene was increasingly activated in the older mice due to the exercise program. Further studies will show whether the findings can be used to derive possibilities for the prevention and therapy of heart disease in humans.

Promotion of Women Scientists  
Project lead

FKZ: 81X3500120

Carolin Lerchenmueller (Heidelberg/Mannheim)

📌 Restoration of cardiomyogenesis in aged mouse hearts by voluntary exercise. *Circulation*, 6 July 2022





## PREVENTION OF SUDDEN CARDIAC DEATH

# Implanted monitor predicts complications after heart attack

After a heart attack, many patients experience a reduction in cardiac output, known as ejection fraction. If this is below 35 percent, those affected often suffer malignant arrhythmias, which is why they are implanted with a defibrillator as a preventive measure. However, the vast majority of fatal and non-fatal complications after an infarction occur in a large group of patients with an ejection fraction of over 35 percent, for whom there are no specific preventive measures.

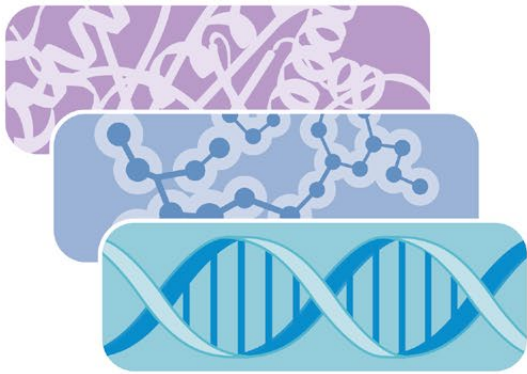
Most often, malignant arrhythmias announce themselves through smaller, less noticeable arrhythmias. Therefore, the SMART-MI-DZHK9 study investigated whether a small, implanted monitor can detect such early arrhythmias in patients with intermediate cardiac output. The study included only those patients in whom the ECG also indicated nerve damage from the infarction, i.e., what is known as so-called cardiac autonomic neuropathy. These patients are particularly at risk for arrhythmias and other complications.

Within 21 months, predefined rhythm events were registered in 60 patients in the cardiac monitor group and in comparison, only in twelve patients in the control group receiving a regular follow-up. Thus, an implanted monitor is suitable for detecting early disturbances of the heart rhythm in the vulnerable group of patients with intermediate ejection fraction. Appropriate preventive measures can then be taken in these individuals.

<p>Clinical Study Principal investigators</p>	<p>SMART-MI-DZHK9 Axel Bauer, Stefan Kääh, Steffen Massberg (Munich)</p>
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📌 Telemedical cardiac risk assessment by implantable cardiac monitors in patients after myocardial infarction with autonomic dysfunction (SMART-MI-DZHK9): a prospective investigator-initiated, randomised, multicentre, open-label, diagnostic trial. *The Lancet Digital Health*, February 2022





## ATRIAL FIBRILLATION

# Risk scores for atrial fibrillation established

Atrial fibrillation affects more than 30 million people worldwide. To better treat this and other cardiovascular diseases, it is crucial to understand them in detail. For this reason, scientists wanted to find out whether, in patients with atrial fibrillation, correlations can be observed between genetics and molecular changes in human heart tissue.

For the molecular investigation of cardiovascular diseases, biomedical research intensively studies nucleic acids, proteins, lipids, and other metabolites using high-throughput analytical methods. However, the data obtained in this way can only present a one-sided picture, which is why a combining approach is needed. To get an overview, the researchers used a complex analytical procedure – a so-called multi-omics analysis, which captures data from several molecular levels, thus representing the interconnectedness between these levels.

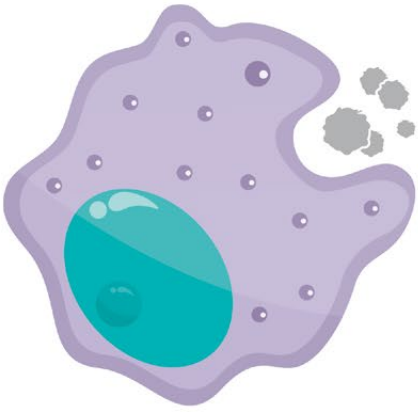
The multi-omics approach in atrial fibrillation is unprecedented and enables the identification of genes and pathophysiological pathways in cardiovascular disease, even in smaller datasets. A DZHK team from the Hamburg/Kiel/Lübeck site has succeeded in identifying genetic alterations, so-called single nucleotide polymorphisms (SNPs), which are associated with atrial fibrillation. These gene sequences can now be used to calculate a risk score and thus contribute to a more accurate prediction of the risk of atrial fibrillation.

Partner site project | FKZ: 81Z1710103  
Project lead | Renate Schnabel (Hamburg/Kiel/Lübeck)

📌 Tissue-specific multi-omics analysis of atrial fibrillation. *Nature Communications*, 21 January 2022

Nature  
Communications





## SUDDEN CARDIAC DEATH

# Scavenger cells protect against life-threatening cardiac arrhythmias

After a heart attack, the risk of sudden cardiac death increases. This is because the reduced supply of oxygen-rich blood to the heart muscle can lead to life-threatening cardiac arrhythmias, so-called ventricular tachycardias. At the same time, the composition of the white blood cells in the heart muscle changes. White blood cells are cells of the immune system.

A DZHK team from the Berlin partner site has discovered in an animal model that specific white blood cells, the neutrophils, increase dangerous rhythm disturbances. When the researchers removed the neutrophils close to the heart muscle cells that were out of sync, the dangerous ventricular tachycardia was reduced.

Other white blood cells, the macrophages, on the other hand, had a protective function. Macrophages are also called phagocytes because they can actively take up particles into their cell interior. Apparently, this process, called phagocytosis, keeps the heart muscle cells from dying. It also eliminates cells that are already dead, which prompts wound healing after a heart attack. Thus, targeting the two types of white blood cells represents a potential therapeutic approach to reduce the risk of sudden cardiac death.

Postdoc Start-up Grant | FKZ: 81X3100209  
Project lead | Jana Grune (Berlin)

🚩 Neutrophils incite and macrophages avert electrical storm after myocardial infarction.  
*Nature Cardiovascular Research*, 11 July 2022

Nature  
Cardiovascular  
Research

# Publications & Awards



## PUBLICATIONS

In 2022, the total number of publications with DZHK affiliation, i.e., mentioning the DZHK, slightly increased to 1,564 compared to the previous year.

The number of publications in high-impact journals (with an impact factor > 10) was 189 (2021: 195).

A list of publications can be found on our website:

[dzhk.de/en/research/research-focus/publications/publications-2022/](https://dzhk.de/en/research/research-focus/publications/publications-2022/)

<sup>1</sup> including Lancet Neurology, Lancet Respiratory Medicine, Lancet Planetary Health

<sup>2</sup> including JAMA Cardiology, JAMA Internal Medicine

<sup>3</sup> including JACC Cardiovascular Imaging

<sup>4</sup> including Science Translational Medicine, Science Advances

### Overview: Publications

	Number 2022	2021
Total publications	1,564	1,515
of which:		
First authorship of a DZHK PI	40	58
Last authorship of a DZHK PI	276	280
First authorship of a YOUNG DZHK member	319	307
First authorship of a DZHK scientist	104	119
Last authorship of a DZHK scientist	398	357
Publication involving several DZHK partner sites	156	168
<b>Publications published in:</b>		
Nature Publishing Group	63	44
Cell Press	7	0
NEJM, Lancet <sup>1</sup> , JAMA <sup>2</sup>	9	20
Circulation, Circ Res, EHJ, JCI, JACC <sup>3</sup>	103	124
Science <sup>4</sup>	7	7
<b>Total</b>	<b>189</b>	<b>195</b>



## PAPERS OF THE MONTH 2022

### JANUARY

**Tissue-specific multi-omics analysis of atrial fibrillation.** Assum, I.\* (Technical University of Munich; Helmholtz Munich – German Research Center for Environmental Health), Krause, J. (University Heart & Vascular Center Hamburg), Zeller, T.\* (University Medical Center Hamburg-Eppendorf, UKE), Schnabel, R. B.\* (University Medical Center Hamburg-Eppendorf, UKE), Heinig, H.\* (Technical University of Munich; Helmholtz Munich – German Research Center for Environmental Health), et al. [Nature Communications](#). 🏠 Hamburg/Kiel/Lübeck, Greifswald, Munich

### FEBRUARY

**A human cell atlas of the pressure-induced hypertrophic heart.** Nicin, L.\* (Johann Wolfgang Goethe University Hospital Frankfurt), Schroeter, S. M.\* (Johann Wolfgang Goethe University Hospital Frankfurt), Glaser, S. F.\* (Johann Wolfgang Goethe University Hospital Frankfurt), et al. [Nature Cardiovascular Research](#). 🏠 Rhine-Main, Hamburg/Kiel/Lübeck, Heidelberg/Mannheim

### MARCH

**Protective immune trajectories in early viral containment of non-pneumonic SARS-CoV-2 infection.** Pekayvaz, K.\* (Ludwig Maximilian University of Munich), et al. [Nature Communications](#). 🏠 Munich

### APRIL

**Loss of endothelial cytochrome P450 reductase induces vascular dysfunction in mice.** Malacarne, P. F. (Johann Wolfgang Goethe University Hospital Frankfurt), et al. [Hypertension](#). 🏠 Rhine-Main

### MAY

**Neuroimmune cardiovascular interfaces control atherosclerosis.** Mohanta, S.K.\* (Ludwig Maximilian University of Munich), Peng, L.\* (Guizhou University of Traditional Chinese Medicine), Weber, C.\* (Ludwig Maximilian University of Munich), Lembo, G.\* (Sapienza University of Rome), Carnevale, D.\* (Sapienza University of Rome), Habenicht, A. J. R.\* (Ludwig Maximilian University of Munich), et al. [Nature](#). 🏠 Munich

### JUNE

**A YAP/TAZ-TEAD signalling module links endothelial nutrient acquisition to angiogenic growth.** Ong, Y. T. (Max Planck Institute for Heart and Lung Research), et al. [Nature Metabolism](#). 🏠 Berlin, Rhine-Main

Each month, the DZHK Board of Directors selects a paper of the month which is announced in the DZHK newsletter and published on the DZHK website.

🏠 = DZHK partner sites involved

### JULY

**Origin and function of activated fibroblast states during zebrafish heart regeneration.** Hu, B.\* (Max Delbrück Center for Molecular Medicine in the Helmholtz Association), Lelek, S.\* (Max Delbrück Center for Molecular Medicine in the Helmholtz Association), Spanjaard, B.\* (Max Delbrück Center for Molecular Medicine in the Helmholtz Association) et al. [Nature Genetics](#). 🏠 Berlin, Rhine-Main

### AUGUST

**Smartphone-based screening for atrial fibrillation: a pragmatic randomized clinical trial.** Rizas, K. D.\* (Ludwig Maximilian University of Munich), Freyer, L.\* (Ludwig Maximilian University of Munich), Sappler, N.\* (Medical University of Innsbruck), et al. [Nature Medicine](#). 🏠 Munich

### SEPTEMBER

**Contractile force of transplanted cardiomyocytes actively supports heart function after injury.** Stüdemann, T. (University Hospital Hamburg-Eppendorf), et al. [Circulation](#). 🏠 Hamburg/Kiel/Lübeck

### OCTOBER

**NIMA-related kinase 9 regulates the phosphorylation of the essential myosin light chain in the heart.** Müller, M. (Heidelberg University Hospital) et al. [Nature Communications](#). 🏠 Heidelberg/Mannheim

### NOVEMBER

**Lamin A/C-dependent chromatin architecture safeguards naive pluripotency to prevent aberrant cardiovascular cell fate and function.** Wang, Y. (University Medical Center Mannheim) et al. [Nature Communications](#). 🏠 Heidelberg/Mannheim

### DECEMBER

**Targeting myeloid cell coagulation signaling blocks MAP kinase/TGF-beta1 driven fibrotic remodeling in ischemic heart failure.** Garlapati, V. (University Medical Center of the Johannes Gutenberg University Mainz) et al. [Journal of Clinical Investigation](#). 🏠 Rhine-Main

\* These authors contributed equally.



## PRIZES, GRANTS, PERSONALIA

(In alphabetic order)

**Dr. Philipp Bengel & Petros Tirilomis**  
(Göttingen)

Oskar Lapp Research Award of the German Society of Cardiology (DGK)

**Prof. Stefanie Dimmeler**  
(Rhine-Main)

Otto Warburg Medal of the Society for Biochemistry and Molecular Biology (GBM)  
ERC (European Research Council) Advanced Grant

**Prof. Ingrid Fleming**  
(Rhine-Main)

Ernst Jung Prize for Medicine

**Prof. Matthias Gorenflo**  
(Heidelberg/Mannheim)

Prize of the Fritz Acker Foundation of the DGK

**Prof. Michael Gotthardt**  
(Berlin)

ERC Advanced Grant

**Prof. Florian Leuschner**  
(Heidelberg/Mannheim)

Arthur Weber Prize of the DGK

**Dr. Jan Philipp Junker**  
(Berlin)

ERC Consolidator Grant

**Prof. Thorsten Kessler**  
(Munich)

ERC Starting Grant

**Dr. Gabriele Schiattarella**  
(Berlin)

ERC Starting Grant

**Prof. Fabian Theis**  
(Munich)

ERC Advanced Grant

**Prof. Christian Weber**  
(Munich)

ESC William Harvey Lecture Award  
in Basic Sciences

**Prof. Andreas Zeiher**  
(Rhine-Main)

ERC Advanced Grant

**Prof. Tanja Zeller**  
(Hamburg/Kiel/Lübeck)

Albert Fraenkel Prize of the DGK



Prof. Florian Leuschner (m.) at the award ceremony of the Arthur Weber Prize.



Prof. Ingrid Fleming (m.) at the award ceremony of the Ernst Jung Prize for Medicine.



# Preclinical Research



New technologies and findings from basic research are the basis for translational projects at the DZHK. To boost translational research in a targeted way, we use various funding instruments.

## Translational Research Projects

Translational Research Projects (TRP) bridge the gap between basic research and the first clinical trials. This phase is generally a weak point in the translational chain, which is why the DZHK focuses on such projects.

In the year under review, ten TRPs were running, and three were completed. Among the completed ones is the project "GMP production of artificial heart tissue for use in myocardial infarction" (Wolfram-H. Zimmermann, Göttingen); see figure p. 20. In the project, biological heart patches, were produced in accordance with current Good Manufacturing Practice (cGMP) for the BioVAT-HF-DZHK20 clinical trial that started directly afterwards. These formed the basis for the first application in humans. Thus, two decisive translational steps were carried out in succession, which would not have been possible without the DZHK.

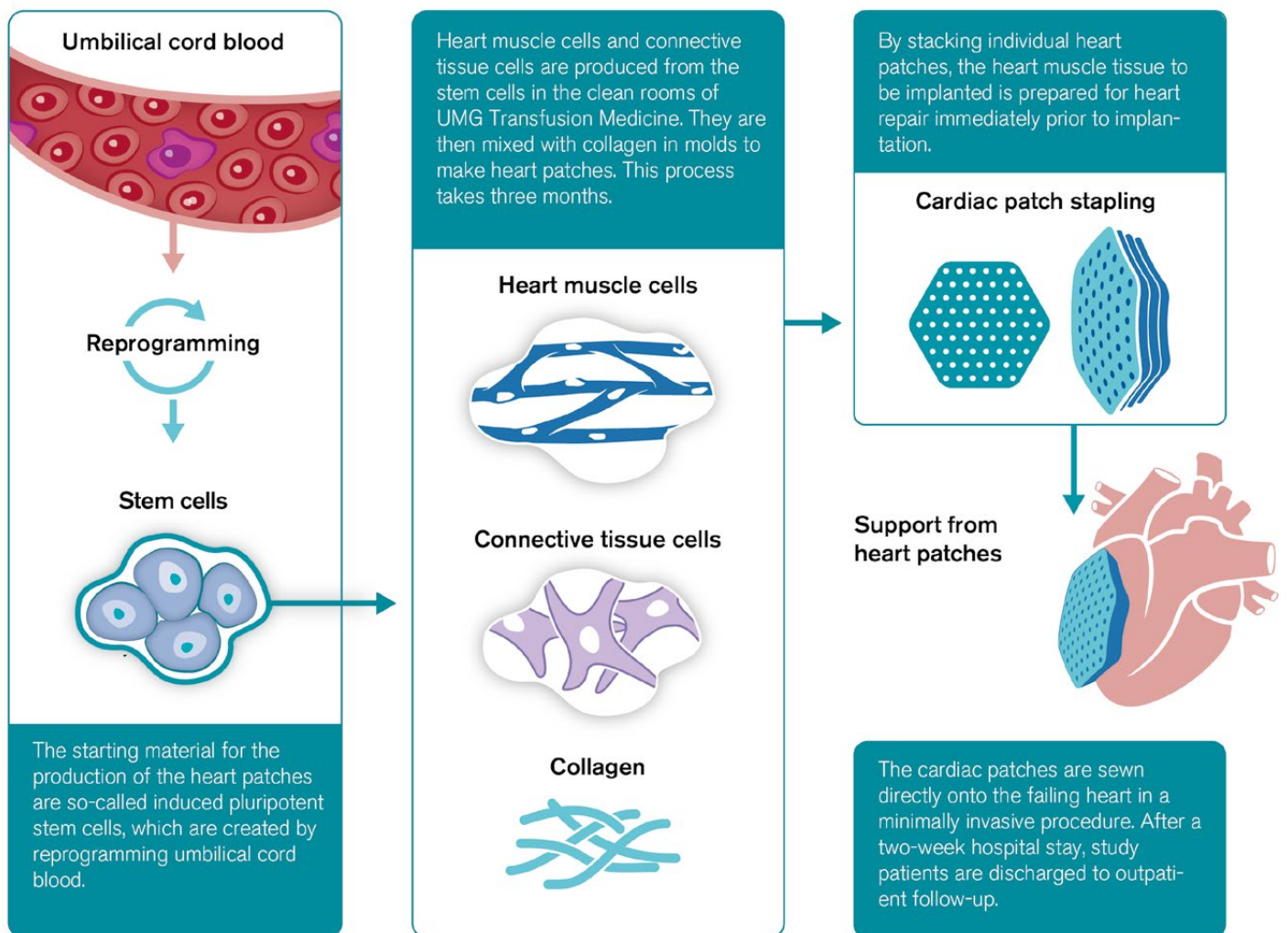


Fig.: Production of biological tissue patches at the University Medical Center Göttingen (UMG) as part of a translational research project: the patches are currently being tested on human subjects for the first time in the BioVAT-DZHK20 clinical trial, also funded by the DZHK.

## TRP Starter Grants

Specific requirements are necessary for a TRP to be approved. First and foremost, a proof-of-concept must be available, and preliminary regulatory considerations must have been made. Since the preparatory steps for a TRP are quite challenging, we introduced a new instrument in 2022 to support these steps: TRP Starter Grants.

With this funding, scientists can prepare their project ideas scientifically and validate early research results. The funding provides expert advice and financial support of up to €150,000 for a maximum duration of 18 months. A total of eleven TRP Starter Grants were applied for in the reporting year, of which three were approved. One of these is headed by the Lübeck biologist Zouhair Aherrahrou:

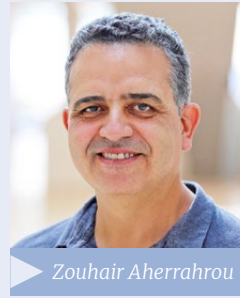
## TRP Starter Grant: a jump-start to the clinical phase

### Non-reclosable – protection against restenosis in CHD

In patients with coronary heart disease (CHD), the coronary arteries narrow due to deposited fatty tissue. When a narrowed blood vessel is reopened, and a stent is placed, small injuries to the inner vessel wall often occur. The body responds by remaking parts of the injured layer. Over time, this causes the blood vessel to narrow again. This process, called restenosis, is one of the most common clinical complications. Zouhair Aherrahrou, a DZHK scientist at the Institute of Cardiogenetics at the University of Lübeck, has been researching a gene related to CHD together with Jeanette Erdmann\* since 2011. In collaboration with Oliver Müller from the University Hospital Schleswig-Holstein, Campus Kiel, the team is using a promising RNA-based therapeutic target to prevent such restenosis in the future. The TRP Starter Grant supports Aherrahrou in optimally preparing his treatment idea for the preclinical phase. In addition to financial support for one and a half years, he will also receive expert advice. “When applying for the TRP Starter Grant, you must present the planned clinical follow-up project to a committee. Among others, scientists from industry sit on this committee and assess whether the outlined idea has potential for the preclinical phase, but also provide valuable suggestions for improvement,” says Aherrahrou.

### Knockout protects against restenosis

Mice lacking the ADAMTS7 gene, known as knock-out mice, are protected from having a blood vessel reocclude. The fact that these knock-out mice were completely healthy made the gene, or its product, an interesting therapeutic target. Aherrahrou and his team developed an inhibitor of



Zouhair Aherrahrou

ADAMTS7 that produces less of the gene product. In a mouse model of atherosclerosis, he has already shown that this inhibitor protects the animals from narrowed vessels. Now, Aherrahrou wants to develop the RNA therapy further to help patients with CHD one day.

### Industry contact and patent planned

“The path from basic research to the patient is long, and for me it is also a completely new world,” says the biologist from Lübeck. The TRP Starter Grant, which started in 2022, arrived just at the right time for him. He plans to use mini pigs in the preclinical phase to test whether his developed inhibitor protects the animals from restenosis. With the TRP Starter Grant, Aherrahrou can test the inhibitor in the laboratory on tissue from the carotid artery of mini pigs. If the results are as good as the data from the mouse, he would like to apply for a TRP project next year. A company from Braunschweig is already supporting the project, and Aherrahrou is also in the process of patenting his idea.

### Inhibition of ADAMTS7 by siRNA to prevent restenosis: first steps towards a preclinical study

Project lead: Zouhair Aherrahrou (Hamburg/Kiel/Lübeck) | Participating scientists: Jeanette Erdmann\*, Oliver Müller (both Hamburg/Kiel/Lübeck partner site) | Duration: 2023–2024 | Budget: €147,747

\* Jeanette Erdmann passed away unexpectedly in summer 2023. For the obituary dated July 11, 2023, see

[dzhk.de/en/the-dzhk/press/article/obituary-of-dzhk-professor-jeanette-erdmann/](https://dzhk.de/en/the-dzhk/press/article/obituary-of-dzhk-professor-jeanette-erdmann/)

These two projects also received a TRP Starter Grant in 2022:

### Development of a novel platelet inhibitor for the prevention and treatment of atherothrombosis

Platelet aggregation inhibitors have been shown to protect against heart attacks and are, therefore, a cornerstone of cardiovascular medicine. They prevent coronary arteries

from closing when atherosclerosis breaks down and activates platelets. However, the use of conventional platelet aggregation inhibitors does not provide complete protection and is associated with bleeding complications. The project team has developed a new platelet inhibitor that prevents plaque-induced platelet aggregation in vitro and arterial thrombosis in a mouse model without interfering with hemostasis.

The group plans to investigate whether their findings can be translated to the human system. To do so, they plan to reproduce their previous results and generate additional data using alternative measurements of thrombus formation in stromal chamber models. In addition, the scientists will investigate the pharmacodynamics and pharmacokinetics of the new inhibitor.

Project lead: Philipp von Hundelshausen, Christian Weber (Munich) | Participating scientists: Tilman M. Hackeng, Stijn Agten (Cardiovascular Research Institute Maastricht, The Netherlands), Götz Münch (AdvanceCOR GmbH) | Duration: 2023–2024 | Budget: €150,000

### Cardiomyocyte-specific restoration of endogenous transcription of KLF15 as a novel therapeutic concept in heart failure

Many factors, including coronary artery disease and hypertension, contribute to a high prevalence of cardiovascular disease. These are characterized by weakening of the myocardium due to a loss of functional cardiomyocytes. The cause may be a dysregulation of healthy gene transcription. Researchers hypothesize that precise restoration of this healthy transcription may prevent the deterioration of cardiomyocyte function or rescue it from failure. Among these factors, the team of scientists has identified a repressor of disease pathways, Krüppel-like factor 15 (KLF15), which is lost during hypertrophic remodeling of the heart. When a genetic system is used to normalize transcription of KLF15 in cardiac muscle cells, attenuation of the pathological response and preservation of cardiac function is observed in mice. The scientists were also able to replicate the loss of KLF15 and repair the loss in a human heart muscle model. In this project, they will test the safety and efficacy of this novel therapeutic principle in a pig model.

Project lead: Laura C. Zelarayán-Behrend (Göttingen) | Participating scientists: Eric Schoger, Rabea Hinkel (both Göttingen partner site), Lorenz Lehmann (Heidelberg/Mannheim) | Duration: 2023–2024 | Budget: €149,976

## Collaboration with Product Development Unit of DZIF

In 2021, the DZHK and the German Center for Infection Research (DZIF) have agreed on closer collaboration in the development of novel drugs and medical devices. The DZHK's project leaders now can call on the DZIF's Product Development Unit (PDU) for expert advice. In the year under review, two ongoing translational research projects used the PDU's advisory services. The PDU supports the projects in project management and regulatory approval issues.

### Interview on the Product Development Unit



Lars Mägdefessel from the Technical University of Munich

**“We were able to take important steps toward commercialization.”**

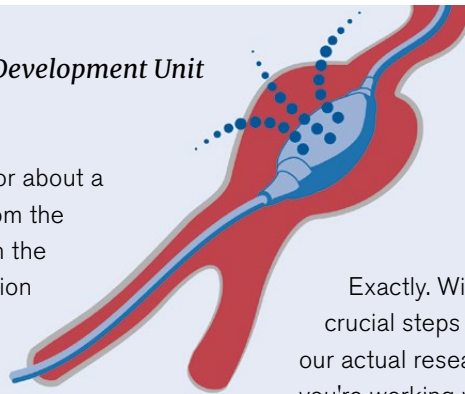
### What is your project about?

We have been conducting research since 2019 in a [Translational Research Project \(TRP\)](#) supported by the DZHK. In this project, we are pursuing an entirely new approach to treat abdominal aortic aneurysms, i.e., vascular outpouchings of the aorta in the abdomen. To prevent them from growing further, we are using a microRNA-based therapy. Using a coated balloon catheter, we can deliver the drug locally into the vessel wall and inhibit microRNA-29b in the aortic tissue. This would be the first approach to inhibit aortic growth with a drug. All approaches to date have been surgical and not without risk to the patient.



### When and why did the Product Development Unit (PDU) come into play?

The PDU has been supporting us for about a year and a half to make the leap from the large animal model to the patient. In the TRP, we have mastered the translation from mouse to pig, and now we are looking at translating to humans to move our research into a clinical trial. To this end, the PDU has brought us together with the BfArM, the German Federal Institute for Drugs and Medical Devices. On the other hand, it has put us in touch with companies helping us, for example, to build a prototype for the balloons. That alone is of high value to us. Also, we highly appreciate advice on contracts and agreements.



### Do you mean you were able to continue to do mainly research and at the same time keep the wheel turning in the direction of the medical device?

Exactly. With the PDU, we were able to take these crucial steps toward commercialization in addition to our actual research. The significant advantage is that you're working with scientists who speak the same language and have the expertise in commercialization and regulatory affairs that basic scientists like me often need to gain. That can speed up projects tremendously.

## DZHK Innovation Cluster

In the year under review, the Board of Directors and the Research Coordinating Committee (RCC) launched a new translational and collaborative funding line. The goal of the "DZHK Innovation Cluster" is to call for collaborative projects on urgent topics in cardiovascular research that have national and international appeal and to which several partner sites can contribute their expertise. In an extensive process in which all partner sites were involved, the following main topics were reconciled.

### Research on nucleic acid therapies

Including the development of non-viral approaches based on oligonucleotides/RNA or viral vectors, and technologies to improve delivery/targeting.

### Exploration of the heart-brain axis

Interplay of heart and brain, e.g., takotsubo cardiomyopathy, stroke heart syndrome, vascular, ventricular, and atrial innervation.

All DZHK registered scientists were eligible to submit an outline in November 2022. The selection process will be completed in the first half of 2023.

## Goals achieved in 2022?



- ✓ Introduced funding for scientific work that serves to prepare a Translational Research Project
- ✓ Established collaboration with the Product Development Unit of the German Center for Infection Research in a cooperation agreement
- ✓ Conducted webinar for technology transfer departments and application consultations of our member institutions to raise awareness of translational project grants

## Goals 2023



- Scouting of translational projects based on PI evaluation
- Decision on a continuation of the DZHK Innovation Cluster call for proposals



# Clinical Research



Clinical trials are a significant focus of the DZHK's research strategy. The financial support for clinical studies of the DZHK amounted to about €5.1 million in the reporting year. Early clinical trials are a crucial step in the translational chain. They are the first step from the laboratory to humans and serve to prove the fundamental applicability of a therapeutic or diagnostic procedure in patients. Early clinical trials are therefore a focus of the DZHK. Another emphasis lies on guideline-relevant studies, to bring a therapy or a new treatment strategy into application.

The results of these studies are incorporated into the groundbreaking treatment guidelines and lead directly to improved treatment for patients. In the reporting year, the DZHK financially requested 25 clinical trials. For their recruitment, 22 studies use the DZHK Clinical Research Platform (see p. 30). In addition, there were three DZHK-associated studies (non-material funding without DZHK funding) whose recruitment is supported by our network.

An overview of all studies can be found in the table on p. 28 and at [dzhk.de/en/research/clinical-research/dzhk-studies/](https://dzhk.de/en/research/clinical-research/dzhk-studies/)



## Results of our funded studies\*

One clinical study of the DZHK was able to publish its results in a high-ranking journal during the reporting year. A large part of the results will influence the treatment of patients.

\*first publications only

### SUDDEN CARDIAC DEATH

#### Implantable cardiac monitors in high-risk post-infarction patients with cardiac autonomic dysfunction (SMART-MI-DZHK9)

An implanted cardiac monitor detects more precursors of dangerous complications in high-risk patients after surviving myocardial infarction than conventional follow-up. The focus was on patients with a mean ejection fraction between 36 and 50 percent and cardiac control disorders caused by the autonomic nervous system. To date, there has been no intensive monitoring for this group. The results of the study suggest that more cases of sudden cardiac death could be prevented in this group with an implanted monitor.

Early clinical trial | Principal investigators: Axel Bauer (Munich and Innsbruck), Stefan Kääb, Steffen Massberg (Munich) | Funding (DZHK): €2.1 million | Participants: 401 | Study centers (Germany): 29 | Publication: Lancet Digit Health, 2022 Feb

Press release dated August 27, 2021, at [dzhk.de/en/news](https://dzhk.de/en/news)

📌 Implanted heart monitor can predict life-threatening complications after heart attack (Study SMART-MI-DZHK9)



## Trials started in 2022

### INFLAMMATORY CARDIOMYOPATHY

#### A multicenter, randomized, double-blind, placebo-controlled trial to evaluate immunosuppressive treatment in patients with chronic virus-negative inflammatory cardiomyopathy (TRINITY-DZHK26)

Approximately 35 percent of patients with heart failure and impaired cardiac function may have chronic myocarditis (CMPi). To determine whether immunosuppressive therapy can improve heart failure, the TRINITY study was initiated. In this study, CMPi is treated with the drugs mycophenolate



mofetil (MMF) and prednisolone and compared to a placebo. Participants will be randomly assigned to one of the two treatment groups and will receive the study drug or a placebo for six months. The effects and side effects are closely monitored. A total of 130 patients from twelve German centers are participating.

Early clinical trial | Principal investigators: Ulrich Grabmaier, Steffen Massberg (Munich) | Funding (DZHK): €1.7 million | Planned participants: 130 | Multicenter

Press release dated June 6, 2023, at [dzhk.de/en/news](https://dzhk.de/en/news)  
 📌 New DZHK Study: Immunosuppressants to improve heart function (TRINITY-DZHK26 trial)

### ATRIAL FIBRILLATION WITH HEART FAILURE

#### Catheter-based ablation of atrial fibrillation compared to conventional treatment in patients with heart failure with preserved ejection fraction (CABA-HFPEF-DZHK27)

This study investigates the effects of catheter ablation in patients with heart failure and atrial fibrillation. About 2.5 million people in Germany suffer from heart failure, and more than one million of them also suffer from atrial fibrillation. The study aims to determine whether catheter ablation improves patients' condition by reducing mortality, stroke incidence, and hospitalization. While atrial fibrillation was previously thought to cause heart failure, it is now known that the opposite can also be true. Atrial fibrillation can worsen heart failure, creating a vicious cycle. Catheter ablation aims to obliterate the heart tissue that interferes with the rhythm, improving symptoms. Smaller observational studies have already shown that catheter ablation can achieve better results than drug treatment in heart failure patients with atrial fibrillation.

Guideline-relevant study | Principal investigators: Abdul S. Parwani (Berlin), Paulus Kirchhof (Hamburg), Stefan Kääb (Munich), Roland R Tilz (Lübeck), Tim Friede (Göttingen), Burkert Pieske | Funding (DZHK): €3.3 million | Planned participants: 1,548 | Multicenter

Press release dated August 29, 2022, at [dzhk.de/en/news](https://www.dzhk.de/en/news)

📌 Improved therapy for patients with heart failure and atrial fibrillation (CABA-HFPEF-DZHK27 trial)

#### HEART VALVE DEFECT

### A first-in-human feasibility study to evaluate the safety (and short-term efficacy) of the autologous GrOwnValve transcatheter pulmonary heart valve (GECT-DZHK28)

In the study, Berlin researchers are testing a unique heart valve replacement made from the patient's tissue. The goal is to develop safe implants that will function over the long term. Conventional heart valves calcify over time or require long-term medication. In addition, artificial heart valves do not grow with the patient, which is a problem in children. Seven young adults with congenital pulmonary valve defects are participating in the study. If successful, a larger follow-up study is planned to investigate its use in adults and children. Co-growing heart valves are particularly relevant for children with a narrowed pulmonary valve, a common congenital heart defect because they typically require surgery every four to five years to receive a new valve.



Early clinical trial | Principal investigator: Boris Schmitt (Berlin) | Funding (DZHK): €420,000 Euro | Planned participants: 7 | Monocentric

Press release dated August 22, 2022, at [dzhk.de/en/news](https://www.dzhk.de/en/news)

📌 Durable and adaptable for life – DZHK study investigates heart valves made of autologous tissue (GECT-DZHK28 study)



### Studies with completed recruitment in 2022

- | Comparison of TAVI versus surgical treatment in patients with symptomatic severe aortic valve stenosis and intermediate risk (DEDICATE-DZHK6)
- | Telemedical Monitoring via Smartwatch in COVID-19 Patients (COVID-SMART)

### Recruitment

By December 31, 2022, a total of 12,161 patients were enrolled in DZHK studies, including 1,589 in 2022 (2021: 1,508). In total, just over 17,400 patients have been enrolled in all DZHK-funded studies over the years.

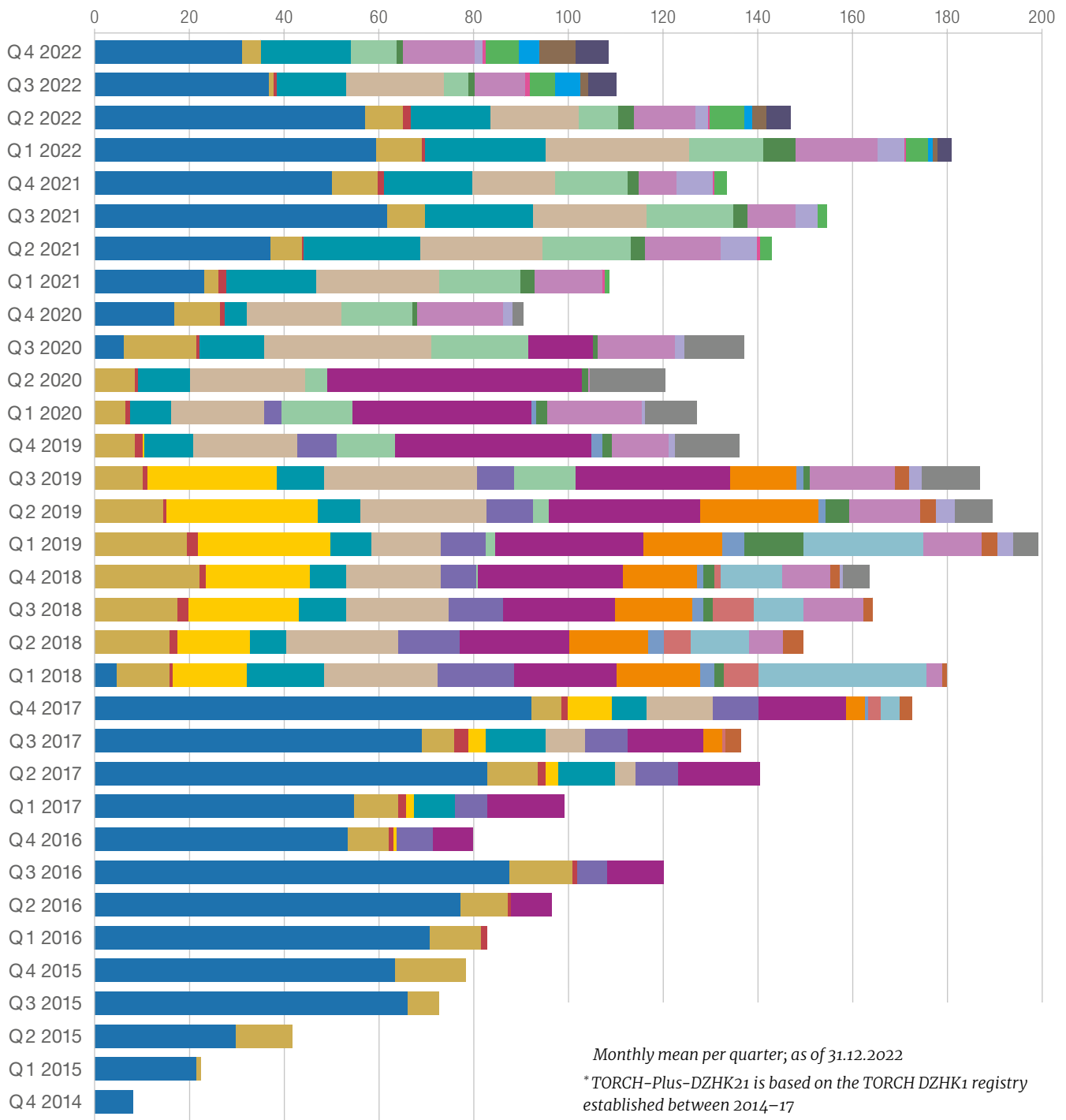
### Global Cardiovascular Research Funders Forum (GCRFF)

Since 2021, the DZHK has been involved as a German partner in the Multinational Clinical Trials Initiative of the GCRFF. In October 2021, the first round of calls for proposals started. The DZHK is involved in the review of "Expressions of Interest" for international co-funding of multicenter trials. We report on this in the chapter "Collaborations" ([see p. 39](#)).

### DZG Patient Participation Working Group

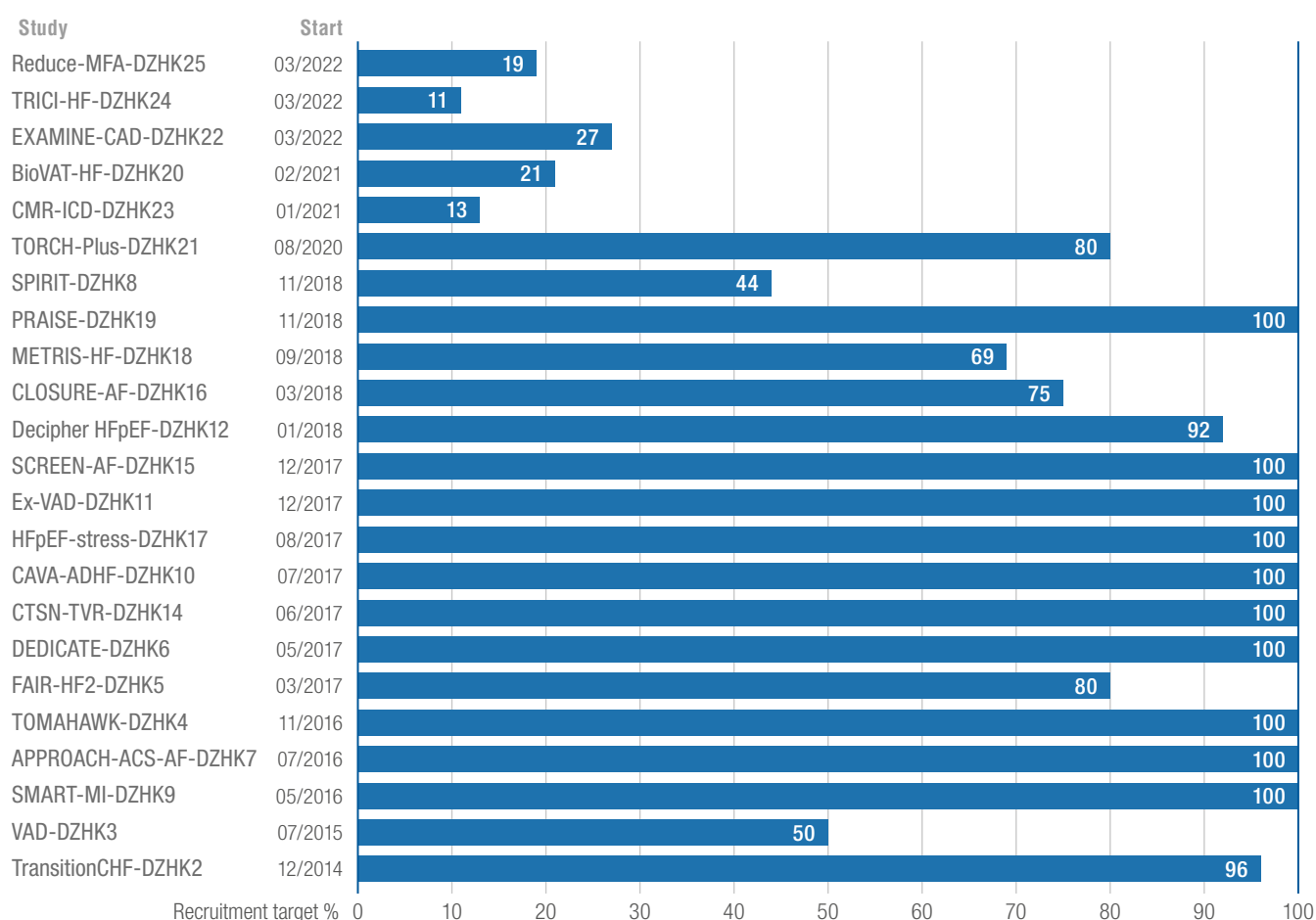
The DZHK is involved in this overarching working group of the German Centers for Health Research. More details can be found in the chapter "Collaborations" ([see p. 39](#)).

OVERVIEW – PATIENTS RECRUITED IN DZHK STUDIES



- TORCH-Plus-DZHK21\*
- SMART-MI-DZHK9  
(Study and registry)
- HfPEF-stress-DZHK17
- TransitionCHF-DZHK2
- CAVA-ADHF-DZHK-10
- METRIS-HF-DZHK18
- VAD-DZHK3
- Ex-VAD-DZHK11
- PRAISE-DZHK19 | DZNEB001
- TOMAHAWK-DZHK4
- Decipher HFpEF-DZHK12
- BioVAT-HF-DZHK20
- FAIR-HF2-DZHK5
- CTSN-TVR-DZHK14
- CMR-ICD-DZHK23
- DEDICATE-DZHK6
- SCREEN-AF-DZHK15
- EXAMINE-CAD-DZHK22
- APPROACH-ACS-AF-DZHK7
- CLOSURE-AF-DZHK16
- TRICI-HF-DZHK24
- SPIRIT-HF-DZHK8
- Reduce-MFA-DZHK25

## OVERVIEW – ENROLLMENT STATUS OF PATIENTS IN DZHK STUDIES



Data in percent (as of 31.12.2022)

## STUDIES AT THE DZHK (EXCLUDING PARTIALLY FUNDED AND ASSOCIATED STUDIES)

DZHK studies	Condition/treatment/ diagnostics	Study type	Responsible PI (DZHK partner site)	Recruitment target	Enrolled
GECT-DZHK28	Heart valve replacement from autologous tissue	ECS	Schmitt (Berlin)	7	Recruitment in preparation
CABA-HFPEF-DZHK27	Atrial fibrillation and heart failure	GRS	Parwani, (Berlin), Kirchhof (Hamburg), Kääb (Munich), Titz (Lübeck), Friede (Göttingen), Pieske (Berlin)	1,548	Recruitment in preparation
TRINITY-DZHK26	Inflammatory myocarditis	ECS	Grabmaier, Massberg (Munich)	130	Recruitment in preparation
Reduce-MFA-DZHK25	Myocardial fibrosis	ECS	Puls, Zeisberg (Göttingen)	300	57
TRICI-HF-DZHK24	Tricuspid regurgitation, TAVI	GRS	Hausleiter, Stocker, Braun, Massberg (Munich)	360	38
CMR-ICD-DZHK23	MRI examination in patients with heart failure	GRS	Eitel (Lübeck)	760	97
EXAMINE-CAD-DZHK22	Disturbed microcirculation	ECS	Landmesser, Stähli (Berlin)	132	35

## STUDIES AT THE DZHK (EXCLUDING PARTIALLY FUNDED AND ASSOCIATED STUDIES)

DZHK studies	Condition/treatment/ diagnostics	Study type	Responsible PI (DZHK partner site)	Recruitment target	Enrolled
TORCH-Plus-DZHK21**	Cardiomyopathy	Registry	Meder (Heidelberg)	4,340	3,458
BioVAT-HF-DZHK20	Artificial heart tissue in severe heart failure	ECS	Zimmermann (Göttingen)	53	11
PRAISE-DZHK19	Acute coronary syndrome in stroke patients	ECS	Endres, Landmesser, Nolte (Berlin)	251	complete
METRIS-HF-DZHK18	Metformin treatment in heart failure	ECS	Döhner (Berlin), Friede (Göttingen), Pieske (Berlin)	144	101
HfpEF-stress-DZHK17	Real-time MRI diagnostics in heart failure	ECS	Schuster (Göttingen)	70	complete
CLOSURE-AF-DZHK16	Stroke prophylaxis by atrial appendage closure	GRS	Landmesser, Boldt (Berlin), Eitel (Lübeck)	1,000	748
SCREEN-AF-DZHK15	Early detection of atrial fibrillation	GRS	Wachter (Göttingen and Leipzig), Hummerts (Göttingen)	267 (in GER)	complete
CTSN-TVR-DZHK14	Tricuspid valve	GRS	Falk (Berlin)	76 (in GER)	complete
Decipher HFpEF-DZHK12	Heart failure, MRI	ECS	Nagel (Rhine-Main)	185	170
Ex-VAD-DZHK11	Exercise with a ventricular assist device	ECS	Edelmann, Falk (Berlin), Halle (Munich), Pieske (Berlin)	64	complete
CAVA-ADHF-DZHK-10	Acute decompensated heart failure	ECS	Jobs (Lübeck), Thiele (Leipzig)*	388	complete
SMART-MI-DZHK9	Sudden cardiac death after myocardial infarction	ECS	Bauer (Munich and Innsbruck, AT), Käab, Massberg (Munich)	400	complete
SPIRIT-HF-DZHK8	Heart failure	GRS	Edelmann (Berlin), (formerly Pieske)	1,300	582
APPROACH- ACS-AF-DZHK7	Circulatory disorders of the heart in combination with atrial fibrillation	GRS	Wakili (Munich and Frankfurt), Massberg (Munich)	400	complete
DEDICATE-DZHK6	Aortic valve stenosis	GRS	Blankenberg, Seiffert (Hamburg)	1,403	complete
FAIR-HF2-DZHK5	Heart failure and iron supplementation	GRS	Karakas (Hamburg), Anker (Berlin)	1,200	957
TOMAHAWK-DZHK4	Cardiac arrest	GRS	Desch (Lübeck and Leipzig), Thiele (Leipzig)*	558	complete
VAD-DZHK3	Severe heart failure, heart transplantation	GRS	Falk, Knosalla (Berlin), Hasenfuß, Friede (Göttingen)	200	100
TransitionCHF-DZHK2	Heart failure	Cohort	Hasenfuß (Göttingen), Wachter (Leipzig)*, Edelmann (Berlin)	1,000	954
TORCH-DZHK1**	Myocardial diseases	Registry	Katus (Heidelberg), Hoffmann (Greifswald)	2,300	complete

ECS: Early clinical study

GRS: Guideline-relevant study

\* Principal investigators who are former DZHK scientists

\*\*TORCH-Plus-DZHK21 is based on the TORCH DZHK1 registry established between 2014-17



# Clinical Research Platform & Heart Bank



## CLINICAL RESEARCH PLATFORM

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The Clinical Research Platform is the backbone of DZHK studies. It ensures that data and biospecimens are collected according to uniform standards and are thus available for high quality, cross-study reuse. In 2022, five new studies ("first patient in") were integrated into the platform and research teams have started patient recruitment. Approximately 120 national and international institutions recruited patients into our studies by the end of 2022.

## Extension of the research platform projects and user study

The decentralized Clinical Research Platform comprises various IT systems and is funded through a project call. For 2024–2028, a new request for proposal was developed and approved by the RCC. The General Assembly voted on it in spring 2023. A total of €8.3 million was approved for five years to continue the Clinical Research Platform.

A user survey was conducted in the reporting year to evaluate the strengths and weaknesses of the IT systems (ethics coordination, independent trust office, data storage, LIMS/ biobanking data, image data management, data/biospecimen use) from the users' point of view.



Users are individuals who enter data into the Clinical Research Platform, essentially study staff at participating study sites, or users who request data and samples from the Heart Bank, mainly researchers. Of 2,000 respondents, five percent completed the rather extensive questionnaire in full. Predominantly positive ratings were given for accessibility, communication, competence, and expectations. In some subsystems, there is room for improvement in user-friendliness and the comprehensibility of forms. The results provide valuable information for further improvement of the systems in the coming term.

### Centralization of biobanking – preparation phase

To date, all study centers have stored biospecimens collected in DZHK studies locally. This approach has long-term disadvantages, especially when it comes to releasing samples to users. The DZHK makes more than 250,000 biospecimens available to researchers worldwide for secondary use for specific purposes. In order to make the

valuable resource of blood samples, urine samples, and snap-frozen punch biopsies even more usable for research, the Executive Board and the RCC have decided to establish two central DZHK biobanks. For this purpose, after a coordination of the content by the Biobanking working group, a requirement and procedure guideline, as well as a template for a project description, were created and published in January 2023. All national biobanks were eligible to apply. The DZHK will provide a total of two million euros for five years for the centralization.

### Harmonization of DZHK cohorts

The DZHK partner sites have contributed many resources to the DZHK that have been built up over many years. Of particular importance are the cardiovascular population-based cohorts (HCHS, SHIP, GHS, KORA) and a clinical cohort study (BeLOVE). The **German Cardiovascular Collaborative Cohorts within the DZHK (G-CCC @DZHK)** initiative was launched and discussed in the year under review to make these more accessible to cross-site research.

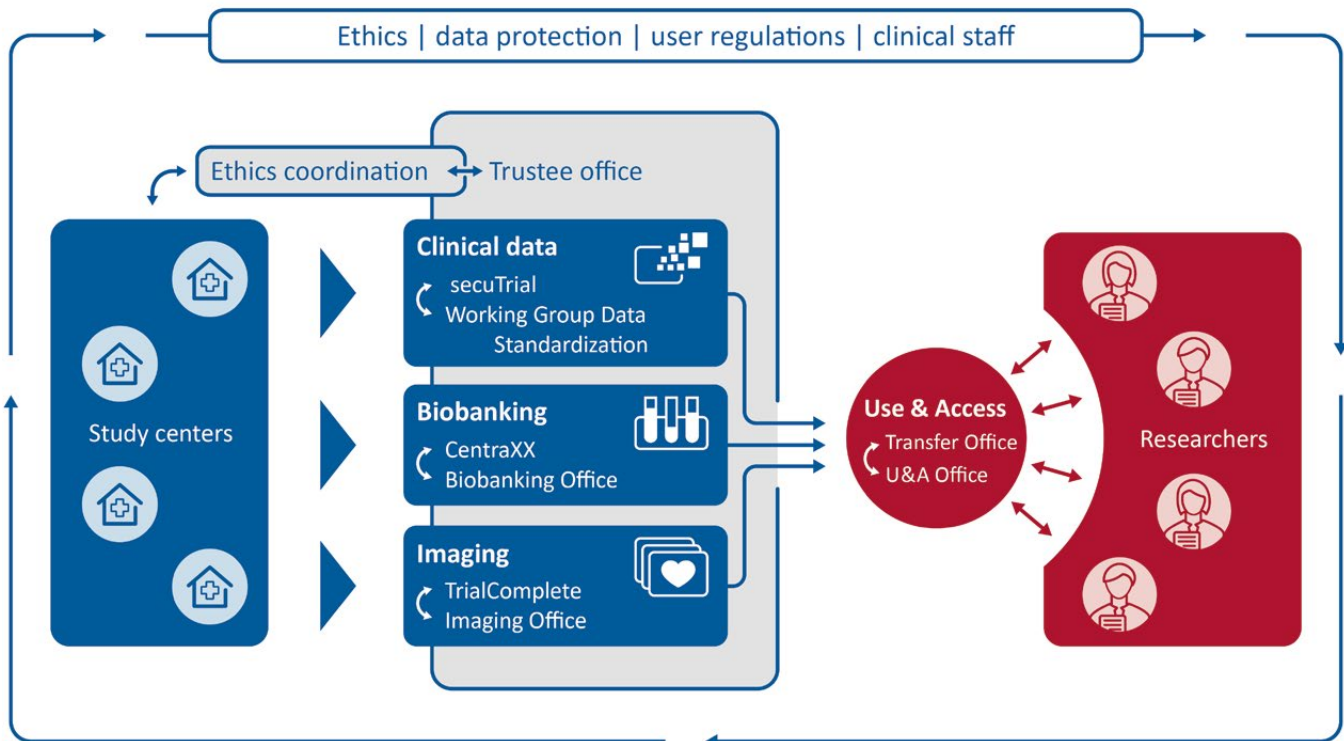


Fig.: The Clinical Research Platform consists of IT infrastructures, processes, and rules. All studies funded by the DZHK use this platform. It is designed to record data and biospecimens in a standardized way and make them available for subsequent research questions.

The initiative aims to develop the basis for low-threshold access and use of harmonized cohort data within the DZHK and beyond. Components should include a compact overview of available cohorts and data as well as a lean and fast application procedure. Standardized data transfer agreements shall accelerate administrative processes and make the platform available to all members of the DZHK.

## DZHK HEART BANK

The DZHK Heart Bank contains high quality clinical data, image data, omics data as well as liquid and tissue samples including associated data, whose processing and storage is performed under standardized conditions. They originate predominantly from the DZHK studies of the Clinical Research Platform. This is an important prerequisite for reproducible research results. At the end of 2022, data and samples from 7,000 patients were recorded.

## Call for data and sample use

We do not collect data and samples as an end in itself, but as a valuable resource for research. To request the use of our data and samples, we published the DZHK-internal call "Utilisation of the DZHK Collection" for the second time, with which we also support this use financially. Four requests for use were received, all of which were recommended for funding by the Use and Access Committee (UAC). The RCC followed this recommendation and thus released a funding totaling €40,000 per project. Other secondary use projects were also evaluated by the UAC outside of the call. The publication of the utilization projects was started at different times, partly still in the reporting year, partly not until the following year. The brief descriptions of the projects and the responsible scientists were presented on the DZHK Heart Bank website.

[dzhk.de/en/dzhk-heart-bank/secondary-use-projects/](https://dzhk.de/en/dzhk-heart-bank/secondary-use-projects/)

## Goals achieved in 2022?



*(incl. goals clinical studies)*

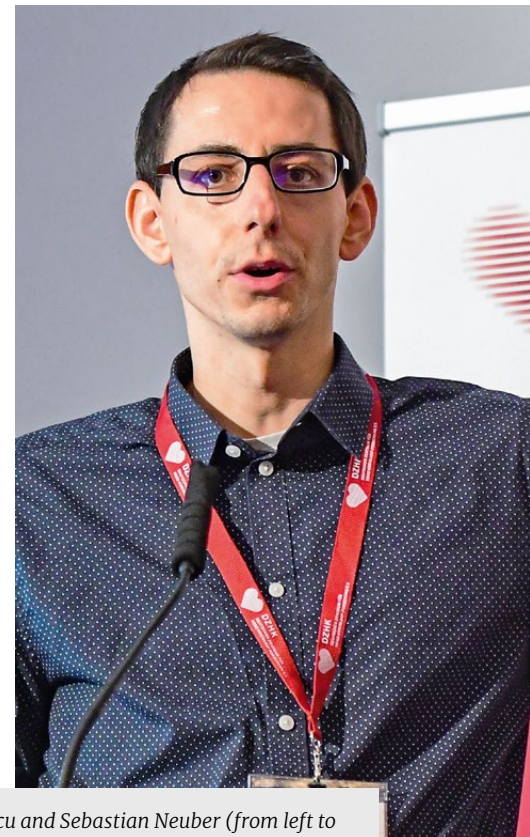
- ✓ Recruitment into at least one large study completed
- Publication on Clinical Research Platform published
- ✓ Extension of research platform projects underway
- ✓ At least three new studies connected to the Clinical Research Platform
- ✓ Concept for centralized DZHK Heart Bank
- ✓ Clinical Study Units: Audits 3.0 done
- ✓ Second call for data and sample projects

## Goals 2023



- Data filter tool for Heart Bank improved
- Publication on Clinical Research Platform published
- Two central DZHK biobanks selected
- New funding guideline for Clinical Staff published
- Three studies represented in Clinical Research Platform

# Promoting Young Talent



Nicolai Spicher, Maria Ercu and Sebastian Neuber (from left to right) were awarded for the best presentations at the Young DZHK Retreat in Potsdam in September 2022 (see p. 42).

Translational research needs inquiring medical scientists and basic scientists who think outside the box of their discipline and their institution. With our extensive support for young scientists, we facilitate laboratory exchanges, release doctors from their daily clinical routine so that they can carry out research and support young scientists in taking the step towards scientific independence.

In 2022, we have earmarked €8.7 million for our eleven junior researcher funding lines. This is a record amount for the excellence, mentoring and training program – in 2021 it was €5.1 million and the year before €3.5 million. The funding for 2022 is higher than usual because we have bestowed three Junior Research Groups, which account for just under €5 million.

## YOUNG DZHK

Of the approximately 2,200 scientists in the DZHK network, almost two-thirds belong to the Young DZHK. With 1,415 young researchers from the partner institutions, it is the largest network in the DZHK.

The Young DZHK actively determines the future of the DZHK: 14 young scientists – two from each of the seven DZHK partner sites – are involved in the Young DZHK Postdoc Committee. The spokesperson is a voting member of the RCC, the committee that decides on strategic issues in the DZHK.

Current overview of speakers:

- [dzhk.de/en/early-career/the-young-dzhk/young-dzhk-postdoc-committee/](https://dzhk.de/en/early-career/the-young-dzhk/young-dzhk-postdoc-committee/)

Since 2014, the Postdoc Committee has organized the annual Young DZHK Retreat (see p. 41), which always takes place prior to the DZHK Retreat. After a two-year break due to the pandemic, 90 young researchers from the DZHK partner sites came to Potsdam in September to learn about current topics at the other partner sites, to make contacts, and to present and discuss their own research.

The Young DZHK also networked internationally: in February 2022, a virtual kick-off symposium entitled "Dutch and German hearts: crossing borders" was organized jointly with the Dutch organization Young@Heart.

Because successful translational research requires interdisciplinary and well-connected researchers, the six DZGs offer opportunities for young researchers in a joint working group (see p. 39).

## TRAINING & MENTORING

The four modules of our training program, which is aimed at PhD students and postdocs, were again well attended in the year under review. In particular, the number of applications for travel grants was significantly higher than in the previous year, as the pandemic in recent years has led to the majority of congresses being held online. In addition to travel grants, the training program includes the Visiting Scientist Program and grants for medical doctoral students. Furthermore, the funds can be used to organize own workshops and networking meetings.

### Mentoring: back to face-to-face formats

During the reporting period, the mentoring year ended for the 14 mentees of the 8th cohort (2021/2022). Since we were only able to offer virtual workshops and exchange formats to the 2021/2022 and 2020/2021 mentoring cohorts during the Corona pandemic, we invited them to the second Alumni Reunion in Berlin in the summer of 2022. Sixteen former and current mentees took advantage of the opportunity to attend workshops, get to know each other personally and exchange ideas. In this program the "presence" format is a big benefit, as it is crucial to prepare the mentees – physicians, scientists or science managers – for leadership tasks, among other things through open discussions in a trusting atmosphere and self-reflection exercises.

The mentoring program will remain in its current form, so we have decided to make only minor changes: the program will take place every two years, and there will be a mix of face-to-face and online workshops.

### AWARDED GRANTS TRAINING & MENTORING

	Amount 2022	2021
Travel grants for high-level conferences	272	116
Doctoral scholarships (including partner site-financed scholarships)	48	48
Visiting Scientist Program	25	11
Attendance of external workshops	98	66
New mentees	12	14

### Joint workshops of DGK and DZHK

Together with the German Society of Cardiology (DGK), we have offered a joint junior researcher support program "Fundamentals of Cardiovascular Research" since 2013. In 2022, young cardiologists could participate in these three workshops:

- | **Basic Mechanisms of Cell Biology** | April 20, Mannheim (in the context of the DGK Annual Meeting)
- | **Formalia and soft skills** | June 8, online
- | **Going in vivo – animal models** | September 30, Bonn (in the context of the DGK Heart Days)

## EXCELLENCE GRANTS

The Excellence Program was developed almost ten years ago on the initiative and with the participation of the Young DZHK Postdoc Committee and is the flagship of the DZHK's support of young researchers. €7.9 of a total of €8.7 million allocated to the Young Investigator Call in 2022 went to the Excellence Call alone. Among the excellence projects that received funding, there were also three DZHK Junior Research Groups, each funded by the DZHK with €1.65 million for six years.

One of them – the Junior Research Group of Jana Grune at the Berlin partner site – started already in 2022.

## Two DZHK Junior Research Groups launched

Leading one's own Junior Research Group is an important step toward scientific independence for young researchers. The heart-lung specialist Jana Grune from the German Heart Institute of the Charité in Berlin and the molecular biologist Daniel Andergassen from the Technical University of Munich (TUM) each started their own DZHK Junior Research Group at the end of the year and in the summer of 2022, respectively. Daniel Andergassen's Junior Research Group had already received funding in 2021.

### Project title | Elucidating the contribution of sex chromosomes to the CVD gender bias



Daniel Andergassen and his Junior Research Group are investigating the role that genes on the X and Y chromosomes play in the differences between men and women in cardiovascular disease. He is following the trail of "escaped"

genes. These so-called "escape genes" outpace a natural process: In women with two X chromosomes, one of the two X chromosomes in each cell is randomly "silenced" early in development. However, about three percent of the escape genes get away from silencing and remain active on both X chromosomes. Women thus have a double dose of these genes compared to men and appear to have slightly better protection against cardiovascular disease than men until menopause. Daniel Andergassen is investigating whether this might be related to the escape genes.

### Project title | Immune modulatory effects of aldosterone in pulmonary hypertension-associated lung vascular maladaptations



Jana Grune studies the communication between the heart and the lungs. When the left side of the heart becomes diseased, pulmonary hypertension can quickly develop, with dramatic consequences for the right side of the heart, which

can fail in the worst case. There is still no effective treatment for patients with pulmonary hypertension caused by left heart disease. At the same time, the number of people

with left heart disease, such as some forms of heart failure, is increasing. It is still unclear why some patients develop pulmonary hypertension while others do not. Jana Grune suspects specific inflammatory processes in the immune system. She hypothesizes that in those who develop a pulmonary phenotype, more monocytes migrate into the tissue, leading to an exaggerated immune response. Jana Grune spent several years as a postdoc in the USA before returning to Germany from Boston.

Press releases from 23.07.2022 and 26.01.2023 at [dzhk.de/en/news/latest-news/](https://dzhk.de/en/news/latest-news/)

- 📄 New DZHK Junior Research Group leader follows trail of "escaped" genes
- 📄 Two new Junior Research Groups started at the DZHK

## Second round for Postdoc Start-up Grant on Advancing Digital Aspects

For the second time, researchers with Young DZHK status had the opportunity to apply for a Postdoc Start-up Grant on Advancing Digital Aspects. Five projects were recommended for the call. The research projects focus, for example, on using machine learning to improve prognosis or creating a digital twin for patient treatment planning. The call was launched for the first time in 2021 to support young scientists, especially in the field of digitalization. They will receive seed funding for an independent research project. In 2022, four of the five projects recommended for the call started. From 2024, after three individual rounds, the Postdoc Start-up Grant on Advancing Digital Aspects will be integrated into the regular Postdoc Start-up Grant, making it permanent.

## EXCELLENCE GRANTS – FUNDED PROJECTS

Funding line	Name	Institution	Project title
<b>Junior Research Group</b>	Daniel Andergassen*	Technical University of Munich	Elucidating the contribution of sex chromosomes to the CVD gender bias
	Claudia Crocini	Charité – Universitätsmedizin Berlin	Sex dimorphism in human cardiac health and disease
	Pieterjan Dierickx	Max Planck Institute for Heart and Lung Research	Circadian rhythms and metabolism in heart failure: from molecular insights to therapeutic targets
	Jana Grune	German Heart Center Berlin	Immune modulatory effects of aldosterone in pulmonary hypertension-associated lung vascular maladaptations
<b>Clinician Scientist Program</b>	Christian Gräßer	German Heart Centre Munich	Targeting the cation channel TRPC6 to reduce restenosis after stent implantation
	Sara Hadzibegovic	Charité – Universitätsmedizin Berlin	Assessment of cardiac wasting-induced cardiomyopathy with cardiac MRI in advanced cancer patients
	Lauren Eleonore Sams	University Hospital of Munich	Re-EVALuating the diagnosis and prognosis of Myocardial Infarction type 1 (REAL-MI)
	Helen Ullrich	University Medical Center of the Johannes Gutenberg University Mainz	Modulation of coronary sinus pressure to develop a new treatment for microvascular disease
<b>Postdoc Start-up Grant</b>	Maja Bencun	Heidelberg University Hospital	Characterizing the role of the RNA-binding protein Mbnl2 during cardiac remodelling
	Dena Esfandiyari Shahvar	Technical University of Munich	Non-coding RNA control of the maternal heart remodelling in pregnancy and lactation
	Francesca Fasolo	Klinikum rechts der Isar of the Technical University of Munich	Exploiting long non-coding RNAs as targets and templates in RNA therapy for vascular disease
	Sandra Hemkemeyer	University Medical Center Hamburg-Eppendorf	The role of lymphatic cyclooxygenases in cardiovascular disease
	Jasper Iske	German Heart Center Berlin	Delineating molecular patterns of MINOCA for diagnostic and therapeutic purposes
	Julian Leberzammer	Johann Wolfgang Goethe University Frankfurt	The impact of COVID-19 on long-term vascular and cardiac inflammation
	Christian Oeing	Charité – Universitätsmedizin Berlin	mTOR in diabetic cardiomyopathy
	Christiane Ott	German Institute of Human Nutrition Potsdam-Rehbruecke	The role of Pank4 as novel key player in cardiac remodelling and energy metabolism
	Mario Pavez-Giani	University Medical Center Göttingen	Targeting mtDNA heteroplasmy by modulating mitochondrial turnover in human iPSC-derived cardiomyocytes
	Kami Alexander Pekayvaz	University Hospital of Munich	Temporal and functional resolution of neutrophil phenotypes at different stages of venous thrombosis
	Julian Uwe Gabriel Wagner	Johann Wolfgang Goethe University Frankfurt	Impact of aging on the cardiac lymphatic system

## EXCELLENCE GRANTS – FUNDED PROJECTS

Funding line	Name	Institution	Project title
Postdoc Start-up Grant on Advancing Digital Aspects	Jan Brüning	Charité – Universitätsmedizin Berlin	Digital twins for diagnosis and treatment-planning of patients with complex univentricular physiology
	Jennifer Furkel	Heidelberg University Hospital	Towards a non-invasive diagnostic classifier in transthyretin amyloidosis
	Djawid Hashemi	Charité – Universitätsmedizin Berlin	Machine learning-based prognosis: assessment of novel CMR features in a prospective patient cohort
	Amir Moussavi	German Primate Center Göttingen	Automatic species-independent myocardial segmentation of real-time cardiovascular MRI
	Ann-Kathrin Rahm	Heidelberg University Hospital	HoloHeart – Development of a toolkit for a virtual interactive experience of the human heart
Promotion of Women Scientists	Olympia Bikou	Technical University of Munich	AAV microRNA Tough Decoy for treating pulmonary hypertensi- on: a new translational approach in pig
	Susanne Helena Karbach	University Medical Center of the Johannes Gutenberg University Mainz	Mechanisms of the increased cardiovascular risk in autoimmune diseases
	Anja Zeigerer	Environmental Health Center – Helmholtz Munich	Endosomal transport regulators in metabolic cardiovascular diseases
	Gabrijela Dumbović	Johann Wolfgang Goethe University Frankfurt	Discovering the functionality of splicing-driven subcellular RNA localization across cardiac cell types
	Manar El Kenani	University Medical Center Göttingen	Reverse cardiac remodelling in murine models of low-flow low-gradient aortic stenosis
Rotation Grant	Anastasia Kyselova	Johann Wolfgang Goethe University Frankfurt	Glutamine rewiring to proline biosynthesis is indispensable for endothelial cell growth
	Daniel Finke	Heidelberg University Hospital	The role of the nuclear receptor ROR in the metabolic stress response of the heart
	Klara Kirschbaum	Frankfurt University Hospital – Goethe University	Old, but new? – A randomized, controlled trial to study the effect of colchicine in patients with CHIP mutations and heart failure with reduced ejection fraction (HFrEF) – CHIP-HF (EudraCT: 2021-001508-13)
	Alexander Heinrich Nave	Charité – Universitätsmedizin Berlin	Cardiometabolic hemostasis during aerobic fitness training early after acute ischemic stroke
	Janek Salatzki	Heidelberg University Hospital	Biomarker- and Cardiac-MRI-based identification of risk factors for functional impairment and structural remodeling in patients with ventricular arrhythmias
Lisa Voigtländer	University Medical Center Hamburg-Eppendorf	Advanced echocardiography in patients undergoing trans- catheter aortic valve implantation (TAVI)	

\*Funding already made in 2021

## Goals achieved in 2022?



- ✓ Face-to-face mentoring alumni meeting organized, especially for mentees who had only been able to meet online due to the pandemic
- ✓ Mentoring Program further developed
- Postdoc Start-up Grant on Advancing Digital Aspects evaluated

## Goals 2023



- Conception of DZG Training Program on Translational Medicine



# Collaborations

## COLLABORATION WITH THE DZG

Collaboration with the German Centers for Health Research (DZG) was further intensified in the year under review. Four of the six DZGs jointly celebrated their **10<sup>th</sup> anniversary** in May ([see p. 4–5](#)).

To improve the management of joint processes and activities, a **virtual DZG office** was established, in which the managing directors of each DZG and one person at speaker level are active.

Together with the **DZG Innovation Fund (DZGIF)**, the concept for a joint research funding program was developed, which was launched in 2022 with two calls for proposals: "Gene and Cell Therapy" (June 2022) and "Microbiome" (September 2022). With the help of the fund, the DZG aims to strengthen the networking of its members within the German research landscape and create interdisciplinary synergies in research into common diseases.

In the first call for proposals on the topic of "Gene and Cell Therapy", researchers from five of the six DZGs joined forces and submitted a successful proposal:

### Cell type-specific targeting for future in vivo delivery in cell & gene therapy

#### Project participants are:

DKTK: Annette Künkele (Charité Berlin), Angela Krackhardt (TU Munich) | DZD: Gerhard Przemeczek, Heiko Lickert (Helmholtz Munich) | DZHK: Alessandra Moretti (TU Munich), Johannes Backs (Heidelberg University), Oliver J. Müller (Kiel University) | DZIF: Tobias Feuchtinger (LMU Munich), Boris Fehse (UKE Hamburg) | DZL: Nico Lachmann (MHH Hannover), Soni Savai Pullamsetti (JLU Giessen)

Duration: 2022–2024 | Total budget: €788,000

### First joint symposium

At the end of October, the DZG organized its first joint interdisciplinary symposium on post-COVID syndrome in Frankfurt (80 participants). This was followed by a public event for citizens to ask questions about the state of research with a focus on post-COVID and sports (approx. 60 participants). Both events were mainly organized by the DZHK Rhine-Main partner site with the support of the DZHK office ([see p. 42](#)).



## From the DZG working groups

### Patient participation

For the first time, the Patient Participation Working Group (WG) held two meetings with patient representatives from all six DZGs. In addition, the working group developed a communication campaign on the topic of "Patient participation in data-intensive research in the DZGs", which was recommended for implementation by the DZG Board. Furthermore, the working group contributed to a declaration on patient participation in health research, which was developed under the auspices of the Health Research Forum of the BMBF.

### Promotion of young scientists

As part of its efforts to promote the next generation of scientists, the DZG offered a number of well-attended courses for young scientists, such as the DZG Symposium for Young Scientists on "Single Cell Analysis" and several lectures on the topics of science communication, career development and business start-up. In addition, intensive efforts were made to support young researchers in balancing clinical practice and research.

### Research IT

The Research IT WG continued to work on the harmonization and interoperability of the various IT infrastructures of the DZG. A DZG-wide data set was discussed, which could be mandatory for all DZG-funded studies in the future. The working group also worked on improving the searchability of studies requested by the DZG. To this end, the first DZG-wide queries were carried out and collaboration with the NFDI4Health initiative was started. Technical proof of concepts for data sharing, decentralized data analysis, and cross-study patient search were conducted and further developed. The plans and first results of the working group were presented at the annual meeting of the German Society for Medical Informatics, Biometry and Epidemiology (GMDS).

### Public relations

The Public Relations Working Group published two more issues of the joint health research journal SYNERGIE and developed a website for the DZG, which went online in time for the anniversary celebrations in May 2022 (see p. 43).

## RESEARCH COLLABORATIONS

### British Heart Foundation and Hartstichting

The joint funding line was retendered with the British Heart Foundation (BHF) and the Dutch Hartstichting (or Dutch Heart Foundation, DHF). The three organizations agreed to focus this year's call on established mid-career researchers. Out of a total of 23 applications, four were recommended for the call by the international selection committee, and the RCC of the DZHK endorsed this recommendation. The DZHK is involved in each of the selected projects, which will start in 2023 and will be reported subsequently.

### Global Cardiovascular Research Funders Forum (GCRFF)

There is interest in this call within the DZHK and during the reporting period the first two full proposals with a "GCRFF Endorsement" were received for review. Due to the results of the pitch and the foreseeable lack of access to the patient populations to be studied, neither of the two projects was proposed for a funding by the Clinical Trials Group.

Supporting multinational clinical trials is a focus of the GCRFF, which was established in 2021. Seven of the 12 GCRFF member organizations participate in the Multinational Clinical Trials Initiative.

## Goals achieved in 2022?



- ✓ First call of the DZG Innovation Fund announced
- ✓ Regular Science & Career Day for all DZG young scientists launched

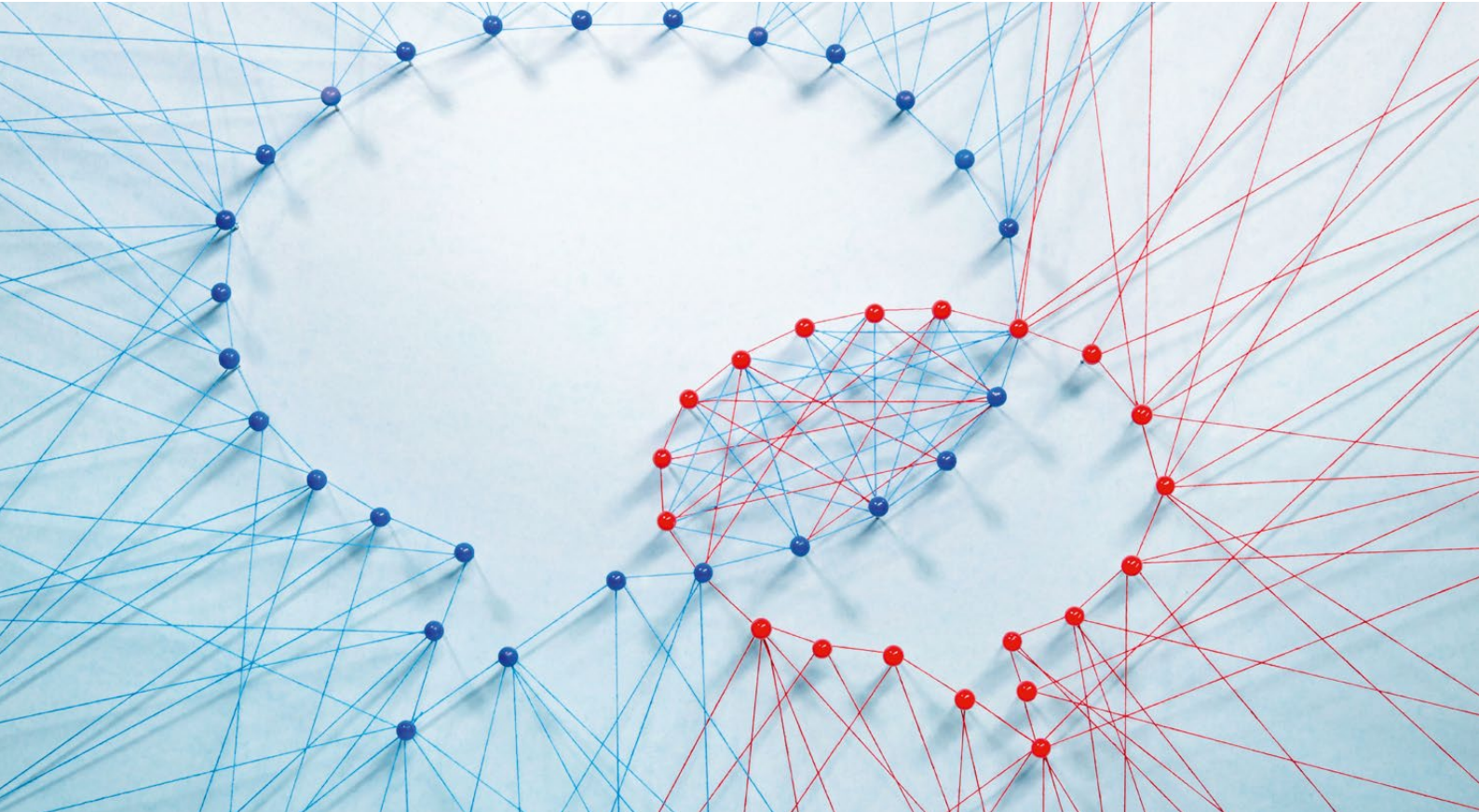
## Goals 2023



- ↗ Renewed Announcement of DZG Innovation Fund
- ↗ Communication campaign on patient involvement launched



# Communication & Public Relations



## SCIENTIFIC EXCHANGE

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### "We're back! DZHK Retreat 2022"

After a two-year break, our annual and largest network meeting – the DZHK Retreat – could be held again as a face-to-face meeting. In addition, the 9<sup>th</sup> edition of the retreat was available via livestream. For the first time, those who could not make it to the idyllically located Seehotel in Potsdam on the banks of the Havel River were able to follow the keynote lectures of invited top scientists and researchers online.

Approximately 200 people attended the two-day event on September 15 and 16, 2022, and 100 followed the technical presentations and discussions online. The keynote lectures were held by two U.S. professors: atherosclerosis expert Alan R. Tall of Columbia University Medical Center and Saptarsi Haldar, who as Vice President of Research at the biotechnology company Amgen is primarily responsible for advancing research into cardiometabolic diseases. Saptarsi Haldar is a member of the Scientific Advisory Board of the DZHK.

## Discussion on the Gender Career Gap

What can be done to ensure that men and women have equal opportunities to pursue careers in cardiovascular research? This was the topic of a panel discussion at the DZHK retreat. The discussion provided an impetus to create more space for gender equality in research and especially in the DZHK. In the ten years since the DZHK was founded, i.e. from 2012 to 2022, the proportion of female principal investigators has increased from 19 percent to 31 percent (see p. 50). This is a gratifying development and an incentive for even more women to work as PIs at our seven sites in the future. They play an important role as role models. At the DZHK, the picture is similar to that of the scientific landscape: While women and men are on an equal level at the beginning of their scientific careers, the situation changes in the later stages of an academic career. Women are increasingly underrepresented. In Germany, only 23 percent of C4/W3 professorships will be held by women in 2021.

## Young DZHK Retreat

Prior to the main retreat, the Postdoc Committee, representing the Young DZHK, hosted the Young DZHK Retreat for the eighth time. About 90 young researchers were present on September 14 and participated in the DZHK Retreat afterwards.

Leon de Windt from the University of Maastricht gave a keynote speech on "Molecular and machine learning-assisted steps to heal a broken heart". A second keynote was given by Anja Hennemuth from Charité – Universitätsmedizin Berlin with the title "Image-based cardiac valve modeling – a multidisciplinary approach for diagnosis and therapy planning".



Three winners emerged from the oral sessions, each assigned to a specific topic, who then presented again to a large audience at the main retreat:

| Oral Session „Cellular biology of the heart“:  
**Activation of phosphodiesterase 3A for cardio-protection**  
 Maria Ercu (Max Delbrück Center for Molecular Medicine)

| Oral Session „Vascular biology“:  
**Aortic and carotid remodeling after transverse aortic constriction in mice**  
 Sebastian Neuber (German Heart Institute Berlin)

| Oral Session „E-cardiology“:  
**Opening the black box: Investigating deep learning models for 12-lead ECG classification**  
 Nicolai Spicher (University Medical Center Göttingen)

## Symposia, lectures, co-funded congresses

Six symposia and five congresses were financed or co-financed by the DZHK in 2022. All symposia and congresses were attended by participants. The events were intended to increase the visibility of the DZHK in the scientific community. The RCC has decided to take a different approach in the future. Therefore, the modules of scientific exchange (co-funded congresses, DZHK lectures) will be discontinued or suspended from 2023 until a new format has been developed (DZHK symposia).

## Symposia 2022

2<sup>nd</sup> DZHK Symposium on Lifestyle-based prevention of non-communicable diseases | 16–17 May 2022, Potsdam

Cardiovascular Bioengineering (CVBE) Symposium | 9–11 June 2022, Göttingen

Research highlights 2022 from the DZHK @ ISHR 2022 | 12–15 June 2022, Berlin

At the heart of translational research: Development of Target-Specific Small Molecule Inhibitors | 23 September 2022, Mannheim

Prevention of Cardiovascular Disease – Insights from Epidemiological Studies | 26–28 September 2022, Greifswald

Post-COVID Syndrome – a joint DZHK / DZL / DZIF / DZNE Symposium | 31 October 2022, Frankfurt

The event on post-COVID syndrome was the first time that the expertise of the German Centers for Health Research was brought together on a joint podium (see also p. 38) with one part for experts and one part for citizens. The DZHK partner site Rhine-Main organized the event with the support of the DZHK office.



Citizens' forum on the topic of post-COVID and sports: Martin Halle, sports cardiology TU Munich; Winfried Banzer, Head of Medicine of Eintracht Frankfurt and team physician; Sascha Zoske (moderator), Frankfurter Allgemeine Zeitung; Anke Steinmetz, Physical and Rehabilitative Medicine, University Medicine Greifswald; Andreas Zeiher, Johann Wolfgang Goethe University Frankfurt (from left to right).

**Co-funded congresses & lectures 2022**

Joint Meeting German and British Microcirculation and Vascular Biology Societies | 7–8 July 2022, Berlin

Targets in heart failure treatment | 15–16 July 2022, Göttingen

TransitionCHF: Improving Recruitment and Follow-ups Through 8 Years of Experience | 14–15 September 2022, Potsdam

3<sup>rd</sup> Joint DGK/DZHK Translational Workshop: Research Data Management in Cardiovascular Science | 28 September 2022, Bonn

CRC1123 Atherosclerosis – Mechanisms and Networks of Novel Therapeutic Targets – International Symposium 2022 | 10–11 October 2022, Munich

Extracellular Vesicles as discovery toolkit and therapeutic opportunity | Costanza Emanuelli (London, UK), DZHK-Lecture

The microtubule network in cardiac hypertrophy and heart failure | Benjamin Prosser, (Pennsylvania, USA), DZHK-Lecture

**Science on Friday**

The “Science on Friday” webinar series entered its third year in 2022. In 2020, we had launched the free offering to coincide with the pandemic. The idea: One hour online via Zoom for Science on a Friday afternoon to promote scientific exchange, especially within the DZHK. As we advertise these dates on social media, external people from the scientific community are increasingly interested in participating. They can register with us and are invited for topics that are not exclusively internal in nature. In this way, we have a tool that serves not only the scientific exchange but also the visibility of the DZHK in the community.

In the reporting year, we were able to offer six events with a wide range of topics: In addition to the research status on individual cardiovascular areas such as cardiac arrhythmias, there was a special issue on Long Covid, in which representatives of the DZHK sites presented locally running research projects. In April, the Postdoc Committee, the representative of the young scientists' network Young DZHK invited and

provided an insight into the careers of scientists who have meanwhile "outgrown" the Young-DZHK. On average, about 70 participants joined in.

**Metabolic control of the cardiovascular system**  
| 4 March 2022, Chairs: Alexander Bartelt (München), Ingrid Fleming (Frankfurt), Oliver Müller (Kiel)

**Whatever happened to...? Post Young DZHK careers**  
| 1 April 2022, Chairs: Nadya Al-Wakeel-Marquard (Berlin), Anne Dueck (München), Eileen Moritz (Greifswald)


**Long COVID Special: What's going on at the partner sites?** | 6 May 2022, Chair: Stefanie Dimmeler (Frankfurt)

**Clonal hematopoiesis** | 1 June 2022, Chairs: Florian Leuschner (Heidelberg), Christian Schulz (Munich), Andreas Zeiher (Frankfurt)

**DZHK Rhythm** | 24 June 2022, Chairs: Paulus Kirchhof (Hamburg), Renate Schnabel (Hamburg)

**Diabetes and cardiovascular research: Added value by collaboration projects, shared technologies and data – a joint DZD/DZHK meeting** | 15 July 2022, Chairs: Stefanie Dimmeler (Frankfurt), Martin Hrabé de Angelis (DZD, Munich)

The webinars are available as recordings on the DZHK intranet (login required):

 [intern.dzhk.de/scientific-exchange/science-on-friday/](https://intern.dzhk.de/scientific-exchange/science-on-friday/)

**PUBLIC RELATIONS**

In 2012, the DZHK was founded as one of six German Centers for Health Research (DZG): In 2022, we celebrated our 10th anniversary together with three other DZG ([see p. 4–5](#)). In a working group with representatives of the anniversary DZGs and with the support of an event agency, we organized a large joint celebration that took place in Berlin in May 2022 with about 200 guests from politics and science.

To coincide with the anniversary, all six DZGs launched a joint website, [www.deutschezentren.de](http://www.deutschezentren.de). The DZHK was significantly involved in the conception and implementation. On the website, which is available in German and English the centers report from six DZG working groups and provide

information on joint events and funding. An interactive map shows where each DZG partner site is located.

With the 10<sup>th</sup> anniversary celebration and the website, the DZG also introduced a revised DZG logo, which was developed in the Public Relations Working Group and in which the DZHK is involved. For more on this, [see p. 39](#).

## Website and social media

Compared to the previous year, the number of users for the entire site increased by 40 percent to just over 400,000 (2021: 285,000). While about 75 percent of visitors came to the site via Google in the previous year, more than 90 percent came via the search engine in 2022. The strong growth is mainly due to a very high interest in news articles and pages about Corona-related diseases, which achieved (and still achieve) high rankings in Google for various keywords. In addition, the other disease pages also saw year-over-year growth – especially heart attacks, but also sudden cardiac death, arrhythmias, and cardiomyopathies.

The percentage of visitors who accessed the website via mobile device increased significantly from 55 percent (in 2021) to over 75 percent.

On Twitter, 2,147 people or organizations followed us by the end of 2022, an increase of 35 percent (2021: +31 percent). On Facebook, we had 2,772 fans, an increase of 15 percent (2021: +11 percent). The Instagram channel had 1,544 subscribers, 17 percent more than last year. On the business network LinkedIn, we had 1,583 followers at the end of the year, more than twice as much in the previous year.

## Further public relations activities

In the year under review, we published 18 press releases in German and English. We designed and implemented study websites, study logos and study flyers for eight new clinical trials. We supported the METRIS-HF study with a landing page and social media posts for patient recruitment.

For the first time since the pandemic, the DZHK had a booth at the annual meeting of the German Society of Cardiology in Mannheim. The public relations department of the DZHK was also responsible for a large part of the publicity for the DZG Post-COVID Symposium ([see p. 42](#)), especially for the public event, as well as for the DZHK Retreat and all scientific events of the DZHK.

We postponed the revision of the DZHK's corporate design and the relaunch of the website to the following year, as the preparation of the 10th anniversary celebration tied up a lot of resources. However, some of the preparations were still going on in the background.



## Goals achieved in 2022?



- 🔄 Corporate design revised
- ✓ Relaunch website started
- ✓ After a two-year break: Retreat held as in-person meeting with hybrid participation options
- ✓ Postponed symposia (due to pandemic) held

## Goals 2023



- ↗ Corporate design revised
- ↗ Relaunch website completed
- ↗ Science-on-Friday series continued on a regular basis



# Success Indicators for Translational Research



## SHORT- AND MEDIUM-TERM INDICATORS

Indicator	Definition	2022	2021
1. "Physician Scientists"	Share of scientifically active (licensed) physicians among the scientists registered in the DZHK ("DZHK scientist" status only)	53 %	56 %
2. Collaboration between DZHK partner sites	a. Number of Shared Expertise projects (year)	28	0*
	b. Number of publications with participation of multiple partner sites	156	168
	c. Number of ongoing large multicenter projects (recruiting DZHK studies and TRPs, as of 31/12/22) involving multiple DZHK partner sites	14	11
	d. Number of Visiting Scientist residencies at other DZHK partner sites (year)	10	4
3. Communication with regulatory authorities	Consulting appointments (e.g. PEI, BfArM) in the context of recruiting DZHK studies, TRP and partner site projects (year)	5	7
4. Collaboration with industry	Collaborations with industry partners in the context of recruiting DZHK studies, TRP and site projects (as of 31/12/22)	11	14

\*Due to a change in the application deadline, there were no newly approved projects in 2021.

## SUCCESS INDICATORS FOR TRANSLATIONAL RESEARCH

Indicator	Definition	2022	2021
5. Collaborative structures in clinical research	a. Type (quality) of collaborative structures (as of 31/12/22)	Clinical Research Platform (Data storage, Trusted Third Party, LIMS, BDMS and ethics project, Use & Access transfer office), stem cell registry, omics resource	
	b. Number (quantity)		
	• Patients included in Clinical Research Platform (as of 31/12/22)	11,245	10,572
	• SOPs (as of 31/12/22)	19	19
	• Data and biospecimen usage applications/notifications (year)	12/6	13/2
	• Approved usage applications and notifications (year)	11/6	13/2
6. High-ranking publications	All publications with DZHK affiliation with impact factor > 10	189	195
7. Preclinical projects and clinical studies	a. Number of Translational Research Projects and recruiting DZHK studies (as of 31/12/22)	24	22
	b. Publications from Translational Research Projects and DZHK clinical studies	30	35

## LONG-TERM SUCCESS INDICATORS

Indicator	Definition	2022	2021
8. Revised medical guideline	Number of guidelines changed as a result of DZHK trials and Competence Network Trials	5	2*

### 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 DZHK partner site projects.

The values for indicators 3, 4, 7b and 8 come from a query to all PIs.

\* The value for 2021 has been corrected from 0 to 2 compared to the 2021 annual report due to late reporting.





# Facts and Figures



*Keeping an eye on the DZHK's finances: Magdalena Milsch-Hetzig (left) and Mumtaz Kasim from DZHK Funding Management Department*

## FINANCES AND STAFF

In 2022, the DZHK had access to around €43.4 million in new funding (2021: €42.4 million) from federal and state budgets as a full annual funding sum. In addition, €5.1 million in accumulated funds will not be spent in 2021 and will be carried over to 2022.

The annual budget in 2022 thus totaled €48.5 million. Of this, funds totaling €44.6 million were used in 2022 (2021: €41.3 million). The allocation of funds as of the reporting date of December 31, 2022, was therefore higher than in the previous year.

The year continued to be strongly influenced by the budget freeze imposed on the Helmholtz Association of German Research Centres by the Budget Committee of the German

Bundestag. The budget freeze affects the DZHK through the Max Delbrück Center for Molecular Medicine in the Helmholtz Association. For the budget to be unblocked, 75 percent of the funds and all accumulated funds had to be spent by the beginning of the year. Intensive communication took place with the partner site management and third-party funding departments of the partner institutes. As a result, most of the funds were used regularly and as planned. The budget committee of the German Bundestag approved the release of the blocked funds in September 2022.

In total, more funds were used than were budgeted in the 2022 business plan, resulting in a reduction of €1.2 million in accumulated funds in 2022.

The funds spent in 2022, amounting to €44.6 million, break down as follows:

- Partner site funds: €21.5 million
- Partner site management: €975,000
- Flexible funds: €19.0 million, of which:
  - Clinical research: €9.2 million
  - Preclinical research: €5.2 million
  - Promotion of young scientists: €4.3 million
  - Funding of externals: €388,000  
(including competence networks: €62,000 and collaboration with external partners: €326,000)
- Membership fees: €2.3 million
- Funding management department: €845,000

In the reporting year, both the membership fees for 2022 and a large part of the membership fees for 2023 have already been spent. Of the total €2.3 million spent, €1.3 million were planned funds for the overall 2022 budget of the association management.

In 2022, about half of the DZHK budget was again allocated to competitive research projects. The DZHK has

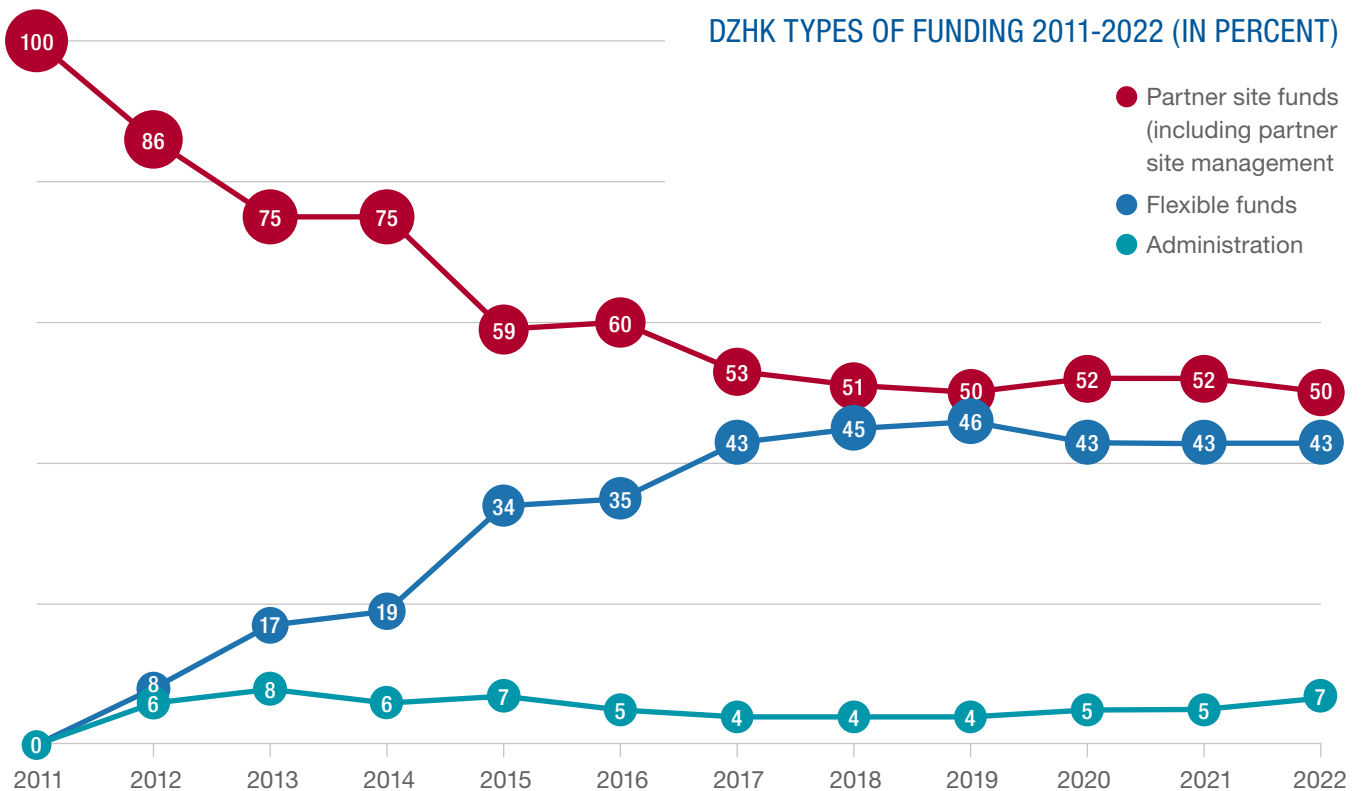
competitively awarded funds totaling €19.0 million. This consolidates the strategic goal of using about 50 percent of the budget as flexible funds. The focus is on excellence, translational research projects and clinical trials.

## BUDGET OF THE ASSOCIATION MANAGEMENT

The total budget of the association management of the DZHK e.V. amounted to €1.4 million in the year under review. This budget was fully financed by membership fees of €1.3 million, a carryover from 2019 of €38,536 and a carryover from 2021 of €75,000. The latter was used to finance the 10th anniversary celebration, which the DZHK organized together with three other DZGs.

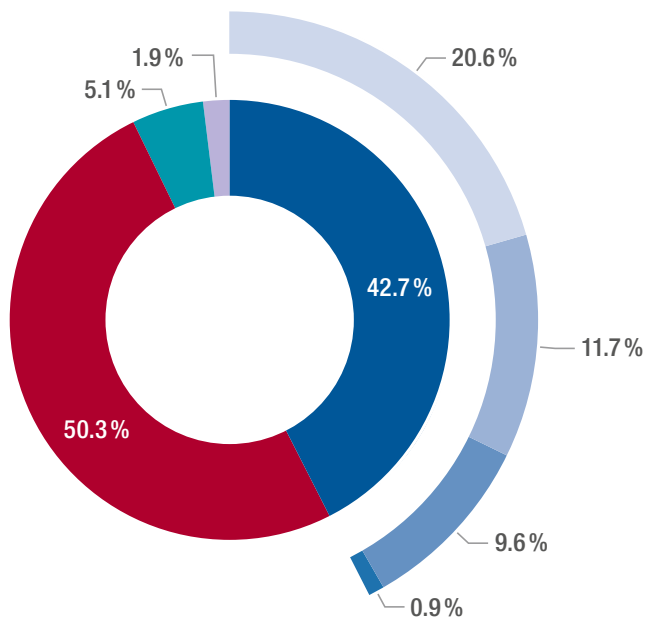
€1.3 million were spent (2021: €1.2 million). Other income amounted to approximately €14,142 (including from health insurance reimbursements).

This results in a surplus of €181,281. The carryover from 2019 thus remained untouched.



\*Any totals deviating from 100 percent are the result of rounding individual share values.

### ALLOCATION OF SPENT DZHK FUNDS 2022 BY EXPENDITURE AREAS\*



- Flexible funds (2021: 43.1 %)
- Partner site funds (2021: 51.5 %)
- Membership fees (2021: 3.3 %)
- Funding management department (2021: 2.1 %)

Flexible funds are made up of

- Clinical research (2021: 19.4 %)
- Preclinical research (2021: 14.2 %)
- Promotion of young scientists (2021: 7.9 %)
- External (2021: 1.7 %)

### STAFF EXPENDITURES, MATERIAL EXPENSES AND INVESTMENTS OF THE DZHK\*

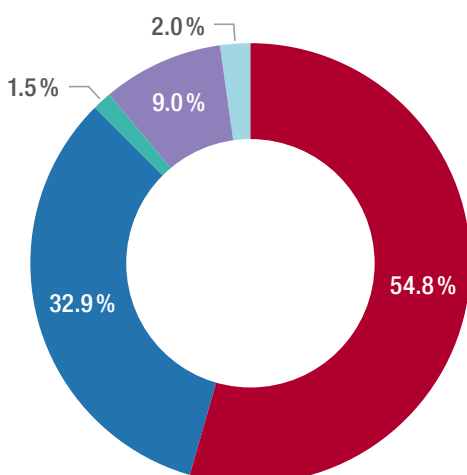


### STAFF

As of December 31, 2022, 594 (2021: 582) persons or "heads" were financed from DZHK funds. This corresponds to 418.72 (2021: 411.64) full-time equivalents (FTE). As in the previous year, this also includes 20 DZHK association

management employees, 14 (2021: 15) employees of the funding management department and one competence network employee (2021: 9).

### STAFF EXPENDITURES, MATERIAL EXPENSES AND INVESTMENTS OF THE ASSOCIATION MANAGEMENT\*



- Staff expenses: €694,508 (2021: €677,315)
- Material expenses: €416,829 (2021: €335,113)
- Investments: €18,465 (2021: €38,547)
- Public relations: €113,558 (2021: €136,041)
- Membership fees (TMF e.V.): €25,000 (2021: €25,000)

\*Totals deviating from 100 percent, if applicable, are the result of rounding individual share values.

## NUMBER OF STAFF FINANCED BY DZHK 2020–2022

	2020	2021	2022
Number of employees (as of 31 December) – FTE	411.70	411.64	418.72
Number of employees (as of 31 December) – capita	568	582	594
thereof men	194	207	215
thereof women	374	375	379
Number of scientists and physicians – FTE	225.68*	244.45*	240.28
Number of scientists and physicians – capita	311*	336*	325
thereof men	147	168	173
thereof women	164	168	152
These include:			
DZHK Professors and Junior Research Group leaders – FTE	19.31	17.51	21.10
DZHK Professors and Junior Research Group leaders – capita	23	18	22
thereof men	18	15	18
thereof women	5	3	4
Senior Scientists and Postdocs – FTE	170.42	181.75	180.78
Senior Scientists and Postdocs – capita	227	243	242
thereof men	100	116	127
thereof women	127	127	115
Doctoral students** – FTE	35.95	45.19	38.4
Doctoral students** – capita	61	75	61
thereof men	29	37	28
thereof women	32	38	33
Non-scientific employees and others – FTE	150.91*	133.59*	150.37
Non-scientific employees and others – capita	216*	202*	234
thereof men	35	31	38
thereof women	181	171	196

\* without employees of the DZHK association management, funding management department and competence networks

\*\* in previous annual reports: PhD students

### Principal Investigators, DZHK scientists, members of the Young DZHK

The DZHK is more than just a contact point for project inquiries: In the course of eleven years, a lively network of meanwhile 2,208 scientists and research physicians (as of December 31, 2022) at all career levels has developed. They work on important questions in cardiovascular research across institute boundaries and locations and from the different perspectives of molecular biologists, bioinformaticians, imaging specialists or cardiogeneticists.

In the year under review, 643 DZHK scientists (2021: 572) and 1,415 young researchers with Young DZHK status (2021: 1,260) were also part of the DZHK's extensive network.

A special role in our research profile is played by the 150 scientists who have been granted the status of "Principal Investigator" – in short: PI – at the DZHK: They shape the DZHK with their research focus.

## New Principal Investigators at the partner sites


In 2022, twelve new PIs were appointed, eight of whom are women. They bring to the DZHK outstanding expertise in epigenetics, genome biology, and vascular biology, among others. The PIs are nominated by the sites and confirmed by the General Assembly.

The DZHK has a total of 150 PIs (as of 31/12/2022). The proportion of female PIs has remained constant at around 28 percent for several years. Our goal is that at least one third of the PIs at the seven DZHK locations are women. In the year under review, the proportion of female PIs increased to 31 percent.

As a rule, the PIs do not receive funding from the DZHK, but lead their own research projects and provide important impetus for DZHK research. With Professor Ralf Gilsbach as the new PI, a DZHK W3 professorship in RNA biology has also been filled at the Heidelberg/Mannheim site. At the Munich site, Professor Donato Santovito was appointed to a W2 professorship in vascular immunotherapy.

DZHK professors are appointed by their respective institutions and financed by the DZHK site funds. They contribute significantly to the scientific profile of the sites. In 2022, there were 18 DZHK professorships.

All professorships can be found at:

 [dzhk.de/en/the-dzhk/scientists/dzhk-professorships/](https://dzhk.de/en/the-dzhk/scientists/dzhk-professorships/)

In 2022, the following new PIs were appointed. Their terms will run through 2025:

### Berlin

- Sofia Forslund (Max Delbrück Center for Molecular Medicine in the Helmholtz Association)
- Sabine Klaassen (Charité – Universitätsmedizin Berlin, Department of Pediatrics with a focus on Cardiology)

### Hamburg/Kiel/Lübeck

- Larissa Fabritz (UKE, Clinic and Polyclinic for Cardiology)
- Raphael Twerenbold (UKE, Epidemiological Study Center)

### Heidelberg/Mannheim

- Daniel Durschmied (University Medicine Mannheim)
- Sandy Engelhardt (Heidelberg University Hospital)
- Eileen Furlong (EMBL Heidelberg, Department of Genome Biology)

- Ralf Gilsbach (Heidelberg University Hospital)
- Carolin Lerchenmüller (Heidelberg University Hospital, Clinic for Cardiology, Angiology, Pneumology)

### Munich

- Christian Hagl (University Hospital Munich)
- Esther Lutgens (University Hospital Munich)
- Konstantin Stark (University Hospital Munich)

### Rhine-Main

- Sofia-Iris Bibli (Johann Wolfgang Goethe University Hospital Frankfurt)

## SCIENCE MANAGEMENT

The scientific management of the DZHK consists of 53 employees. Some of them work in the Berlin office in the association management and in the Funding Management Department (FMM). Another part works in the DZHK's seven branch offices throughout Germany. The FMM is institutionally part of the Max Delbrück Center for Molecular Medicine of the Helmholtz Association (MDC).

As of December 31, 2022, the association management had 20 employees (15.74 FTE), including the managing director. The FMM had 14 employees (10.90 FTE). The DZHK usually finances one full-time position for a site manager and one full-time position for an administrative assistant within the partner site management offices. They coordinate all activities of their site, such as application and reporting, financial control, and the organization of site retreats and PI meetings. The FMM is responsible for the legal review of all DZHK funding applications in addition to the review of the proof of use and financial controlling. It forwards project funds to the partner institutions at the seven partner sites and external cooperation partners. A total of 511 ongoing projects were funded in the year under review (previous year: 496). The total number of DZHK projects to date is 1909.

The members of the management team coordinate the areas of Clinical Research, Preclinical Research, the Clinical Research Platform, the Young DZHK, Scientific Exchange, and Public Relations. In addition, the management supports the organs and committees of the DZHK in strategic processes.

In 2022, in addition to standard tasks, these topics and projects were of particular relevance to the association management:

- 10<sup>th</sup> anniversary of the DZHK (p. 5)
- New funding instrument TRP Starter Grants launched, and first projects approved (p. 20)
- First call for DZHK Innovation Clusters (p. 23)
- First call for proposals of the DZG Innovation Fund for cross-DZG projects (p. 38)
- First joint DZG symposium on Post-Covid Syndrome (p. 39)
- Second call "Utilisation of the DZHK Collection" for secondary use of data and biospecimens of the DZHK collection and public announcement of the utilization projects (p. 32)
- Preparation of the centralization of biobanking (p. 31)
- Start of an initiative to harmonize DZHK cohorts (p. 31)
- DZHK Retreat and Young DZHK Retreat for the first time in two years (p. 40)
- Second round for Postdoc Start-up Grant on Advancing Digital Aspects (p. 35)
- Preparation of external evaluation, due in 2024, started

# ..... Partner Sites



## DZHK PARTNER SITE BERLIN

### Partner site spokesperson

Holger Gerhardt, Max Delbrück Center for Molecular Medicine in the Helmholtz Association, Head of "Integrative Vascular Biology"; Professor of Experimental Cardiovascular Research at Charité; DZHK Professor and BIH Professor (Berlin Institute of Health)

### Deputy spokespersons

Sabine Klaassen, Charité – Universitätsmedizin Berlin – Clinic for Pediatric Cardiology, Experimental and Clinical Research Center (ECRC). Until 11/2022: Burkert Pieske, Charité – Universitätsmedizin Berlin, Clinic Director Medical Clinic with focus on Cardiology (Virchow-Klinikum) and Clinic for Internal Medicine – Cardiology (DHZB). From 12/2022: Frank Edelmann, Charité – Universitätsmedizin Berlin Campus Virchow-Klinikum German Heart Center of the Charité (DHZC) Clinic for Cardiology, Angiology & Intensive Care Medicine – HSA

### Partner site management

Until 12/2022: 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 (Charité) | German Heart Center of the Charité (DHZC, formerly: German Heart Center Berlin, DHZB) | German Institute of Nutrition Research (DIFE) | Max Delbrück Center for Molecular Medicine in the Helmholtz Association | Robert Koch Institute (RKI)

## What was important in 2022

At the turn of the year to 2023, the cardiac medical facilities of the German Heart Institute Berlin (DHZB) and Charité were merged to form the new German Heart Center of Charité (DHZC). The DHZC comprises eight clinics and institutes, making it one of the largest cardiac centers in Germany.



Gabriele G. Schiattarella (Max Delbrück Center and Charité) successfully attracted third-party funding. He received an ERC Starting Grant endowed with €1.8 million to study the molecular mechanisms of heart failure. Jan Philipp Junker of the Max Delbrück Center received an ERC Consolidator Grant of €2 million for his research on how the heart can heal itself. One of the prestigious ERC Advanced Grants, awarded annually by the European Research Council, went to Michael Gotthardt, also of the Max Delbrück Center: He received funding of €2.5 million to investigate the contractile and elastic properties of the heart. DZHK researcher Franziska Seidel from the DHZC investigates disease mechanisms of cardiac myocarditis in children – supported by the Gerd-Killian project call of the Heart Foundation. The site also obtained a grant for the German arm of the US PRIMARY study, led by Volkmar Falk at the DHZC.

Five DZHK researchers from Berlin are among the Highly Cited Researchers in 2022. They belong to the most cited researchers worldwide. Since June 2022, Wolfram Döhner from the Charité has been a new board member of the European Society of Cardiology (ESC).

Various events were held to promote scientific exchange at the site and beyond: Around 100 guests attended the fifth DZHK site retreat in Berlin. In May 2022, researchers met in Berlin at the DZHK symposium, "Translational Symposium on Lifestyle-based Prevention of Non-communicable Diseases". In June 2022, basic researchers from all over the world met at the "XXIV World Congress" of the International Society for Heart Research, which was associated with a DZHK symposium.



## DZHK PARTNER SITE GÖTTINGEN

### Partner site spokesperson

Wolfram-H. Zimmermann, Director of the Institute of Pharmacology at the University Medical Center Göttingen

### Deputy spokespersons

Rabea Hinkel, Professor of Laboratory Animal Science at the German Primate Center Until 11/2022: Eberhard Bodenschatz, Director of the Max Planck Institute for Dynamics and Self-Organization. From 12/2022: Elisabeth Zeisberg, Professor of Cardiac Stroma, Department of Cardiology and Pneumology at the University Medical Center Göttingen

### Partner site management

Axel Kaul (partner site manager), Vanessa Kruse (scientific project manager), Sylvia Vann and Sabine Effenberger (partner site administrators), Marie-Christin Ernst (assistance), University Medical Center Göttingen

### Partner institutions at the DZHK partner site Göttingen

Georg August University Göttingen | University Medical Center Göttingen (UMG) | German Primate Center (DPZ) | Max Planck Institute for Dynamics and Self-Organisation (MPI-DS) | until 12/2021: Max Planck Institute for Experimental Medicine and Max Planck Institute for Biophysical Chemistry | as of 01/2022 merged into the Max Planck Institute for Multidisciplinary Natural Sciences (MPI-NAT)

## What was important in 2022

In 2022, the Heart and Brain Center Göttingen (HBCG) could be completed, and the move-in is planned for April 2023. The HBCG will be used for joint research into heart and brain diseases, and the construction costs of around €38 million will be funded by the state of Lower Saxony and the federal government.



A team led by Elisabeth Zeisberg (UMG) received €1.5 million in additional funding in the nationwide innovation competition SPRIND-Challenge of the Federal Agency for Leap Innovation to develop a novel antiviral therapy. Within the framework of the DZHK investment program, urgently needed equipment for producing genetic vectors (AAV) for therapeutic genome editing and preclinical testing was purchased.

Tobias Brüggemann (UMG) has accepted a call to a W2 professorship in physiology and pathophysiology in 2022. Lutz Ackermann (University of Göttingen) received the French-German Georg Wittig-Victor Grignard Prize 2022 of the Société Chimique de France, Stefan Hell (MPI-NAT) received the Werner-von-Siemens-Ring 2022 and was accepted into the Order Pour le mérite.

The Cardiovascular Bioengineering Symposium, jointly organized with the NIH, was held in Göttingen in June 2022. With 40 international speakers, the symposium aimed to promote international networking and offered young scientists an excellent platform to present themselves and their projects to a large scientific audience through the Young Investigator Award presentations. The symposium was very well received, with 170 participants from Germany and abroad.

The Translational Networks Meeting took place on 16.11.2022 in Göttingen at the MPI for Multidisciplinary Natural Sciences to support the networking of translational research. Scientists from DZHK, DZNE, DZKJ, Fraunhofer ITMP, and MBExC met to intensify their collaboration on translational projects at the site.





## DZHK PARTNER SITE GREIFSWALD

### Partner site spokesperson

Until 06/2022: Stephan B. Felix, Director of the Clinic and Polyclinic for Internal Medicine B, University Medicine Greifswald. From 06/2022: Marcus Dorr, Clinic and Polyclinic for Internal Medicine B, University Medicine Greifswald

### Deputy spokespersons

Until 06/2022: Marcus Dörr and Jens Fielitz, Clinic and Polyclinic for Internal Medicine B, University Medicine Greifswald. From 06/2022: Jens Fielitz and Stephan B. Felix, Clinic and Polyclinic for Internal Medicine B, University Medicine Greifswald

### Partner site management

Stefan Groß (partner site manager), Susanne Franck (partner site administrator/controlling), Kornelia Sadewasser (partner site administrator/finances), University Medicine Greifswald

### Partner institutions at the DZHK partner site Greifswald

University Medicine Greifswald (Clinic & Polyclinic for Internal Medicine B, Interfaculty Institute for Genome Research, Institute for Clinical Chemistry & Laboratory Medicine, Institute for Community Medicine (Dept. of Prevention Research & Social Medicine, Dept. of SHIP-Clinical Epidemiological Research, Dept. of Health Services Research & Community Health))

## What was important in 2022

At the partner site in Greifswald, the new laboratory animal facility, which is directly connected to the molecular biology research laboratories of the cardiology department, was moved into and is available to the DZHK projects for all animal experimental work. It is equipped with modern operating and examination rooms for the phenotyping of cardiovascular diseases.



The DZHK symposium "Prevention of Cardiovascular Diseases – Insights from Epidemiologic Studies" with numerous international speakers was held in Greifswald in September 2022 as part of the annual meeting of the DGEpi.

Recruitment for the population-based cohort "SHIP-NEXT-0" with a planned enrollment of 4,500 subjects was successfully continued in 2022. Population-based cohorts (incl. NAKO) with a total number of > 220,000 subjects will be available to DZHK projects for cardiovascular research from 2025. In SHIP-NEXT, new innovative e/m health-based research approaches such as contactless pulse wave measurements or long-term actimetry/GPS tracking will be used for the first time.

Construction of the William B. Kannel Center for Community Medicine, recommended by the Science Council, will begin in 2022. The nationally significant research building will raise the profile of the campus in population-based epidemiologic research. Upon completion in 2026, the building will house the DZHK Research and Training Center and DZHK scientists, as well as the Study of Health in Pomerania (SHIP) study center.

In 2021, the Helmholtz Institute for One Health was founded at the Greifswald site, which will lead to synergies in 2022, such as the joint acquisition of a fully automated nitrogen storage facility in the field of biobanking.

Scientists from the Greifswald site were also involved in nationwide COVID projects in 2022 within the framework of the Network University Medicine, in many cases also in leading or spokesperson positions (e.g., Steering Committee of the "National Pandemic Cohort Network" [NAPKON], Use and Access Committee NAPKON, spokesperson FOSA Cardiology and Laboratory Medicine). Greifswald was the leading recruitment center of the NAPKON cross-sector platform (SUP cohort) and has also established local Post-COVID cohorts ("PoCoRe," "PoCoReCONNECT"), which received state funding of €1.48 million at the end of 2022.

## DZHK PARTNER SITE HAMBURG/KIEL/LÜBECK

### Partner site spokesperson

Stefan Blankenberg, Clinic Director, Medical Director of the University Heart and Vascular Center Hamburg, University Medical Center Hamburg-Eppendorf (UKE)

### Deputy spokespersons

Derk Frank, Medical Director of the Clinic for Internal Medicine III with a focus on cardiology, angiology and internal intensive care, University Hospital Schleswig-Holstein Campus Kiel; 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 (finances at partner site), University Medical Center Hamburg-Eppendorf

### Partner institutions at the DZHK partner site Hamburg/Kiel/Lübeck

University Hospital Hamburg-Eppendorf; Asklepios Klinik St. Georg | University of Lübeck (UKSH, Campus Lübeck) | Kiel University (UKSH, Campus Kiel)

## What was important in 2022

At the partner site, interdisciplinary research teams study heart diseases from different perspectives and close gaps in the research chain. Scientific priorities include identifying genetic risk factors, biomarker research, stem cell and tissue engineering, and systems medicine approaches to decipher disease mechanisms and new therapeutic targets of congenital and acquired heart disease.

The site has valuable research infrastructures for multi-omics analyses, disease-relevant model systems (e.g., large animal, small animal, as well as iPSC platforms), imaging and phenotyping techniques, large patient cohorts, artificial intelligence and digital health, and clinical trials.



In January 2022, the UKE and Science Senator Katharina Fegebank held the topping-out ceremony for the new Heart and Vascular Center, which features state-of-the-art equipment and expanded diagnostic capabilities. The new building offers excellent conditions for treating highly complex and rare cardiovascular diseases and provides holistic care for patients by integrating the entire pediatric cardiac area.

The future Cardiovascular Imaging Center will be a highly specialized imaging center that will enable diagnostics at very early stages of disease and image-guided minimally invasive therapies. The new building is scheduled to be ready for occupancy in 2023.

Translational research at the UKSH Kiel Campus has been strengthened by establishing a new DZHK W2 Professorship for Translational Cardiology and Angiology, which Prof. Oliver J. Müller successfully filled as of July 1, 2022. This will enable him to continue his work on new therapeutic approaches for heart failure, Marfan syndrome, and pulmonary hypertension as well as the development of adeno-associated viral vectors for cardiovascular gene transfer. In addition, Prof. Derk Frank was nominated for the W3-Professorship in Cardiology and Angiology – connected with the direction of the Clinic for Internal Medicine III (Cardiology, Angiology, Intensive Care Medicine) at the Campus Kiel. At the Lübeck Institute of Human Genetics (Director: Prof. Malte Spielmann), Prof. Martin Kircher founded the WG Computational Genome Biology and Regulatory Genomics. The team focuses on research into computer-based methods for identifying functionally relevant genomic sequences and sequence variants.

Prof. Markus Schwaninger has acquired an Intravital 2-photon STED microscope for the research building "Center of Brain, Behavior and Metabolism" (CBBM) at the University of Lübeck.



## DZHK PARTNER SITE HEIDELBERG/MANNHEIM

### Partner site spokesperson

Johannes Backs, Director of the Institute for Experimental Cardiology, Heidelberg University Hospital

### Deputy spokespersons

Jörg Heineke, University Medicine Mannheim; second deputy: Patrick Most, Department of Internal Medicine III, Heidelberg University Hospital

### Partner site management

Tanja Weis (partner site manager), Denise Kampffmeyer (partner site administrator), Melissa Schank (finances), Heidelberg University Hospital

### Partner institutions at the DZHK partner site

#### Heidelberg/Mannheim

Heidelberg University | Heidelberg University Hospital | Mannheim University Medical Center | German Cancer Research Center (DKFZ) | European Molecular Biology Laboratory (EMBL)



### What was important in 2022

The Heidelberg/Mannheim partner site contributes the scientific focus "Hereditary and inflammatory cardiomyopathies and arrhythmias" to the DZHK. Twelve site projects are currently being worked on within this scientific topic.

Under the leadership of Prof. Johannes Backs and Prof. Norbert Frey, the full proposal submitted last year for the SFB entitled "Molecular Circuits of Heart Disease" was finally approved, and the funding started in the second half of 2022.

During the general meetings in March and September 2022, Jun. Prof. Sandy Engelhardt, Prof. Daniel Dürschmied, Prof. Ralf Gilsbach, Dr. Carolin Lerchenmüller, and Dr. Eileen Furlong were appointed site PI.

Apl. Prof. PD Dr. Constanze Schmidt from the Department of Cardiology at Heidelberg University Hospital was awarded the prestigious Else Kröner Clinician Scientist Professorship for Atrial Arrhythmopathy.

Prof. Mirko Völkers was accepted into the Heisenberg Program of the DFG in the reporting year with the proposal "mRNA metabolism and translational control in cardiomyocytes."

Internal Medicine VIII (Prof. Johannes Backs) and Internal Medicine III (Prof. Norbert Frey) and another department of Heidelberg University Hospital are receiving extensive new laboratory space totaling more than 2,000 square meters in an external building close to the campus. More than €1.5 million will be provided by the Medical Faculty of the University of Heidelberg for the new equipment.



## DZHK PARTNER SITE MUNICH

### Partner site spokesperson

Christian Weber, Director of the Institute for Prophylaxis and Epidemiology of Circulatory Diseases, Hospital of the Ludwig Maximilian University of Munich

### Deputy spokespersons

Stefan Engelhardt, Director of the Institute of Pharmacology and Toxicology of the Technical University of Munich

### Partner site management

Sandra Rauser (partner site manager), Hospital of the Ludwig Maximilian University of Munich; Elif Alkan (assistance), Technical University of Munich

### Partner institutions at the DZHK partner site Munich

Hospital of Ludwig Maximilian University of Munich (KUM) | Ludwig Maximilian University of Munich (LMU) | Technical University of Munich (TUM) | German Heart Center Munich (DHM) | Klinikum rechts der Isar (MRI) der Technischen Universität München | Helmholtz Munich – German Research Center for Environmental Health (HMGU) | Max Planck Institute for Biochemistry (MPI)

## What was important in 2022

In 2022, more than 80 DZHK projects at the Munich site investigated the center's goals. For example, researchers at MRI found in porcine hearts that human ventricular progenitor cells (HPVs) can challenge the formation of new cardiac tissue, improve cardiac function, and reduce scar tissue (Poch et al., Nat Cell Biol 2022). At KUM, a previously unknown neutrophil-mediated mechanism was discovered to lead to an increased risk of recurrent ischemia



after myocardial infarction (Petzold et al., Immunity 2022). Furthermore, it could be shown for the first time that in atherosclerosis, nerve signals are exchanged between blood vessels and the brain (Mohanta et al., Nature 2022), which in the long run offers chances for a causal therapy.

In March, Prof. Christian Hagl, Prof. Esther Lutgens, and Prof. Konstantin Stark, three new DZHK PIs, joined the site. Dr. Daniel Andergassen started his DZHK Junior Research Group at the Institute of Pharmacology and Toxicology (IPT) of the TUM on June 1, 2022, Prof. Donato Santovito started his DZHK professorship for "Vascular Immunotherapy" at the Institute for Prophylaxis and Epidemiology of Circulatory Diseases (IPEK) of the LMU Klinikum on September 15, 2022 (IPEK) of the LMU Hospital.

Apart from the primary DZHK activities, the Munich scientists were also very successful. For example, the SFB 1123 "Atherosclerosis: Mechanisms and Networks of Novel Therapeutic Targets" (spokesperson: Prof. Christian Weber) was successfully reviewed and extended for another four years. C-NATM (co-speaker: Prof. Stefan Engelhardt) won one of a total of seven clusters in the second round of the BMBF's Clusters4Future initiative, which aims to develop RNA-based drugs and vaccines that expand the spectrum of drug-treatable diseases. Prof. Fabian Theis received an ERC Advanced Grant, and PD Dr. Thorsten Kessler an ERC Starting Grant.



## DZHK PARTNER SITE RHINE-MAIN

### Partner site spokesperson

Andreas Zeiher, Distinguished Professorship at Goethe University Frankfurt

### Deputy spokespersons

Philipp Wild, Professor of Clinical Epidemiology, Head of Preventive Cardiology and Medical Prevention, Center for Cardiology, Head of Clinical Epidemiology and Systems Medicine, Center for Thrombosis and Hemostasis, University Medicine, Johannes Gutenberg University Mainz.  
Ralf Brandes, Director of the Institute of Cardiovascular Physiology, Goethe University Frankfurt

### Partner site management

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

### Partner institutions at the DZHK partner site

#### Rhine-Main

Goethe University Frankfurt | Max Planck Institute for Heart and Lung Research Bad Nauheim | Kerckhoff-Klinik Bad Nauheim | University Medical Center of the Johannes Gutenberg University Mainz

## What was important in 2022

At the University Hospital in Frankfurt am Main, Prof. Stefanie Dimmeler and Prof. Andreas Zeiher each received an ERC Advanced Grant for a total of €7.2 million. In July, the SFB 1513 "Damage Control by the Stromavascular Compartment" started with Prof. Ralf Brandes as a speaker and Prof. Ingrid Fleming as co-spokesperson. Prof. Dimmeler received the Otto Warburg Medal and Prof. Fleming the Ernst Jung Prize for Medicine.



In October, a DZG Symposium on Post-COVID Syndrome (see p. 42) and the Merz Award Symposium of Prof. Joseph C. Wu from Stanford took place in Frankfurt.

Scientific highlights included the Atlas of the Human Hypertrophied Heart (Nicin et al., Nat Cardiovasc Res. 2022), the impact of mild SARS-CoV-2 infection on cardiovascular health (Puntmann et al., Nat Med. 2022), and publications on lncRNA triplex formation (Leisegang et al., Nat Commun; Warwick et al., Brief Bioinform 2022). At the MPI-HLR, Dr. Pieterjan Dierickx has opened his laboratory focusing on the circadian regulation of cardiac metabolism.

The joint project GARY of Prof. Eva Herrmann and Prof. Christian Hamm of the Kerckhoff Clinic was successfully completed after two years with twelve publications and €4.6 million raised for the project "PeriOP-CARE HF".

The University Medical Center of the Johannes Gutenberg University in Mainz, was selected as a core partner in the BMBF's curATime future cluster "Cluster for Atherothrombosis and Individualized Medicine" for the first three of a total of nine years (total funding: €15 million). For the multi-disciplinary consortium DIASyM, the second funding phase (2023–2026) was approved with €3.6 million. For the characterization of heart failure (MyoVasc) using proteomic profiling, €2.4 million were granted by Bayer AG.

Scientific highlights include a paper presenting a new approach for the treatment of stress-dependent vascular dysfunction in coronary artery disease (AG Wenzel, Efentakis et al., Eur Heart J. 2022), a review of environmental risk factors for cardiovascular disease (Munzel et al., Cardiovasc Res. 2022) and the identification of the aldosterone/renin relationship for long-term prediction of arterial hypertension (AG Wild, Arnold et al., Cardiovasc Res. 2022).

## ACRONYMS

<b>AAV</b>	Adeno-Associated Virus	<b>Fig.</b>	Figure
<b>AI</b>	Artificial intelligence	<b>FKZ</b>	Funding Code (all projects can be found in the project database at <a href="https://dzhk.de/en/resources/data-manual/">https://dzhk.de/en/resources/data-manual/</a> )
<b>BDMS</b>	Image Data Management System	<b>FMM</b>	Funding Management Department
<b>BfArM</b>	Federal Institute for Drugs and Medical Devices	<b>FTE</b>	Full-time equivalent
<b>BHF</b>	British Heart Foundation	<b>GCRFF</b>	Global Cardiovascular Research Funders Forum
<b>BMBF</b>	Federal Ministry of Education and Research	<b>GRS</b>	Guideline-relevant study
<b>DCM</b>	Dilated cardiomyopathy	<b>LIMS</b>	Laboratory Information Management System
<b>DGK</b>	German Cardiac Society	<b>MRT</b>	Magnetic resonance imaging
<b>DHF</b>	Dutch Heart Foundation (Hartstichting)	<b>NAKO</b>	NAKO Health Study = formerly National Cohort
<b>DHZC</b>	Deutsches Herzzentrum der Charité (engl. German Heart Center of the Charité), formerly German Heart Center Berlin (DHZB)	<b>NAPKON</b>	National Pandemic Cohort Network
<b>DKTK</b>	German Consortium for Translational Cancer Research	<b>NUM</b>	Network University Medicine
<b>DNA</b>	Deoxyribonucleic acid	<b>PDU</b>	Product Development Unit
<b>DZD</b>	German Center for Diabetes Research	<b>PEI</b>	Paul Ehrlich Institute
<b>DZG</b>	German Centers for Health Research	<b>PI</b>	Principal Investigator
<b>DZHK</b>	German Center for Cardiovascular Research	<b>RCC</b>	Research Coordinating Committee
<b>DZIF</b>	German Center for Infection Research	<b>RNA</b>	Ribonucleic acid
<b>DZKJ</b>	German Center for Child and Adolescent Health	<b>SFB</b>	Collaborative Research Center
<b>DZL</b>	German Center for Lung Research	<b>SHIP</b>	Study of Health in Pomerania
<b>DZNE</b>	German Center for Neurodegenerative Diseases	<b>SOP</b>	Standard Operating Procedure
<b>ECG</b>	Electrocardiogram	<b>StM</b>	Site Management
<b>ECS</b>	Early clinical study	<b>TAVI</b>	Transcatheter Aortic Valve Implantation
<b>ERC</b>	European Research Council	<b>TRP</b>	Translational Research Project
<b>ESC</b>	European Society of Cardiology	<b>UAC</b>	Use and Access Committee
		✓	Goal achieved
		↻	In progress
		—	Goal not achieved

# IMPRINT

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