



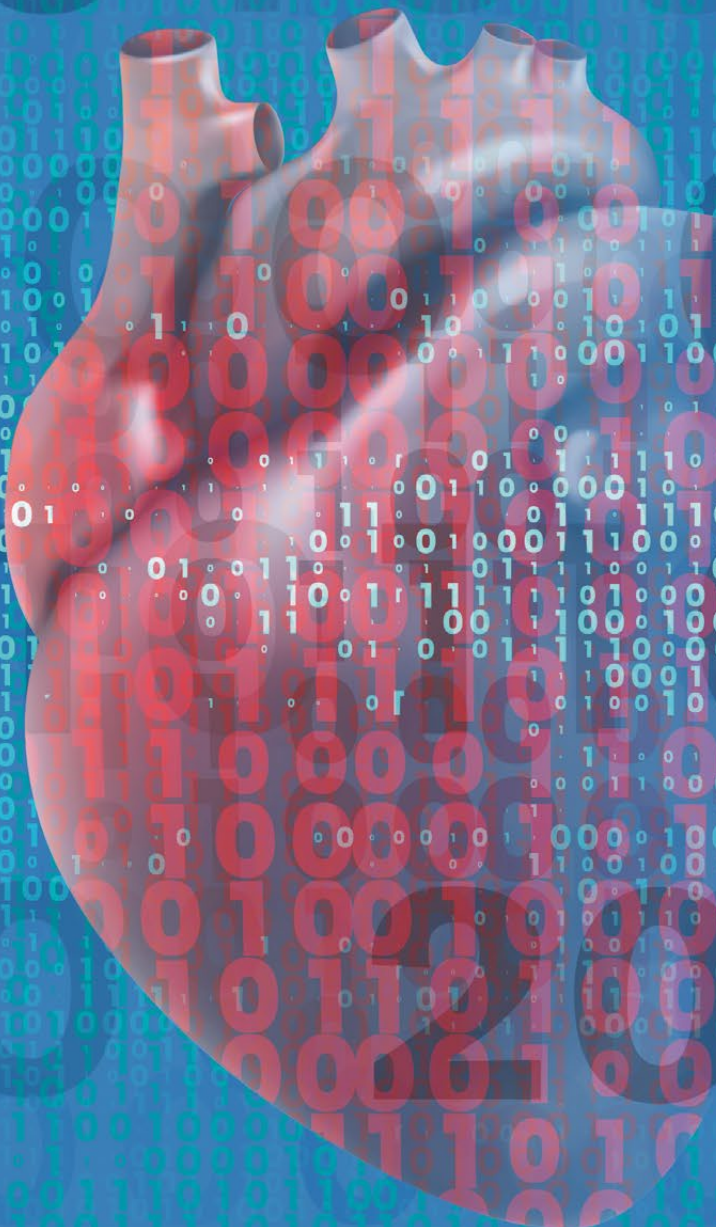
DZHK
DEUTSCHES ZENTRUM FÜR
HERZ-KREISLAUF-FORSCHUNG E.V.



DEUTSCHE ZENTREN DER
GESUNDHEITSFORSCHUNG

German Centre for Cardiovascular Research

ANNUAL REPORT



2021



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

At the beginning of 2021, two talented individuals joined the DZHK's senior management team. Prof. Stefanie Dimmeler was appointed Spokesperson of the Board of Directors and Dr. Katharina Eulenburg was appointed Managing Director. We would like to offer our sincere thanks to Thomas Eschenhagen as Board Spokesperson and Joachim Krebs as Managing Director for their outstanding achievements in managing the DZHK in the past nine years.

2021 was marked by reflections on strategic development while continuing to address operational challenges brought about by the Corona pandemic. In the first year of the pandemic, the DZHK started to collect data and biospecimens on behalf of the Network University Medicine (NUM) for COVID-19 research. After one year, this successful and fruitful collaboration ended on schedule in December 2021. The NUM now intends to set up future COVID-19 research following the success of the DZHK model.

With a focus on strategic development, we aimed to improve research translation and digitalization in 2021.

In cardiovascular medicine, big data and AI solutions hold great potential for innovative solutions for improving patient care. We therefore launched new funding opportunities with the goal of driving digital transformation.

We also explored in depth how translation – i.e. the transfer of results from basic research to clinical application – could be even more successful. Surveys and internal discussions revealed that translational research requires significant preparation and external expertise and support. We have begun to plan appropriate measures.

We are delighted that our scientists were able to further increase their numbers of published papers, including in high-ranking journals.

Despite continued challenges following the Corona pandemic, we are incredibly proud of our achievements in 2021. Our board of directors and management team would like to thank each and every individual for their resilience, commitment and excellent work.



Stefanie Dimmeler
Spokesperson of the
Board of Directors



Steffen Massberg
Board of Directors



Thomas Sommer
Board of Directors



Katharina Eulenburg
Managing Director

Focus Digitalization

In medicine and the life sciences, Big Data and AI have great potential for innovative solutions and improving efficiency. Wearables and devices are already providing diagnostic support for cardiovascular patients today.



Digital and AI applications are particularly appealing in cardiovascular research and clinical cardiology, as most diagnostic electrophysiology and imaging data are already collected digitally.

With the DZHK Heart Bank (see p. 35), the DZHK also has a digital data, metadata, and image data collection that originates from clinical studies and continues to grow. These datasets are a valuable basis for AI analysis and Deep Learning. Due to this, the Board of Directors, Research Coordinating Committee (RCC), and General Assembly initiated several activities in this area during the reporting year. This direction also aligned with our Scientific Advisory Board's strategic recommendation to further promote digitalization.

As the requirements and problems in preclinical and clinical research differ, a clinical task force (spokespersons Philipp Wild and David Leistner) and a preclinical task force (spokespersons Titus Kühne and Marcel Schulz) with representatives per partner site were set up to manage digitalization.

The task forces are mandated to develop strategic priorities and evaluate research ideas for their relevance and feasibility. In clinical research, the focus should be on apps and smart devices in particular. Preclinical research and basic research should focus on data sharing and research resources. DZHK announced funding for the following project type:

Digital partner site projects

DZHK invited each partner site to submit up to two projects (total budget per site: €100,000, Greifswald €66,000).

The partner sites submitted ten projects, of which two were preclinical and eight clinical.

The applications were roughly divided into three thematic clusters: Processes, Infrastructures, and Data Collection (four applications, including both preclinical projects), Data Processing and Analysis (two applications), and Algorithms (five applications). One of the ten applications was assigned to two clusters.

The task forces awarded funding to every project, with a total funding value of €625,000.

All projects are available online in our project database under the project type "Digital Technologies":

<https://dzhk.de/en/resources/projektdatenbank/>

Central digitalization projects

Following the important and productive work of each task force, a need for multi-site digitalization projects that add value to the entire DZHK became clear. The task forces were responsible for developing these projects and all sites participated. The General Assembly approved the following three projects with a total funding value of €275,000:

Federated deep learning to support prostheses selection from TAVI-CT (clinic)

This multicenter project aims to establish a federated learning consortium to address a clinical question regarding TAVI prosthesis selections.

Nine clinics from seven DZHK sites and one additional hospital are involved. Novel concepts of federated learning (FL) train decentralized neural networks without the need for the underlying data to leave the individual sites (data sovereignty remains at the sites; possibility to use reproducibility cohorts that represent a wide range of patient characteristics and admission technique). The project aims to reach its first milestone regarding data preparation of more than 10,000 available patient datasets and implementing a test architecture.

Locations: Berlin, Göttingen, Greifswald, Hamburg/Kiel/Lübeck, Heidelberg/Mannheim, Munich, Rhine Main

FEDEX – Extension of the Feasibility Explorer for a better visualization of DZHK data (Clinic)

The goal of this project is the functional extension of current possibilities provided by the [Feasibility Explorer](#)[↗], to search the data and sample collection of the [DZHK Heart Bank](#)[↗] and confirm its scientific question suitability.

To this end, the project partners are integrating the Medex2 software for interactive web-based analysis of clinical data into the Feasibility Explorer.

Another essential component is risk impact assessment in addition to countermeasures regarding a possible re-identification of individuals and the unauthorized use of generated hypotheses.

Locations: Göttingen, Heidelberg/Mannheim

DZHK preclinical RNA-seq data analysis portal (D-DAP) (Preclinical)

This project aims to build a pilot portal for the DZHK community to analyze preclinical data, host public and private datasets, and provide data owner-centered use and access management.

This portal will initially focus on bulk RNA-seq and single-cell RNA-seq data, as such datasets are well

standardized, widely available in the DZHK community, and can be used with existing data analysis portal solutions.

The portal will enable scientists from all disciplines to analyze, visualize, and integrate their datasets into the wealth of existing DZHK and other published RNA-seq datasets from human and experimental model systems.

Locations: Berlin, Göttingen, Greifswald, Hamburg/Kiel/Lübeck, Heidelberg/Mannheim, Munich, Rhine Main

Postdoc Start-up Grant digitalization

To maximize the potential of young scientists for this future topic, a Postdoc Start-up Grant on Advancing Digital Aspects for members of the Young DZHK was announced for the first time in 2021, in addition to the conventional grant. Five projects were funded, three of which started in the reporting year.

Envision! Virtual reality for a better understanding and treatment of congenital heart defects

Nikolaus Thierfelder | Munich

Standardized ECG processing pipeline for AI/ML-based classification of cardiovascular diseases

Marcus Vollmer | Greifswald

Digital HeART (DHART) research portal

Etienne Boileau | Heidelberg/Mannheim

Assessment of heart failure mouse models by systematically comparing single cell transcriptomics data in mice and man

David John | Rhine Main

DZHK-Omics: Intuitive and standardized bulk RNA-sequencing analysis for the coding-naïve basic scientist

Mark Emile Pepin | Heidelberg/Mannheim

Further activities

The funding guidelines for translational research projects (TRP) (see p. 22) have been expanded to explicitly allow applications for the development of digital technologies.

On 14 and 15 October 2021, the Young DZHK from the Hamburg/Kiel/Lübeck site organized an online workshop on digitalization to highlight the diverse potential of digitalization in cardiovascular research and to further promote it.

RESEARCH THAT MATTERS — TRANSLATIONAL ACHIEVEMENTS IN 2021

The journey from innovation to clinic is often extensive. For example, the rapid introduction of the mRNA vaccine against the coronavirus by the company BioNTech was only possible because 20 years of basic and translational research took place beforehand.

The DZHK is active in the field of cardiovascular medicine at all stages of translation, from basic research to patient care. Here, we describe some successful projects in 2021.





CLINICAL RESEARCH

COVID-19 – Pausing antihypertensives can boost recovery

At the beginning of the pandemic, there was much uncertainty. Are antihypertensive drugs from the group of ACE inhibitors and angiotensin receptor blockers to blame for so many cardiovascular patients suffering with severe COVID-19?

Shortly after the pandemic outbreak, DZHK researchers at the Ludwig Maximilian University Hospital in Munich and colleagues at the University of Innsbruck designed the ACEI-COVID study to investigate the role of antihypertensive drugs. The DZHK had already launched an emergency program in 2020 for clinical trials that would investigate the effects of SARS-CoV-2 on the cardiovascular system.

The team published the results of the [ACEI-COVID Study](#)[↗] in *The Lancet Respiratory Medicine* in 2021. According to the study, temporarily discontinuing ACE inhibitors and angiotensin receptor blockers may improve the recovery period of high-risk patients suffering from COVID-19. However, the severity of the disease is not affected by the drugs. According to the study, pausing the medication could be particularly useful in older cardiovascular patients, but this must be reviewed by treating physicians in each individual case.

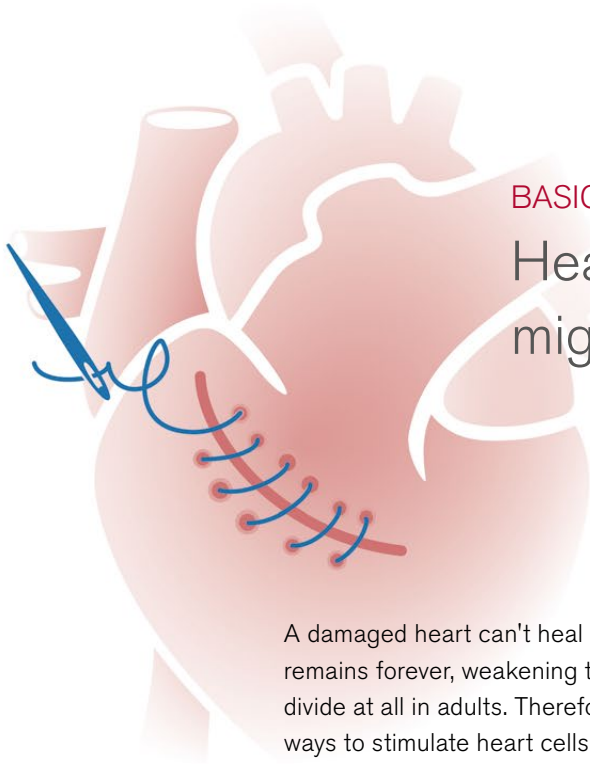
For high-risk COVID-19 patients with damaged cardiovascular systems, the study provides further guidance in treatment and follow-up.

Clinical trial
Principal investigator

Stopping ACE-inhibitors in COVID-19
Steffen Massberg (Munich)

[↗] Discontinuation versus continuation of renin-angiotensin system inhibitors in COVID-19 (ACEI-COVID): a prospective, parallel group, randomised, controlled, open-label trial. *The Lancet Respiratory Medicine*, 11 Jun 2021





BASIC SCIENCE

Heart attack – How scars might heal

A damaged heart can't heal like a wound in the skin. A scar caused by a heart attack remains forever, weakening the heart muscle. This is because heart muscle cells hardly divide at all in adults. Therefore, researchers worldwide are desperately searching for ways to stimulate heart cells to divide – or regenerate.

A DZHK team from the Max Planck Institute for Heart and Lung Research in Bad Nauheim, together with international colleagues, has reprogrammed heart muscle cells in mice so they can divide again. However, it is crucial how long and how strongly the cells are reprogrammed. If conditions are not ideal, the heart can't recover or even tumors could form.

The researchers used transgenic mice in which the expression of four stem cell factors in the heart can be switched on and off. These factors allow the heart muscle cells to regress and divide again. The animals' cardiac output improved, and scars were also smaller when expression of the factors was briefly turned on before or shortly after a heart attack. Isolated heart cells also began to regenerate when the factors were turned on.

Because improved regeneration in the experiments was partially at the cost of increased cancer risk, further research is needed before this method can reach clinical use.

Partner site project
Project lead

Rhine Main FKZ: 81Z0200302
Thomas Braun

📌 Reversible reprogramming of cardiomyocytes to a fetal state drives heart regeneration in mice .
Science, 23 Sept 2021



BASIC SCIENCE

Heart attack – Blood cells boost wound healing

Special white blood cells, called basophils, could boost heart healing after a heart attack, scientists from Heidelberg showed in an animal model. Basophils are mainly known to play a role in allergies and asthma.

In the case of a heart attack, heart muscle cells die and are broken down by immune cells during inflammation. Basophils also form part of the immune system and migrate to the area of inflammation. There they release messenger substances, IL-4 and IL-13, that stimulate wound healing. The messengers convert phagocytes, from phagocytes that promote inflammation to those that inhibit inflammation. The researchers observed that mice lacking these white blood cells had a significantly worse prognosis – the same was true for patients with few basophils at the time of a heart attack.

The team also wanted to find out whether a particular molecule could further accelerate healing. They already knew the anti-inflammatory effect of the molecule IPSE/alpha-1 – the eggs of an intestinal parasite release the molecule, causing the basophils to release more messenger substances which boosts the healing process.

In an animal model, the scientists observed exactly this effect in mice treated with IPSE/alpha-1 after a heart attack.

Partner site project
Project lead

Heidelberg/Mannheim FKZ: 81Z0500107
Florian Leuschner

Basophils balance healing after myocardial infarction via IL-4/IL-13. *The Journal of Clinical Investigation*, 1 Jul 2021

The Journal
Of Clinical
Investigation



BASIC SCIENCE

Congenital heart defects – How left heart syndrome develops

Left heart syndrome is a severe congenital heart defect that, if left untreated, can lead to death shortly after birth. Scientists at the DZHK, together with other partners, have now investigated the genetic causes of the disease in more detail.

Complex molecular programs at the cellular level control the development of the human heart. Mutations may alter this genetic network, and the sensitive cellular processes are disturbed. This is how hypoplastic left heart syndrome (HLHS) develops, which is characterized by underdevelopment of the left ventricle.

Using gene sequence analyses, the researchers have now identified the gene programs that control heart muscle development and are responsible for the heart's abnormal structural changes. In their multidisciplinary study, they also examined cardiac stem cells from HLHS patients during heart development and performed 3D modeling of ventricular development. They found that the cell cycle of heart cells from HLHS patients is disrupted.

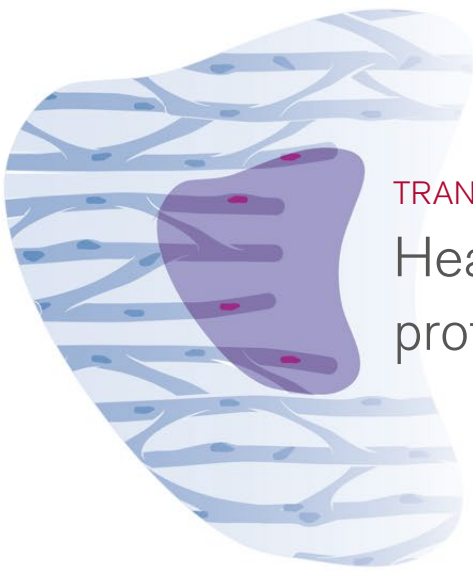
The cells do not undergo the regulated maturation process and lose their ability to respond to growth signals. Therefore, the heart cells die. The consequence is genetically-determined underdevelopment of the heart. With knowledge of these specific molecular defects, scientists hope to develop new therapeutic approaches that could improve the life expectancy of patients with HLHS in the future.

Partner site project
Project lead

Munich FKZ: 81Z0600601
Karl Laugwitz

📌 Sequential Defects in Cardiac Lineage Commitment and Maturation Cause Hypoplastic Left Heart Syndrome. *Circulation*, 25 Oct 2021





TRANSLATIONAL RESEARCH

Heart failure – Truncated protein weakens muscle

Titin is the human body's largest protein and provides muscle fiber elasticity. If defective, affected individuals can develop dilated cardiomyopathy (DCM) – when the heart muscle is weakened. What happens in a certain form of DCM has been demonstrated for the first time by a team including DZHK researchers from Göttingen.

Like most genes, the titin gene occurs twice in humans. One of the two titin genes is shortened in patients with the special form of DCM, while the other is still full-length and healthy. The mutation causes many shortened and less healthy titin proteins to be present in the heart muscle cells.

Theoretically, the healthy gene could produce enough titin to supply the heart muscle cells. Using more than 100 heart tissue samples, the research team found that although the healthy gene was more abundant in DCM patients, there was still significantly less healthy titin in them than in heart-healthy people or DCM patients with another cause of the disease. Less titin means fewer units capable of contracting in the muscle. As a result, the muscle develops less strength, and the heart is weakened.

The shortened titin proteins are also not recognized by cellular “quality control” and thus are not broken down. They clump together in the cells, similar to harmful proteins in Alzheimer's disease. The researchers were also able to show that the CRISP/Cas9 gene scissors can repair the mutation. However, this would have to start at the heart muscle cell's precise location. This is not yet possible, however if this changes, researchers suggest it could lead to a cure for this patient group.

Shared Expertise (SE)-Project

Munich-Göttingen FKZ: 81X2600611,
81X2300156 | SE-Nr. 155

Project lead

Alexander Goedel, Wolfgang Linke

Truncated titin proteins and titin haploinsufficiency are targets for functional recovery in human cardiomyopathy due to TTN mutations. *Science Translational Medicine*, 3 Nov 2021





TRANSLATIONAL RESEARCH

Heart failure – More elasticity and less heart stiffening

In a specific form of heart failure, the heart chambers can contract but are stiff and unable to expand effectively – like a dried-up leather bag. Not enough blood gets into the ventricles to supply the body's circulation. This is called heart failure with preserved ejection fraction and it is virtually untreatable. DZHK researchers from Berlin have demonstrated how stiffened heart muscle could become elastic again.

How elastic a muscle is is partly determined by the protein titin, the largest protein in the human body. The body makes titin in various subtypes that are more or less elastic. In heart muscle cells, titin wears out quickly due to the high stress of pumping and is, therefore, regularly renewed. In heart failure with preserved ejection fraction, increasingly less elastic titin variants are incorporated and the heart muscle stiffens.

Researchers have now developed an active substance that influences a specific step in titin synthesis – alternative splicing. In this process, a factor called RBM20 plays an unfavorable role in the elasticity of titin. If it is very active, stiffer titin molecules are formed. If it is inhibited, titin is more elastic. This was also shown in animal models whereby genetically modified mice that can produce only half as much RBM20 as their peers have more elastic titin. This finding was also confirmed with artificial heart tissue in the laboratory.

The next step is to stabilize the inhibiting compound so that it remains in the body long enough. Then it could be used as a drug for heart failure with preserved ejection fraction.

Partner site project
Project lead

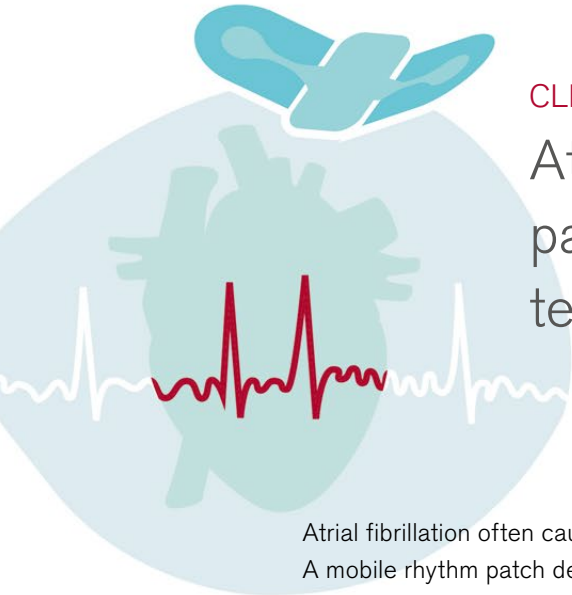
Berlin FKZ: 81Z0100105
Norbert Hübner

Shared Expertise (SE)-Project
Project lead

Berlin-Heidelberg/Mannheim FKZ: 81X2100151 | SE-Nr. 152
Michael Gotthardt, Christoph Dieterich

📌 Therapeutic inhibition of RBM20 improves diastolic function in a murine heart failure model and human engineered heart tissue. *Science Translational Medicine*, 1 Dec 2021

Science
Translational
Medicine



CLINICAL RESEARCH

Atrial fibrillation – Mobile patch detects arrhythmia ten times more often

Atrial fibrillation often causes no symptoms and can therefore be difficult to detect. A mobile rhythm patch detects atrial fibrillation in high-risk patients ten times more frequently than conventional diagnostics. The mobile procedure could thus be suitable for the early detection of atrial fibrillation and prevent subsequent strokes. This is the result of a study involving researchers from Canada and DZHK researchers from the Göttingen site, as well as a network of family doctors.

The multi-center, randomized study, called [SCREEN-AF- DZHK15](#)[↗], tested a rhythm patch that records every heartbeat and can detect silent atrial fibrillation. The study involved 856 people from 48 primary care practices between 2015 and 2019. Participants were 75 years or older and had high blood pressure but no known atrial fibrillation.

Half of the participants received the rhythm patch, which was placed on the chest twice for two weeks at a time and recorded the heart rhythm continuously. The other half received standard medical care. Atrial fibrillation was detected in 23 participants in the rhythm patch group and only two in the control group. The episodes of atrial fibrillation were usually several hours long. Of the patients found to have atrial fibrillation, 75 percent were receiving a blood-thinning medication to protect against strokes.

This impressive study demonstrates that atrial fibrillation can be detected early in the course of primary care and effectively prevent strokes.

<p>Clinical study Project lead (in Germany)</p>	<p>SCREEN-AF-DZHK15 Rolf Wachter (Göttingen and Leipzig)</p>
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↗ Screening for Atrial Fibrillation in the Older Population – A Randomized Clinical Trial. *JAMA Cardiology*, 24 Feb 2021





CLINICAL RESEARCH

Atrial fibrillation – Early rhythm maintenance is beneficial in heart failure

Starting rhythm-maintenance treatment early is beneficial for patients with heart failure and recently diagnosed atrial fibrillation, as shown by a subgroup analysis of the EAST-AFNET-4 study population. The [EAST-AFNET-4-Study](#) [↗] was largely funded by the DZHK and investigated whether rhythm-maintaining therapy using anti-arrhythmic drugs or catheter ablation improves patient outcome when started in the first year after diagnosis of atrial fibrillation.

The study's main finding was that early rhythm-maintaining therapy with drugs or ablation resulted in fewer deaths, strokes, and hospitalizations for worsening heart failure or acute coronary syndrome, compared with usual care.

In another evaluation, researchers analyzed data from the [EAST-AFNET-4-Study](#) [↗] to determine whether the beneficial effects of early rhythm maintenance could be extended to the subgroup of patients with heart failure. The analysis included 798 patients with heart failure, half of whom were in the early rhythm-maintenance study group and 402 in the standard care group.

During the median follow-up period of 5.1 years, the primary study endpoint (cardiovascular death, stroke, or hospitalization for worsening heart failure or acute coronary syndrome) occurred in 23 percent of participants with early rhythm maintenance. In the treatment-as-usual group, this was the case in 32 percent of patients.

Clinical study	EAST – AFNET 4
Principal investigator	Paulus Kirchhof (Hamburg/Kiel/Lübeck and AFNET)

📄 Early Rhythm Control Therapy in Patients With Atrial Fibrillation and Heart Failure.
Circulation, 30 Jul 2021





CLINICAL RESEARCH

Arrhythmias – Implanted monitor protects against complications after a heart attack

An implanted cardiac monitor detects more precursors to dangerous complications in patients who have survived a heart attack than in conventional follow-up. This is the result of the [SMART-MI-DZHK9 study](#)[↗], led by DZHK researchers at the Munich partner site.

The focus was on patients who had an ejection fraction of between 36 and 50 percent after a heart attack and disturbances in cardiac control by the autonomic nervous system. Their cardiac performance is thus still relatively good, yet many suffer life-threatening complications in the course of the disease.

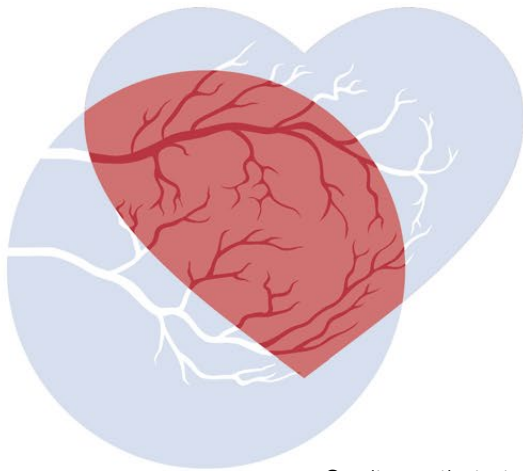
Those with poorer ejection fraction (below 35 percent) are known to have a high incidence of severe arrhythmias, so they are implanted with a defibrillator that delivers electricity shocks in the event of dangerous arrhythmia, bringing the heart back into rhythm. However, there are no specific preventive measures for the large group of patients with intermediate ejection fraction (36-50 percent). Unfortunately, life-threatening arrhythmias also occur in them, and are usually less noticeable. This study investigated whether implantable monitors can detect such early arrhythmias.

Four hundred patients were divided into two groups. The study group were implanted with the thumbnail-sized heart monitor under the skin and monitored by telemedicine. The control group received normal follow-up. In the monitor group, the researchers detected predefined severe rhythm events in 60 patients within 21 months, compared with only 12 patients in the control group. The researchers, therefore, recommend that even high-risk patients with moderately reduced ejection fraction and cardiac autonomic dysfunction should receive intensive follow-up and arrhythmia monitoring.

Clinical study | SMART-MI-DZHK9
Principal investigator | Axel Bauer (Graz and Munich)

[↗] 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*, 1 Feb 2022





CLINICAL RESEARCH/PATIENT CARE

Sudden cardiac arrest
– Challenging immediate
angiography if cause is
unclear

Cardiac catheterization examinations should not be performed immediately after arrival to hospital in resuscitated cardiac arrest patients with an unclear cause, as shown by the [TOMAHAWK-DZHK4](#) [↗] study.

Sudden cardiac arrest is caused by a heart attack in about half of cases. Other causes may include primary cardiac arrhythmias, cerebral hemorrhage, pulmonary embolism, or trauma. In some of the revived patients, heart attack can be clearly identified by special features in the ECG. They are examined by cardiac catheterization (angiography) immediately upon arrival at the hospital, which allows narrowed coronary arteries to be visualized and dilated.

For all others who come to the hospital, the cause often remains unclear at first. Since cardiac causes are the most common, all of these patients usually receive an immediate angiography. Whether or not this is the best course of action for this group of patients has been the subject of disagreement among physicians.

In this study, 554 patients were randomly divided into two groups. Patients in the immediate group underwent coronary angiography about three hours after arriving at the hospital. Of them, 143 had died after 30 days. The other group received intensive care for a mean of two days before cardiac catheterization was performed. If other causes of circulatory arrest were identified, the treatment team did not carry out coronary angiography. In this delayed group, 122 individuals died within the first 30 days. Severe neurological damage was even slightly more common in the immediate group.

The results suggest that when cardiac arrest is unclear in the emergency department, there is no rush to perform coronary angiography. Thus, the study brings more certainty to the decision-making process for emergency department personnel and prevents unnecessary testing for those in cardiac arrest.

<p>Clinical study</p> <p>Principal investigator</p>	<p>TOMAHAWK-DZHK4</p> <p>Steffen Desch (Leipzig and Hamburg/Kiel/Lübeck)</p>
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↗ Angiography after Out-of-Hospital Cardiac Arrest without ST-Segment Elevation. *New England Journal of Medicine*, 29 Aug 2021



Publications & Awards



PUBLICATIONS

In 2021, the total number of publications with DZHK affiliation, i.e. naming the DZHK, matched the previous year's figure of around 1,500.

The number of publications in high-impact journals (with an impact factor > 10) increased to 195.

A list of publications can be found on our website:

dzhk.de/en/research/research-focus/publications/publications-2021/

¹ including Lancet Neurology, Lancet Respiratory Medicine, Lancet Planetary Health

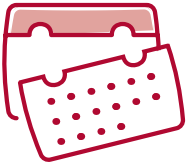
² including JAMA Cardiology, JAMA Internal Medicine

³ including JACC Cardiovascular Imaging

⁴ including Science Translational Medicine, Science Advances

Publications

	Number 2021	2020
Total publications	1,515	1,511
of which:		
First authorship of a DZHK PI	58	61
Last authorship of a DZHK PI	280	313
First authorship of a Young DZHK member	307	277
First authorship of a DZHK Scientist	119	122
Last authorship of a DZHK Scientist	357	309
Publications involving several DZHK sites	168	128
Publications published in:		
Nature Publishing Group	44	33
Cell Press	0	8
NEJM, Lancet ¹ , JAMA ²	20	10
Circulation, Circ Res, EHJ, JCI, JACC ³	124	110
Science ⁴	7	1
Total (Impact Factor > 10)	195	162



PAPERS OF THE MONTH 2021

JANUARY

Exercise-stress real-time cardiac magnetic resonance imaging for non-invasive characterisation of heart failure with preserved ejection fraction: The HFpEF stress trial. Backhaus, S. J. (University Medical Center Göttingen) et al. *Circulation*. Göttingen

FEBRUARY

The GEF Trio controls endothelial cell size and arterial remodeling downstream of Vegf signaling in both zebrafish and cell models. Klems, A.* (Karlsruhe Institute of Technology, KIT), le Noble, F.* (Heidelberg University Hospital), van Buul, J.D.* (University of Amsterdam), Ramms, A.S.* (Karlsruhe Institute of Technology, KIT), van Rijssel, J.* (University of Amsterdam) et al. *Nature Communications*. Heidelberg/Mannheim, Munich, Göttingen

MARCH

Single cell sequencing reveals endothelial plasticity with transient mesenchymal activation after myocardial infarction. Tombor, L.S. (Frankfurt University Hospital) et al. *Nature Communications*. Rhine Main

APRIL

Epigenetic gene expression links heart failure to memory impairment. Islam, R. (German Center for Neurodegenerative Diseases) et al. *EMBO Mol Med*. Göttingen

MAY

Fasting alters the gut microbiome reducing blood pressure and body weight in metabolic syndrome patients. Maifeld, A. (Max Delbrück Center for Molecular Medicine) et al. *Nature Communications*. Berlin

JUNE

Impairment of the ER/mitochondria compartment in human cardiomyocytes with PLN p.Arg14del mutation. Cuello, F. (University Medical Center Hamburg-Eppendorf) et al. *EMBO Mol Med*. Hamburg/Kiel/Lübeck, Berlin

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

Basophils balance healing after myocardial infarction via IL-4/IL-13. Sicklinger, F. (Heidelberg University Hospital) et al. *Journal of Clinical Investigation*. Heidelberg/Mannheim

AUGUST

Pathogenic variants associated with dilated cardiomyopathy predict outcome in pediatric myocarditis. Seidel, F. (German Heart Center Berlin) et al. *Circulation*. Berlin

SEPTEMBER

Angiography after out-of-hospital cardiac arrest without ST-segment elevation. Desch, S. (University Medical Center Schleswig-Holstein / Campus Lübeck) et al. *New England Journal of Medicine*. Hamburg/Kiel/Lübeck

OCTOBER

Reversible reprogramming of cardiomyocytes to a fetal state drives heart regeneration in mice. Maatz, H. (Max Delbrück Center for Molecular Medicine), Chen, Y. (Max Planck Institute for Heart and Lung Research) et al. *Science*. Göttingen, Rhine Main

NOVEMBER

Long noncoding RNA MIAT controls advanced atherosclerotic lesion formation and plaque destabilization. Fasolo, F.* (Klinikum rechts der Isar of the Technical University of Munich), Jin, H.* (Karolinska Institute), Winski, G.* (Karolinska Institute) et al. *Circulation*. Munich

DECEMBER

Therapeutic inhibition of RBM20 improves diastolic function in a murine heart failure model and human engineered heart tissue. Radke, M. (Max Delbrück Center for Molecular Medicine) et al. *Science Translational Medicine*. Heidelberg/Mannheim, Hamburg/Kiel/Lübeck

* These authors contributed equally.



PRIZES, GRANTS, PERSONALIA

Editors' picks

Dr. Hendrik Bartolomaeus

(Berlin)

Siegenthaler Medal in silver of the Walter Siegenthaler Society

Dr. Sofia-Iris Bibli

(Rhine Main)

Oskar Lapp Research Prize of the German Cardiac Society (DGK)

Prof. Stefanie Dimmeler

(Rhine Main)

Paul Morawitz Prize of the DGK

Prof. Jeanette Erdmann

(Hamburg/Kiel/Lübeck)

Coordination of the international consortium PROGRESS selected by ERA PerMed – a consortium of funding organisations

Member of the Leopoldina – German National Academy of Sciences

Dr. Benedikt Fels

(Hamburg/Kiel/Lübeck)

Young Investigator Award of the Deutsche Hochdruckliga

Magdalena Ellen Haid

(Greifswald)

Young Investigator Award at the Preventive Cardiology Congress of the European Society of Cardiology (ESC)

Prof. Dr. Dr. Mahir Karakas

(Hamburg/Kiel/Lübeck)

€4.1 million of project funding of the Federal Ministry of Education and Research (BMBF)

Angelos Karlas

(Munich)

Science Award of the German Society for Vascular Surgery (DGG)

PD Dr. Thorsten Kessler

(Munich)

Becht Research Prize of the German Foundation for Heart Research

Karolin Kleemann

(Göttingen)

Hans Georg Borst Award of the German Society for Thoracic and Cardiovascular Surgery (DGTHG)

Prof. David M. Leistner & Prof. Ulf Landmesser

(Berlin)

Funding from the Federal Joint Committee's Innovation Fund for the Project PräVaNet

Prof. Florian Leuschner

(Heidelberg/Mannheim)

Albert Fraenkel Prize of the DGK

Prof. Oliver J. Müller

(Hamburg/Kiel/Lübeck)

Funding of the BMBF for two projects in the amount of €360,000 and €280,000

Prof. Burkert Pieske

(Berlin)

Franz Loogen Prize of the DGK

Prof. Hendrik Sager

(Munich)

Franz Maximilian Groedel Research Prize of the DGK

Dr. Marie Schafstedde

(Berlin)

Young Investigator Award of the German Society for Pediatric Cardiology and Congenital Heart Defects (DGPK)

Prof. Dr. Jan Scheitz

(Berlin)

Stroke Prize by the German Society for Neurology (DGN) and the German Stroke Society (DSG)

Dr. Moritz von Scheidt

(Munich)

Uta und Jürgen Breunig-Forschungspreis of the German Heart Foundation and the German Society of Internal Medicine

Dr. Mirko Völkers

(Heidelberg/Mannheim)

Arthur Weber Prize of the DGK

Dr. Christoph Waldeyer und Dr. Fabian J. Brunner

(Hamburg/Kiel/Lübeck)

Dr. Martini Prize of the Paul Martini Foundation

Dr. Florian Weinberger

(Hamburg/Kiel/Lübeck)

Galenus Research Prize

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17 DZHK researchers among the most influential scientists in the world

Each year, the list of “Highly Cited Researchers” includes the scientists whose work is cited particularly often by their peers.

17 DZHK researchers belonged to the top one percent of the most cited researchers in their respective fields.

17 DZHK researchers were among the top one percent of the most frequently cited scientists in their respective fields worldwide in 2021.

Lutz Ackermann | Göttingen
Chemistry

Ulf Landmesser | Berlin
Clinical Medicine

Stefan D. Anker | Berlin
Clinical Medicine

Matthias Mann | Munich
Molecular Biology and Genetics

Andreas Daiber | Rhine Main
Cross-Field

Thomas Münzel | Rhine Main
Cross-Field

Stefanie Dimmeler | Rhine Main
Cross-Field

Annette Peters | Munich
Cross-Field

Sofia Forslund | Berlin
Biology and Biochemistry

Burkert Pieske | Berlin
Clinical Medicine

Uwe Haberkorn | Heidelberg/Mannheim
Clinical Medicine

Nikolaus Rajewsky | Berlin
Molecular Biology and Genetics

Paulus Kirchhof | Hamburg/Kiel/Lübeck
Clinical Medicine


Fabian J. Theis | Munich
Cross-Field

Karl-Heinz Kuck | Hamburg/Kiel/Lübeck
Clinical Medicine

Holger Thiele | Herzzentrum Leipzig – Universität Leipzig
Clinical Medicine

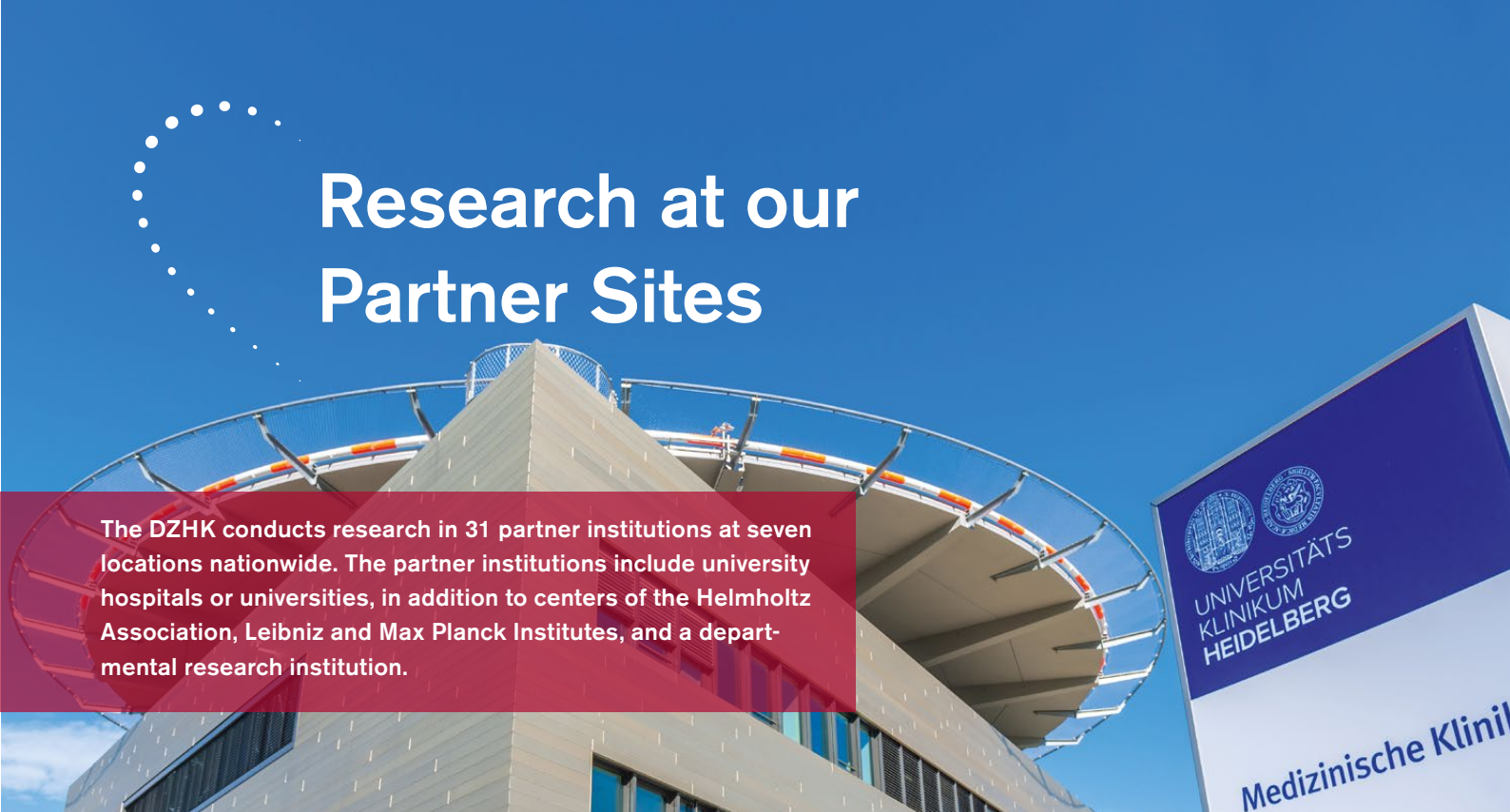
Christian Weber | Munich
Cross-Field

Press release from 16 November 2021 at dzhk.de/en/news/latest-news/2021/

 17 DZHK researchers are among the most cited scientists worldwide




Research at our Partner Sites



The DZHK conducts research in 31 partner institutions at seven locations nationwide. The partner institutions include university hospitals or universities, in addition to centers of the Helmholtz Association, Leibniz and Max Planck Institutes, and a departmental research institution.

The new five-year funding phase for the partner site projects began in 2021 and will run until 2025. Some of these projects involve continuing site-specific research priorities, however are also dedicated to new research topics. In line with the principle of boosting strengths, the partner sites can use these funds to sharpen their scientific profile in the long term. As a rule, these are projects in which basic research is conducted and which are suitable for further development in applied and patient-oriented research.


All partner site projects are listed at:

 dzhk.de/en/resources/projektdatenbank/
(project type: partner site project)

In addition, ten projects on the topic of research digitalization were started at the partner sites (see p. 4).

The DZHK professorships are also financed by site funds. Sixteen scientists held a DZHK professorship in the reporting year.

All DZHK professorships can be found at:

 dzhk.de/en/research/research-groups/dzhk-professorships

New Principal Investigators at the sites

Nine new Principal Investigators (PI) were appointed by the General Assembly for five years (2021–2025) at the partner sites. As excellent scientists in their field, the PIs shape the scientific profile of the DZHK. They are usually not directly funded by the DZHK, however lead their research projects and contribute to the committee work. In total, the DZHK has 147 PIs as of December 2021.

Greifswald

- Oliver Otto, University Medical Center Greifswald
- Alexander Teumer, University Medical Center Greifswald

Hamburg/Kiel/Lübeck

- Ingo Eitel, University Hospital Schleswig-Holstein/Campus Lübeck
- Paulus Kirchhof, University Medical Center Hamburg-Eppendorf
- Malte Spielmann, University of Lübeck/University Hospital Schleswig-Holstein/Campus Lübeck

Heidelberg/Mannheim

- Constanze Schmidt, Heidelberg University Hospital

Munich

- Matthias Mann, Max Planck Institute of Biochemistry
- Fabian Theis, Helmholtz Center Munich

Rhine Main

- Valentina Puntmann, University Hospital Frankfurt



Preclinical Research



New technologies and findings from basic research form the basis of translational projects in the DZHK.

A scientist from Göttingen measures the contraction force of a tiny ring of artificial heart tissue.

The DZHK supports Translational Research Projects (TRP) and collaborative projects through Shared Expertise and collaborations with external partners (since no new projects were funded this reporting year for organizational reasons, they are not listed in this report). The DZHK allocated €2.1 million in 2021 to new projects in the field of pre-clinical research.

Translational Research Projects (TRP)

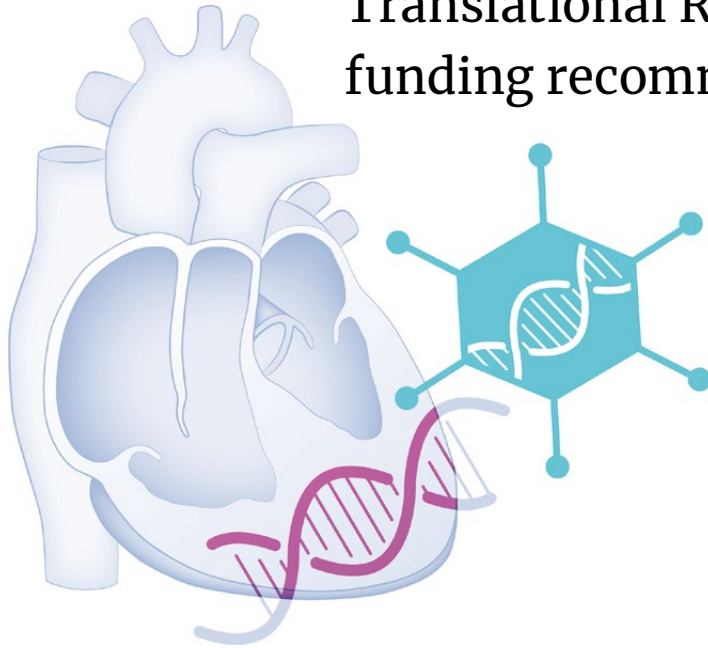
The DZHK funds TRPs with a focus on improved patient care. Since 2021, it has also been possible to apply for projects that involve the development of digital technologies or solutions using artificial intelligence. A prerequisite for funding is that they must align with the DZHK's strategic goal of positively influencing the lives of people with cardiovascular diseases.

The projects funded so far are incredibly diverse in both topic and method. This also applies to the projects recommendation for funding or continuation in 2021.

Members of the Translational Research Group (TRG) reviewed the applications and observed and monitored aspects to be considered in project implementation. Common to all projects is a well-characterized target and the potential to develop medical treatments for patients, or to develop new diagnostic procedures.

Due to the pandemic, the implementation of two projects was prolonged and therefore no TRP was completed in 2021.

Translational Research Projects with funding recommendations in 2021



Gene therapy of cardiac hypertrophy

A thickened heart muscle can result from narrowing of the aortic valve or inherited heart muscle disease. If left untreated, it can lead to heart failure. Treatments for thickened heart muscle are limited and surgery is often required.

In this project, researchers are testing a new therapeutic approach in a pig model. The activity of a protein, the transcription factor NFAT, which regulates the gene program involved in cardiac muscle enlargement, will be neutralized in cardiac muscle cells.

Preliminary work in a mouse model has provided initial evidence. A nucleic acid sequence, corresponding to a sequence in the target genes of the protein NFAT to which it binds, was transferred into mice. A virus-derived shuttle,

called a vector, was used to transfer this sequence into the mouse model. NFAT bound itself to the sequence introduced into the cells via the vector, and therefore did not bind exclusively to the regulatory regions of its actual target genes. This had a therapeutic effect on the thickened heart muscle and prevented the development of heart failure.

To bring the neutralization of NFAT closer to clinical application, in this project the team will investigate this approach further in an aortic valve stenosis porcine model. The results could pave the way for a clinical trial in patients with thickened hearts.

 **Project title:** *Gene therapy of cardiac hypertrophy*



Duration

2022–2024



Budget

€894.000



Project lead

- Oliver Müller (Hamburg/Kiel/Lübeck)



Participating scientists

- Rabea Hinkel (Göttingen)
- Norbert Frey, Markus Hecker (Heidelberg/Mannheim)

Translational Research Projects with a second funding period

Hit-to-lead development of CaMKII-HDAC4 inhibitory compounds to treat heart failure

Principal investigator: Johannes Backs (Heidelberg)
| Duration: 2019–2022 | Budget: €1,280,687

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











Principal investigator: Lars Maegdefessel (Munich)
| Duration: 2019–2023 | Budget: €995,190

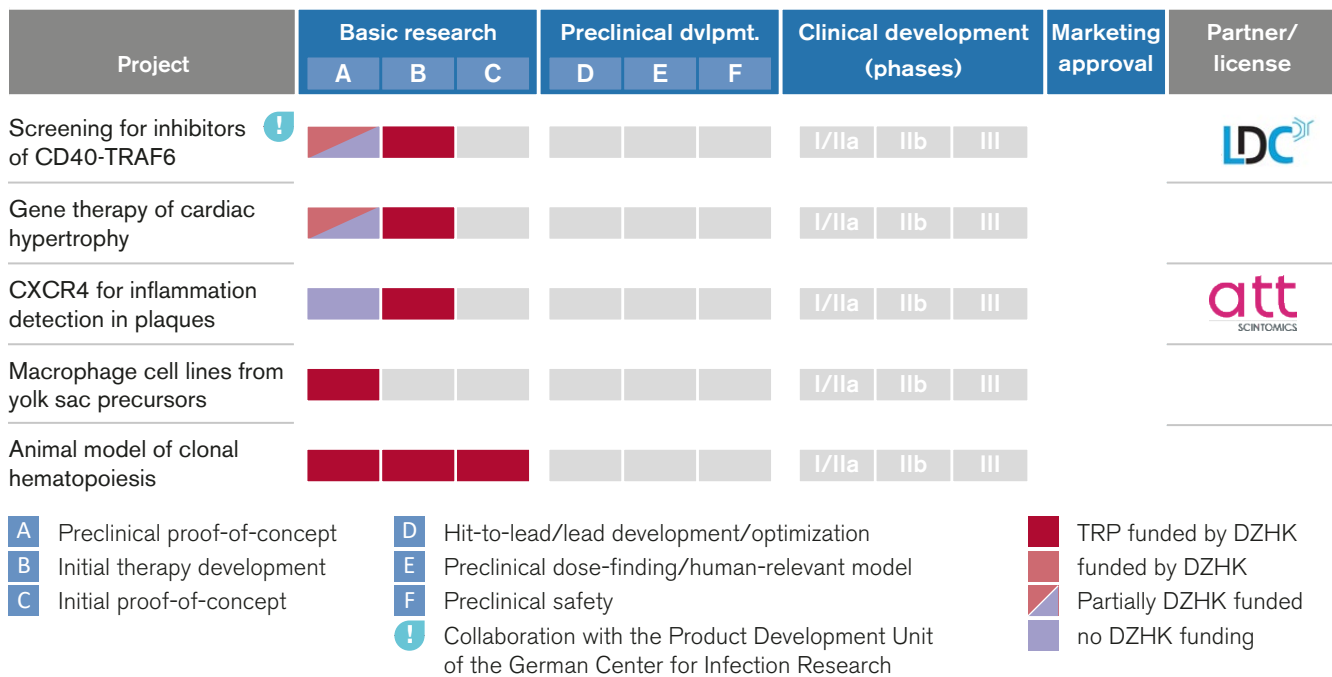
Collaboration with the Development Unit of DZIF

In 2021, the DZHK and the German Center for Infection Research (DZIF) agreed to collaborate more closely on developing novel drugs and medical devices. As a result, project leads at the DZHK now have the opportunity to call on the DZIF's Product Development Unit (PDU) for expert advice. The PDU specializes in new product development strategies and regulatory issues.

The table below illustrates in which phase of product development the TRPs (dark red) are located.

PROJECT PHASES OF A PRODUCT DEVELOPMENT

Project	Basic research			Preclinical dvlpmnt.			Clinical development (phases)			Marketing approval	Partner/ license
	A	B	C	D	E	F	I/IIa	IIb	III		
Production of cardiac tissue under GMP conditions											
Inhibitors of miR-92a											
Inhibitors of CAR											
Inhibitors of miR-29b to treat abdominal aortic aneurysms											
Transcatheter mitral valve implantation											
Transplantation of engineered cardiac tissue											
HCM gene therapy											
NIRF-IVUS imaging system											
rrAAV.MRTF-A based gene therapy											
Cardiac biopsy under real-time MRI											
Therapeutic peptides for heart failure											
Low-energy defibrillation											
Inhibitors of CaMKII-HDAC4 protein tein interaction											
Development of inhibitors of CD40-TRAF6											



Survey on translational projects

Far too often, promising therapeutic approaches uncovered in preclinical research are delayed because translational research is time-consuming, expensive, and often face significant setbacks. Translation is, however, crucial for driving clinical development forward. That is why the DZHK is further increasing its focus on this area.

Between June and October 2021, the DZHK conducted systematic surveys in three target groups: Those eligible to apply, technology transfer offices, and Young DZHK scientists. The results revealed in detail how all stakeholders use the existing translational research funding offer and which hurdles still need to be removed.

For example, it became apparent that one-third of the Young DZHK members would like to conduct research closer to the patient, but that a lack of specialist know-how can be a barrier. The technology transfer departments showed that they need to become more familiar with the ultimate goal and conditions of TRP funding.

Strategy for more translational project applications

Based on the survey results and the experience of the TRG so far, DZHK created a strategy to grow and better support the translational research pipeline at the DZHK.

Specifically, the strategy includes communicating more strongly what the TRP funding line offers and what support services are already available in the run-up to the application. In addition, we want to provide funding for scientific work in preparation for a TRP (Translational Research Project Starter Grant). To raise awareness of the TRP funding line and increase the number of project applications, we plan to offer a webinar targeted at technology transfer departments and application advisors at DZHK member institutions. These strategic objectives fed into the goals for 2022.

Goals achieved in 2021?

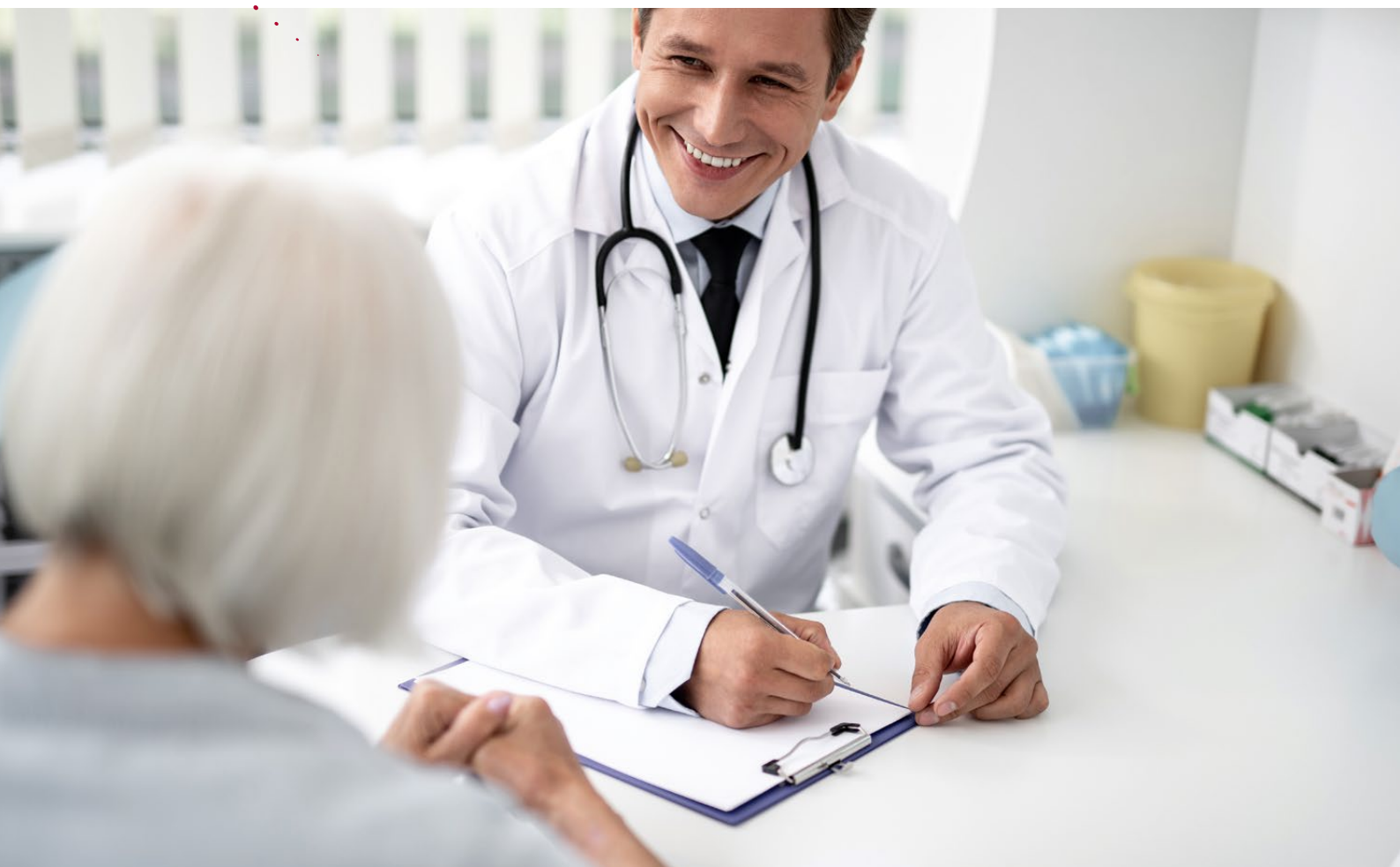
- ✓ A strategy designed to increase the number of TRPs submitted and approved

Goals 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



Clinical Research



Clinical trials are a key focus of the DZHK's research strategy. We specifically support early clinical trials that test an innovative therapy or diagnostic test in patients for the first time. Another focus is on guideline-relevant studies, to bring a new treatment or a new treatment strategy into practice. The results of these studies are incorporated into groundbreaking treatment guidelines and provide a direct link to improved patient care.

In the reporting year, the DZHK financially supported 25 clinical trials, including three studies on COVID-19 research. For their recruitment, 21 studies use the DZHK Clinical Research Platform (see p. 32).

In addition, there were five DZHK-associated studies (non-material funding without DZHK funding) whose recruitment is supported by our network. An overview of the studies can be found in the table on p. 30 and at dzhk.de/en/research/clinical-research/dzhk-studies/

The financial support of clinical studies at the DZHK amounted to approximately €4.4 million in the reporting year.



Results of our funded studies*

Six clinical studies of the DZHK were able to publish their results in high-ranking journals in the reporting year. A large part of the results will influence the treatment of patients.

*First publications only

HEART FAILURE

Cardiovascular magnetic resonance real time exercise stress testing in heart failure with preserved ejection fraction (HFpEF-stress-DZHK17 [↗])



Breathing and moving allowed in the MRI machine: A real-time MRI can take images of the heart under exercise stress.

Result: Diastolic heart failure can be reliably detected using real-time MRI under stress.

Potential for clinical practice: The stressful and time-consuming catheter examination under stress could be replaced by the non-invasive diagnostics of real-time MRI.

Early clinical trial | Principal investigator: Andreas Schuster (Göttingen, Germany) | Funding: €317,880 | Participants: 75 | Monocenter | Publication: Circulation 2021 January

Press release of 29 January 2021 at dzhk.de/en/news/

Diastolic heart failure: Non-invasive diagnosis with real-time magnetic resonance imaging can be an alternative to invasive cardiac catheterization

HEART VALVE DISEASE

Evaluating the benefit of concurrent tricuspid valve repair during mitral surgery (CTSN-TVR-DZHK14 [↗])

Results: Simultaneous surgical reconstruction of the mitral valve and mildly leaking tricuspid valve is beneficial to patients but connected with a slightly increased pacemaker rate.

Potential for clinical practice: More certainty for physicians and patients when deciding on co-treatment of the tricuspid valve.

Guideline-relevant study | Principal investigators: Volkmar Falk (Berlin), Annetine C. Gelijns (Icahn School of Medicine at Mount Sinai, New York City) | Cooperation: Cardiothoracic Surgical Trials Network (CTSN) | Funding (DZHK): €722,863 | Participants: 76 (Germany) | Study centers (Germany): 11 | Publication: New England Journal of Medicine 2021 November

Press release 3 December 2021 at dzhk.de/en/news/

Benefits of simultaneous mitral and tricuspid valve surgery (German only)

HEART ATTACK

Revacept – a novel inhibitor of platelet adhesion in patients with stable coronary artery disease undergoing elective percutaneous coronary intervention (ISAR-PLASTER [↗])

Results: The locally-acting antiplatelet agent Revacept is safe and effective in dilating stenosed blood vessels via a balloon catheter.

Potential for clinical practice: The rate of heart attacks was not reduced. Revacept would have to be tested in a different group of patients with a higher risk of heart attacks.

Early clinical trial | Principal investigators: Steffen Massberg, Adnan Kastrati (Munich) | Funding: €990,152 | Participants: 332 | Trial sites (Germany): 7 | Publication: JAMA Cardiology 2021 July

Press release of 7 April 2021 at dzhk.de/en/news/

Innovative platelet inhibitor tested for the first time in cardiovascular patients

Results from the TOMAHAWK-DZHK4, SCREEN-AF-DZHK15, and ACEI-COVID-19 studies are presented in Translational Successes (see p. 6).



Trials started in 2021

HEART VALVE DISEASE

Tricuspid Intervention in Heart Failure (TRICI-HF-DZHK24 [↗](#))

An insufficient tricuspid valve represents a severe and progressive disease that often leads to a worsening of the clinical condition. Until some time ago, only cardiac surgical procedures – open heart surgeries – were available for treating the valve. Minimally invasive treatment methods using cardiac catheter techniques have only become available in the last few years.

The DZHK study TRICI-HF-DZHK24 is the first industry-independent, multi-center study to evaluate whether several catheter-based interventions benefit patients, compared to drug-based therapy only. For this purpose, the scientists will assess how many patients survive after twelve months, and whether hospitalization due to heart failure is necessary.

Early clinical trial | Principal investigators: Jörg Hausleiter, Thomas Stocker, Steffen Massberg (Munich) | Funding: €1,692,566 | Planned participants: 360 | Multi-center

Press release dated 16 February 2022 at [dzhk.de/en/news/](https://www.dzhk.de/en/news/)

[↗](#) Percutaneous tricuspid valve repair: a future pathway out of right heart failure?

HEART FAILURE

Effect of antifibrotic therapy on regression of myocardial fibrosis after transcatheter aortic valve implantation (TAVI) in aortic stenosis patients with high fibrotic burden (REDUCE-MFA-DZHK25 [↗](#))

Despite the successful treatment of narrowed aortic valves using catheter-assisted aortic valve implantation (TAVI), people with a severely scarred heart have a significantly increased risk of dying within the first year after that.

To date, individuals have not received drug therapies to counteract scarring. The REDUCE-MFA-DZHK25 study is now the first to use two antifibrotic drugs to test whether they can reduce scarring and improve prognosis in heart valve patients after TAVI.

Early clinical trial | Principal investigators: Elisabeth Zeisberg, Miriam Puls (Göttingen) | Funding: €1,796,937 | Planned participants: 300 | Multi-center

Press release dated 21 December 2021 at [dzhk.de/en/news/](https://www.dzhk.de/en/news/)

[↗](#) New DZHK study to reduce scarring in narrowed heart valves



Studies with completed recruitment in 2021

The [COVID-Prevent trial](#) [↗](#) ended enrollment early in the reporting year, due to ever decreasing hospitalization rates of COVID-19 patients. This made effective recruitment no longer possible. The statistical analysis will be adapted to the lower patient number of 111.

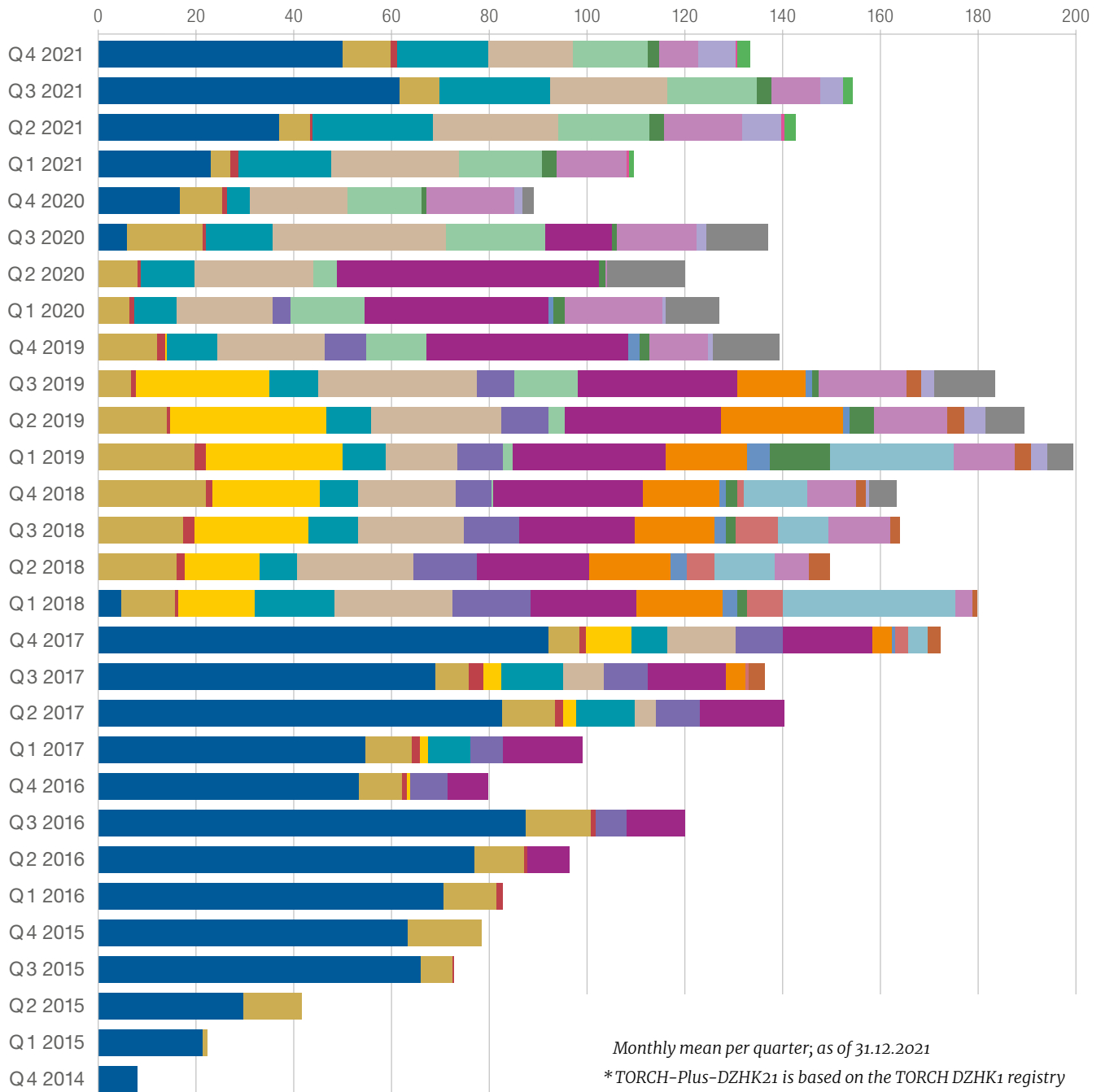
Recruitment recovers

Recruitment recovered slowly during the year and was slightly higher overall than the previous year across all DZHK studies (Fig. on p. 29), however only two new studies started recruitment in 2021.

The pandemic continued to impact recruitment performance. This includes a significantly delayed recruitment start of centers in new multi-center studies ([EXAMINE-CAD-DZHK22](#) [↗](#), [CMR-ICD-DZHK23](#) [↗](#)). This was due to COVID-19-related bottlenecks on the wards, travel restrictions, overloaded commissions and legal departments partly in the home office or pandemic prioritization mode, as well as delayed patient inclusion in [BioVAT-HF-DZHK20](#) [↗](#) due to missing materials (supply bottleneck).

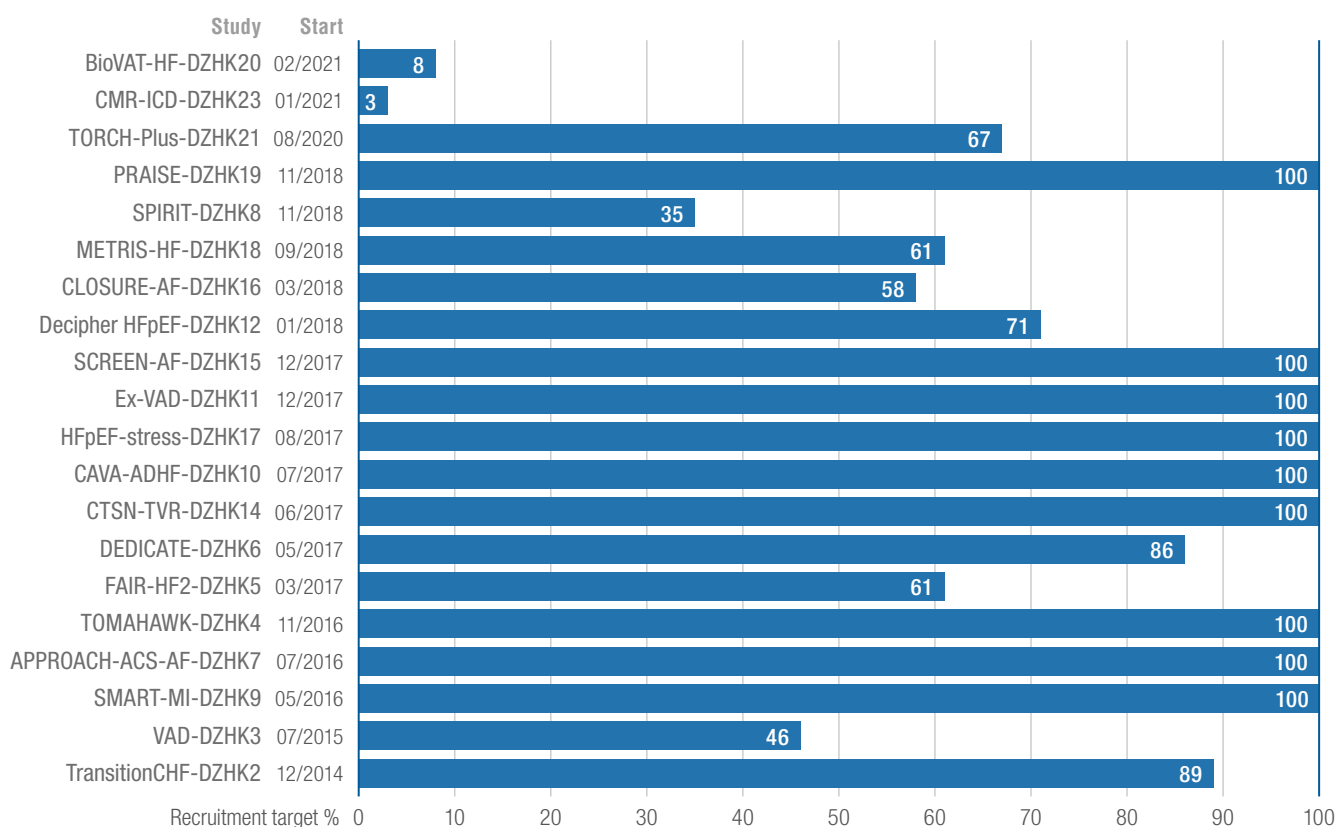
By 31 December 2021, 10,572 patients were enrolled in DZHK studies, including 1,508 in 2021 (2020: 1,419). In total, just over 15,500 patients have been enrolled in all DZHK-funded studies over the years.

OVERVIEW – PATIENTS RECRUITED
DZHK STUDIES



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

OVERVIEW – ENROLLMENT STATUS OF PATIENTS IN DZHK STUDIES



Data in percent (as of 31.12.2021)

STUDIES AT THE DZHK

DZHK studies	Condition/ Treatment/ Diagnostics	Study type	Responsible PI (DZHK partner site)	Recruitment target	Enrolled
TORCH-DZHK1	Myocardial diseases	Registry	Katus (Heidelberg/Mannheim), Hoffmann (Greifswald)	2,300	complete
TransitionCHF-DZHK2	Heart failure	Cohort	Hasenfuß, Wachter, Edelmann (Göttingen)	1,000	885
VAD-DZHK3	Severe heart failure, heart transplantation	GRS	Falk, Knosalla (Berlin), Hasenfuß, Friede (Göttingen)	200	91
TOMAHAWK-DZHK4	Cardiac arrest	GRS	Desch (Hamburg/Kiel/Lübeck), Thiele	558	complete
FAIR-HF2-DZHK5	Heart failure and iron administration	GRS	Karakas (Hamburg/Kiel/Lübeck), Anker (Berlin)	1,200	730
DEDICATE-DZHK6	Aortic valve stenosis	GRS	Blankenberg, Seiffert (Hamburg/Kiel/Lübeck)	1,403	1,212
APPROACH-ACS-AF-DZHK7	Circulatory disorders of the heart in combination with atrial fibrillation	GRS	Wakili, Massberg (Munich)	400	complete
SPIRIT-HF-DZHK8	Heart failure	GRS	Pieske, Edelmann (Berlin)	1,300	466
SMART-MI-DZHK9	Sudden cardiac death after myocardial infarction	ECS	Bauer, Kääb, Massberg (Munich)	400	complete

STUDIES AT THE DZHK

DZHK studies	Condition/ Treatment/ Diagnostics	Study type	Responsible PI (DZHK partner site)	Recruitment target	Enrolled
CAVA-ADHF-DZHK10	Acute decompensated heart failure	ECS	Jobs (Hamburg/Kiel/Lübeck), Thiele	388	complete
Ex-VAD-DZHK11	Exercise with a ventricular assist device	ECS	Edelmann, Pieske, Falk (Berlin), Halle (Munich)	64	complete
Decipher HFpEF-DZHK12	Heart failure, MRI	ECS	Nagel (Rhine Main)	185	132
CTSN-TVR-DZHK14	Mitral valve insufficiency	GRS	Falk (Berlin)	76 (in D)	complete
SCREEN-AF-DZHK15	Early detection of atrial fibrillation	GRS	Wachter, Hummers-Pradier (Göttingen)	267 (in D)	complete
CLOSURE-AF-DZHK16	Stroke prevention by closure of the atrial ear	GRS	Landmesser, Boldt (Berlin), Eitel (Hamburg/Kiel/Lübeck)	1,000	580
HFpEF-stress-DZHK17	Real-time MRI diagnostics for heart failure	ECS	Schuster (Göttingen)	70	complete
METRIS-HF-DZHK18	Metformin treatment in heart failure	ECS	Doehner, Pieske (Berlin), Friede (Göttingen)	180	110
PRAISE-DZHK19	Acute coronary syndrome in stroke patients	ECS	Endres, Landmesser, Nolte (Berlin)	251	complete
BioVAT-HF-DZHK20	Engineered human myocardium in terminal heart failure	ECS	Zimmermann (Göttingen)	53	4
TORCH-Plus-DZHK21	Myocardial diseases	Registry	Meder (Heidelberg/Mannheim)	4,340	2,906
EXAMINE-CAD-DZHK22	Impaired microcirculation	ECS	Landmesser, Stähli (Berlin)	Recruitment in preparation	
CMR-ICD-DZHK23	MRI examination in heart failure	GRS	Eitel (Hamburg/Kiel/Lübeck)	760	24
TRICI-HF-DZHK24	Tricuspid regurgitation, TAVI	GRS	Hausleiter, Braun, Stocker, Massberg (Munich)	Recruitment in preparation	
Reduce-MFA-DZHK 25	Myocardial fibrosis	ECS	Puls, Zeisberg (Göttingen)	Recruitment in preparation	

DZG Working Group Patient Involvement

The DZHK is involved in this joint working group of the German Centers for Health Research. You can find more details in the chapter “Collaborations” (see p. 42).

Global Cardiovascular Research Funders Forum (GCRFF)

Since 2021, the DZHK has been involved as a German partner in the GCRFF's Multicenter Trials Initiative. 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 multi-center trials. We report on this in the chapter “Collaborations” (see p. 43).

We list the goals for our area “Clinical Trials” together with the goals for the area “Clinical Research Platform & Heart Bank” (see p. 36).



Clinical Research Platform & Heart Bank



CLINICAL RESEARCH PLATFORM

The Clinical Research Platform is the backbone of DZHK studies. It ensures data and biospecimens are collected according to uniform standards and are available for high quality, cross-study reuse. In 2021, two new studies (“first patient in”) were integrated into the platform and research teams have started patient recruitment. In 2021, approximately 120 national and international institutions recruited patients into our studies.

DZHK supports NAPKON

In 2020, the DZHK’s Clinical Research Platform division was funded to collect Corona research data as part of the Network University Medicine (NUM). The NUM had been looking for a provider that could quickly capture data and samples from Corona clinical trials across institutions and in a privacy-compliant manner. By the end of 2021, DZHK collected data from 4,500 individuals from three NAPKON cohorts for NUM using the Clinical Research Platform system.

We are particularly proud that the NUM has continued to operate data collection via the DZHK’s Clinical Research Platform in 2022. In the reporting year, the DZHK shared collected data with the NUM.

Press release from December 28, 2021

Cardiovascular research provides the blueprint for university COVID-19 research

The German Center for Cardiovascular Research pioneered clinical COVID-19 research by making its Clinical Research Platform available to the nationwide Network University Medicine (NUM) in 2020. Starting in early 2022, the NUM operated its own research platform modeled by the DZHK, thus serving as a blueprint for future research infrastructure at the NUM.

“Without the DZHK, university-based Corona research would not have been able to get off the ground with nationwide studies within a few months. In April 2020, in the face of the Corona crisis, the DZHK was ready without hesitation to make its structures and know-how available to the NUM,” says Prof. Heyo Kroemer, Chairman of the Board of Charité – Universitätsmedizin Berlin, who had launched the NUM.

Ralf Heyder, Head of the NUM Coordination Office, adds: “We have benefited enormously from the DZHK partners' many years of experience with logistics for large multicenter studies. We thank them for their extremely successful collaboration over the past year and a half.”

A quick solution was needed

When the novel Coronavirus became known in March 2020, it quickly became clear that University researchers had to join forces to fight the disease. To collect data and biospecimens from sick and infected people across Germany, the NUM, launched by the German Federal Ministry of Education and Research, rapidly needed a robust data and biospecimen infrastructure.

The research platform of the DZHK was selected at that time because it fulfilled all requirements for COVID-19 research. It can capture clinical data, patient samples, and diagnostic images pseudonymously and entirely digitally. “We only had to adapt our platform, which we normally use to run multicenter clinical trials from the cardiovascular field, to support COVID-19 research and adapt data acquisition systems and processes,” says Dr. Julia Hoffmann, project manager at the DZHK office.

Data with a globally unique depth of detail

Since November 2020, the platform has collected data and samples from 4,500 individuals from three cohorts of the National Pandemic Network (NAPKON), one of the NUM's projects. “The data collected in the research platform and planned molecular investigations will allow us to obtain a uniquely detailed picture of COVID-19 and its long-term consequences,” says Prof. Janne Vehreschild, who coordinates NAPKON

with his team at the University Hospitals of Frankfurt and Cologne. “This will allow us to break down the causes of severe courses and subsequent damage even more precisely and give us clues as to how we can better protect and treat our patients.” More than 60 research projects have already been applied for or started.

NUM continues to operate a platform based on DZHK model

In the future, the DZHK's infrastructure partners will collect Corona data under the direction of NUM, following the DZHK's model. “We believe our providing of the blueprint for a NUM research platform reflects the quality and high standard of DZHK's model. With our platform, data acquisition was able to start quickly. Now we are happy to be able to turn our focus back to cardiovascular research,” says DZHK board spokesperson Prof. Stefanie Dimmeler.

Service4Studies – New portal for study staff

In 2021, we launched the new web-based portal [Service4Studies](#) for study directors and recruiting center staff. It collates information, checklists, and documents from the subsystems and projects of the Clinical Research Platform. Users can also apply for IT access and participate in training and consultation sessions.

Around 2,400 people from more than 120 institutions have therefore been given a single point of contact for all questions relating to the Clinical Research Platform.

Service4Studies
Das Service-Portal für klinische Studien im DZHK

How This Site Works | Research Platform | Study Centres | Participants | Contacts

Warm Welcome!
This is how the DZHK's clinical research platform works.
[Read more](#)

Service4Studies
We can help you
You can learn how to activate a study center, obtain access to the documentation

News
8th November 2022
Digital forms are online

DZHK HEART BANK

In the year under review, we combined the Clinical Research Platform's data and biospecimens with additional resources to form the "DZHK Heart Bank". Information surrounding this valuable research resource was shared on our website (dzhk.de/en/dzhk-heart-bank). This allows researchers to test their questions with data and specimens from our DZHK Heart Bank.

The DZHK Heart Bank contains high-quality clinical, image, and OMICs data in addition to liquid and tissue biospecimens, including associated data, which are processed and stored under standardized conditions. This is an essential prerequisite for reproducible research results.

The DZHK Heart Bank comprises the following:

Resource with liquid samples and image data

- Liquid biospecimens (serum, EDTA plasma, citrated plasma, buffy coat, urine)
- Patient datasets with an extensive range of cardiological diagnoses
- Image data (ECG, echo)



Samples and data originate from DZHK-funded studies, obtained according to standardized procedures at all study centers via the DZHK research platform. Through this, our resource continues to grow.

Resource with cardiovascular tissue samples

- 8,000 tissue samples
- EDTA blood and untreated PAXGene samples
- Associated clinical data



The German Heart Center Berlin resource contains samples and clinical data from patients with cardiac disease diagnoses.



DZHKomics resource (DNA and RNA)

- 1,200 genetic data sets from healthy individuals
- 1,150 whole genome sequences
- 700 RNA sequences



This resource can be used to assess the differences between healthy and diseased individuals. Scientists in life sciences can access and use this resource for their research.

Call for the use of data and biospecimens

Data and biospecimens provide a valuable resource for cardiovascular research. To boost the use of our data and specimens, the first call for "Utilisation of the DZHK Collection" started in early 2021. A second call followed in 2022. Nine applications were received, all of which were recommended for funding by the Use and Access Committee and received funding totaling €40,000 per project. Further applications were received outside the funding call. The data and biospecimens were released during the reporting year, and all projects were shared on the website:

dzhk.de/en/dzhk-heart-bank/secondary-use-projects/
A second call will follow in 2022.

DZG Research IT Working Group

The DZHK is involved in this German Centers for Health Research working group. More details can be found in the Collaboration chapter (see p. 42).

Goals achieved in 2021?



- ✓ First call for secondary use projects implemented
- ✓ NUM project handed over to the Medical Informatics Initiative and the NUM research platform
- ✓ DZG-AG data management started
- ✓ At least two new DZHK studies started

Our goals for clinical trials, which are presented in a separate chapter (see p. 26), were:

Goals 2022



- ↗ 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



Promoting Young Talent



Young physicians in the clinics see and closely assess their patients every day. They are highly motivated and, due to their clinical exposure, are able to take research questions from the bedside to the lab and from the lab to the bedside. To do this, they require good working conditions, freedom to carry out research, financial support and interactions with their peers. This also applies to clinical scientists and basic researchers. The DZHK has therefore allocated €5.1 million in 2021 for its extensive programs to promote early career scientists and excellence.

YOUNG DZHK

In 2021, 1,260 young scientists from DZHK partner institutions were members of the [Young DZHK](#) ↗, forming the largest network within the DZHK. The Young DZHK Postdoc Committee is the voice of the Young DZHK and

each of the seven DZHK sites is represented by two persons. The spokesperson is a voting member of the RCC – the body that determines the strategy of the DZHK.

Current overview of the spokespeople:

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

Normally, the members of the Postdoc Committee organize the Young DZHK Retreat, which takes place every year in the run-up to the DZHK Retreat (see p. 44). No face-to-face event took place due to the pandemic in 2021, however there was a digital replacement event for the DZHK retreat, which was also directed at junior scientists. The partner site representatives in the Postdoc Committee can also organize two workshops per year for the members of the Young DZHK. In the reporting year, DZHK partner site Greifswald offered two cross-site online meetings:

6 August 2021 (Greifswald) | **Figures in science and welcome to the dark side**
 6–7 December 2021 (Greifswald) | **Scientific writing, a structured approach**

Young scientists at the DZHK have access to a total of eight funding lines that are specially designed for them – from travel grants and the Clinician Scientist Program, which releases young physicians for research, to the Mentoring Program and support for mothers on their way to professorships.

AWARDED GRANTS TRAINING & MENTORING

	Number 2021	2020
Travel grants for high-level conferences	116	54
Doctoral scholarships (including partner site-financed scholarships)	48	36
Visiting Scientist Program	11	9
Attendance of external workshops	66	29
New mentees	14	13

TRAINING & MENTORING

Doctoral students and postdocs of the Young DZHK can use the four different modules of our training program. Although in 2021 more travel grants were awarded, there were still significantly fewer applications than before the Corona pandemic.

During the reporting period, the mentoring program for the 7th year (2020/2021) ended. The new year (2021/2022) started with 14 new mentees, however due to continued regulations, communication had to be virtual for the new group. The mentees are physicians, natural scientists or science managers. They can choose a mentor themselves and are prepared for future leadership tasks.

Together with the German Cardiac Society (DGK), we have been offering a jointly run early career workshop program called “Fundamentals of Cardiovascular Research” since 2013. In 2021, young cardiologists were able to participate in three workshops:

10 April 2021, online | **Heart failure mechanisms**
 2 June 2021, online | **Getting started in the lab – Methods in cardiovascular research**
 30 September 2021, Bonn (as part of the DKG Heart Days) | **Drug development – The long road to a drug**

Further offers for young scientists have been launched by the joint working group for the promotion of young scientists at the German Centers for Health Research (see p. 42).

EXCELLENCE GRANTS

In addition to the five established funding lines, in 2021 there was an initial one-time call for Young DZHK members to submit applications for the Postdoc Start-up Grant on Advancing Digital Aspects (see p. 5). The funding line is based on the Postdoc Start-up Grant and aims to promote scientific independence at an early stage by providing start-up funding for an independent research project. Three of the five funded projects, which use technologies such as artificial intelligence or virtual reality, started in the year under review.

In 2021, we started evaluating the success of the funding lines. For example, three quarters of the scientists who have received a Postdoc Start-up Grant since 2015 have achieved the funding goal. They were able to submit a grant proposal to a larger third-party funding body or have since successfully acquired further third-party funding. In the Rotation Grant funding line, an evaluation of curricula vitae showed that funded individuals tended to remain in research, and at the DZHK, more than individuals who did not receive funding. The other three funding lines (Clinician Scientist Program, Promotion of Women Scientists, Junior Research Group) have not yet been evaluated, as not enough projects have been completed or the funding line is too premature to draw conclusions.

EXCELLENCE GRANTS – FUNDED PROJECTS

Funding line	Name	Institution	Project title
Clinician Scientist Programme	David Bode	Charité – Universitätsmedizin Berlin	FoxO1 and caloric restriction as regulators of lipotoxic left atrial dysfunction in metabolic HFpEF
	Elias Rawish	University Medical Center Schleswig-Holstein – Campus Lübeck	The complement system as an inflammatory link between obesity and atherosclerosis
	Mridula Balakrishnan	Max Planck Institute for Heart and Lung Research	Sympathetic reinnervation during zebrafish heart regeneration
	Zhifen Chen	German Heart Centre Munich	Discovery and exploration of novel drug targets for lowering cardiometabolic risk
	Claudia Crocini	Max Delbrück Center for Molecular Medicine	Interaction between sarcomere mechanics and chromatin remodelling in engineered heart tissue
Postdoc Start-up Grant	Badder Kattih	Frankfurt University Hospital	Impact of MRC2 on cardiac fibroblast plasticity during chronic cardiac injury in the human heart
	Michael Molitor	University Medical Center of the Johannes Gutenberg University Mainz	Immune modulation of cardiac monocytes/macrophages due to metabolic acidic stress and the role of the transcription factor inducible cyclic AMP early repressor (ICER) in ischemic heart disease
	Laura Parma	Ludwig-Maximilians-University Munich	Role of the CXCL12-CXCR4/ACKR3 axis in atherosclerotic plaque instability
	Christian Schulte	University Medical Center Hamburg-Eppendorf	Characterisation of VEGF-Beta regulation networks in monocytes – a transcriptomics approach
	Eric Schoger	University Medical Center Göttingen	CRISPR/Cas9 gene activity control with all-in-one mini-dCas9 transcription factors in cardiomyocytes
	Florian Sicklinger	University Hospital Heidelberg	The impact of tricuspid regurgitation on gut microbiome, immune homeostasis, and its consequences on the progression of atherosclerosis
	Chi-Chung Wu	Max Planck Institute for Heart and Lung Research	Role of Slit/Robo signaling in cardiomyocyte cytokinesis and regeneration
Postdoc Start-up Grant on Advancing Digital Aspects	Etienne Boileau	University Hospital Heidelberg	Digital HeART (DHART) Research Portal
	David John	Johann Wolfgang Goethe University Frankfurt	Assessment of heart failure mouse models by systematically comparing single cell transcriptomics data in mice and man
	Mark Emile Pepin	University Hospital Heidelberg	DZHK-Omics: Intuitive and standardized bulk RNA-sequencing analysis for the coding-naïve basic scientist
	Nikolaus Thierfelder	Ludwig-Maximilians-University Munich	Envision! Virtual reality for a better understanding and treatment of congenital heart defects
	Marcus Vollmer	Greifswald University Hospital	Standardized ECG processing pipeline for AI/ML-based classification of cardiovascular diseases
Promotion of Women Scientists	Stefanie Fenske	Ludwig-Maximilians-University Munich	A mutation-independent gene therapy to treat RyR2 gain-of-function mutations causing CPVT
	Klytaimnitra Kiouptsi	University Medical Center of the Johannes Gutenberg University Mainz	The microbial effect on thrombus growth and platelet function in a deep vein thrombosis model
	Laura Michalick	Charité – Universitätsmedizin Berlin	The role of heteromeric TRPV1/4 channel complexes in endothelial mechanotransduction
	Daniela Panáková	Max Delbrück Center for Molecular Medicine	PCP-dependent control of muscle differentiation through modulation of nuclear mechanics
	Olga Schweigert	University Medical Center Hamburg-Eppendorf	Contribution of blood pressure related gene CRIP1 on pathology and progression of hypertension
Maria-Patapia Zafeiriou	University Medical Center Göttingen	Investigation of neuronal remodelling in a human iPSC-derived innervated cardiac muscle model	

EXCELLENCE GRANTS – FUNDED PROJECTS

Funding line	Name	Institution	Project title
Rotation Grant	Jeremy Epah	Johann Wolfgang Goethe University Frankfurt	Fetal hemoglobin (HbF) induction as protein translation treatment option for inherent anaemia
	Djawid Hashemi	Charité – Universitätsmedizin Berlin	Validation and evaluation of a non-invasive assessment of central venous oxygen saturation by CMR
	Johannes Benjamin Holle	Charité – Universitätsmedizin Berlin	Attenuating cardiovascular risk by targeting microbial metabolism and premature T cell aging
	Jona Benjamin Krohn	University Hospital Heidelberg	The role of M4 macrophages in extracellular vesicle-mediated atherosclerotic plaque calcification
	Lukas Damian Weberling	University Hospital Heidelberg	Oxygenation-sensitive CMR: A medication-free protocol for cardiovascular imaging and stress tests

Goals achieved in 2021?



- ✓ Evaluated whether the objectives of the Excellence Program are being achieved with funding
- Mentoring Program further developed
- ✓ Young DZHK brochure reissued

Goals 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



Collaborations



COLLABORATION WITH THE DZG

Many people still suffer from diabetes, infectious diseases, cancer, and cardiovascular, lung and neurodegenerative diseases. With the German Centers for Health Research (DZG), the Federal Ministry of Education and Research has established powerful research structures to better detect, treat and prevent these diseases in the future. To this end, the DZGs bring together non-university and university partner institutions from all over Germany and have been working together on an interdisciplinary basis since the beginning.

At the center of this cross-DZG collaboration are various committees and working groups that are dedicated to strategic and disease-independent topics.

In the DZG Forum, board members and representatives of the funding authorities meet four times a year. One meeting

outcome in 2021 was the creation of the DZG Innovation Fund – a joint research funding program that will start in 2022. This program is coordinated by the virtual DZG head office which was also newly established in the reporting year. DZG managing directors and their respective coordinators form the head office team. Together, they will further strengthen and accompany the collaborations of the DZG in the future.

New: Joint website of the



www.deutschezentren.de



From the working groups

Research IT

The [Research IT working group](#) ↗, newly established in 2021, is working on harmonizing processes and IT systems between the DZGs. The aim is to use intelligent data management to accelerate the acquisition of knowledge on both common and rare diseases, to reduce the number of patient examinations required, and to jointly explore new avenues for the diagnosis and treatment of serious diseases.

The working group works closely with the respective IT developers, data managers and infrastructure operators of the six DZGs. In addition to developing a DZG metadata catalog, with the aim of making research data transparent and accessible across the DZGs, the working group is designing a basic data set for harmonizing study data. Initial development work has begun in order to implement a common authentication for DZG services and a “record linkage” to determine patient overlap between DZGs. The working group collaborates with other infrastructure initiatives, such as the Network University Medicine, the Medical Informatics Initiative, and the National Research Data Infrastructure for Personal Health Data (NFDI4Health).

Patient participation

Patient participation is becoming increasingly important in research. For this reason, the six DZGs have set up a [Patient Participation Working Group](#) ↗, whereby six patient representatives participate alongside 17 scientists from the DZGs. Together they are committed to:

- better participation of patients in (data-rich) research
- greater awareness of patient participation
- increased communication on the topics of “data-rich medicine” and “data donation” and for
- a better perception of the values, interests and needs of patients in research.

Promotion of young scientists

In 2021, the [working group](#) ↗ launched a new workshop series, the “Lunchtime Career Talks”. Here, selected individuals from translational research and science-related professional fields present their personal career paths as role models, thus giving participants impetus for their own careers. In the first half of the year, the workshop series “Translating Science into Clinical Practice”, organized by the German Center for Diabetes Research, took place for the first time as an online event.

The DZHK also organized another online workshop on “Epigenetic techniques” on 21st October, which was attended by over 100 young scientists from all six DZGs.

Public relations

The [public relations working group](#) ↗ is largely responsible for the joint DZG magazine SYNERGIE. In 2021, the magazine was awarded the “Berliner Type in Silber” prize in the B2C – magazines / periodicals category. With the award, the jury acknowledged the expressive design, which precisely and vividly shows the diverse research topics of the DZGs. The award honors print products from Germany, Austria and Switzerland.

Two more issues were published in 2021 (German only):

- “The game of life – genome”
issue #1 | 2021
- “Individual and targeted – precision medicine”
issue #2 | 2021



2021
BERLINER TYPE

The magazine is available in digital form and print. The website www.dzg-magazin.de was completely revised in 2021, in particular the search engine optimization.



Other cross-DZG working groups

Working groups on the topics of biobanking, global health and regulatory aspects of clinical trials also exist. Due to the pandemic, these groups were less active in 2021. We will report on this again from 2022 onwards.

RESEARCH COLLABORATIONS

Global Cardiovascular Research Funders Forum (GCRFF)

In the GCRFF, worldwide cardiovascular research funders join forces. Twelve large public funding organizations from Australia, Canada, Denmark, France, Germany, New Zealand, the Netherlands, Sweden, and the United Kingdom have come together to form a global partnership. The DZHK is a member for Germany.

The goal of the forum is to accelerate progress in independent cardiovascular research by enabling countries to work more closely together. In a first step, the organizations want to collect respective funded projects in a joint database. To this end, the organizations first want to record the projects they each have funded in a joint database. This should help to make global research funding in the cardiovascular field more transparent. In addition, the forum supports researchers in planning and funding large multinational clinical trials that would not be feasible in a single country.

In 2021, the GCRFF Multinational Clinical Trials Initiative launched the first call for Expressions of Interest (EOI) for multinational clinical trials. As an interim result, out of a total of nine EOIs submitted, the Initiative Panel recommended three for further assessment by national funders, two of which involved DZHK.

British Heart Foundation and Hartstichting

Since 2018, the DZHK has been running a joint funding program with the British Heart Foundation (BHF), in which the Dutch Heart Foundation (Hartstichting) has also been participating since 2019.

Through the program, the partners aim to promote research that would not be possible on a national level alone. Funding is provided for bi- or tri-national research projects that focus on improving the diagnosis, prevention and treatment of cardiovascular diseases. The BHF and the DZHK each provide two million euros per call, while the Hartstichting provides one million euros. In the fall of 2021, three applications were recommended for funding, one of which involved partners from the DZHK and aims to develop innovative approaches to tissue regeneration after damage to the heart tissue.

ReGenLnc – Exploiting endothelial long non-coding RNAs to promote regenerative angiogenesis in the damaged myocardium



Lead scientists: Germany– Ralf Brandes (Goethe University Frankfurt) | UK – Andy Baker (University of Edinburgh) | Netherlands – Reinier A. Boon (Amsterdam UMC)

Other co-applicants: Christian Kupatt (Klinikum Rechts der Isar, Technical University of Munich) | Rabea Hinkel (DPZ Göttingen) | Monika Gladka (Amsterdam UMC) | Christine Mummery (Leiden University) | Mairi Brittan (University of Edinburgh) | Julie Rodor (University of Edinburgh)

Duration: 4 years | Funding amount DZHK: €395.900 | Total funding amount of the project (including share UK and Netherlands): €1,184,497

Goals achieved in 2021?

- ✓ Clinical trials initiative of the Global Cardiovascular Research Funders Forum launched

Goals 2022

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



Communication & Public Relations



SCIENTIFIC EXCHANGE

Due to the continuing impact of COVID-19 in 2021, we had to choose an alternative format for our annual meeting – the DZHK Retreat and the connected Young DZHK Retreat. The DZHK Retreat is our largest network meeting. In replacement, we were able to offer the DZHK network a partial substitute for the scientific content with two extended online meetings offered to all researchers in the DZHK community – both senior and junior. The topics were “Large cohorts in the DZHK” (16 September) and “New options for translational research” (3 December). The biobank expert Naomi Allen (UK Biobank, Oxford) and the geneticist Leslie

Leinwand (University of Colorado, Boulder) who are outstanding speakers and scientists in their field gave keynote lectures at these meetings.

Science on Friday

We continued offering one hour of science to our DZHK community on Friday afternoons. The webinar series, “Science on Friday”, launched at the end of 2020 has become a fixed date for the scientific exchange of the DZHK.

On average, around 120 participants attended eight dates in 2021. The highest number of participants, 215, attended the webinar on “Gene Therapy” in January 2021, which covered topics ranging from artificial intelligence and the latest research findings on diseases, such as heart failure and atherosclerosis, to an overview of the DZHK Heart Bank. The format was also well received by our Young DZHK members, who usually formed approximately half of participants.

Gene therapy | 21 January 2021

Artificial intelligence in cardiovascular research
| 19 February 2021

Heart failure with preserved ejection fraction: What’s new in the DZHK? | 19 March 2021

In vitro and large animal models for cardiovascular disease
| 23 April 2021


Atherosclerosis: What’s new in the DZHK? | 28 May 2021

Bio databases of the DZHK – Design, methods and examples of use | 23 July 2021

“Vascular Biology” co-hosted by DGK AG4 Vascular Biology | 29 October 2021

DZHK Clinician Scientist – Science between bench and bedside | 19 November 2021

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

 intern.dzhk.de/wissenschaftlicher-austausch/science-on-friday/

Symposia, lectures and co-funded congresses

After an adjustment phase in 2020, when the majority of events planned after March 2020 were cancelled or had to be postponed due to the pandemic, more events were held again in the reporting year. Many of them were delivered in an online format. The DZHK co-funded six congresses, two of which were held online, one in Göttingen and one as a hybrid event in San Servolo/Italy. In addition, two DZHK Lectures on psychocardiology were held in Munich. By co-funding major congresses, the DZHK ensures visibility in the national and international cardiovascular research community.

Dutch German Joint Meeting (DGK) | 11–13 March 2021, online
organized by Jörg Heineke (Heidelberg/Mannheim)

#science of the Young DGK | 18 February–10 June 2021, online (series with 4 dates)
organized by Rabea Hinkel (Göttingen)

European Council for Cardiovascular Research (ECCR) Meeting 2021 | 8–9 October 2021, online
organized by Michael Bader (Berlin)

9th “Cardiac Regeneration and Vascular Biology” conference | 18–20 October 2021, San Servolo, hybrid
organized by Christian Kupatt (Munich)


3rd Joint Dutch German Vascular Biology Meeting
| 3–5 November 2021, Göttingen
organized by Rabea Hinkel (Göttingen)


InGENe-ious Cardiology, Genetics of Con-genital Heart Disease | 6–7 November 2021, online
organized by Felix Berger and Holger Gerhardt (Berlin)


Psychobiological basics of psychocardiology and psychocardiological treatment – concepts and effects. (Lectures)
| 6 November 2021, Munich
organized by Karl-Heinz Ladwig (Munich)

Four internal DZHK symposia were applied for during the reporting period and approved at the end of 2021.

PUBLIC RELATIONS

In the reporting year, we made central content more easily and clearly accessible online: The portal service4studies.dzhk.de/en  was launched at the end of 2021. This web-based service is aimed at staff in study centers who recruit patients for DZHK clinical trials (see p. 34).

With the DZHK Heart Bank, we make it easy for researchers worldwide to get an overview of the most valuable resources on our website at dzhk.de/en/dzhk-heart-bank/ : Biospecimens, clinical, genomic, and imaging data, that originated primarily from DZHK clinical trials (see p. 35).

We also upgraded the Translational Research Projects section of our website (see p. 22), which forms the core of DZHK translational research: At dzhk.de/en/research/preclinical-research/translational-research-projects/ , the projects are illustrated and presented individually with results.

As part of the collaboration between the six DZGs, the DZHK is involved in the public relations working group. For more information, see p. 42.

120/80 – The cardiovascular podcast

Can smartwatches provide helpful clues in cardiology or the coronavirus? What do we know about COVID-19 and the heart? What is the state of research in heart muscle diseases in children? Answers to these and other questions were discussed by DZHK researchers and Christine Vollgraf, Head of Communications and Public Relations, in the DZHK podcast launched in 2021. The first of three episodes of the new podcast on cardiovascular research were shared online in June 2021 on the popular podcast platforms and our website.



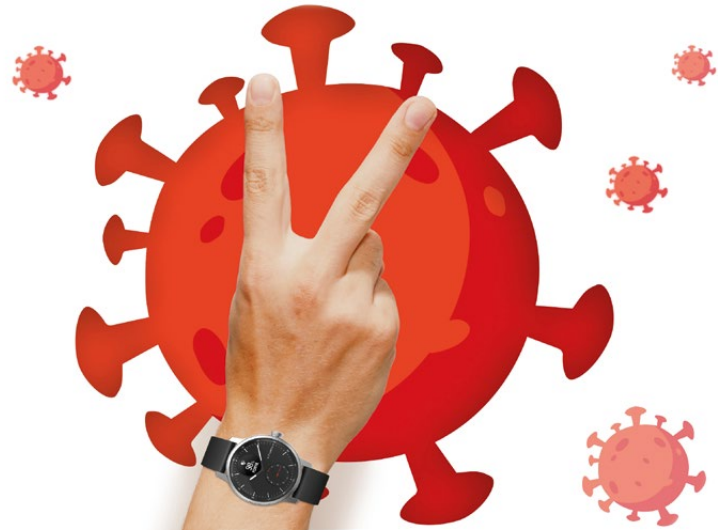
To listen to all episodes:

dzhk.de/en/news/media-centre/podcast/

Study: Patient recruitment supported by press work

The Munich COVID SMART study, funded by the DZHK, was looking for patients in the Munich area who were in isolation at home due to a recent COVID-19 infection.

The time window for patient recruitment was very small, as it was not foreseeable at the time that the pandemic would involve further waves. In order to motivate as many patients as possible to participate in a short period of time, we launched a public campaign via press and radio, regionally focused Facebook posts, and posters and flyers in health offices and doctors' practices. On the landing page covid-smart.de, interested parties could easily sign-up for participation in the study. As a result, the study reached the target figure of 600 patients.



Facebook, Instagram, LinkedIn, Twitter

The number of followers on our social media channels continued to rise in 2021, however at a lower rate of increase than in previous years. On [Twitter](#), 1,591 people or organizations followed the DZHK by the end of 2021 – an increase of 31 percent (2020: +66 percent). On [Facebook](#), we had 2,416 followers – an increase of eleven percent (2020: +32 percent). Our [Instagram channel](#) had 1,319 subscribers, 30 percent more than in the previous year. On the business network [LinkedIn](#), we strengthened our presence and had 782 followers at the end of the year.

For the first time, our profiles saw a significant decline in reach and response on Facebook and Instagram. On the one hand, this was due to the fact that the start of the coronavirus pandemic in 2020 attracted more attention for



scientific and medical news than in a “normal” year. On the other hand, organic reach declined significantly in 2021, especially on Facebook, because the company is increasingly relying on advertising revenue. Profiles with little advertising budget, such as that of the DZHK, therefore reach fewer users for equivalent topics than in previous years.

Website: News and information on diseases are traffic drivers

Compared to the previous year, we were able to increase user numbers of the DZHK website by 43 percent to 285,000 (2020: 200,000). The website's major traffic drivers continue to be [news](#) ↗ and [general disease information](#) ↗. Slightly more than one fifth of visitors came directly to the site and three quarters came via Google.

The DZHK continued to perform well, mainly because Google rates various DZHK contents as particularly recommendable. In particular, search queries related to diseases in the cardiovascular context attract visitors to the site (top: "sudden cardiac death"). As expected, the list of top keywords in 2021 continued to be strongly influenced by Corona (top: "myocarditis Corona").

Goals achieved in 2021?



- ✓ DZHK podcast launched
- ✓ Online platform "service4studies" launched (together with team Clinical Research Platform)
- ✓ Detailed presentation of the Translational Research Projects on DZHK website
- ✓ "Science on Friday" online workshop series established

Goals 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



Success Indicators for Translational Research



SHORT- AND MEDIUM-TERM INDICATORS

Indicator	Definition	2021	2020
1. "Physician Scientists"	Share of scientifically active (licensed) physicians among the scientists registered in the DZHK	56 %	56 %
2. Collaboration between DZHK partner sites	a. Number of Shared Expertise projects (year)	0*	32
	b. Number of publications with at least two DZHK authors from different partner sites	168	128
	c. Number of ongoing large multicenter projects (recruiting DZHK studies and TRPs) (31/12/21) involving multiple DZHK partner sites	11	13
	d. Number of Visiting Scientist residencies at other DZHK sites (year)	4	1
3. Communication with regulatory authorities	Consulting appointments (e.g. PEI, BfArM) in the context of recruiting DZHK studies, TRP and partner site projects (year)	7	4
4. Collaboration with industry	Collaborations with industry partners in the context of recruiting DZHK studies, TRP and partner site projects (31/12/21)	14	14

* Due to a change in the application deadline, there were no newly approved projects in 2021 (see p. 22)

Indicator	Definition	2021	2020
5. Collaborative structures in clinical research	a. Type (quality) of collaborative structures (31/12/21)	Clinical Research Platform (data storage, Trusted Third Party, LIMS, BDMS and ethics project, Use & Access), stem cell registry, OMICs resource	
	b. Number (quantity)		
	• Patients included in Clinical Research Platform (31/12/21)	10,572	9,064
	• SOPs (31/12/21)	19	17
	• Data and biospecimen usage applications/notifications (year)	13/2	0/3
	• Approved usage applications and notifications (year)	13/2	0/3
6. High-ranking publications	All publications with DZHK affiliation with impact factor > 10	195	162
7. Preclinical projects and clinical studies	a. Number of Translational Research Projects and recruiting DZHK studies (31/12/21)	22	18
	b. Publications from Translational Research Projects and DZHK clinical studies	35	31

LONG-TERM SUCCESS INDICATORS

Indicator	Definition	2021	2020
8. Revised medical guidelines	Number of guidelines changed as a result of DZHK trials and Competence Network Trials (total)	0	2
9. New therapeutic and diagnostic principles	Number of new therapeutic and diagnostic principles developed within the framework of DZHK projects that have entered clinical application	0	0
10. Patients treated according to new therapeutic or diagnostic principles	Number of patients treated according to new therapeutic or diagnostic principles developed by DZHK researchers (measurability is questionable)	0	0

Remarks on the table:

Definition of DZHK studies: from competitive/flexible funds; predominantly or fully DZHK financed; study uses the infrastructure for clinical studies of the DZHK.

All indicators refer exclusively to projects financed from DZHK funds; no indicator refers to otherwise financed research by DZHK member institutions. Because they are easier to record, indicators 2a, 2c, 2e, 5, 7 and 8 refer exclusively to the competitive/flexible DZHK funds and not to DZHK partner site projects.

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

Facts and Figures



FINANCES AND STAFF

In the reporting year 2021, the DZHK had approximately €42.4 million of funding at its disposal, in addition to a carryover of €4 million from 2020 (2019: €5.8 million). Of this amount, €41.3 million were used (2020: €42.9 million).

The allocation of funds in 2021 was slightly less than in the previous year. The pandemic-related restrictions at the research facilities and supply bottlenecks meant that fewer funds were spent than forecasted in the 2021 business plan. The reduction of our positive balance since 2017 could therefore not be continued in 2021.

Accumulated funds amounting to €5.14 million were not spent and were carried over into 2022. A considerable proportion of the remaining balance has been approved for

clinical trials. The late withdrawal of funds was due to pandemic-related delays in patient recruitment. Therefore, these remaining funds are well-justified reserves for clinical trials. For ethical reasons, the studies cannot be discontinued and the approved funds cannot be reduced.

2021 was again significantly impacted by the budget freeze for the Helmholtz Association of German Research Centers (HGF), decided by the German Bundestag's Budget Committee. The budget freeze affects the DZHK via the Max Delbrück Center for Molecular Medicine (MDC). To lift the freeze, 75 percent of the annual budget and all remaining funds from the previous year must be spent early in the year. Thanks to the close collaboration with the scientists, partner site managements, third-party funding departments

of the partner institutions, and the finance department of the MDC, this target was achieved. The Budget Committee of the German Bundestag agreed in September 2021 to release the funds blocked for 2021. The agreed budget freeze will continue to affect the DZHK to the same extent in 2022.

The funds spent in 2021 amounting to €41.3 million* broke down as follows:

- **Partner site funds:** €20.2 million
- **Partner site management:** €1.1 million
- **Flexible funds:** €17.8 million
(including clinical research €8 million, preclinical research €5.9 million, promotion of young scientists €3.2 million and funding of externals €0.7 million [including competence networks €0.5 million and collaborations with external partners €0.2 million])
- **Membership fees:** €1.4 million
- **Funding management department:** €0.9 million

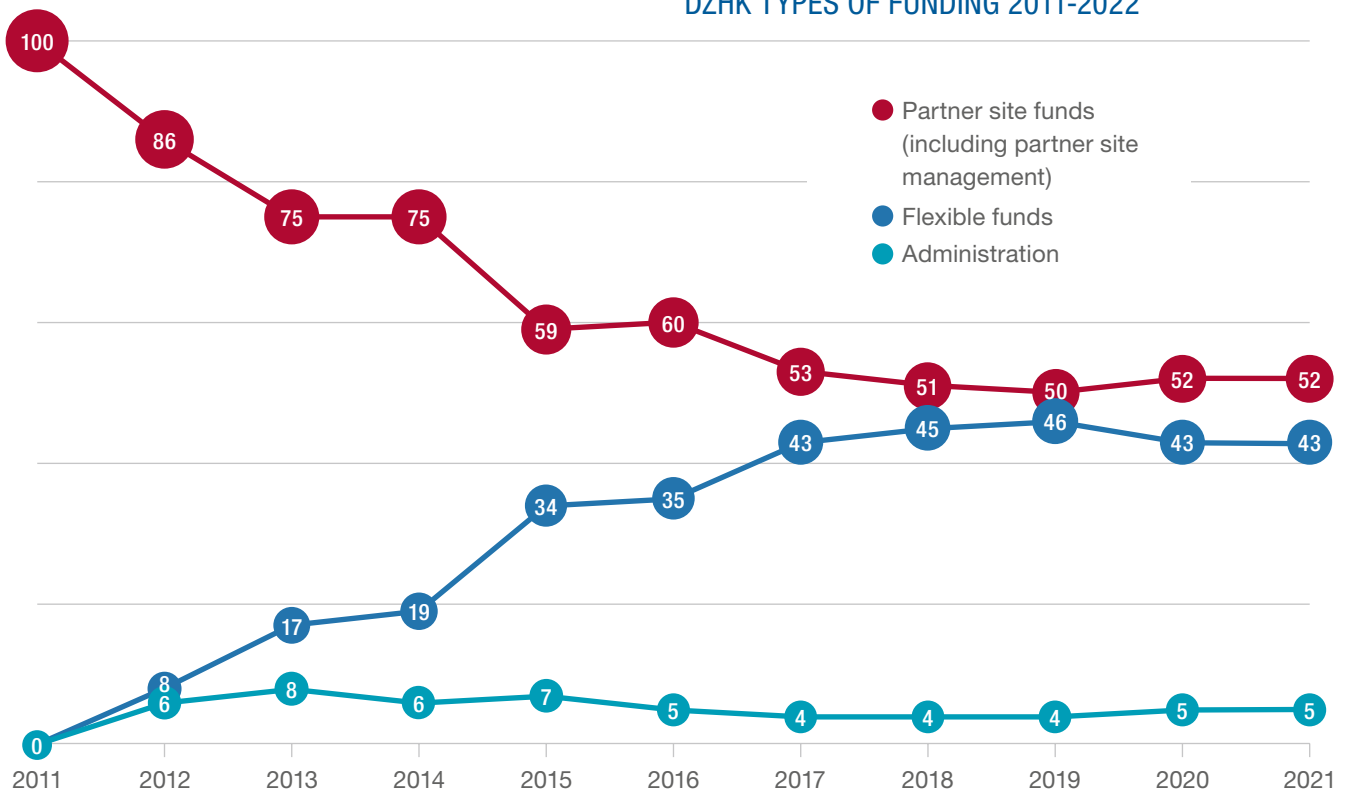
In addition to the partner site projects, the DZHK funds

competitive research projects with about half of the budget. These are mainly the Excellence Grants, Translational Research Projects and clinical studies. These flexible funds are allocated through internal competition. It remains a strategic goal that about 50 percent of funds in the DZHK are awarded competitively. This is the fifth consecutive year that we have achieved this strategic goal.

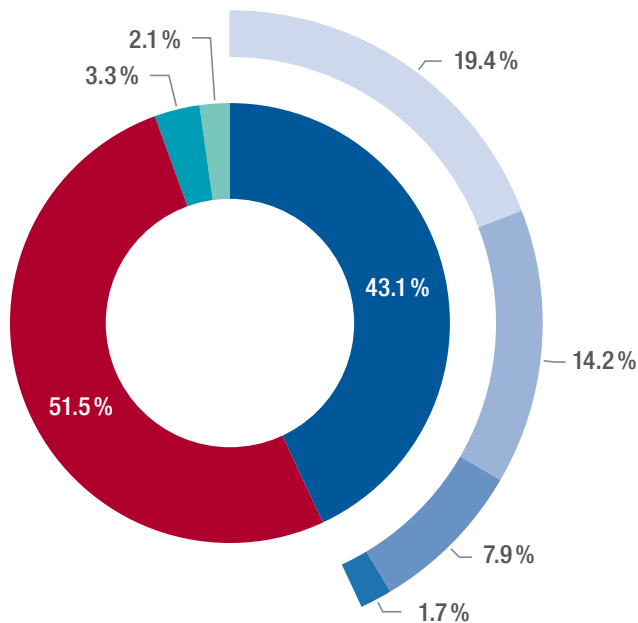
BUDGET OF THE ASSOCIATION MANAGEMENT

The budget of the association management (in previous annual reports: head office) of the DZHK e.V., financed by membership fees, amounted to €1.35 million in 2021 as in the previous year. This budget was fully financed by membership fees of €1.25 million and by a carryover of €98,174 from 2018. €1.21 million were spent (2020: €1.32 million). Other income amounted to approximately €4,503 (including health insurance reimbursements). This results in a surplus of €44,313. The carryover from 2018 remained untouched.

DZHK TYPES OF FUNDING 2011-2022



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



ALLOCATION OF SPENT DZHK FUNDS 2021 BY EXPENDITURE AREAS*

- Flexible funds (2020: 43.4%)
- Partner site funds (2020: 51.9%)
- Membership fees (2020: 2.8%)
- Funding management department (2020: 1.9%)

Flexible funds are made up of

- Clinical research (2020: 24.0%)
- Preclinical research (2020: 11.0%)
- Promotion of young scientists (2020: 6.8%)
- External (2020: 1.7%)

STAFF EXPENDITURES, MATERIAL EXPENSES AND INVESTMENTS OF THE DZHK*

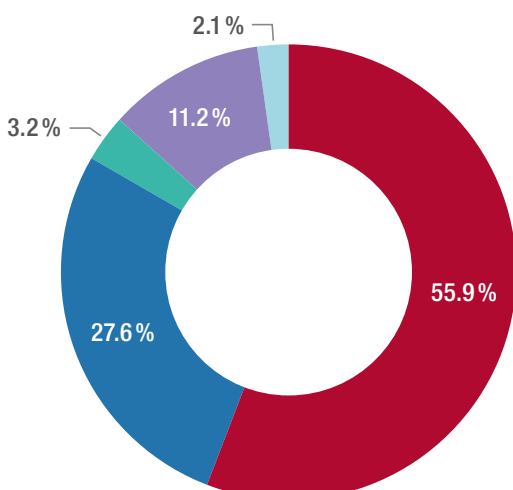


STAFF

As of December 31, 2021, 582 (2020: 568) persons or "heads" were financed from DZHK funds. This corresponds to 411.64 (2020: 411.70) full-time equivalents (FTE).

This also includes 20 (2020: 19) DZHK association management employees, 15 employees of the funding management department (2020: 12) and nine employees in the competence networks (2020: 10).

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



- Staff expenses: €677,315 (2020: €618,165)
- Material expenses: €335,113 (2020: €443,057)
- Investments: €38,547 (2020: €49,301)
- Public relations: €136,041 (2020: €180,116)
- Membership fees (TMF e. V.): €25,000 (2020: €25,000)

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

NUMBER OF STAFF FINANCED BY DZHK 2019–2021

	2019	2020	2021
Number of employees (as of 31 December) – FTE	408.71	411.70	411.64
Number of employees (as of 31 December) – capita	515	568	582
thereof men	174	194	207
thereof women	341	374	375
Number of scientists and physicians – FTE	226.55*	225.68*	244.45*
Number of scientists and physicians – capita	308*	311*	336*
thereof men	139	147	168
thereof women	169	164	168
These include:			
DZHK Professors and Junior Research Group leaders – FTE	19.81	19.31	17.51
DZHK Professors and Junior Research Group leaders – capita	22	23	18
thereof men	18	18	15
thereof women	4	5	3
Senior scientists and postdocs – FTE	161.73	170.42	181.75
Senior Scientists and postdocs – capita	212	227	243
thereof men	84	100	116
thereof women	128	127	127
Doctoral students** – FTE	45.01	35.95	45.19
Doctoral student** – capita	74	61	75
thereof men	37	29	37
thereof women	37	32	38
Non-scientific staff and others – FTE	116.6*	150.91*	133.59*
Non-scientific staff and others – capita	163*	216*	202*
thereof men	163*	35	31
thereof women	141	181	171

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

** in previous annual reports: PhD students

CHANGE IN THE BOARD AND MANAGEMENT

At the end of 2020, Stefanie Dimmeler from the Rhine Main partner site (Goethe University Frankfurt) began the role as spokesperson of the board of directors for the next three years. Her predecessor Thomas Eschenhagen from the Hamburg/ Kiel/Lübeck partner site ended his very successful nine-year term in office at the end of 2020. Stefanie Dimmeler is a biologist and has been principal investigator at the Rhine Main partner site since it was formed.

There was also a change in the management of the DZHK. Our long-standing managing director Joachim Krebs began a new professional journey at the beginning of 2021.

He is succeeded by Katharina Eulenburg, who previously worked as a scientific officer in the DZHK office since its foundation.

PRINCIPAL INVESTIGATORS, DZHK SCIENTISTS, MEMBERS OF THE YOUNG DZHK

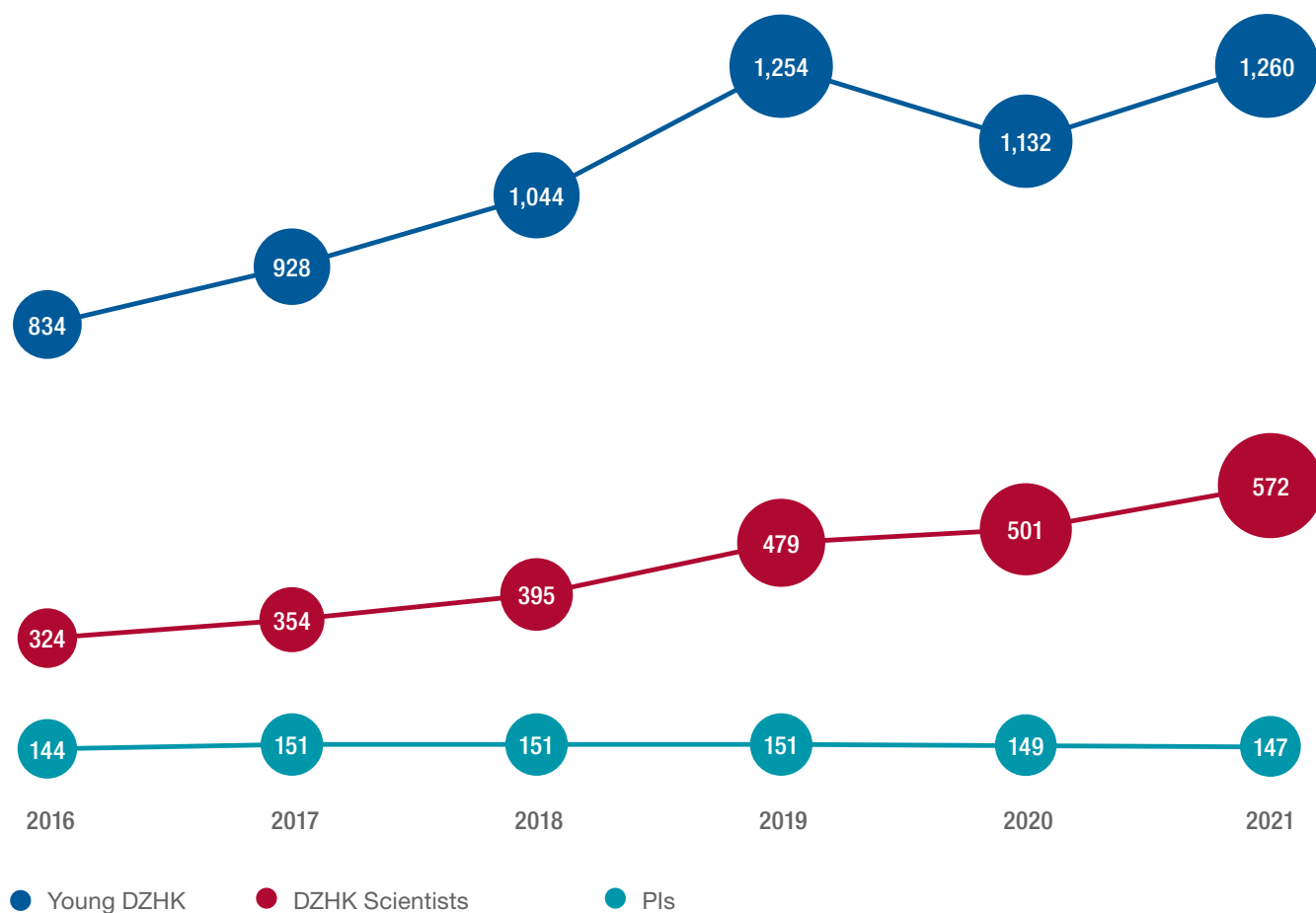
At the end of 2021, the DZHK's research network included around 2,000 researchers and physician scientists dedicated to cardiovascular research from various fields, such as molecular biologists, bioinformaticians, imaging specialists or cardiogeneticists. 147 principal investigators (PIs, 2020: 149), 572 DZHK scientists (2020: 501) and 1,260 Young DZHK members (2020: 1,132) have official DZHK status.

DZHK scientists and Young DZHK members contribute at least a quarter of their working time to a DZHK project and can, for example, conduct research with DZHK project funds. The PIs are particularly renowned researchers. With their expertise, they shape the profile of the DZHK, both in research and through their involvement in the committees. PIs are nominated by the partner sites and confirmed by the general assembly. In the year under review, the general assembly decided who would receive DZHK PI status or whether the status would be extended. The PIs were last appointed in 2017. Nine new PIs were appointed for the term 2021-2025 (see p. 21). The target of 30 percent women PIs at each partner site has not yet been met.

Overall, the new appointments kept the percentage of women constant at 28 percent (as of 31/12/21), compared to the previous year. Of the 147 PIs, 41 are women. Each of the partner institutions, with the exception of Asklepios Kliniken Hamburg, has appointed at least one PI since 2021.

Each partner site has a maximum of 20 PI positions. PIs holding a DZHK professorship are counted separately. The professorships are established at the partner sites from DZHK funds. PIs, on the other hand, are generally not funded by the DZHK.

PIS, DZHK SCIENTISTS AND MEMBERS OF THE YOUNG DZHK 2016–2021



RESEARCH MANAGEMENT

The employees of the association management (in previous annual reports: head office), the funding management department (FMM) and the seven partner site management teams form the DZHK's research management. The joint head office of the association management and the FMM is in Berlin. The partner site managements are decentralized branches of the association management and are located at each of the seven partner sites.

In the year under review, 20 employees including the managing director were working in the association management (16.27 FTEs as of 31/12/21). The FMM had 15 employees (12.33 FTE). In the partner site managements, the DZHK usually finances one full scientist position for a partner site manager and one full administrative assistant position.

Central tasks of the DZHK are performed in the association management. The staff coordinates the areas of clinical research, preclinical research, clinical research platform, promotion of young scientists, scientific exchange and public relations. The association management also supports the bodies and committees of the DZHK in strategic discussions.

In 2021, in addition to standard tasks, these topics and projects were of particular relevance to the association management:

- Coordination of newly established digitization task forces for preclinical and clinical research and call for tenders for digitization projects. (p. 4)
- Development of new funding guideline Translational Research Project Starter Grant (p. 25)
- Launch of a new service portal for all those involved in clinical studies at the DZHK (p. 34)

- Launch of the DZHK Heart Bank with clear presentation of all data and biospecimens of the DZHK collection (p. 35)
- First call "Utilisation of the DZHK Collection" for secondary use of data and biospecimens of the DZHK collection (p. 35)
- Handover of Corona research data which the DZHK collected on a transitional basis as part of the University Medicine Network (p. 32)
- Participation in the first call of the Global Cardiovascular Research Funders Forum multinational clinical trials initiative (p. 43)
- Preparation of the 10th anniversary celebration of the DZHK
- Success evaluation of the funding lines Postdoc Start-up Grant and Rotation Grant
- Conceptual design and preparation of the procurement procedure for the digital grant management system
- Contribution to the draft of a DZG-wide exploitation regulation
- Start of the virtual head office of the DZG

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 496 ongoing projects were funded in the 2021 (2020: 456). The DZHK's total project count to date is 1773.

The partner site managements coordinate all activities of their partner site. This includes, but is not restricted to, the application and reporting system, financial controlling, and the organization of partner site retreats and PI meetings.

..... Partner Sites



DZHK PARTNER SITE BERLIN

Partner site spokesperson

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

Deputy spokesperson

Burkert Pieske, Charité – Universitätsmedizin Berlin, Director at University Medical Centre, Division of Cardiology, and at the Clinic for Internal Medicine – Cardiology (DHZB)

Partner site management

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

Partner institutions at the DZHK partner site Berlin

Charité – Universitätsmedizin Berlin (Charité), German Heart Centre Berlin (DHZB); German Institute of Human Nutrition Potsdam-Rehbrücke (DIfE); Max Delbrück Center for Molecular Medicine in the Helmholtz Association (MDC); Robert Koch Institute (RKI)

What was important in 2021

The Käthe-Beutler-Haus at the MDC research campus and the Charité campus Berlin Buch, completed in 2020, was occupied by the research groups in 2021. The building houses facilities for the latest OMICS technologies, single-cell analysis, and microscopy techniques. The new center for blood vessel medicine is also home to the DZHK-PI research groups of Prof. Holger Gerhardt and Prof. Michael Potente.

In December 2021, the merger of the two DZHK partner institutions, Charité and DHZB, was finalized to form the German Heart Center of Charité (DHZC). The DHZC will combine the cardiac medical expertise of Charité and DHZB. The construction of an associated new building will also be starting in 2023.



In the newly acquired Collaborative Research Center SFB1470 headed by Professors Burkert Pieske (Charité/DHZB) and Michael Gotthardt (MDC), a research team of basic scientists and clinicians are leading a study titled “Heart Failure with Preserved Ejection Fraction (HFpEF)”. The team will analyze the mechanical, metabolic, inflammatory and immunological triggers of the disease, the respective downstream signaling pathways, and specific reactions on the cardiovascular system. The SFB Center will be funded with approximately €12 million for an initial four years.

In the transatlantic Leducq network, research groups from Europe and the USA led by Prof. Michael Gotthardt (MDC) and Prof. Leslie Leinwand (Boulder) are investigating the role of alternative splicing in heart disease. The project will run for five years and is funded with €7 million by the Leducq Foundation.

As one of ten PIs, Prof. Michael Bader (MDC) is investigating the function of serotonin during embryonic development in the EU-funded Innovative Training Network “Serotonin & Beyond”. The EU funded the project with a total of €4 million for three years and enables 15 young scientists – two at MDC – to conduct multidisciplinary research.

Since 2021, clinical innovations have been researched through the DIGIPREDICT project. As part of this EU project, a digital twin of a patient is being created using novel biosensors, artificial intelligence, and organ-on-a-chip technology. This comprehensive patient data helps scientists paint a fuller picture of disease and the best therapeutic approaches. In this study specifically, complications in patients with systemic inflammatory response syndrome (including COVID-19 and after cardiac surgery) will be detected early, and patient monitoring and treatment will be improved. The project at Charité is funded with €643,000 under the direction of Prof. Volkmar Falk and Prof. Alexander Meyer (DHZB/Charité).



DZHK PARTNER SITE GÖTTINGEN

Partner site spokesperson

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

Deputy spokesperson

Eberhard Bodenschatz, Director of the Max Planck Institute for Dynamics and Self-Organisation, Rabea Hinkel, Professor of Laboratory Animal Science at the German Primate Center

Partner site management

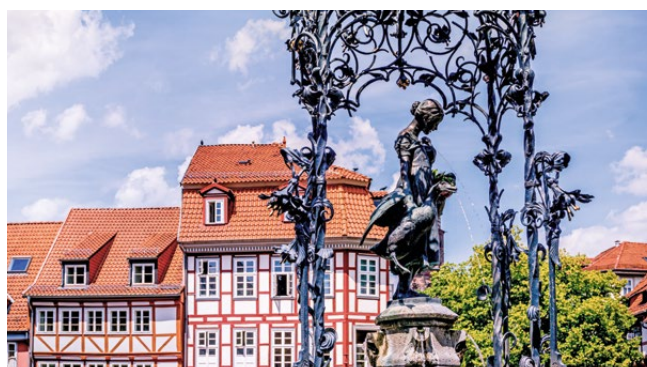
Axel Kaul (partner site manager), Vanessa Kruse (scientific project manager), Sylvia Vann and since 03/2021 Sabine Effenberger (partner site administrator), Marie-Christin Ernst (assistance), University Medical Centre Göttingen

Partner institutions at the DZHK partner site Göttingen

Georg August University Göttingen; University Medical Centre Göttingen (UMG); German Primate Center; Max Planck Institute for Dynamics and Self-Organisation (MPIDS) 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 2021

In the presence of Lower Saxony's Minister for Science and Culture, Björn Thümler, the completion ceremony for the Heart and Brain Center Göttingen (HBCG) took place in May 2021. The construction costs of around €38 million will be financed by the state of Lower Saxony and the federal government. The HBCG will be jointly managed by Prof. Gerd Hasenfuß and Prof. Mathias Bähr. In the HBCG, collaboration between DZHK and DZNE scientists will be fostered by an interdisciplinary and holistic approach to patient care. The HBCG is expected to be ready for occupancy by the end of 2022.



In April 2021, the EU project ESCAPE started under the leadership of Prof. Christoph Herrmann-Lingen. It aims to improve the quality of life of multimorbid heart patients with personalized treatments. Prof. Elisabeth Zeisberg received funding in the Leap Innovation Competition (SPRIN-D Challenge) to develop CRISPR/Cas13-mediated antiviral therapy.

Prof. Dr. Metin Tolan has been president of the University of Göttingen since April 1, 2021. On May 1, 2021, Prof. Dr. Lorenz Trümper began his new role as Chief Medical Officer of UMG. Prof. Dr. Andreas Fischer (German Cancer Research Center Heidelberg and University of Heidelberg) took over as Head of Clinical Chemistry and Laboratory Medicine at UMG in the fourth quarter of 2021 and will move into a laboratory in the DZHK Heart Research Building in due course.

On September 24, 2021, the Heart Center of the University Medical Center Göttingen celebrated its 20th anniversary in the Aula am Wilhelmsplatz with approximately 100 invited guests. In November, the "Microcirculation and Vascular Biology Meeting", supported by the DZHK, took place at the DPZ with an opening lecture by Nobel Laureate Stefan Hell and 30 other international speakers. In December, the DZHK site Göttingen met at the DPZ for the site retreat focused on interdisciplinary networking as a basis for translational cardiac research in Göttingen.



DZHK PARTNER SITE GREIFSWALD

Partner site spokesperson

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

Deputy spokesperson

Marcus Dörr and Jens Fielitz, Department of Internal Medicine B, University Medical Centre Greifswald

Partner site management

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

Partner institutions at the DZHK partner site Greifswald

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

What was important in 2021

In 2021, epidemiological research at the Greifswald partner site was strengthened by the Science Council's recommendation to include the William B. Kannel Center for Community Medicine research building in the 2022 funding phase. This is a research building of national significance. The estimated funding totals €65.6 million, with the federal government and the state of Mecklenburg-Vorpommern each contributing 50 percent. In addition to the examination center for the Study of Health in Pomerania (SHIP) subjects, the DZHK examination and training center and DZHK scientists will also move into the William B. Kannel Center.



In addition, Greifswald became one of the sites of the newly founded DZG "German Center for Pediatric and Adolescent Medicine" (DZKJ) in 2021. The DZHK will be under one roof with the other German Health Centers at the Greifswald site (DZNE, NAKO, DZKJ) from 2025, further promoting joint projects.

In May 2021, recruitment of the third independent population-based local cohort SHIP-NEXT-0 started. This strengthens the site's profile in cardiovascular epidemiology. In the future, four population-based cohorts with a sample size of over 220,000 will be available to DZHK projects for cardiovascular research. 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. This will further expand the partner site's profile in medical digitalization.

Since the end of 2019, a state-of-the-art laboratory animal house has been under construction in Greifswald and was completed in 2021. The opening and commissioning took place in early 2022. The laboratory animal house is directly connected to the molecular biology research laboratories of cardiology. It is available to DZHK projects for all experimental animal work, including its own intervention and examination rooms for phenotyping cardiovascular diseases.

At the end of 2021, a new DFG-funded research training group (RTG2719-PRO – Proteases in pathogen and host: importance in inflammation and infection; spokesperson: Prof. Barbara M. Bröker) was established at the University Medical Center and University of Greifswald. In a subproject with DZHK participation, mechanisms of septic cardiomyopathy are being investigated.

DZHK PARTNER SITE HAMBURG/KIEL/LÜBECK

Partner site spokesperson

From 11/2020 until 12/2021: Heimo Ehmke, Director of the Institute of Cellular and Integrative Physiology, University Hospital Hamburg-Eppendorf

Deputy spokesperson

Derk Frank, Medical Director of the Clinic for Internal Medicine III with a focus on cardiology, angiology and internal intensive care medicine, 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); Christian Albrecht University Kiel (UKSH, Campus Kiel)

What was important in 2021

The partner site's research pipeline of large-scale epidemiological cohort studies, high molecular biology expertise, biomarker research, and innovative bioinformatics enables translation from lab to bedside and from bedside to lab. The comprehensive biospecimen collections and clinical data also enable cross-disease approaches, e.g., in cardio-oncology, cardio-neurology, and cardio-nephrology.



The partner site specializes in omics technologies, imaging, and phenotyping techniques. It is characterized by a broad spectrum of methods, such as large animal, small animal, and iPSC platforms for human cardiovascular disease models. Several translational therapeutic approaches have been successfully tested and are currently in clinical trials through structured collaborations with biotech companies e.g., gene therapy (Dinaqor AG Switzerland) and heart repair (Evotec AG Hamburg).

In 2021, the University Center of Cardiovascular Science (UCCS) was founded at the UKE, aiming to transfer scientific findings from epidemiological, genetic, and molecular-experimental research into clinical application in a targeted manner. The Clinic for Pediatric and Adolescent Medicine (Kinder-UKE) of the UKE was selected by the BMBF in March 2021 as one of the sites of the German Center for Child and Adolescent Health (DZKJ). With its pediatric transplant center and focus on research into rare genetic diseases, the UKE brings important building blocks to the new health center. Future collaboration between the DZHK and DZKJ will strengthen the site's appeal to young scientists.

The University Heart Center Lübeck, a multidisciplinary facility of the Medical Clinic II and the Clinic for Cardiac and Thoracic Vascular Surgery of the University Hospital Schleswig-Holstein, was the first center in northern Germany to receive the certificate "Mitral Valve Center" of the German Society of Cardiology.

DZHK PARTNER SITE HEIDELBERG/MANNHEIM

Partner site spokesperson

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

Deputy spokesperson

Jörg Heineke, University Hospital Mannheim and Patrick Most, Department of Internal Medicine III, University Hospital Heidelberg

Partner site management

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

Partner institutions at the DZHK partner site Heidelberg/Mannheim

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



What was important in 2021

The Heidelberg/Mannheim site contributes the scientific focus “Hereditary and inflammatory cardiomyopathies and arrhythmias” to the DZHK. In the context of this scientific focus, twelve site projects are currently underway.

In addition, the site successfully filled a DZHK W3 professorship for RNA biology with Prof. Ralf Gilsbach at the Institute of Experimental Cardiology (Director Prof. Johannes Backs).

Under the direction of Prof. Johannes Backs and Prof. Norbert Frey, an outline for an SFB entitled “Molecular Circuits of Heart Disease” had been submitted to the DFG in the previous year, which was reviewed in the reporting year 2021. In April 2021, the advisory meeting at the DFG took place, which ended with the request to prepare a full SFB proposal. The full proposal was prepared in 2021.

In September 2021, Prof. Dr. Constanze Schmidt from Heidelberg University Hospital joined the site as a new member and Prof. Dr. Martin Borggrefe from Mannheim University Medical Center stepped down.

The Departments of Internal Medicine III (Prof. Norbert Frey) and Internal Medicine VIII (Prof. Johannes Backs) will have several thousand square meters of research space available in a new leased building close to campus. Detailed plans for the space were made in 2021. Occupation of the space will be prepared in 2022. Extensive support from the School of Medicine will enable the purchase of high-quality 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-Maximilians-University Munich

Deputy spokesperson

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

Partner site management

Sandra Rauser (partner site manager), Ludwig Maximilian University of Munich (LMU); Elif Alkan (assistant), Technical University of Munich

Partner institutions at the DZHK partner site Munich

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



What was important in 2021

The research focus at the Munich partner site (“Munich Heart Alliance”, MHA) of the DZHK is molecular mechanisms of cardiovascular diseases that have not yet been understood, the development of new therapeutic approaches based on these, and their translation into clinical trials. In this context, more than 80 research projects from the various funding lines of the DZHK were processed at the seven Munich member institutions. 418 publications with DZHK affiliation and a cumulative impact factor of more than 4,000 were published by Munich scientists in 2021, including on the DZHK-funded clinical trials ACEI-COVID-19, REVACEPT, ISAR-REACT 5, and APPROACH-ACS-AF. As before, a broad spectrum of methods was available for DZHK collaborative projects, including state-of-the-art OMICS technologies, various imaging and phenotyping methods, and large-animal, small-animal, and iPSC platforms for human cardiovascular disease models.

Among others, Prof. Christian Kupatt (ERC Advanced Grant with €2.5 million) and Dr. Moritz von Scheidt (“Junior Research Group Cardiovascular Diseases” of the Corona Foundation with €1 million) were successful in obtaining third-party funding. Awards were presented to Prof. Fabian Theis (Hamburg Science Prize) and PD Dr. Thorsten Kessler (Becht Research Prize of the German Foundation for Heart Research), among others. Furthermore, four Munich DZHK members were among the “Highly Cited Researchers” 2021.

To support the scientific exchange at the site, two meetings with lectures on Munich DZHK research projects were held virtually due to the pandemic.



DZHK PARTNER SITE RHINE MAIN

Partner site spokesperson

Andreas Zeiher (until 09/2021): Director of the Cardiology Department of the University Hospital Frankfurt, since 10/2021: Distinguished Professorship at the Goethe University Frankfurt

Deputy spokesperson

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 Medical Center of the Johannes Gutenberg University Mainz; Ralf Brandes, Director of the Institute for Cardiovascular Physiology, Goethe University Frankfurt

Partner site management

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

Partner institutions at the DZHK partner site Rhine Main

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

What was important in 2021

At the University Hospital in Frankfurt am Main, Reinier Boon started his ERC Consolidator project in April to study the role of ncRNA in aging. Stefanie Dimmeler was awarded the Paul Morawitz Prize for her contribution to cardiovascular research. Sebastian Cremer received a €240,000 Pitzer grant to establish an outpatient clinic for clonal hematopoiesis in cardiovascular disease. In addition, Jaya Krishnan's translational research project on the prevention of cardiotoxicity and cardiac injury was awarded €9.8 million through the EIC Accelerator.



Scientific highlights include research on the cellular response of endothelial cells after myocardial infarction (Tombar et al., Nat Commun. 2021) and the discovery of the composition and alteration of cardiomyocytes in children with cardiomyopathy (Nicin et al., Circulation 2021).

At the Max Planck Institute for Heart and Lung Research, Didier Stainier was approved for €2.5 million of funding from the European Research Council (ERC) in April 2021 to study the genetic processes by which cells compensate for the consequences of genetic defects. At the Kerckhoff Clinic in Bad Nauheim, the acquired analysis platform was integrated into the site project's laboratory system, and DZHK project-bound biomarker measurements have been taken since the beginning of the year. The evaluations of the clinical project GARY could be published in four publications.

At Mainz University Medical Center, €3.3 million (EU-REACT) was obtained for the interdisciplinary investigation of the effects of the SARS-CoV-2 pandemic at the individual and population level (Gutenberg COVID-19 study). Based on this, the interdisciplinary Gutenberg Long COVID Study, funded with €400,000, was initiated in December 2021 (PI Philipp Wild). Mainz University Medicine (PIs Philipp Wild, Wolfram Ruf) was selected for the final round of the BMBF Future Cluster Initiative in 2021, with the project curATime (Cluster for Atherothrombosis and Individualized Medicine) together with TRON gGmbH and the German Research Center for Artificial Intelligence.

ACRONYMS

AI	Artificial Intelligence	HBCG	Heart and Brain Center Göttingen
BDMS	Image Data Management System	HLHS	Hypoplastic left heart syndrome
BfArM	Federal Institute for Drugs and Medical Devices	IF	Impact faktor
BHF	British Heart Foundation	iPSC	induced pluripotent stem cells
BMBF	Federal Ministry of Education and Research	LIMS	Laboratory Information Management System
CRC	Collaborative Research Centers (SFB)	MDC	Max Delbrück Center for Molecular Medicine
DCM	Dilated cardiomyopathy	MRI	Magnetic resonance imaging
DGK	German Cardiac Society	NAKO	German National Cohort
DFG	German Research Foundation	NAPKON	National Pandemic Cohort Network
DHF	Dutch Heart Foundation (Hartstichting)	NUM	University Medicine Network
DHZB	German Heart Center Berlin	PDU	Product Development Unit
DNA	Deoxyribonucleic acid	PEI	Paul Ehrlich Institute
DPZ	German Primate Center	PI	Principal Investigator
DZG	German Centers for Health Research	RCC	Research Coordinating Committee
DZHK	German Center for Cardiovascular Research	RNA	Ribonucleic acid
DZIF	German Center for Infection Research	SHIP	Study of Health in Pomerania
DZKJ	German Center for Child and Adolescent Health	SOP	Standard Operating Procedure
DZNE	German Center for Neurodegenerative Diseases	TAVI	Standard Operating Procedure
ECG	Electrocardiogram	StM	Standortmanagement
ECS	Early clinical study	TAVI	Transcatheter aortic valve implantation
EOI	Expression of Interest	TRG	Translational Research Group
ERC	European Research Council	TRP	Translational Research Project
ESC	European Society of Cardiology	UKE	University Medical Center Hamburg-Eppendorf
FKZ	Funding code	UMG	U07niversitätsmedizin Göttingen
FMM	Funding Management Department	✓	Goal achieved
FTE	Full-time euqivalent	↻	In progress
GCRFF	Global Cardiovascular Research Funders Forum	—	Goal not achieved
GRS	Guideline-relevant study		

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