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

DZG DEUTSCHE ZENTREN
DER GESUNDHEITSFORSCHUNG

German Centre for Cardiovascular Research

ANNUAL REPORT

2020

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

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

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Foreword

Covid-19 has impacted every corner of our lives – and has significantly influenced our work at the DZHK. Despite the devastation of the pandemic, it has presented us with new opportunities and allowed us to demonstrate our strengths.

This past year, we have shown that we are fast and flexible when it comes to adapting structures and research when faced with challenge. We are also proud that the DZHK's Clinical Research Platform was selected by the Network University Medicine in a competitive process to collect the data for the National Cohort Platform (NAPKON). Our platform ensured that the data of corona patients from German university hospitals could be collected promptly, stored digitally and in compliance with data protection regulations. With this data, knowledge about the disease is continuously growing, forming the basis for new approaches to Covid-19 research, prevention and therapies.

Successfully adapting our platform to Covid-19 research, while navigating the stress and uncertainty posed by the pandemic, is testament to our people, both at the partner sites and in our head office. The Board of Directors would like to express their sincere gratitude to all staff at the DZHK.

Special thanks also to two people who have shaped the DZHK from conception and navigated many challenges in the last year. Thomas Eschenhagen, Chairman of the Board, and Joachim Krebser, Managing Director, have created an atmosphere of respect and open communication that has undoubtedly contributed to the DZHK's successes. Both did an excellent job of navigating us through the pandemic and ensuring a smooth transition into new leadership, with Stefanie Dimmeler as Spokesperson of the Board of Directors and Katharina Eulenburg as Managing Director.

After ten years of annual reports, we are delighted to present a new and improved format. Our 2021 report will provide you with even more research-related content and will illustrate the impact and relevance of our work for cardiovascular disease patients and our wider society.

The DZHK Board of Directors

Stefanie Dimmeler
Spokesperson of the Board of Directors

Steffen Massberg
Board of Directors

Thomas Sommer
Board of Directors

In Focus

The German Centre for Cardiovascular Research was founded with the aim of translating results from basic research into patient benefit. The year 2020 has shown how important this work is.

The significant challenge for translational cardiovascular research

Since March 2020, the pandemic has presented great challenge to the DZHK. Scientists and colleagues in research management adapted quickly - and with great team spirit - to new demands and research questions.

Cardiovascular patients are particularly affected by Covid-19 because they are at high risk for a severe course of the disease. Accordingly, many groups in the DZHK have dedicated their work to a wide variety of coronavirus research topics. As a result of this research, 74 publications related to Covid-19 were published in the reporting year (see p. 12). We reported on specific research projects in the 2019 annual report, as editorial deadlines fell in the middle of the 2020 pandemic year.

In August 2020, a Circulation Covid-19 paper was selected as Paper of the of the Month ↗ (see pp. 10 and 13). Researchers at the Munich partner site were able to determine the mechanism that causes the small lung vessels of severely ill Covid-19 patients to develop numerous clots, which ultimately lead to lung failure.

Detailed knowledge of risk factors, disease progression and treatment successes of infected and diseased persons is the basis for effective therapies and protection against Covid-19. Another focus in this reporting year was the adaptation of our Clinical Research Platform to the requirements

of the coronavirus research of the Network University Medicine (NUM), which we report on in detail in the chapter "Clinical Research Platform" (see p. 34).

To keep the public updated on the latest developments, we set up the DZHK corona blog ↗ (see p. 46).

Internal evaluation – ascertaining the status quo

The DZHK's mission is translation, which means transferring results from basic research into clinical application. As a decentralised centre, we have established special structures, funding programmes and expertise for this purpose. Our second major evaluation took place on the 13th and 14th of January 2020. This internal review was led by our scientific advisory board and additionally accompanied by four external reviewers. The aim of the evaluation was to ascertain the status quo and the partner sites' contribution to the success of the DZHK.

We are very pleased about the extremely positive assessment of the review panel. In particular, they emphasised the DZHK-enabled networking of cardiovascular research throughout Germany, which had not existed like this before the founding of the DZHK. The reviewers also stated that the programmes, research and exchange platforms, training measures and scientific excellence of the DZHK's members were a considerable success and add value to the cardiovascular research community.

In particular, the panel praised the established and internationally visible clinical research at the DZHK, which not only includes all DZHK partner sites, but also takes place in over 70 external study centres. Essential for this is the DZHK's own Clinical Research Platform with standardised and mandatory infrastructures such as central data storage and decentralised biobanking, to name but a few (see p. 33).

The centre's achievements in basic and translational research were also highlighted. New therapeutic approaches and medical devices developed through DZHK-funded research, such as the inhibitor antimiR-92a or engineered heart tissue, are currently undergoing clinical trials.

The DZHK's commitment to promoting young scientists with numerous research funding schemes, scholarships and mentoring, as well as the targeted recruitment of DZHK professorships, was appreciated by the review panel and considered an important investment for the future.

Also recognised by the panel were the DZHK measures that further strengthen international networking while increasing the visibility of the DZHK, such as the joint funding programme with the British Heart Foundation (BHF) and the Dutch Heart Foundation (Hartstichting) (see p. 43).

Change in leadership

In 2020, we said goodbye to two personalities who have shaped the DZHK over many years and helped form it from the very beginning.

After nine years, Thomas Eschenhagen from the Hamburg/Kiel/Lübeck partner site stepped down as Chair of Board of Directors in December 2020. Joachim Krebser, who accompanied the founding of the DZHK from the beginning and became the first Managing Director in 2012, also relinquished the position after nine years in January 2021.

The new leadership is formed by Stefanie Dimmeler from the Rhine Main partner site as Chair of the Board of the Directors and Katharina Eulenburg as Managing Director. Both have been active in the DZHK for many years and we look forward to working with them in their new roles.

Highlights and Publications 2020

JANUARY

A research team from the Hamburg/Kiel/Lübeck partner site found a genetic defect that is responsible for leaking heart valves.

News from 09/01/2020:

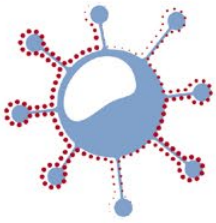
↗ Genetic defect leads to heart valve defects

MARCH

34 external study centres throughout Germany received the label "DZHK Study Partner" as an award for their good patient recruitment in DZHK studies (p. 47).

Two projects each received €1 million to further advance their promising research that had emerged from a one-off ideas competition in 2017 (p. 24).

APRIL



€1 million was provided for three DZHK clinical trials to investigate cardiovascular complications associated with Covid-19 (p. 30).

MAY

JUNE

British, Dutch and German researchers worked closely together to solve urgent questions in cardiovascular medicine: Three trans-national projects were awarded a total funding amount of €5 million (p. 43).

FEBRUARY

How does heart failure develop? An interdisciplinary research team from the Rhine Main partner site received €6.8 million to find more precise answers with the help of mass spectrometry (p. 62).

News from 11/02/2020:

↗ Fighting heart failure: funding of millions for systems medicine in Mainz

With its Clinical Research Platform, the DZHK supported the Covid-19 research of the German university hospitals by temporarily recording clinical data, diagnostic images and samples from coronavirus patients (p. 33).

Together against Corona: The first patients were enrolled in the three cohorts of the National Pandemic Cohort Network (NAPKON). Their data has been collected with the same infrastructure that the DZHK uses for its clinical trials (p. 34).

JULY

NOVEMBER

For the first time, and in response to the Covid-19 pandemic, the DZHK's largest network meeting, the annual retreat, took place as a digital event (p. 40).

SEPTEMBER

AUGUST

The EAST-AFNET-4 study of the Atrial Fibrillation Competence Network, supported by the DZHK, showed that early rhythm-preserving therapy of atrial fibrillation prevents complications (p. 27).

News from 31/08/2020:

Atrial fibrillation: Early rhythm control therapy prevents complications

DECEMBER

New funding guideline "Utilisation of data and specimens" provides impetus for even more scientists to use the DZHK's cardiovascular data and specimens for specific research questions (p. 35).

OCTOBER

The first joint symposium of the DZHK and the HiGHmed initiative in Heidelberg was held, with the topic 'How do you bring together knowledge from patient care and research using digital means?' (p. 41).

The selected news stories are based on publications that were awarded Paper of the Month by the DZHK's Board of Directors.

Atlas of the human heart

The Atlas of the Human Heart is a comprehensive study on heart cell types, subtypes, and blood vessel cells, published for the very first time.

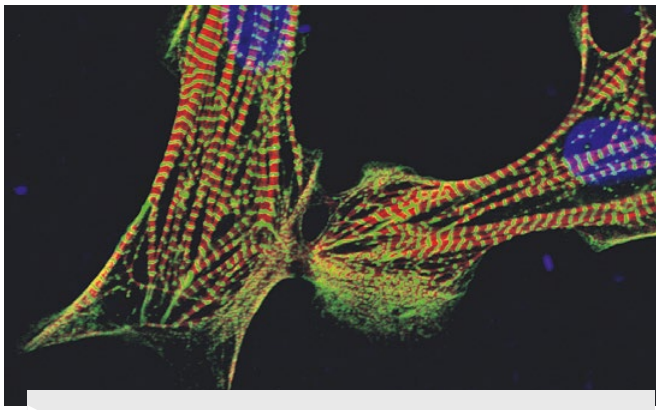
Around half a million individual cells and cell nuclei of the human heart were analysed by an international team of researchers from six countries. The scientists want to understand how the healthy heart "ticks" and what goes wrong in heart disease. This should enable researchers to find new treatments and ways to regenerate damaged heart tissue. In a first draft atlas of the human heart, published in the journal Nature, the researchers show the enormous diversity of cells and molecules.

Unknown subtypes of heart cells discovered

In this study, the team used seven female and seven male hearts from heart-healthy donors between the ages of 40 and 75, who were not eligible for transplantation. To characterise the heart cells as precisely as possible, the team examined which genes were switched on in each of the individual cells and cell nuclei from six different heart regions. In addition to tremendous cell diversity, the atlas reveals previously unknown subtypes of heart muscle cells, supporting heart cells, protective immune cells, and an extensive network of blood vessel cells. It also shows how the cells communicate to keep the heart beating.

Cells differ depending on heart region

Cells in different heart regions were also found to differ significantly. It is possible that this leads to different responses to treatments. The researchers also examined the blood vessels that run through the heart in greater detail than ever before. The atlas shows how cells in veins and arteries have adapted to different pressures and environments. This could help us understand what happens in the blood vessels during coronary artery disease.



The atlas shows significant differences between cells in different heart regions. This could be one reason for different responses to treatment.

Professor Norbert Hübner, Principal Investigator at the DZHK and one of the lead authors from the Max Delbrück Center for Molecular Medicine, says, "This study shows what the technique of single-cell sequencing and international collaborations can do. Knowing the full spectrum of cardiac cells and their gene activity is a fundamental necessity. Only then can we understand how the heart functions and how it responds to stress and disease."

Publication: **Cells of the adult human heart.** Litviňuková, M. et al. *Nature, 24 September 2020,* *DOI: 10.1038/s41586-020-2797-4*

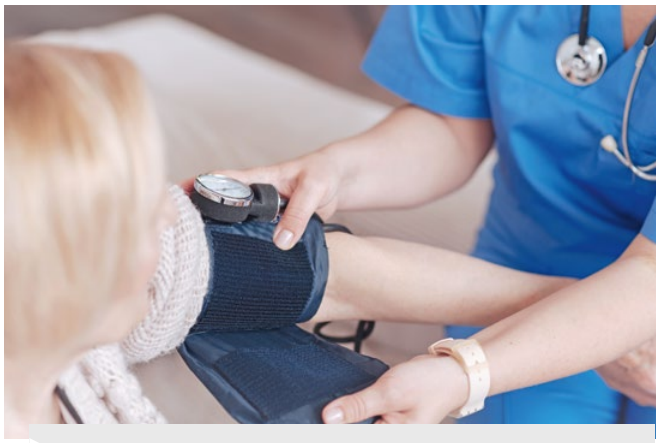
Awarded Paper of the Month | October 2020

Overactive enzyme causes hereditary hypertension

An altered gene for the enzyme PDE3A causes a hereditary form of hypertension. Proof of this has been provided after more than 40 years of research by several teams at the DZHK partner site in Berlin, with the help of two animal models.

In the early 1970s, a physician observed that members of an extended Turkish family had shortened fingers and extremely high blood pressure. The majority of those affected died of a stroke before their 50th birthday.

Since the early 1990s, a team led by Professor Friedrich Luft at the Max Delbrück Center for Molecular Medicine (MDC) in Berlin has been searching for the causes and was finally able to identify an altered gene. It contains the blueprint for an enzyme called phosphodiesterase 3A, also called PDE3A.



Extremely high blood pressure and shortened fingers put scientists on the trail of a gene mutation.

The enzyme, which regulates both blood pressure and indirectly bone growth, becomes more active than usual due to the gene mutation. The hereditary disease is also called Bilginturan Syndrome after its Turkish discoverer.

The missing proof

Until now, there was no proof that the mutated PDE3A is the cause of Bilginturan Syndrome. This evidence has now been provided by an international group of 40 researchers from Berlin, Bochum, Limburg, Toronto (Canada), and Auckland (New Zealand). DZHK working groups from MDC and Charité - Universitätsmedizin Berlin were involved in the study.

The researchers used two animal models. First, they genetically modified mice to produce overactive human PDE3A in the smooth muscle cells that form part of the vascular walls. This gave the animals high blood pressure.

Gene-altered rats with the hereditary disease

Even more interestingly however, was a rat model. In this model, the scientists used the CRISPR/Cas9 gene scissors to alter nine base pairs in a region of the PDE3A gene that is mutated in the syndrome, a so-called mutation hotspot. The resulting enzyme differed in three amino acids from the common variant, and the enzyme's activity also changed. The rats suffered from high blood pressure and the toes of their forelegs were also significantly shortened - similar to the fingers of humans with the syndrome.

This discovery could lead to clinical change. A substance called Riociguat, which is already approved for the therapy of pulmonary hypertension, can slow down overactive PDE3A. The team found that its administration in the diseased rats lowered blood pressure to normal levels.

Publication: **Phosphodiesterase 3A and arterial hypertension.** Ercu, M. et al. *Circulation, 11 Jun 2020,* DOI: 10.1161/CIRCULATIONAHA.119.043061

Awarded Paper of the Month | June 2020

Covid-19: Lung failure and thrombosis are linked

Lung failure and the development of blood clots are closely linked in Covid-19. A research team from the DZHK partner site in Munich gained insights into the mechanism in mid-2020.

Infection with SARS-CoV-2 can lead to lung failure in severe cases. It is then usually necessary to provide invasive ventilation to those affected. In parallel, complications such as pulmonary embolism or thrombosis in the veins can frequently occur in these patients. It was initially unclear whether there was a connection between the two events.

In the blood of severely ill Covid-19 patients with lung failure, researchers found two highly activated cell types. They are responsible for thrombosis in even the smallest blood vessels in the lungs.

The research team from LMU Klinikum München was able to detect numerous thromboses in the smallest blood vessels of the lungs of severely ill Covid-19 patients. Vascular occlusions were also found in the heart and kidney.

Vascular occlusions should prevent the spread of viruses

The thrombi consisted mainly of platelets and activated inflammatory cells, called neutrophil granulocytes. Vascular occlusions are a protective tool for humans. They form because inflammatory processes activate blood clotting and platelets. As a result, vessels become clogged, which should prevent the spread of viruses and bacteria in the body. However, the vascular occlusions also impair blood supply to tissues - contributing to lung failure - and a systemic tendency for thrombosis develops.

Using multi-dimensional fluorescence flow analysis, the researchers showed that highly activated neutrophil granulocytes and platelets are found in the blood of ventilator-dependent Covid-19 patients with lung failure. Both cell types activate each other reciprocally, ultimately leading to vascular occlusion in the lungs.

Blood clotting is strongly activated

An essential component of vascular occlusion are NETs (neutrophil extracellular traps). These net-like structures made of DNA and granule proteins of the neutrophil granulocytes stabilise the blood clots. This initially local process in the lungs also leaves its mark in the blood, where blood clotting is strongly activated. This is then reflected in an increased systemic tendency to develop clots.

These findings contribute to a better understanding of the pathophysiological mechanisms in Covid-19 and may be a starting point in the prevention and therapy of lung failure and other thrombotic complications in patients with Covid-19.

Publication: **Immunothrombotic dysregulation in COVID-19 pneumonia is associated with respiratory failure and coagulopathy.** Nicolai, L. et al. *Circulation, 28 Jul 2020,* DOI: 10.1161/CIRCULATIONAHA.120.048488.

Awarded Paper of the Month | August 2020

Heart attack: Misdirected immune cells can damage vessels

Heart attacks have various triggers, but in each case blood supply to the heart muscle is blocked by a clot. Researchers from the DZHK partner site in Berlin were able to show that blood clots in the coronary vessels can also form in other ways than previously known.

A heart attack occurs when blood clots block the coronary arteries - resulting in life-threatening oxygen starvation of the heart muscle. Blood clots form when the connective tissue sheath of vascular deposits - known as plaques- becomes unstable and ruptures. The released material initiates processes that lead to the clumping of platelets.

In a quarter of the heart attack patients studied, blood clots had formed on intact vascular deposits, triggered by erosions.

Immune cells accumulate near plaques

The findings of the Berlin researchers now indicate that blood clots can also form at intact plaques. Under certain flow conditions, immune cells can collect there, activating blood clotting. The researchers call this process plaque erosion, as opposed to the familiar plaque rupture.

The team examined 170 heart attack patients, and in about 25 percent of them they found that the cause was erosion of the vascular plaque instead of rupture. It turned out that the plaque erosion sites are characterised by special activated immune cells – called T lymphocytes – which accumulate in the walls of coronary vessels under altered flow conditions and can contribute to damage of the inner vessel wall.

Using a special imaging technique, known as optical coherence tomography (OCT), the researchers succeeded in visualising the dangerous plaques in high resolution and accurately dividing them into rupture or erosion. They then removed the blood clot at the infarct-triggering site with a suction catheter and obtained blood to examine immune cells and inflammatory markers.

Composition of immune cells is altered

In blood clots caused by erosion, the team found an altered composition of immune cells. Increased CD4- and CD8-positive lymphocytes and their cytotoxic effector molecules indicated an inflammatory response that damages endothelial cells of the inner vessel wall. The blood clots in these cases were also found more frequently in the vicinity of vessel branches, which are characterised by special flow conditions. The researchers were able to reproduce the processes in a cell model.

These findings could lead to the development of immunomodulating therapies for the treatment and prevention of heart attacks.

Publication: **Differential immunological signature at the culprit site distinguishes acute coronary syndrome with intact from acute coronary syndrome with ruptured fibrous cap: results from the prospective translational OPTICO-ACS study.** Leistner, D. M. et al. European Heart Journal, 1 October 2020, DOI: 10.1093/eurheartj/ehaa703

Awarded Paper of the Month | November 2020

PUBLICATIONS

Published work enables researchers to access the knowledge of others, and discuss, cite and take it further in their own research. Frequently cited articles in recognised journals are also important for a scientist's reputation.

In 2020, the number of publications with DZHK affiliation rose to 1,508. The number of publications with an impact factor over 10 rose to 161. In this reporting year, DZHK scientists published 74 publications related to Covid-19, 14 of which appeared in specialist journals with an impact factor over 10. The Berlin (31), Munich (18) and Rhine Main (13) partner sites were particularly active here. Five publications involved more than one partner site.

A list of the publications can be found on our website:

dzhk.de/en/research/research-focus/publications/publications-2020/

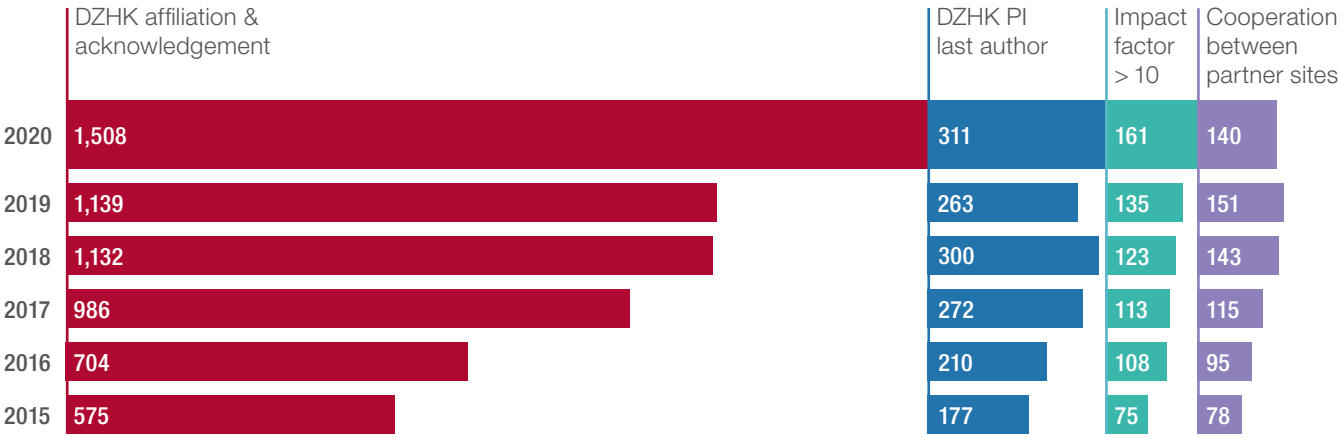
Publications

Amount	2020	2019
Total publications	1,508	1,139
of which:		
First authorship of a DZHK PI	61	55
Last authorship of a DZHK PI	311	263
First authorship of a Young DZHK member	278	249
First authorship of a DZHK Scientist	120	97
Last authorship of a DZHK Scientist	308	239
Publications involving several DZHK partner sites	140	151
Publications published in:		
Nature Publishing Group	33	30
Cell Press[1]	8	8
NEJM, Lancet, JAMA[2]	10	10
Circulation, Circ Res, EHJ, JCI, JACC	109	84
Science[3]	1	3
Total (Impact-Factor > 10)	161	135

1 includes Cell, Cell Stem Cell, Immunity, Cell Metabolism, Molecular Cell, Trends in Biochemical Sciences, Trends in Cell Biology, Trends in Immunology, Trends in Genetics, American Journal of Human Genetics (AJHG), Developmental Cell, Trends in Molecular Medicine, Trends in Biotechnology

2 includes JAMA Cardiology

3 includes Science Translational Medicine



PAPER OF THE MONTH 2020

Each month, the DZHK Board selects a Paper of the Month which is announced in the DZHK newsletter and published on the DZHK website ↗.

⌂ = DZHK partner sites involved

JANUARY

CRISPR-mediated activation of endogenous gene expression in the postnatal heart. Schoger, E. (University Medical Center Göttingen) et al. *Circulation Research.* ⌂ Göttingen, Heidelberg/Mannheim

FEBRUARY

Loss of ADAMTS19 causes progressive non-syndromic heart valve disease. Wünnemann, F. (University of Montreal, Canada), Ta-Shma, A. (University of Münster)* et al. *Nature Genetics.* ⌂ Hamburg/Kiel/Lübeck

MARCH

The histone demethylase JMJD2B regulates endothelial-to-mesenchymal transition. Glaser, S. F. (University Hospital Frankfurt) et al. *PNAS.* ⌂ Rhine Main, Heidelberg/Mannheim

APRIL

AntimiR-21 prevents myocardial dysfunction in a pig model of ischemia/reperfusion injury. Hinkel, R. (German Primate Center Göttingen), Ramanujam, D. (Technical University of Munich)* et al. *JACC.* ⌂ Göttingen, Munich

MAY

Somatic gene editing ameliorates skeletal and cardiac muscle failure in pig and human models of Duchenne muscular dystrophy. Moretti, A., Hoppmann, P., Meier, A. B. (Technical University Munich)* et al.: *Nature Medicine.* ⌂ Göttingen, Munich

JUNE

Phosphodiesterase 3A and arterial hypertension. Ercu, M. (Max Delbrück Center for Molecular Medicine Berlin), Markó, L. (Charité-Universitätsmedizin Berlin)* et al. *Circulation.* ⌂ Berlin

JULY

Noncanonical inhibition of caspase-3 by a nuclear microRNA confers endothelial protection by autophagy in atherosclerosis. Santovito, D., Natarelli, L. (Ludwig Maximillian University Munich)* et al. *Science Translational Medicine.* ⌂ Munich

AUGUST

Immunothrombotic dysregulation in COVID-19 pneumonia is associated with respiratory failure and coagulopathy. Nicolai. L., Leunig, A. (Hospital of the Ludwig Maximilian University Munich)* et al. *Circulation.* ⌂ Munich

SEPTEMBER

A minimal-invasive approach for standardized induction of myocardial infarction in mice. Sicklinger, F., Zhang, Y. (University Hospital Heidelberg)* et al. *Circulation Research.* ⌂ Heidelberg/Mannheim

OCTOBER

Cells of the adult human heart. Maatz, H. (Max Delbrück Center for Molecular Medicine Berlin), Reichart, D. (University Medical Center Hamburg-Eppendorf) et al. *Nature.* ⌂ Berlin, Hamburg/Kiel/Lübeck

NOVEMBER

Differential immunological signature at the culprit site distinguishes acute coronary syndrome with intact from acute coronary syndrome with ruptured fibrous cap: results from the prospective translational OPTICO-ACS study. Leistner, D. M., (Charité – Universitätsmedizin Berlin) et al. *European Heart Journal.* ⌂ Berlin, Munich

DECEMBER

An important role for DNMT3A-mediated DNA methylation in cardiomyocyte metabolism and contractility. Madsen, A. (University Medical Center Hamburg- Eppendorf) et al. *Circulation.* ⌂ Hamburg/Kiel/Lübeck

* contributed equally.

PRIZES, GRANTS, PERSONALIA

Editors‘ picks

Dr. Philipp Bengel
(Göttingen)
Rudi Busse Young Investigator Award from the German Cardiac Society (DGK)

Dr. Bo Eric Christian Beuthner
(Göttingen)
August Wilhelm and Lieselotte Becht Research Prize of the German Heart Research Foundation endowed with €15,000

Dr. Dario Bongiovanni
(Munich)
Young Investigator Award of the European Society of Cardiology (ESC)

Prof. Reinier Boon
(Rhine Main)
Consolidator Grant of the European Research Council (ERC)

Julia Büschges
(Berlin)
Young Investigator Award at the Preventive Cardiology Congress 2020 of the European Society of Cardiology (ESC)

Prof. Lucie Carrier
(Hamburg/Kiel/Lübeck)
Research funding within the framework of the Transatlantic Networks of Excellence by the Leducq Foundation in the amount of €5.6 million

Prof. Stefanie Dimmeler
(Rhine Main)
Gold medal of the European Society of Cardiology (ESC)

Prof. Jens Frahm
(Göttingen)
Werner-von-Siemens-Ring of the Werner-von-Siemens-Ring Foundation

Prof. Gerd Hasenfuß
(Göttingen)
Funding from the German Research Foundation (DFG) for a Collaborative Research Center in the amount of €14.6 million

PD Dr. Thorsten Kessler
(Munich)
Prevention Award 2020 of the German Society for Internal medicine (DGIM) in the amount of €10,000

Prof. Wolfgang Koenig
(Munich)
Paul Morawitz Prize of the German Cardiac Society (DGK)

Prof. Florian Leuschner und Tim Christian Kuhn
(Heidelberg/Mannheim)
Wilhelm P. Winterstein Prize of the German Heart Foundation in the amount of €10,000

Prof. Jeanette Schulz-Menger
(Berlin)
Gold Medal Award 2020 from the Society for Cardiovascular Magnetic Resonance (SCMR)

Prof. Renate Schnabel
(Hamburg/Kiel/Lübeck)
Research funding from the EU research framework program "Horizon 2020" in the amount of €6 million

Prof. Samuel Tobias Sossalla
(Göttingen)
Albert Fraenkel Prize 2020 of the German Cardiac Society (DGK)

PD Dr. Konstantin Stark
(Munich)
Starting Grant from the European Research Council (ERC) in the amount of €1.5 million

Dr. Ludwig Weckbach und PD Dr. Ulrich Grabmaier
(Munich)
Franz Maximilian Groedel Research Prize 2020 from the German Cardiac Society (DGK)

Prof. Wolfram-Hubertus Zimmermann
(Göttingen)
Second winner in the innovation competition "Organ Replacement from the Laboratory" and €2 million in project funding from the Federal Ministry of Education and Research (BMBF)

Research at our Partner Sites

The DZHK conducts research in 32 partner institutions at seven partner sites nationwide. The partner institutions include university hospitals and universities, centres of the Helmholtz Association, Leibniz and Max Planck Institutes and a departmental research institution.

Each partner site has its own research focus. Around 1,800 scientists affiliated with the DZHK ensured that cardiovascular research was carried out in the 67 approved partner site projects in 2019 and 2020. They spent around 49.8 percent of its total funds (€10.6 million) on the partner site projects.

According to the principle of "strengthening strengths", the partner sites are using these funds to sharpen their scientific profile in the long term. As a rule, the projects are basic science and suitable for further development in applied and patient-oriented research.

The DZHK professorships are also financed through partner site funds. 17 scientists held a DZHK professorship in this reporting year. A further professorship for genome editing at the Göttingen partner site has not yet been filled.

All DZHK professorships can be found here:
dzhk.de/en/the-dzhk/scientists/dzhk-professorships/

The DZHK is a driving force for the development and acceleration of cardiovascular research at all sites. In 2020, this was made particularly clear by the fact that new research buildings in which DZHK research groups will work were planned or opened at four of our seven partner sites.

All partner site projects can be accessed at:
dzhk.de/en/resources/projektdatenbank
(Project type: Partner Site Projects)

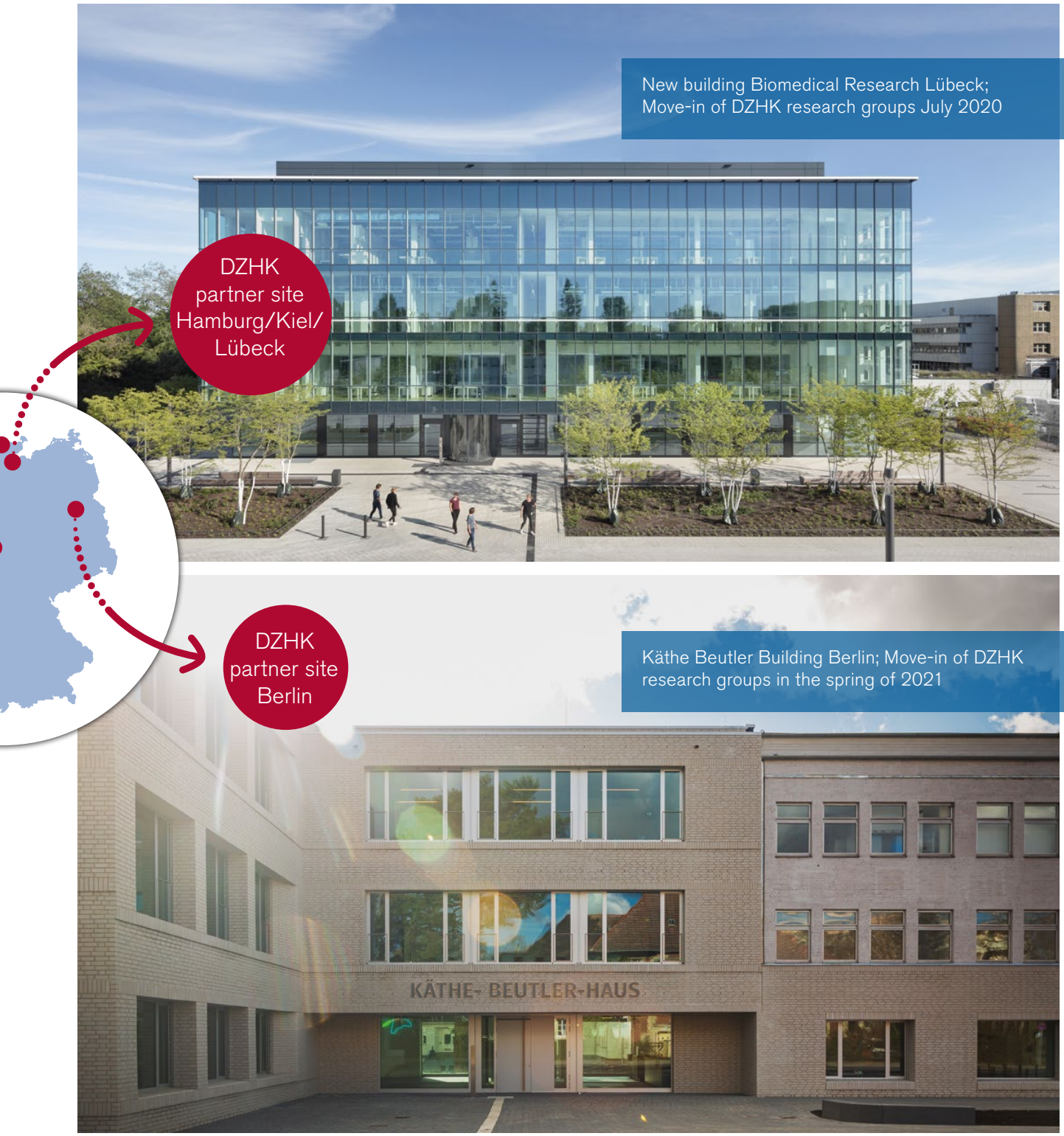
Quinke Research Center Kiel,
Opening February 2020

DZHK
partner site
Hamburg/Kiel/
Lübeck

Heart and Brain Center Göttingen, Laying of
the foundation stone November 2020

DZHK
partner site
Göttingen

Developments at the partner sites can be found
in the chapter "Facts and Figures" from p. 56.



New building Biomedical Research Lübeck; Move-in of DZHK research groups July 2020

Käthe Beutler Building Berlin; Move-in of DZHK research groups in the spring of 2021

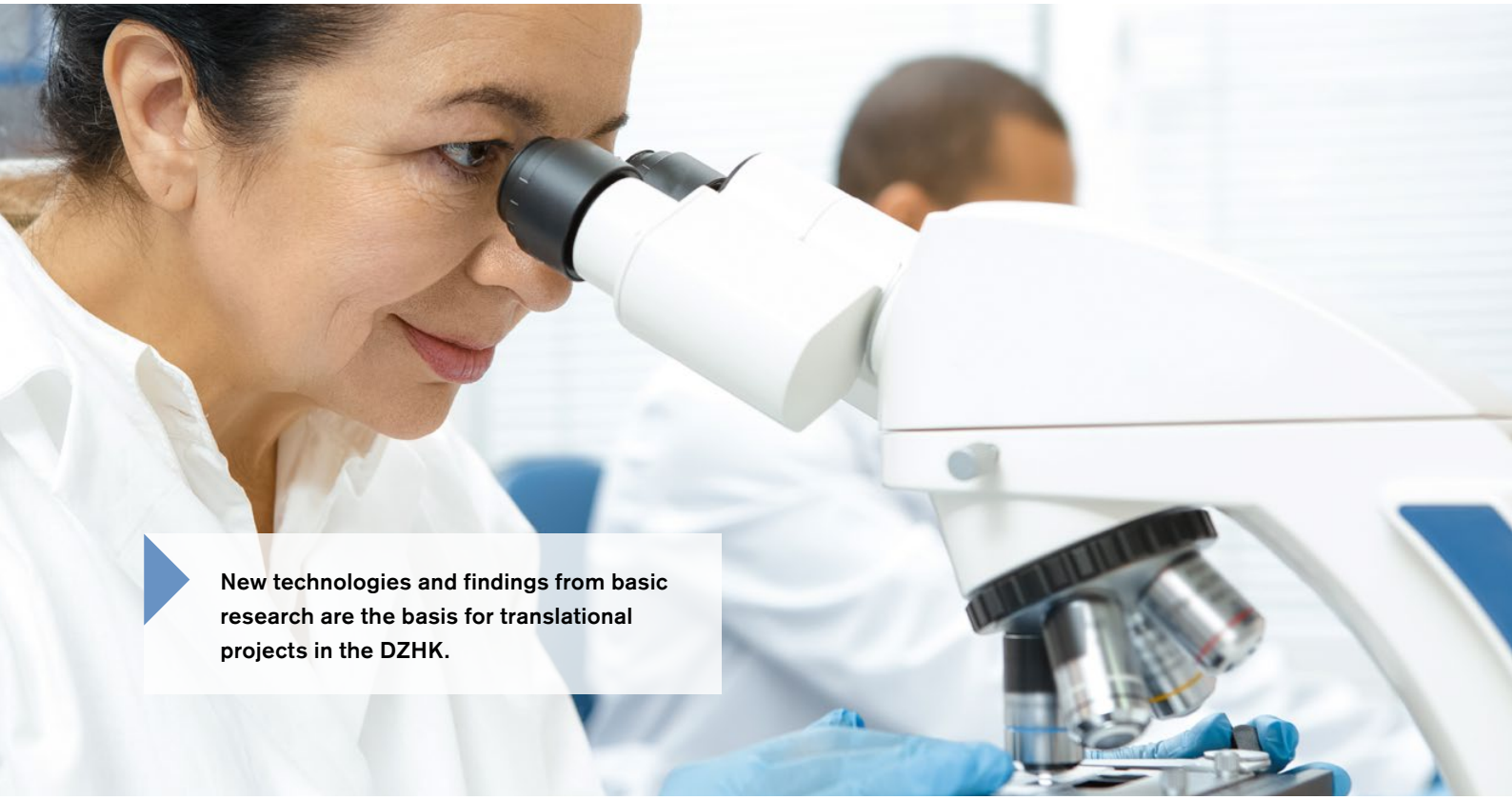
Goals achieved in 2020?

- ✓ Approx. 100 partner site projects from 2021-2025 administratively applied for and approved
- ↻ Share of women DZHK PIs increased from 2021–2025

Goals 2021

- ↗ Digitisation projects initiated at the partner sites
- ↗ Share of women DZHK PIs increased in the years 2021–2025

Preclinical Research



New technologies and findings from basic research are the basis for translational projects in the DZHK.

Preclinical research describes the projects that precede clinical research. It is vital, as it generates new knowledge that may contribute to a better understanding of the mechanisms underlying diseases. In 2020, the DZHK allocated €4.8 million to new projects in the field of preclinical research.

TRANSLATIONAL RESEARCH PROJECTS

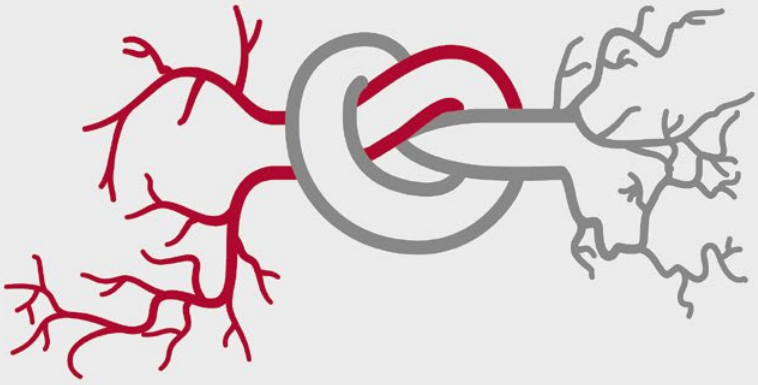
Preclinical research forms the basis for translational projects, which bridge the gap between basic research and early clinical trials. The DZHK supports translational research and collaborative projects using shared expertise with external partners. By supporting translational projects, we aim to provide better care for cardiovascular patients in the future.

The projects funded to date are incredibly diverse in terms of topics and methods. This also applies to the projects awarded in 2020. These have a total volume of €2.2 million.

New projects that have been funded include the search for an inhibitor that prevents the progression of atherosclerosis, the development of a gene therapy that targets the progressive blockage of leg vessels, and of an animal model that can be used to test new diagnostic tools or investigate new treatments. Members of the Translational Research Group reviewed the applications and investigated what would be needed for the projects to be successful. Common to all projects is a well-characterized target and the potential to develop new treatments or diagnostic tools for cardiovascular patients in need.

Due to the pandemic, many projects were delayed and therefore no Translational Research Project was completed in 2020.

Translational Research Projects awarded in 2020



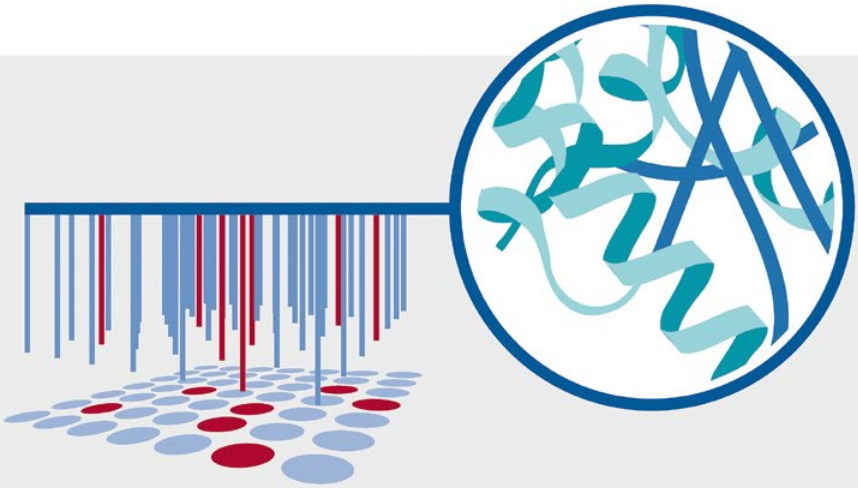
A new gene therapy for peripheral arterial disease

Peripheral arterial disease is caused by impaired blood flow to the limbs, due to the narrowing or blockage of a large artery. A bypass, balloon angioplasty, or stent can be used to reopen the artery, however this is not possible in smaller vessels. In this case, complementary therapy can be used to stimulate the growth and maturation of small vessels. These vessels are often affected by the persistent undersupply of oxygen and inflammation in diabetes or a lipid metabolic disorder.

This therapy involves administering an adeno-associated virus (AAV) that harbors the gene sequence of a factor called MRTFA, which kickstarts blood vessel growth. The factor induces both vessel growth and microvessel stabilisation. This approach will be tested in a pig model with a blocked femoral artery, in healthy and diabetic animals or in animals with elevated lipids and cholesterol levels in the blood. Accompanying studies will be performed on the distribution and side effects of the gene therapy.

rAAV.MRTF-A-based vascular gene therapy in chronic hindlimb ischemia

Duration	Budget	Project lead	Participating investigators
2021–2025	€1,234,600	• Christian Kupatt Munich	• Karl-Ludwig Laugwitz • Alessandra Moretti • Eckhard Wolf Munich



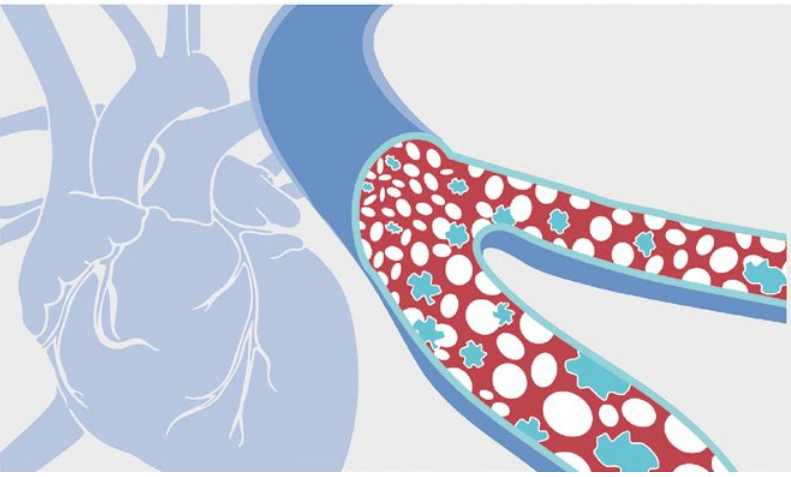
Development of inhibitors for the treatment of atherosclerosis

Previous work has shown that inhibiting the binding of two molecules, called CD40L and CD40, on immune cells, significantly reduces atherosclerosis. However, inhibiting this binding over a long period of time can suppress the body's healthy immune system and increase the risk of clots. The scientists found a solution - by inhibiting the binding of another molecule called TRAF6 to CD40, atherosclerosis is reduced but the immune system is not dangerously suppressed.

This project aims to find new small-molecule inhibitors that specifically inhibit the binding of TRAF6 to CD40, blocking the inflammatory component of atherosclerosis. These small molecule inhibitors could be used as drugs to treat cardiovascular disease caused by inflammation.

Re-screening for novel CD40-TRAF6 interaction inhibitors

Duration	Budget	Project lead	Participating investigators
2021	€405,710	• Dorothee Atzler • Esther Lutgens • Christian Weber Munich	• Bert Klebl (Lead Discovery Center Dortmund)



Development of a large animal model of clonal hematopoiesis

Aging humans can develop mutations, or faults, in stem cells that lead to the formation of white blood cell clones. This process is called clonal hematopoiesis and is a risk factor for cardiovascular disease. Patients with clonal hematopoiesis are also at greater risk of complications or death with surgery. The underlying mechanisms are poorly understood. Experimental findings to date have mainly come from small animal models, which often do not adequately represent disease mechanisms and outcomes in humans.

The researchers plan to develop a pig model with a stem cell mutation that leads to clonal hematopoiesis. Such a large animal model should help the team better understand the mechanisms of clonal hematopoiesis and investigate new treatment options that could benefit humans in the future.

Development and characterization of a pig model of TET2-mediated clonal hematopoiesis

Duration	Budget	Project lead	Participating investigators
2021–2024	€516,826	• Christian Schulz Munich	• Daphne Merkus • Eckhard Wolf Munich

Translational Research Projects since 2015

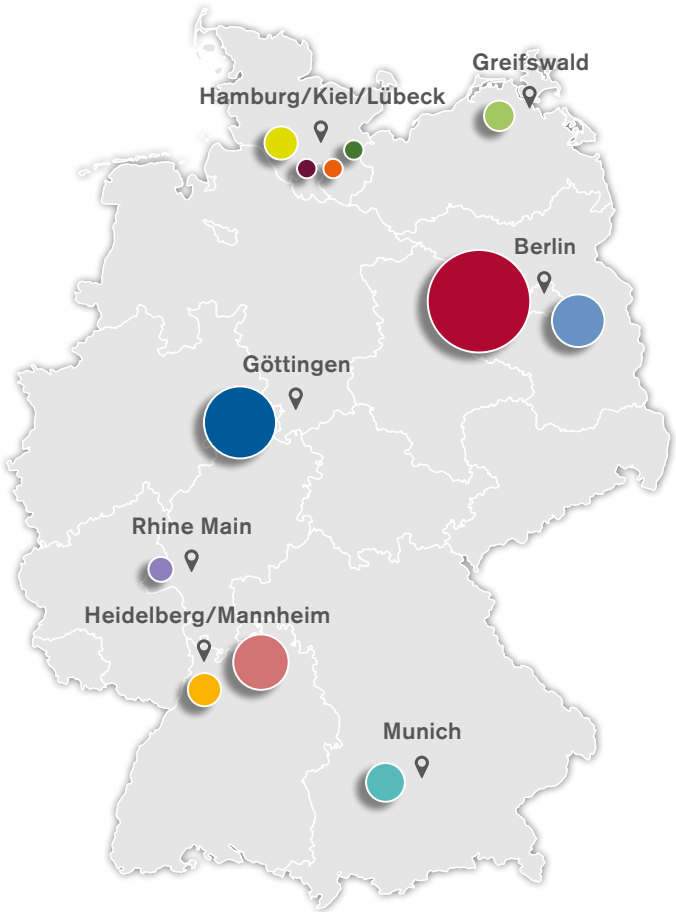
Project title	Project lead	Budget (€)	Duration
Development of miR-92a inhibitors for the treatment of cardiovascular disease	Dimmeler (Rhine Main)	2,458,430	2015–2019
Off-pump transapical mitral valved stent implantation	Lutter (Hamburg/Kiel/Lübeck)	337,290	2016–2017
Low-energy termination of ventricular fibrillation in a porcine heart failure model	Luther (Göttingen)	1,023,000	2016–2019
IPSC-EHT transplantation for cardiac repair – towards first-in-patient	Eschenhagen, Hansen (Hamburg/Kiel/Lübeck)	1,746,314	2016–2022
Gene therapy for neonatal sarcomeric cardiomyopathies: towards first-in-patient	Carrier (Hamburg/Kiel/Lübeck)	451,794	2016–2019
Generation and functional characterization of macrophage cell lines from yolk sac precursors	Schulz (Munich)	248,932	2017–2019
Late pre-clinical development of CD40-TRAF 6 inhibitors	Weber, Lutgens, Atzler (Munich)	396,944	2017–2019
In-vivo characterization of the chemokine-receptor CXCR4 for the detection of inflammation in atherosclerotic plaques by PET/MR	Schwaiger (Munich)	28,140	2017
Novel inotropic/lusitropic biologics against decompensated chronic heart failure	Most, Katus (Heidelberg/Mannheim)	472,896	2018–2019
GMP-production of engineered human myocardium for heart failure repair	Zimmermann (Göttingen)	2,657,936	2018–2021
CAR inhibitors to treat myocardial infarction	Gotthardt (Berlin)	232,681	2019–2021
Local miR-29b inhibition using drug eluting balloons to block abdominal aortic aneurysm progression	Maegdefessel (Munich)	486,080	2019–2021
Real-time MRI-guided targeted endomyocardial biopsy of radiofrequency ablation lesions in a porcine model	Unterberg-Buchwald (Göttingen)	853,003	2019–2024
Hit-to-lead development of CaMKII-HDAC4 inhibitory compounds to treat heart failure (project I: Identification of potent hits)	Backs (Heidelberg/Mannheim)	507,041	2019–2020
Detection of plaque vulnerability with a novel hybrid intravascular NIRF-IVUS imaging system	Joner (Munich)	756,119	2020–2023
rAAV.MRTF-A-based vascular gene therapy in chronic hindlimb ischemia	Kupatt (Munich)	1,243,600	2021–2025
Re-screening for novel CD40-TRAF6 interaction inhibitors	Atzler, Lutgens, Weber (Munich)	405,710	2021
Development and characterization of a pig model of TET2-mediated clonal haematopoiesis	Schulz (Munich)	516,826	2021–2024

SHARED EXPERTISE

Collaborations help us gain access to, and share, the latest research methods and specialised knowledge. They also promote multidisciplinary approaches to solving research questions. Through a large platform of the DZHK, called Shared Expertise, the DZHK gives scientists access to a wealth of information. Shared Expertise is intended to be more than a marketplace of available infrastructures, it offers participating scientists the opportunity to collaborate, and contribute ideas and expertise.

In 2020, the DZHK funded 32 collaborative projects with a total of €2.3 million. These projects have an average duration of 15 months and are focused on a specific question. Young DZHK members were involved as applicants in 34 percent of the applications. Technologies, such as studies of genomes, transcriptomes, and proteomes, the breeding of different animal strains, or the generation of specific induced pluripotent stem cells, formed many of the applications, as in previous years.

Shared Expertise was requested for almost half of the projects (46 percent) and is one of the most frequently used services (see the following overview). However, it is also possible to enter individual collaborations that are specifically tailored to a particular issue. We are proud to facilitate networking within the DZHK through these partnerships.



The most frequently used Shared Expertise at the DZHK (since 2012)

Shared Expertise	Description (Use since 2012 I Requested use in 2020)		
SE006	Genomics/Proteomics	37	4
SE171	Stem cell unit and cardiomyocyte/ engineered heart muscle phenotyping	26	5
SE028	AAV vector platform	20	–
SE001	Generation of transgenic rats	19	–
SE041	OMICS platform	14	–
SE031	Next-generation sequencing platform	12	–
SE161	AAV vector design and production	12	3
SE099	Proteome and metabolome profiling	11	1
SE056	Vascular proteomics	9	–
SE024	EHT screening platform	7	–
SE057	Cardiometrics	7	1
SE063	MicroRNA array platform	7	–

EXTERNAL PARTNERS

Collaborations with scientific institutions outside the DZHK are also supported. They give scientists access to additional expertise and the opportunity to work with outstanding external scientists. In 2020, the DZHK funded five collaborative projects with external partners, totaling €391,082. Of this amount, €220,257 of funding went to external partners.

COOPERATIONS WITH EXTERNAL PARTNERS

Institution	Project Title	DZHK Funding
University of Münster, Institute of Anatomy and Vascular Biology	Decoding endothelial transcriptomic and regulatory responses to homeostatic and dysfunctional fluid flow profiles	€54,744
Philipps University of Marburg, Clinic for Cardiology, Angiology and Internal Intensive Care Medicine	Proof of concept: treating acute myocardial infarction with faecal transplantation in a transgenic animal model	€43,700
Hannover Medical School, Institute of Molecular and Translational Therapeutic Strategies	Identifying new RNA targets in a nonhuman primate model for age-associated cardiovascular diseases	€59,754
Technische Universität Dresden, Faculty of Medicine and Cardiology	Which is the optimal HFpEF animal model: focus on comparison with HFpEF patients and skeletal muscle	€24,000
Fraunhofer Institute for Toxicology and Experimental Medicine (ITEM)	Single cell RNA sequencing in iPSC-derived nodal and atrial cells from patients with atrial fibrillation	€30,809
University Hospital of Düsseldorf, Clinic of Cardiology, Pneumology and Angiology	Role of leukocyte derived Reactive Oxygen Species and Nitric oxide on thrombopoiesis	€7,250

IDEAS COMPETITION

Two projects receive further funding

Two projects from our Ideas Competition will receive additional funding of €1 million each after reaching their first milestone. This was decided by the Research Coordinating Committee in spring 2020.

The competition, which was launched for the first time in 2017, invited DZHK members to propose a bold idea that could lead to a scientific breakthrough in cardiovascular research. In addition, the projects were encouraged to link several DZHK partner sites or other German Centres of Health Research. Three of 19 competitors received start-up funding in 2017 and reached their first milestone in 2019.

Development of gene therapies for the treatment of heart disease

Patrick Most *(Heidelberg/Mannheim)* in collaboration with
Dirk Grimm *(University of Heidelberg, German Center for Infection Research)*
Arne Hansen *(Hamburg/Kiel/Lübeck)* and
Rabea Hinkel and **Wolfram-H. Zimmermann** *(Göttingen)*

So far, it has not been possible to transfer successful gene therapies with adeno-associated viruses from other medical fields to heart diseases. These viruses - called

vectors - serve as clever transporters that introduce genetic material into the body's cells. If successful, the transported material can alter faulty genes and combat diseases. Until now, there has been a lack of suitable vectors for the treatment of heart disease.

The team aims to develop heart-specific vectors, based on adeno-associated viruses derived from the human heart. They will be administered intravenously and will transport the therapeutic genes directly to the heart. Experts from the DZHK and the German Center for Infection Research are working together on this project.

Innovative approaches in precision medicine: The influence of clonal hematopoiesis on cardiovascular diseases

Andreas Zeiher *(Rhine Main)* in collaboration with **Hugo A. Katus** *(Heidelberg/Mannheim)* and **Heribert Schunkert** *(Munich)*

Genetic mutations in hematopoietic stem cells, leading to the growth of abnormal cells, do not necessarily result in blood diseases or cancer. However, they are associated with an increased risk of coronary artery disease and a poor prognosis in patients with heart failure.

The researchers, led by Andreas Zeiher, would like to better understand the effects of the mutations and their role during disease. This could lead to the discovery of new, personalised treatments for patients with these mutations in the future.

NEW MEMBERS TRANSLATIONAL RESEARCH GROUP

In autumn 2020, the Translational Research Group (TRG) was newly appointed by the DZHK General Assembly for the term 2021-2023. The TRG reviews translational research proposals and prepares decisions in the committees of the DZHK.

TRG members 2021–2023

Bechem, Martin (Speaker)	Wuppertal
Brandes, Ralf	DZHK partner site Rhine Main
Domdey, Horst	Martinsried
Ehmke, Heimo (Speaker)	DZHK partner site Hamburg/Kiel/Lübeck
Fielitz, Jens	DZHK partner site Greifswald
Gorczynski, Richard	Holland, USA
Hirsch, Emilio	Turin, Italy
Most, Patrick	DZHK partner site Heidelberg/Mannheim
Ruiz-Lozano, Pilar	Stanford, USA
Zapf, Antonia	DZHK partner site Hamburg/Kiel/Lübeck

Goals achieved in 2020?

- ↻ Development of a concept to promote the results of the Translational Research Projects in the DZHK
- ✓ Continued funding of the projects that emerged from the Ideas Competition in 2017
- ✓ New TRG members recruited

Goals 2021

- ↗ Strategy development to increase the number of TRPs submitted and approved

Clinical Research

Clinical trials are a focal point of the DZHK's research strategy. We are proud to support early clinical trials that test innovative therapies or diagnostic procedures in humans for the first time. Another strategic focus for the DZHK is guideline-relevant studies. The results of these studies are incorporated into guidelines and therefore directly benefit patients.

After eight years of clinical research, we now have clinical trials in all stages of study, from newly awarded, project start, completed recruitment, and follow-up, to publication of results.

In this reporting year, the DZHK funded 26 clinical trials. The studies, which include three on Covid-19, were either fully (11) or partially (11) completed in the past year. The results of the completed trials have been incorporated into clinical guidelines. 22 studies used the DZHK Clinical Research Platform for recruitment (all studies with DZHK numbers). In addition, there were six affiliated studies (without DZHK funding).

An overview of all studies can be found in the table on p. 31–32 and on
dzhk.de/en/research/clinical-research/dzhk-studies/

Financial support for the DZHK's clinical studies amounted to around €7 million in the reporting year.

DZHK studies that started in 2020

Circulatory disorders in the heart do not only occur when large vessels are constricted. They can also result from the impaired circulation of small blood vessels (called microcirculation) that supply the heart muscle. The EXAMINE-CAD-DZHK22 study is investigating which patients with impaired microcirculation benefit from beta-blockers and which benefit from calcium channel antagonists. 192 subjects will be enrolled in the study.

Press release from 28/01/21
Study investigates which drugs help with circulatory disorders of small heart vessels

All patients with severe heart failure receive a defibrillator to protect them from sudden cardiac death. But the procedure is risky and often unnecessary. The CMR-ICD-DZHK23 study is testing whether magnetic resonance imaging (MRI) of the heart can be used to predict which heart failure patients will benefit from an implanted defibrillator before the procedure is performed. A total of 760 people will be included in this study.

Press release from 11/12/20
Avoiding unnecessary interventions – new DZHK study investigates who benefits from an implanted defibrillator

DZHK-associated studies in 2020

The PASSION study is investigating whether the drug Tadalafil can reduce hospital admissions and mortality in patients with combined pre- and post-capillary pulmonary hypertension that developed due to heart failure. The study is funded in part by the German Center for Lung Research (DZL) and is expected to enroll 356 patients.

Studies that published scientific results in 2020

The EAST-AFNET-4 trial of the Atrial Fibrillation Competence Network has shown that early rhythm control using antiarrhythmic drugs or catheter ablation can reduce serious complications of atrial fibrillation such as stroke, heart attack, and worsening heart failure over five years. The study was partially funded by the DZHK from 2015–2020.

Publication: **Early rhythm-control therapy in patients with atrial fibrillation.** Kirchhof, P. et al. *N Engl J Med 2020*

Press release from 31/08/20
Atrial fibrillation: Rhythm-control therapy prevents complications

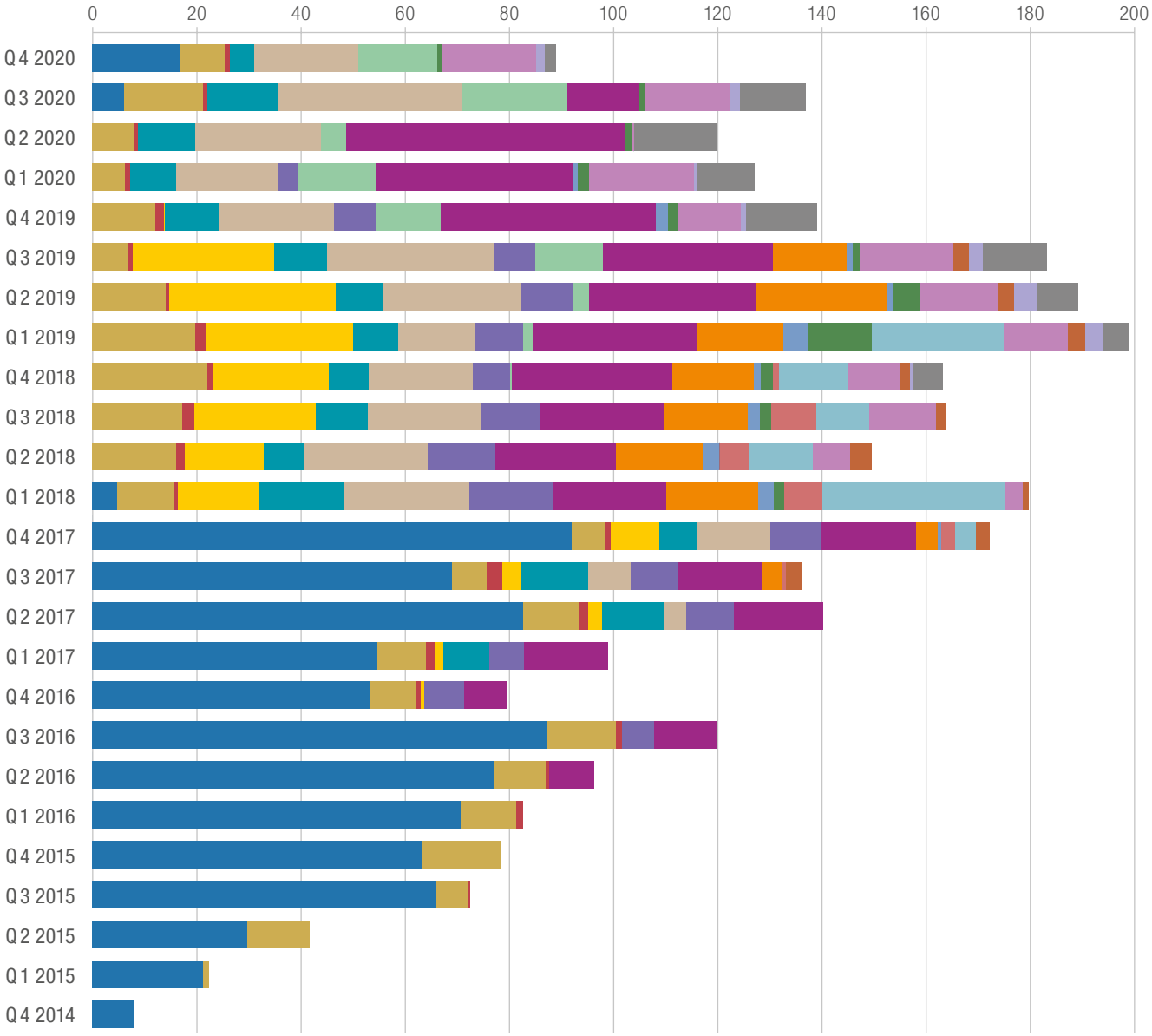
Additional studies have completed recruitment

Despite the pandemic, four studies completed enrollment during the reporting year: PRAISE-DZHK19|DZNEB001, Ex-VAD-DZHK11, APPROACH-ACS-AF-DZHK7, and SMART-MI-DZHK9.

Enrollment declined in 2020 due to the pandemic. The CLOSURE-AF-DZHK16 study had to stop recruitment completely from March to July. TORCH-Plus-DZHK21 was able to start recruitment in August despite the pandemic. A benefit of the temporary decrease in recruitment in 2020 was that some studies were able to complete their recruitment phase successfully.

From 2015 to the end of 2020, a total of 9,064 patients were enrolled in DZHK studies (excluding associated and competence network studies), including 1,419 in 2020 (2019: 2,160).

OVERVIEW: RECRUITED PATIENTS DZHK STUDIES



Monthly averages per quarter; as of 31/12/20

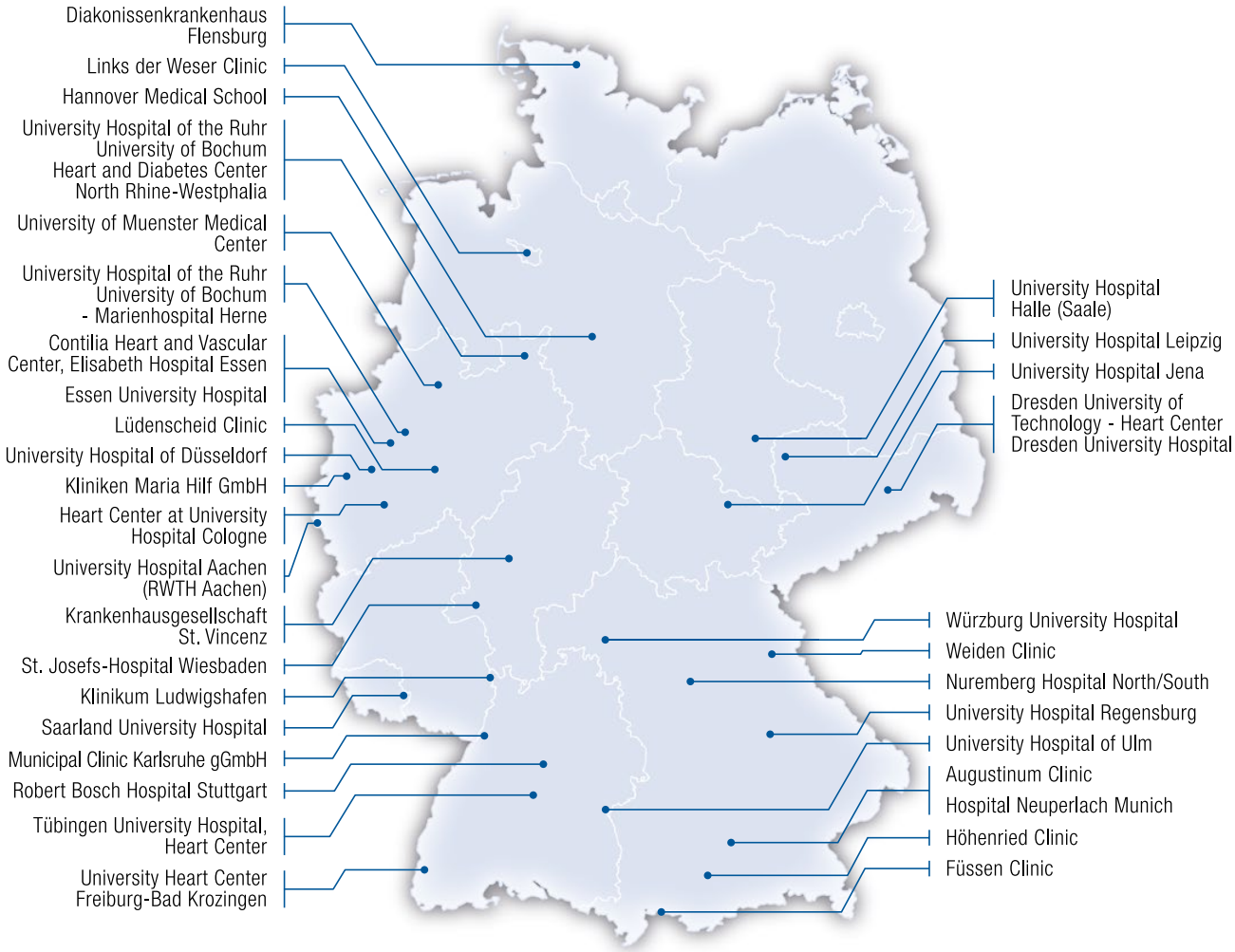
**TORCH-Plus-DZHK21 is based on the TORCH DZHK1 register built up from 2014–171*

- TORCH-Plus-DZHK21*
- TransitionCHF-DZHK2
- VAD-DZHK3
- TOMAHAWK-DZHK4
- FAIR-HF2-DZHK5
- DEDICATE-DZHK6
- APPROACH-ACS-AF-DZHK7
- SPIRIT-HF-DZHK8
- SMART-MI-DZHK9 (Trial & Register)
- CAVA-ADHF-DZHK-10
- Ex-VAD-DZHK11
- Decipher HFpEF-DZHK12
- CTSN-TVR-DZHK14
- SCREEN-AF-DZHK15
- CLOSURE-AF-DZHK16
- HFpEF-stress-DZHK17
- METRIS-HF-DZHK18
- DZHK19IDZNEB001

„DZHK STUDY PARTNER“ AWARD

This reporting year, we granted a first-time award to external trial sites that have included at least ten patients in DZHK studies. The centres can post this award on their website (see chapter "Public Relations" on p. 47). In this way, we want to honour the commitment of the external trial sites, which contribute to the success of the DZHK's clinical research.

These 34 external trial sites received the label "DZHK Study Partner":



CLINICAL STUDIES ON COVID-19

People with pre-existing conditions, especially those that affect the heart and vascular system, are at risk for severe Covid-19 progression. The most important include heart failure, heart attack, diabetes, and hypertension.

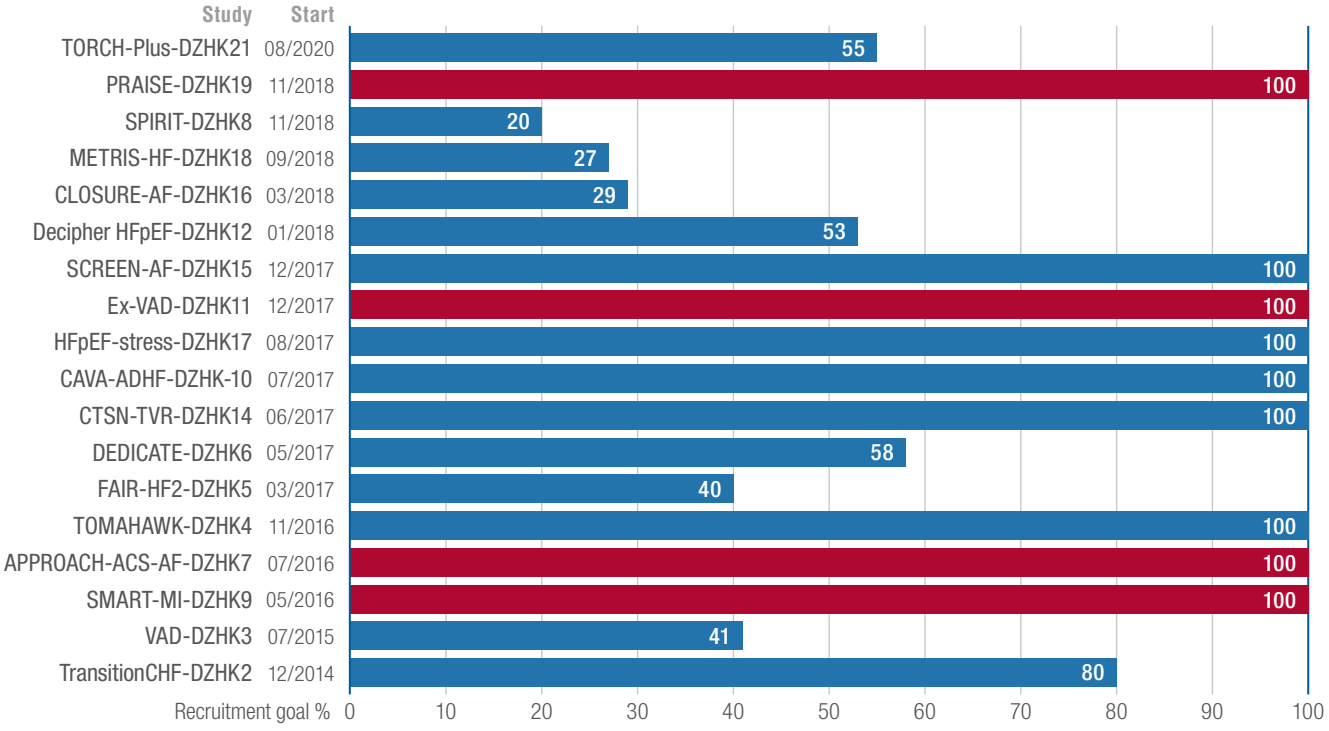
Therefore, the DZHK has allocated €1 million for clinical studies on Covid-19 research, for which all DZHK clinical scientists were eligible to apply. Three studies received funding in May 2020:

The **COVID SMART** (formerly MR SPOC) study investigates whether a smartwatch can help determine the right time to hospitalise people who have Covid-19 and are at risk of severe infection.
Moritz Sinner | Munich

The **COVID-PREVENT** trial investigates whether administration of the blood thinner rivaroxaban can reduce thrombotic events such as heart attack, pulmonary embolism, or stroke, leading to greater likelihood of survival.
Ulf Landmesser | Berlin

The **ACEI-COVID-19** study investigates whether pausing ACE inhibitors, or replacing them with anti-hypertensive drugs, with a different mechanism of action in Covid-19 patients affects the course of the disease.
Steffen Massberg | Munich

OVERVIEW - ENROLLMENT STATUS OF PATIENTS IN DZHK STUDIES



Figures in percent (as of 31/12/20)
● *These studies completed recruitment in 2020*

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	801
VAD-DZHK3	Severe heart failure, heart transplantation	GRS	Falk, Knosalla (Berlin), Hasenfuß, Friede (Göttingen)	200	81
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	475
DEDICATE-DZHK6	Aortic valve stenosis	GRS	Blankenberg, Seiffert (Hamburg/Kiel/Lübeck)	1,403	933
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	258
SMART-MI-DZHK9	Sudden cardiac death after myocardial infarction	ECS	Bauer, Kääb, Massberg (Munich)	400	complete
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	98
CTSN-TVR-DZHK14	Mitral valve insufficiency	GRS	Falk (Berlin)	76 (in GER)	complete
SCREEN-AF-DZHK15	Early detection of atrial fibrillation	GRS	Wachter, Hummers-Pradier (Göttingen)	267 (in GER)	complete
CLOSURE-AF-DZHK16	Stroke prevention by closure of the atrial ear	GRS	Landmesser, Boldt (Berlin), Eitel (Hamburg/Kiel/ Lübeck)	1,000	435
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	49
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)	Recruitment in preparation	
TORCH-Plus-DZHK21	Myocardial diseases	Registry	Meder (Heidelberg/ Mannheim)	4,340	2,391
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)	Recruitment in preparation	

STUDIES AT THE DZHK

	Condition/ Treatment/ Diagnostics	Study type	Responsible PI (DZHK partner site)	Recruitment target	Enrolled
Partially-funded studies					
ISAR-REACT 5	Circulatory disorders of the heart	GRS	Kastrati, Schüpke (Munich)	4,000	complete
Revacept-PCI in CAD	Coronary heart disease	ECS	Kastrati, Massberg (Munich)	332	complete
DZHK-associated studies (without DZHK funding)					
SFB/TR19plus#	Myocarditis	Cohort	Felix (Greifswald)	500	94
CULPRIT-Shock	Myocardial infarction with cardiogenic shock	GRS	Thiele (Lübeck/Leipzig)	706	complete
FIX-HF-5C	Heart failure	GRS	Hasenfuß (Göttingen)	160	complete
SORT-AF	Heart failure, Adipositas	GRS	Willems (Hamburg/Kiel/ Lübeck), Steven (Cologne)	140	complete
PASSION	Heart failure	GRS	Rosenkranz (Cologne), Hoeper (Hanover)	356	71

AUDITING OF THE DZHK CLINICAL STUDY UNITS

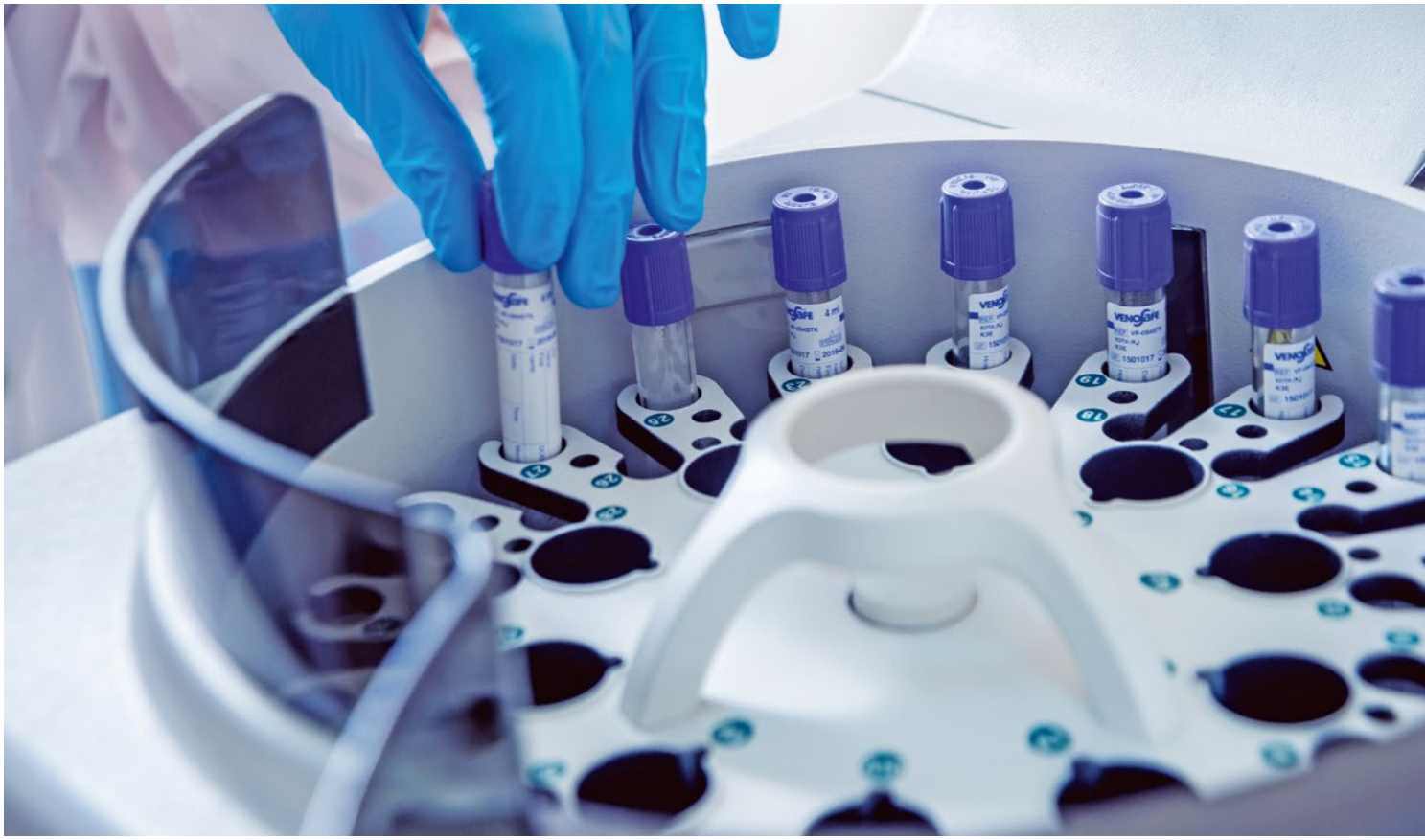
In this reporting year, we audited the DZHK Clinical Study Units (see box) for the second time. The first audits in 2018 focused on whether the rooms were equipped with the prescribed devices and whether the data entry systems of the DZHK Clinical Research Platform are used.

In this second round of audits, we aimed to ensure the quality of processes and technical documentation. In particular, we focused on recruitment and education, sample collection, processing and storage, revocations and re-use requests, and correct documentation in the IT systems of the Clinical Research Platform.

14 of 16 DZHK Clinical Study Units could be audited. The remaining two had to be postponed to the following year due to the pandemic. An interim evaluation showed that about 70 percent of the units were working very well, with about 30 percent showing potential for improvement.

The DZHK Clinical Study Units have examination rooms with standardised equipment for DZHK regulated recruitment. After meeting all quality criteria, all DZHK Clinical Study Units are subject to regular internal audits and receive the official DZHK quality label "DZHK Clinical Study Unit" with the corresponding year specification. The recruitment processes into our DZHK studies are coordinated at these units by the DZHK Clinical Staff. The funding of the DZHK Clinical Staff depends on the recruitment performance of the study centre and the successful completion of the internal audits.

Clinical Research Platform & DZHK Collection



CLINICAL RESEARCH PLATFORM

The Clinical Research Platform serves as the basis for conducting DZHK trials. It ensures that high quality data and samples are collected according to standards and are available for subsequent use across studies. In the year under review, the coronavirus pandemic dominated work on the Clinical Research Platform (see page 34). Covid-19 activities consumed the majority of our resources. We dedicated ourselves to analysing and improving data quality and completeness with the remaining resources, following last year's focus on building the technical and IT components.

To this end, metrics for data completeness were developed in 2019, which are taken from the IT systems of the Clinical Research Platform. The metrics allow us to assess the quality of a study or study centre's work. Previously, their performance could only be assessed on the basis of quantitative success in patient recruitment.

Since 2020, we have been systematically evaluating these metrics. The evaluations were sent to the trials and centres and serve to uncover weaknesses. Furthermore, they aim to encourage a high level of data completeness. When the data are as complete as possible, meaningful follow-up can be achieved.

Initial reports highlighted a large variability in the data between centres and trials. Based on these reports, we contact the relevant units and look for solutions to improve. This has already allowed us to identify systematic errors and make significant improvements. In the end, the metrics lead to a score that evaluates the performance of the study centres in recruitment and is also reflected in the promotion of staff to coordinate patient enrollment. We hope this will be motivating for teams and will ultimately strengthen the success of their research.

NAPKON POWERED BY DZHK

The Clinical Research Platform of the DZHK faced a special test in the coronavirus pandemic. It was selected to rapidly collect high quality data and samples from Covid-19 patients from German university hospitals and clinics as part of the Network University Medicine (NUM).

For this purpose, the DZHK head office, in consultation with the board and all representatives of the subcomponents of the DZHK Clinical Research Platform, submitted a project application to the NUM and received a contract of €1.2 million.

Within a few months, we adapted our systems to the needs of Covid-19 research and made them available to the National Pandemic Cohort Network (NAPKON), a subproject of the NUM. Among other things, the clinical dataset was expanded from 86 to over 3,000 data points.

The DZHK is proud of this contribution to the fight against SARS-CoV-2 and Covid-19. The NUM views this activity as a transitional solution, so the data will be transferred to a follow-up structure at the end of 2021.

The following DZHK partner institutions provide the components of the Clinical Research Platform for NUM:

Image Data Management:
Institute of Cardiovascular Computer-Assisted Medicine, Charité - Universitätsmedizin Berlin and Ludwig-Maximilians-Universität Munich

Trusteeship:
Institute of Community Medicine, University Medical Center Greifswald

Biospecimens (Laboratory Information System):
Institute of Clinical Chemistry and Laboratory Medicine, Greifswald University Medical Center, and DZHK head office in Berlin

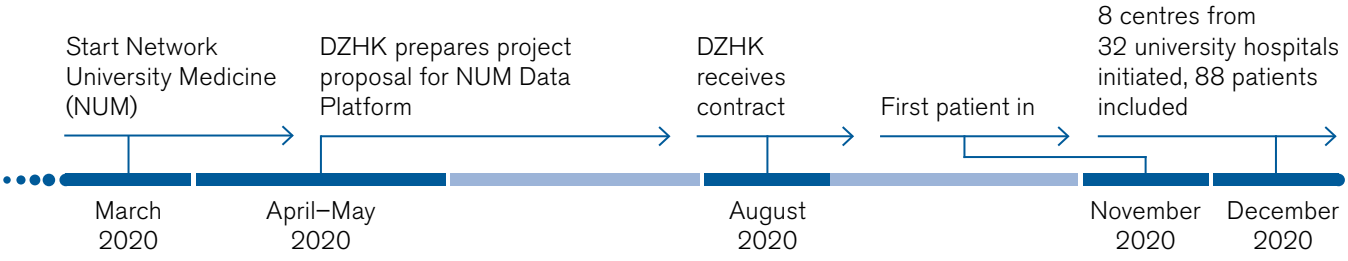
Data Management:
Institute of Medical Informatics, University Medical Center Göttingen

Ethics:
Helmholtz Zentrum München German Research Center for Environmental Health, Department of Molecular Epidemiology

Overall coordination:
DZHK head office Berlin

DZHK press release of 13/11/20

DZHK provides data infrastructure for corona research (in German)



DATA AND SAMPLE COLLECTIONS

The DZHK Data and Sample Collection contains a wealth of high quality biospecimens such as blood and urine with associated image data and clinical data, as well as DNA data. This valuable collection enables comparative studies and meta-utilisation across different studies. To ensure that even more internal and external scientists take advantage of this potential, we have intensively discussed strategies to increase the awareness of our DZHK Collection.

For this purpose, we are planning an improved presence on the website. In addition, we have launched a funding guideline for the use of collected data and specimens ("Utilisation of data and specimens"). It offers scientists from our member institutions the opportunity to receive funding for their research project if they use data and specimens from the DZHK collection.

In addition to the DZHK collection, the funding guideline applies to three other collections: The Tissue Collection of the German Heart Institute Berlin (DHZB), the DZHKomics Resource, and the Registry of the Competence Network for Congenital Heart Defects (KNAHF). The first call was made in early 2021.

Furthermore, we are working towards including the Tissue Collection of the DHZB in our use and access processes. This means the tissue collection will be technically and regulatorily integrated into the Feasibility Explorer ↗.

Scientists can check which data and samples are available via this online platform. In addition to the DZHK collection, the Feasibility Explorer will also include the tissue collection in the future. The request for use can then be submitted to the DZHK and will be reviewed by the Use & Access Committee, according to transparent criteria in accordance with the DZHK Use and Access Policy.

In the year under review, we also revised our Use and Access Policy, particularly regarding adapted processes, wording, and comprehensibility.

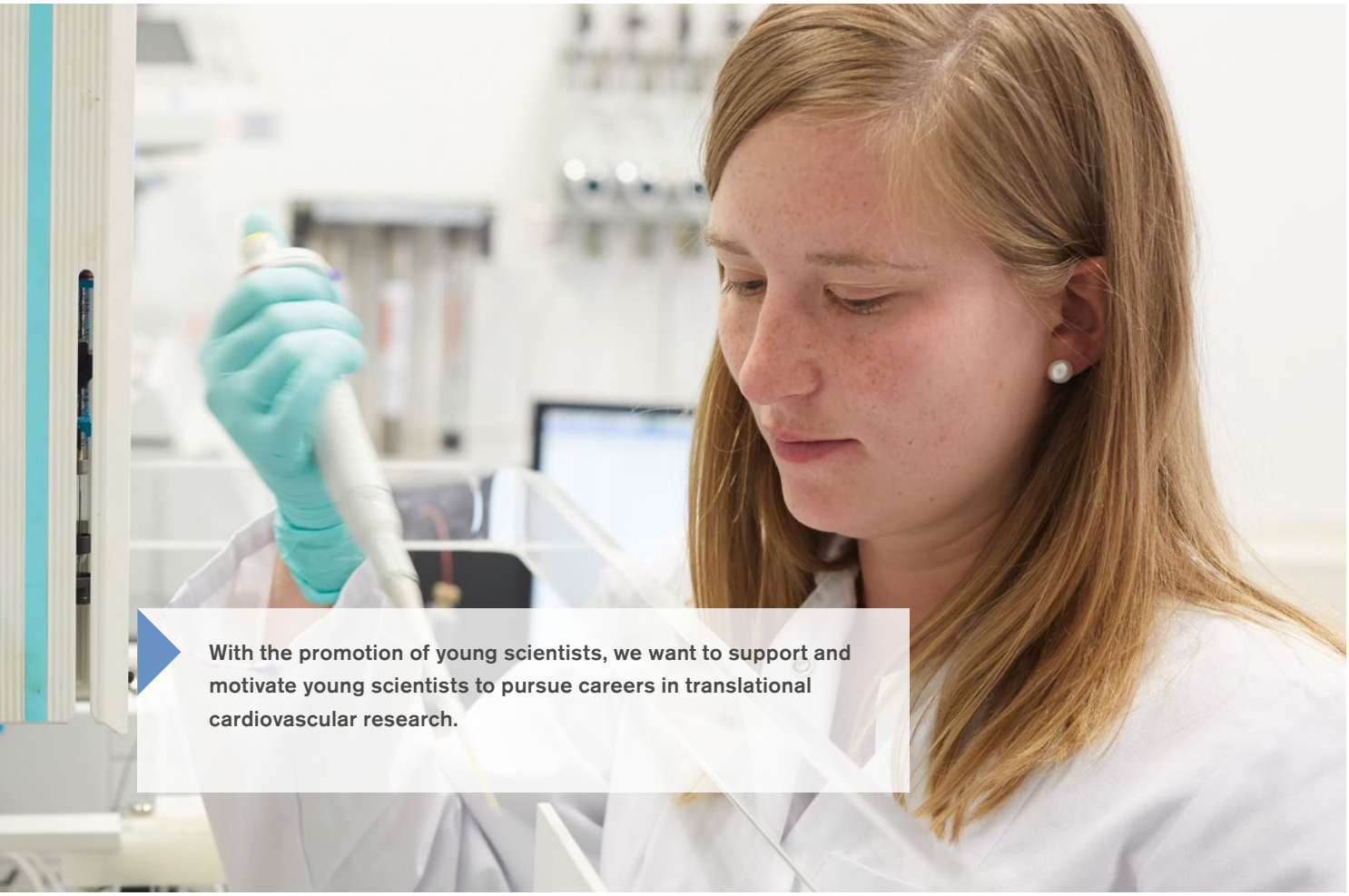
Goals achieved in 2020?

- ✓ Recruitment of three additional DZHK studies completed
- ✓ Focus on data completeness and quality further deepened
- – DZHK audits 2.0 conducted at all DZHK study centres
- ✓ Scope and visibility of data and sample collection increased
- ✓ Commercialisation of OMICs resource: requests for use received

Goals 2021

- ↗ Call on Utilisation of Data and Biospecimen
- ↗ NUM project handed over to Medical Informatics Initiative and NUM research platform
- ↗ DZG working group on data management started
- ↗ At least two new DZHK studies started

Supporting Young Talent



With the promotion of young scientists, we want to support and motivate young scientists to pursue careers in translational cardiovascular research.

Young scientists can apply for funding of their own projects at the DZHK. We also support them in networking in order to share the latest scientific findings and prepare themselves for future leadership roles. In the year 2020, the DZHK has allocated € 3.5 million for this purpose.

YOUNG DZHK

More than 1,130 young scientists formed the Young DZHK in 2020. These include basic researchers, clinical scientists and physicians. Their interests and needs are represented by the Young DZHK Postdoc Committee, to which every partner site appoints two representatives. The members of the committee organise the annual Young DZHK Retreat (see p. 40) and other smaller scientific workshops (see p. 40). Through its participation in other DZHK boards, the Postdoc Committee is involved in strategic decisions of the DZHK. The spokesperson is a voting member of the Research Coordinating Committee, the body responsible for the scientific strategy of the DZHK, as well as a member of the selection panel for the DZHK Excellence Grants which reviews applications and makes funding recommendations.

Young DZHK Postdoc Committee 2020

Speaker | Nadya Al-Wakeel-Marquard
Deputy speakers | Tobias Jakobi, Norman Liaw (from 11/2020: Anne Dueck)

Berlin | Nadya Al-Wakeel-Marquard, Djawid Hashemi
Göttingen | Aline Jatho, Norman Liaw
Greifswald | Eileen Moritz, Martin Bahls
Hamburg/Kiel/Lübeck | Anca Remes, Tobias Reinberger
Heidelberg/Mannheim | Maarten van den Hoogenhof, Tobias Jakobi
Munich | Anne Dueck, Leo Nicolai
Rhine Main | Sven-Oliver Tröbs, Jiong Hu

In 2021, many spokespersons will be newly elected at the partner sites.
Current overview.

TRAINING & MENTORING

The Training Programme offers doctoral students and postdocs funding that helps increase their visibility (participation in conferences), strengthens professional and personal skills (participation in workshops, DZHK Mentoring Programme) and offers financial freedom to conduct research (doctoral scholarships). In addition to scientific training, the programme aims at facilitating networking between the scientists of the different DZHK partner sites as well as exchange beyond the DZHK, such as with the other German Centres for Health Research (DZG).

Due to the pandemic, numerous scientific events were cancelled, held virtually or postponed until 2021. As a result, almost 80 percent fewer travel grants were awarded to attend high-level conferences. In the Visiting Scientist Mobility Programme, only half as many (foreign) lab exchanges were funded than in 2019.

Despite limited opportunities, nine young scientists used the Visiting Scientist Programme to gain fresh insights into different laboratories and to learn new methods and techniques. 54 members were awarded a travel grant to attend and present at high-level congresses. 36 medical students were able to dedicate a year of full-time work to an experimental doctoral thesis in a DZHK project.

In 2020 and 2021, 13 mentees had the opportunity to meet regularly with the mentors of their choice. The programme prepares physicians, natural scientists and science managers for leadership roles. The focus lies on the mentee's personality. Over the course of a year, the mentees learn to better assess their social, communication and professional skills.

AWARDED GRANTS, TRAINING AND MENTORING

	2020	2019
Travel grants for high-level conferences	54	301
Doctoral scholarships (including partner site-financed scholarships)	36	47
Visiting Scientist Programme	9	19
Attendance of external workshops	29	84
Selected mentees	13	13

EXCELLENCE GRANTS

A core element of the DZHK's promotion of young scientists is the Excellence Programme. With various funding opportunities, talented young researchers with doctoral degrees are supported (overview "Projects in the Excellence Programme" on p. 39).

During the pandemic, lab hours were severely restricted in some cases, as fewer people than usual were allowed to work together in one room. Projects with study participants had to be paused, unless research was being conducted on Covid-19. Projects involving laboratory animals were also delayed because animal breeding was switched to emergency mode. Resident or specialist physicians were needed in the clinic hence some had to reduce or postpone their research. In the Excellence Programme, this partly led to the extension of the duration of already approved projects.

In a competitive selection process, twelve postdocs were able to secure a Postdoc Start-up Grant. The grant supports the collection of initial data for the subsequent application for an own third-party funded project. Funding is provided for smaller projects with a clearly defined scientific question.

Eight women conducting excellent research were awarded the DZHK's Promotion of Women Scientists Grant. This funding scheme, introduced in 2019, explicitly addresses female scientists with children. For them, reconciling family and a scientific career still poses a big challenge. In the year under review, the funding amount available to the grantees was increased from €63,000 to €80,000 for one year. The funds can be used for non-scientific personnel and consumables. In addition, the opportunities for younger female scientists have been improved. Female Young DZHK members and female scientists in a more advanced stage in their career can now apply for funding in separate calls.

Three physicians with an interest in research joined the Clinician Scientist Programme in 2020. The programme enables them to gain scientific qualifications while in their specialist training. The Clinician Scientists are closely accompanied by mentors.

Made possible with a DZHK Rotation Grant, one medical doctor is able to take a year off from his patient care duties in order to devote himself to a research project that is in the interest of the DZHK.

Junior Research Groups – On the way to scientific independence

New Junior Research Group leader:

Gabriele Schiattarella

Charité – Universitätsmedizin Berlin

Worldwide, ten per cent of all people over 40 develop heart failure with preserved Ejection Fraction (HFpEF), a condition where the left ventricle is not able to fill properly with blood. HFpEF is one of the most common chronic diseases of the cardiovascular system. So far, however, there is no effective therapy. Metabolic disorders and inflammatory processes are involved in the development of this type of heart failure. How HFpEF develops and what happens at the cellular and molecular level, is the subject of Gabriele Schiattarella's research. He concentrates on the role of two signalling molecules, the liver receptor alpha and the inducible nitric oxide synthase. Both play a role in the emergence and development of the disease.

Gabriele Schiattarella transferred in 2020 from the Southwestern Medical Center of the University of Texas in Dallas, USA, as head of a new Junior Research Group at Charité – Universitätsmedizin Berlin.

Regulation of Lipid Alterations and Metabolic Inflammation in Heart Failure with Preserved Ejection Fraction

Press release from 05/11/20:

↗ New DZHK Junior Research Group focuses on heart failure and cardiometabolic disease

Goals achieved in 2020?

- ✓ Promotion of Women Scientist funding line further developed
- ✓ Maximum funding amounts of Excellence Grants increased

Goals 2021

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

PROJECTS IN THE EXCELLENCE PROGRAMME

Funding line	Name	Institution	Title
Clinician Scientist Programme	Till Josha Demal	University Hospital Hamburg-Eppendorf	Inherited aortic diseases: identification and functional analysis of novel disease-causing genes
	Alexander Dutsch	German Heart Centre Munich	Contribution of SVEP1 and CD209 to vascular and cardiac inflammation - new mechanistic insights and therapeutic avenues
	Simon Martin	Goethe University Frankfurt	Interplay of systemic inflammation, vascular inflammation and microvascular function
Postdoc Start-up Grant	Teresa Gerhardt	Charité – Universitätsmedizin Berlin	Endothelial function and T cell-endothelium crosstalk in coronary macro- and microvascular disease
	Markus Heckmann	University Hospital Heidelberg	Molecular mechanisms and potential therapeutic targets in checkpoint-inhibitor induced myocarditis
	Zegeye Jebessa	University Hospital Heidelberg	Investigating SERCA2a regulators functional and molecular overlap - do DWORF and S100A1 synergistically regulate cardiac performance?
	Thomas Juan	Max Planck Institute for Heart and Lung Research	Investigating cardiac troponin T-related cardiomyopathies using conditional degron strategies
	Vivien Kmietczyk	University Hospital Heidelberg	Cpeb4 controls cardiac remodelling by its dynamic binding behaviour to its mRNA target Zeb1
	Kristin Kräker	Max Delbrück Center for Molecular Medicine in the Helmholtz Association	Microvascular imaging as early predictor for cardiac dysfunction after preeclampsia
	Tim Christian Kuhn	University Hospital Heidelberg	Inhibiting PCSK6 to prevent fibrosis/adverse remodelling and preserve cardiac function
	Christoph Lipps	Kerckhoff Clinic	Endothelial cell-derived extracellular vesicles for therapeutic application in cardiovascular disease
	Leo Nicolai	Hospital of Ludwig Maximilian University of Munich (KUM)	Deciphering single platelet dynamics in thrombosis and chronic vascular inflammation
	Emiel van der Vorst	Hospital of Ludwig Maximilian University of Munich (KUM)	The aryl hydrocarbon receptor (AhR), a friend that turns out to be a foe?
	Jens Wiebe	German Heart Centre Munich	Molecular and morphological characterization of coronary neoatherosclerosis
	Stefanie Zylla	Greifswald University Medical Centre	Elucidating the role of five adipokines in the presence, prediction and treatment of HFpEF
Promotion of Women Scientists	Dorothee Atzler	Hospital of Ludwig Maximilian University of Munich (KUM)	Immuno-metabolic phenotyping of the amino acid homoarginine in atherosclerosis
	Arica Beisaw	Max Planck Institute for Heart and Lung Research	Manipulating the AP-1 response to promote cardiac regeneration in the adult mammalian heart
	Paola Cattaneo	Goethe University Frankfurt	Assembling a multilevel molecular roadmap of cardiomyocyte maturation for cardiac regeneration
	Arpita Chowdhury	University Medical Centre Göttingen (UMG)	Role of protein tyrosine phosphatase receptor sigma (PTPRσ) during maladaptive myocardial remodelling
	Christina Magnussen	University Hospital Hamburg-Eppendorf	Structural and genetic biomarkers in dilated cardiomyopathy: from molecular variants to clinical phenotypes
	Roxana Ola	University Hospital Mannheim	The role of endothelial TGFB/BMP signalling pathway in heart remodelling and homeostasis
	Sonia Singh	University Hospital Hamburg-Eppendorf	The role of Janus kinase 1 in cardiac proteotoxicity
	Laura Cecilia Zelarayán-Behrend	University Medical Centre Göttingen (UMG)	Defining the beta-catenin-dependent posttranscriptional regulation during heart failure progression
Rotation Grant	Richard Schell	University Hospital Heidelberg	Targeting MEF2D-dependent transcription to treat sepsis-induced acute heart failure
Junior Research Group	Gabriele Schiattarella	Charité – Universitätsmedizin Berlin	Regulation of lipid alterations and metabolic inflammation in heart failure with preserved ejection fraction

Scientific Exchange

Due to the pandemic, the scientific exchange within the DZHK and also with other organisations in 2020 was limited to online events. This has helped us learn a lot and develop new formats.

DZHK RETREAT AND YOUNG DZHK RETREAT

In 2020, the DZHK organised its eighth annual scientific meeting, the DZHK Retreat, which is our largest network meeting. Despite being originally planned as a face-to-face meeting, it was held online.

The DZHK Retreat took place on 16th and 17th of September and focused on "Inflammation in Cardiovascular Disease". The programme included twelve lectures and twelve flash talks, in which the Papers of the Month 2019 were presented. The keynote speaker was Zahi Fayad from the Icahn School of Medicine at Mount Sinai, New York. Of a total of 380 registered attendees, up to 200 were online during peak times. An agency supported us with the technical handling of the programme.

The seventh Young DZHK Retreat also took place as a first-time online event on September 17th. 214 people were registered to attend.

Science on Friday

Since the online DZHK Retreat was shorter than usual, we decided to launch a new workshop series to further promote scientific exchange within the DZHK. At "Science on Friday", once a month on a Friday, scientists from the DZHK and other institutions discuss the latest research findings for one hour.

In the year under review, two workshops with high attendance were held.

"Omics and single-cell technologies", 11/11/2020, Chair: Norbert Hübner, 280 participants

"Small molecules, RNA therapeutics and biologicals", 11/12/2020, Chair: Johannes Backs, 159 participants

The recorded workshops are available on the DZHK intranet (login required):

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

New Webinar Format

As further training for resident physicians was cancelled due to the pandemic, Young DZHK members from the Berlin partner site launched a new online training format. Since the end of March 2020, Djawid Hashemi, resident at the Charité Berlin, invited physicians and scientists to a live talk on YouTube, including esteemed high blood pressure expert Professor Friedrich Luft from the Max Delbrück Center for Molecular Medicine and the Charité – Universitätsmedizin Berlin.

In the beginning, the focus was on cardiac issues and on topics related to coronavirus. For example, Professor Dr Junbo Ge from Fudan University in Shanghai reported on his experiences of Covid-19 in China.

The greatest interest was generated by an update on Covid-19 vaccinations, with around 25,000 views in only six weeks.

The service is free and open to all, but primarily attracts a medical audience. Listeners can ask the experts questions via chat and YouTube comments.

All webinars are available on demand on our website:
dzhk.de/en/news/webinars/on-demand/
or on Djawid Hashemi's YouTube channel.

Symposia, Lectures and Co-funded Congresses

Due to the pandemic, the majority of the symposia, co-funded congresses and DZHK lectures planned for 2020 had to be postponed. Of ten planned events two took place:

Nonlinear Dynamics of the Heart (Lecture), 20/03/2020, Göttingen, organised by Stefan Luther

DZHK-HiGHmed Symposium: Cardiology meets Systems Medicine and Digital Health Solutions, 21-22/09/2020, online, organised by Christoph Dieterich (Heidelberg)

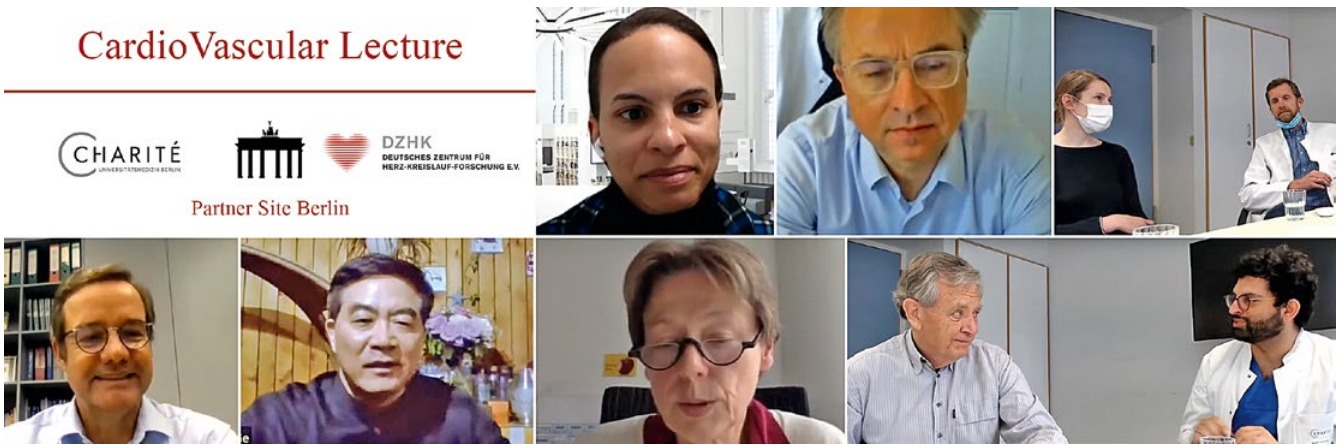
Press release from 09/10/20 (German only):
Was die digitale Medizin in der Kardiologie leistet

Goals achieved in 2020?

✓ Online Retreat formats introduced

Goals 2021

↗ Online workshop series "Science on Friday" further established



Cooperations

COOPERATION WITH THE DZG

The goal of the six German Centres for Health Research (DZG) is to combat widespread diseases more effectively. Founded between 2009 and 2012 on the initiative of the German Federal Ministry of Education and Research (BMBF), the centres bring together non-university research and university partner institutions from all over Germany.

The DZGs have worked closely together since they were formed. In the DZG forums (four meetings in 2020), the focus lies on the strategic development and cooperation of the DZGs. In recent years, cooperation has been further expanded and, among other things working groups for Biobanking, Artificial Intelligence, Data Management, Promotion of Young Scientists, Public Relations, Prevention, Global Health and Regulatory Aspects of Clinical Trials have been established. At the end of 2020, a strategy paper for the future cooperation of the DZGs and use of funding was adopted.

In 2020, the DZGs carried out several coronavirus projects together. For example, a Europe-wide database of health data and biomaterials from patients with Covid-19 was established. This wealth of information formed the basis of additional research projects.

As part of the promotion of young scientists, the DZG held a joint seminar with the National Institute for Science Communication. The communication seminar was directed at the centres' junior researchers.

In order to inform members of the Bundestag about the successful work of the DZGs and to exchange views with parliamentarians, a parliamentary evening was planned for 2020 but was cancelled due to the pandemic.

Two more issues of the joint DZG magazine SYNERGIE on "Diagnosis" and "Therapy" were published in print and online ↗.

NATIONAL AND INTERNATIONAL COOPERATIONS

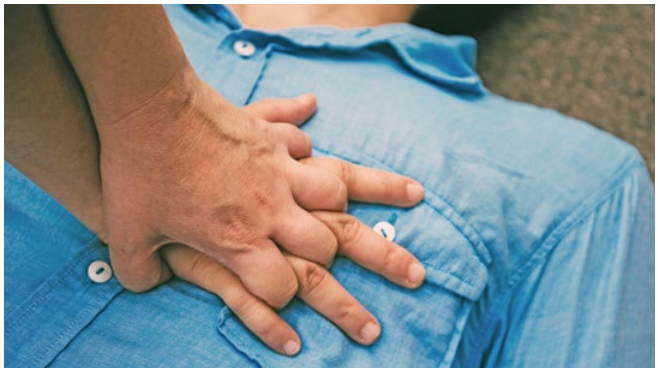
Global Cardiovascular Research Funders Forum

International research funders have come together to form the Global Cardiovascular Research Funders Forum (GCRFF) with the aim of accelerating progress in cardiovascular research. The Research Coordinating Committee of the DZHK agreed for the DZHK to become the German member of the GCRFF. The forum's goal is for the participating countries to work more closely together and for global research funding in the cardiovascular field to become more transparent. Among other things, the funding network wants to support researchers in planning and conducting large multinational trials that would not be feasible in a single country.

British Heart Foundation and Hartstichting

Since 2018, the DZHK has been running a joint funding scheme with the British Heart Foundation (BHF) that was joined by the Dutch Heart Foundation (Hartstichting) in 2019. With the scheme, 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 improved diagnosis, prevention and treatment of cardiovascular diseases. The BHF and DZHK each provide approximately €two million per call, the Hartstichting €one million.

In spring 2020, three projects received funding, each with a DZHK partner involved. This means that in the two rounds of funding to date, all successful projects involved researchers from the DZHK.



GenUCA – The genetic basis of cardiac arrests of unknown cause

German partners: Martin Borggrefe (coordinator), Ibrahim El-Battrawy, University Medical Centre Mannheim | Stefan Kääb, Hospital of the Ludwig-Maximilians-University (LMU) Munich
British partners: Elijah R. Behr (coordinator), Alan Pittman, St George's University of London
Dutch partners: Connie R. Bezzina (coordinator), Arthur Wilde, Carol Ann Remme, Amsterdam University Medical Centers

In five per cent of patients who suffer a cardiac arrest, the causes are not known and a genetic cause is suspected. With the help of genetic studies of a large number of survivors of unexplained cardiac arrest, the researchers hope to reveal the underlying mechanisms and identify target molecules for new drugs, in order to prevent the sudden death of patients.

DnAFiX – Genetic atrial fibrillation: A path towards new treatment and screening strategies

German partners: Niels Voigt (coordinator), University Medical Center Göttingen | Denise Hilfiker-Kleiner, Hanover Medical School (MHH) | Hendrik Milting, Heart and Diabetes Center North Rhine-Westphalia, University Hospitals of the Ruhr-University of Bochum, Bad Oeynhausen
Dutch partners: Bianca J.J.M. Brundel (coordinator), Amsterdam University Medical Centers | Natasja de Groot, Erasmus MC, Rotterdam | Rudolf de Boer, University Medical Center Groningen

Atrial fibrillation can occur in families, and in some cases can more frequently affect younger family members. The hypothesis is that mutated proteins in the cytoskeleton of atrial heart muscle cells are responsible for the development of atrial fibrillation in these individuals. The team wants to understand the exact mechanism behind this process, with the aim of developing new therapies to tackle the disease.

I-CARE – Quantitative imaging of transthyretin amyloidosis of the heart

German partners: Fabian aus dem Siepen (coordinator), Ute Hegenbart, Uwe Haberkorn, Heidelberg University Hospital
British partners: Marc Dweck (coordinator), David Newby, University of Edinburgh | Marianna Fontana, Julian Gillmore, Royal Free Hospital
Dutch partners: Riemer Slart (coordinator), Hans Nienhuis, Peter van der Meer, University Medical Center Groningen

Transthyretin amyloid cardiomyopathy is a condition that involves the build-up of amyloid in the heart and presents as heart failure. In order to be able to better care for patients, a fluorine radioisotope from nuclear medicine skeletal diagnostics is used in an imaging procedure. With this, the researchers want to understand the effects of a drug therapy and which patients respond best to treatment.

OTHER COOPERATION PARTNERS

Cardiological Competence Networks

The Cardiological Competence Networks conduct valuable work in the collaborative research of cardiac diseases. Therefore, the DZHK has been funding selected studies and structures of the Cardiological Competence Networks since 2015. Key areas are guideline-relevant studies in the field of heart failure and atrial fibrillation, and funding for the National Registry for Congenital Heart Defects. Funding of the Competence Network Heart Failure ended in 2021. Atrial fibrillation and congenital funding continued up to and throughout 2021. In 2020, the funding amounted to approximately € 575,000.

German Heart Foundation

The German Heart Foundation offers patients information on all questions concerning cardiovascular diseases. A large number of the leading DZHK scientists are honorary members of the scientific advisory board of the German Heart Foundation. They are on hand to answer patients' questions with expert advice.

The DZHK participated in the Heart Weeks 2020, the motto of which was "The Weak Heart", with social media posts by cardiologists. Board spokesperson Thomas Eschenhagen was also interviewed on the topic of "Tissue patches, gene therapies and artificial heart valves - heart failure research at the DZHK".

German Cardiac Society

Together with the German Society of Cardiology (DGK), the largest cardiological society in Europe, the DZHK has been offering "Fundamentals of Cardiovascular Research" workshops for young scientists since 2013. Three workshops are organised each year.

Due to the pandemic, only one workshop took place in 2020, which was held virtually for the first time. The webinar on "Vascular Biology" was so well-received and evaluated that we would like to continue offering the digital format.

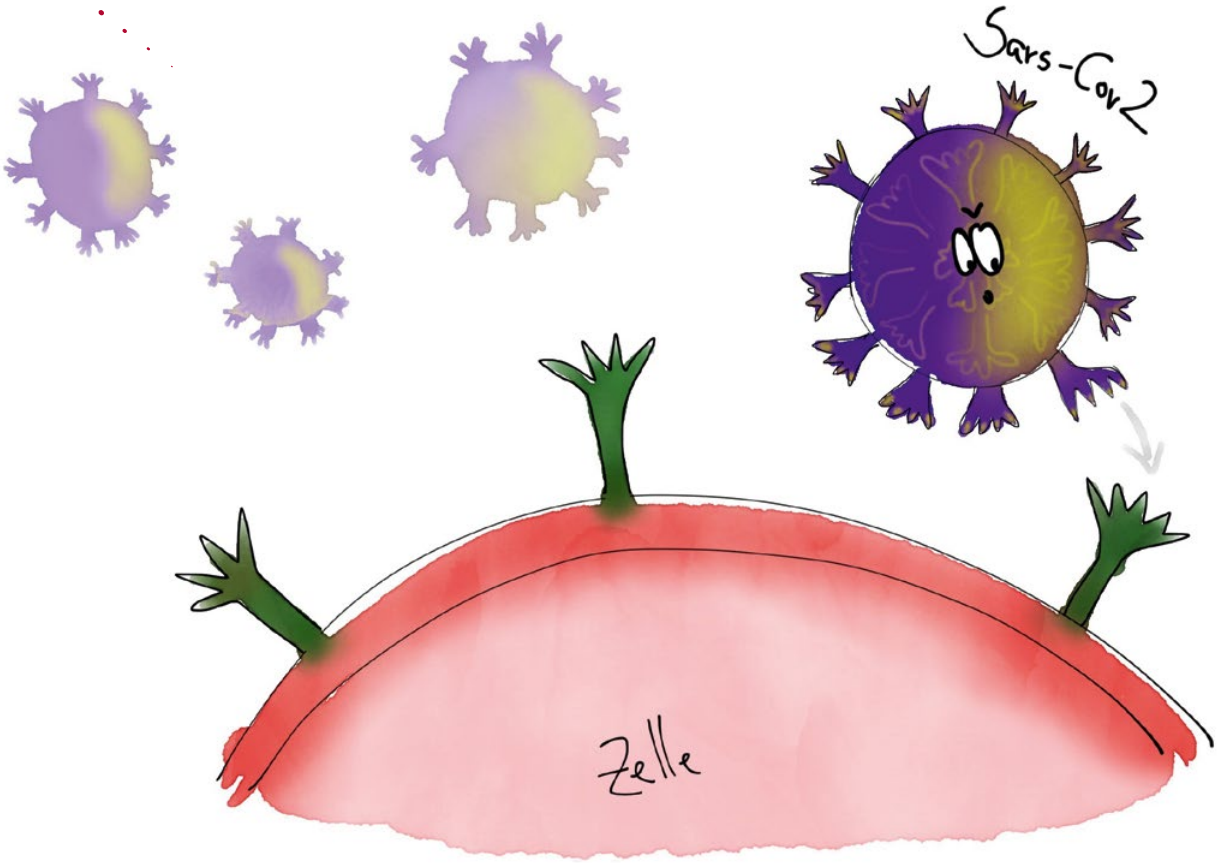
Goals achieved in 2020?

- ✓ Decision on BHF-DHF-DZHK projects made
- ✓ DZG meeting with the German National Cohort on joint application for use held
- ✓ Joint DZG rules on licensing developed

Goals 2021

- ↗ Clinical trials initiative of the Global Cardiovascular Research Funders Forum (GCRFF) launched

Public Relations



In our corona blog we explained with a cartoon how the virus attaches to the cell's receptor and its association with ACE inhibitors.

In 2020, the DZHK's communication was strongly influenced by the public's interest in Covid-19-related topics. In addition to news on coronavirus research in the DZHK, we responded with specifically tailored information offers:

- DZHK corona blog (German only)
- Corona-FAQ for cardiovascular patients on the DZHK website (German only)
- Press briefing at the Science Media Centre (SMC) "COVID-19 and the heart" with DZHK experts
- Press releases on Covid-19 research

We could see that coronavirus-related articles received an above-average number of hits. Although we had recorded a significant rise in the total number of website visitors in the previous year, it was 1.6 times higher in 2020. The views of our news page showed clear peaks during the first (April) and the second (October/November) wave of the pandemic. This illustrates the public's high demand for information on health research from reputable sources in these times.

Most frequently accessed news item:

"Coronavirus: Do not stop taking high blood pressure drugs such as ACE inhibitors and Sartane" (20/03/20), viewed 15,700 times from March to May 2020.

Label for DZHK Study Partners Developed

We have developed a label for "DZHK Study Partners": This enables clinics and practices to show their commitment to research to the outside world. 34 external study centres in Germany (see p. 29) received the label in 2020 as an award for their good recruitment of patients in DZHK studies. Hereby, we want to acknowledge and honour the centres' important contribution to the research goals of the DZHK.

The study partners used the label on social media, their websites or as a certificate in their own premises. The local press also reported on the excellent study partners. The award is presented every two years.

A Look behind the Scenes: Takeover on Instagram

Once again, we were able to increase our follower numbers on social media, with 1,211 on Twitter ↗ (2019: 731) and 2,182 on Facebook ↗ (2019: 1,648). Our Instagram ↗ had 1,006 followers at the end of 2020 (2019: 434).

The high level of interest in Covid-19 topics was also noticeable. Especially in the spring of 2020, reach, interaction and follower numbers increased. On Facebook, users commented on the DZHK posts nearly twice as often as in the previous year.

In September 2020, we started a takeover on Instagram. Since then, Young DZHK member and influencer Florentine Kleemann (@fleurbardot) has taken over the DZHK's Instagram once or twice a month. Through stories or live chats, she allows an insight into the everyday life of our doctors, researchers and students.

Goals 2020 achieved?

- ✓ DZHK Study Partners awarded
- – DZHK podcast launched
- – Online platform "service4studies" launched
- ✓ Two more issues of the DZG magazine "SYNERGIE. Forschen für Gesundheit" published

Goals 2021

- ↗ DZHK podcast launched
- ↗ Online platform "service4studies" launched (together with team Clinical Research Platform)
- ↗ Detailed presentation of the Translational Research Projects on the DZHK website

Success Indicators for Translational Research

SHORT- AND MID-TERM INDICATORS

	Indicator	Definition	2020	2019
1.	„Physician Scientists“	Share of scientifically active (licensed) physicians of scientists registered at the DZHK	56 %	52.5 %
2.	Cooperations between DZHK sites	a. Number of Shared Expertise projects (year)	32	37
		b. Number of publications with at least two DZHK authors from different partner sites	140	151
		c. Number of ongoing large multicentre projects (recruiting DZHK studies and TRPs) (31/12/20) involving multiple DZHK partner sites	13	15
		d. Number of Visiting Scientist stays at other DZHK partner sites (year)	1	4
3.	Communication with regulatory authorities	Consulting appointments (e.g. PEI, BfArM) in the context of recruiting DZHK studies, TRP and partner site projects (year)	4	6
4.	Cooperations with industry	Cooperations with partners from industry within the framework of recruiting DZHK studies, TRP and partner site projects (31/12/20)	14	18

	Indicator	Definition		2020	2019
5.	Cooperative structures in clinical research	a. Type (quality) of cooperative structures (31/12/20)	Clinical Research Platform (data storage, Trusted Third Party, LIMS, BDMS and ethics project, Use & Access), stem cell registry, OMICs resource		
		b. Amount (Quantity)			
			• Patients included in Clinical Research Platform (31/12/20)	9,064	7,645
			• SOPs (31/12/20)	17	23
			• Data and biospecimen usage applications/notifications (year)	0/3	2/8
			• Approved usage applications and notifications (year)	0/3	2/5
6.	High-ranking publications	All publications with DZHK affiliation with impact factor > 10		161	135
7.	Preclinical projects and clinical trials	a. Number of Translational Research Projects and recruiting DZHK studies (31/12/20)		18	26
		b. Publications from Translational Research Projects and DZHK clinical studies		31	40

LONG-TERM SUCCESS CRITERIA

	Indicator	Definition	2020	2019
8.	Revised medical guidelines	Number of guidelines changed as a result of DZHK trials and Competence Network Trials (total)	2	1
9.	New therapeutic and diagnostic principles	Number of new therapeutic and diagnostic principles developed in DZHK projects and entering clinical application (total)	0	0
10.	Patients treated according to new therapeutic or diagnostic principles	Number of patients who have been enrolled according to new, by DZHK researchers developed, therapeutic, or diagnostic principles (overall) (measurability is questionable)	0	0

Remarks on the table:

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

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

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

Facts and Figures

FINANCES AND STAFF

In the reporting year 2020, the DZHK had approximately €41.1 million of funding at its disposal, plus a carryover of €5.8 million from 2019 (2019: €8.3 million). Of this amount, €42.9 million were spent in 2020 (2019: €43.3 million).

The allocation of funds in 2020 was slightly less in 2019 – although the partners committed funds earlier and more regularly throughout the year. Overall, more funds were allocated than originally envisaged in the 2020 business plan, hence the reduction of our positive balance (around €1.9 million), which began in 2017, was continued.

Accumulated funds amounting to €4.0 million were not spent and were carried over into 2021. In relative terms, the outflow of funds in relation to the respective new funds (annual budget without carryovers from previous years) was 97 percent in 2016, 108 percent in 2017, 105 percent in 2018, around 106 percent in 2019 and around 105 percent in 2020.

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

The year 2020 was 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). The budget release was dependent on spending 75 percent of the budget and all positive fund balance early in the year.

Intensive communication with the partner sites and third-party funding departments led to the result that funds were allocated earlier and more regularly. In September 2020, the Budget Committee of the German Bundestag gave its approval for the release of the funds blocked for 2020. The agreed budget freeze will continue to apply to the DZHK to the same extent in 2021.

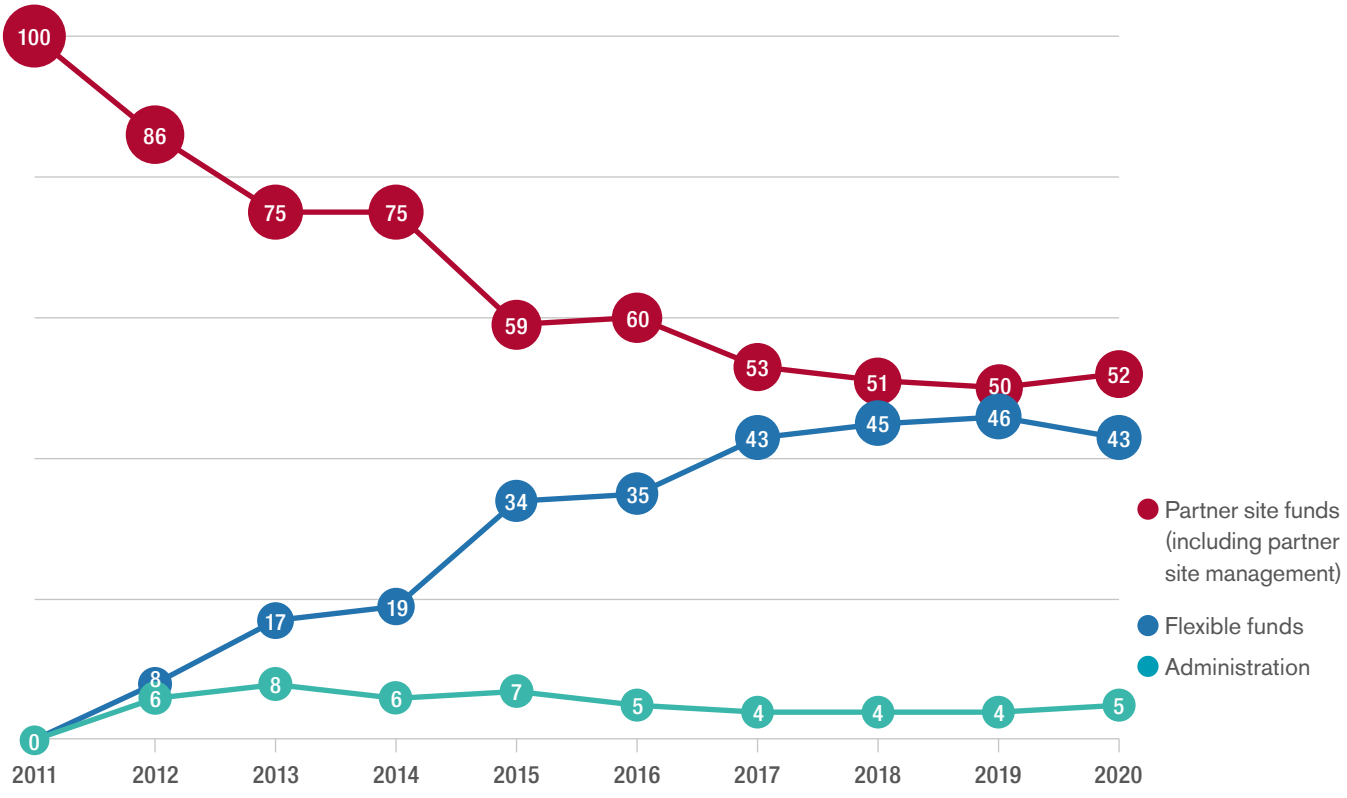
The funds spent in 2020 amounting to €42.9 million were broken down as follows:

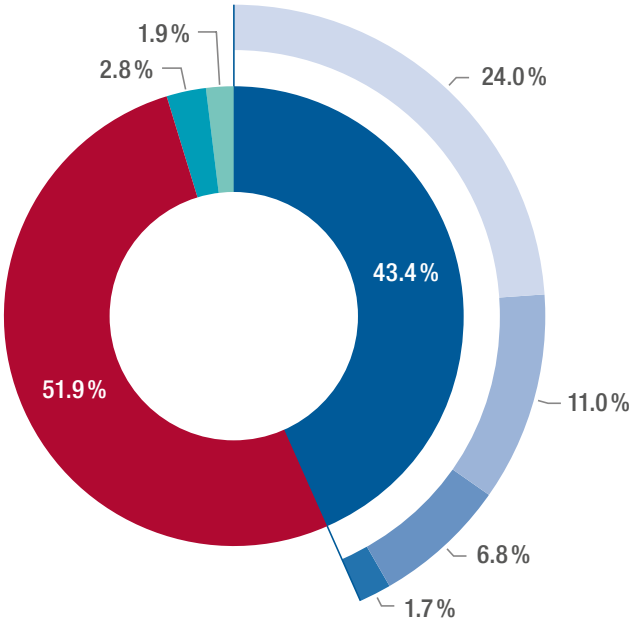
- **Partner site funds:** €22.3 million
- **Flexible funds:** €18.6 million
  (including clinical research €10.3 million, preclinical research €4.7 million, Young DZHK €2.9 million and funding of externals €0.7 million [including competence networks €0.6 million and cooperation with external partner €138,000])
- **Membership fees:** €1.2 million
- **Funding management department:** €0.8 million

In addition to the partner site projects, the DZHK uses approximately half of the budget for competitive research projects. These are mainly Excellence Grants, Translational Research Projects and clinical trials. These flexible funds are allocated in an internal competition. It has remained a strategic goal of the DZHK that approximately 50 percent of funds are awarded competitively. It is the fourth year in a row that we achieved this strategic goal.

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

DZHK TYPES OF FUNDING 2011–2020 IN PERCENT





ALLOCATION OF SPENT DZHK FUNDS 2020 BY EXPENDITURE AREAS*

- Flexible funds (2019: 45.9 %)
- Partner site funds (2019: 50.4 %)
- Membership fees (2019: 1.9 %)
- Funding management department (2019: 1.9 %)

Flexible funds are made up of:

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

STAFF EXPENDITURES, MATERIAL EXPENSES, AND INVESTMENTS*

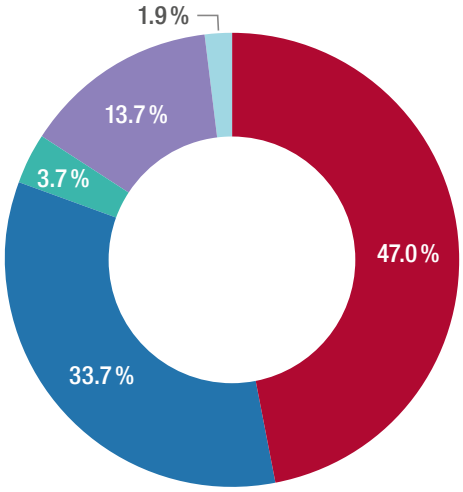
Budget of the DZHK head office

The budget of the head office of the DZHK e. V., financed from membership fees, amounted to €1.35 million in 2020 (2019: €1.17 million). This budget was fully financed by membership fees. Of this amount, €1.32 million (2019: €1.34 million) was spent – other income amounted to €12,625. This results in a surplus of €46,985.

At the reporting date of 31 December 2020, 411.70 (2019:408.71) full-time equivalents (FTEs) or 568 (2019: 515) persons or "heads" were financed by DZHK funds. This included 19 employees of the DZHK head office, twelve employees of the funding management department and ten employees of the competence networks.

STAFF EXPENDITURE, MATERIAL EXPENSES AND INVESTMENTS OF THE HEAD OFFICE*

- Staff costs: €0,62 million (2019: €0.62 million)
- Material expenses: €0.44 million (2019: €0.37 million)
- Investments: €49,301 (2019: €0.11 million)
- Public relations: €0.18 million (2019: €0.16 million)
- Membership fees: €25,000 (2019: €20,000)



**Figures in percent: Totals may not add up to 100 percent due to rounding of individual share values.*

NUMBER OF STAFF FINANCED BY DZHK 2018–2020

At the request of the BMBF, the HR reporting system was changed in 2019, so that only a comparison of the total number of employees is possible for 2018.

	2018	2019	2020
Number of employees (as of 31/12/20) (FTE)	432.73	408.71	**411.70**
Number of employees (as of 31/12/20) (capita)	595	515	**568**
thereof male	191	174	**194**
thereof female	404	341	**374**
Number of scientists and physicians (FTE)	–	226.55*	**225.68***
Number of scientists and physicians (capita)	–	308*	**311***
thereof male	–	139	**147**
thereof female	–	169	**164**
These include:			
DZHK Professorships and Junior Research Group Leader (FTE)	–	19.81	**19.31**
DZHK Professorships and Junior Research Group Leader (FTE) (capita)	–	22	**23**
thereof male	–	18	**18**
thereof female	–	4	**5**
Senior Scientists und Postdocs (FTE)	–	161.73	**170.42**
Senior Scientists und Postdocs (capita)	–	212	**227**
thereof male	–	84	**100**
thereof female	–	128	**127**
PhD students (FTE)	–	45.01	**35.95**
PhD students (capita)	–	74	**61**
thereof male	–	37	**29**
thereof female	–	37	**32**
Non-scientific staff and others (FTE)	–	116.6*	**150.91***
Non-scientific staff and others (capita)	–	163*	**216***
thereof male	–	163*	**35**
thereof female	–	141	**181**

** without employees DZHK head office, FMM and competence networks*

Principal Investigators, DZHK Scientists, Young DZHK Members

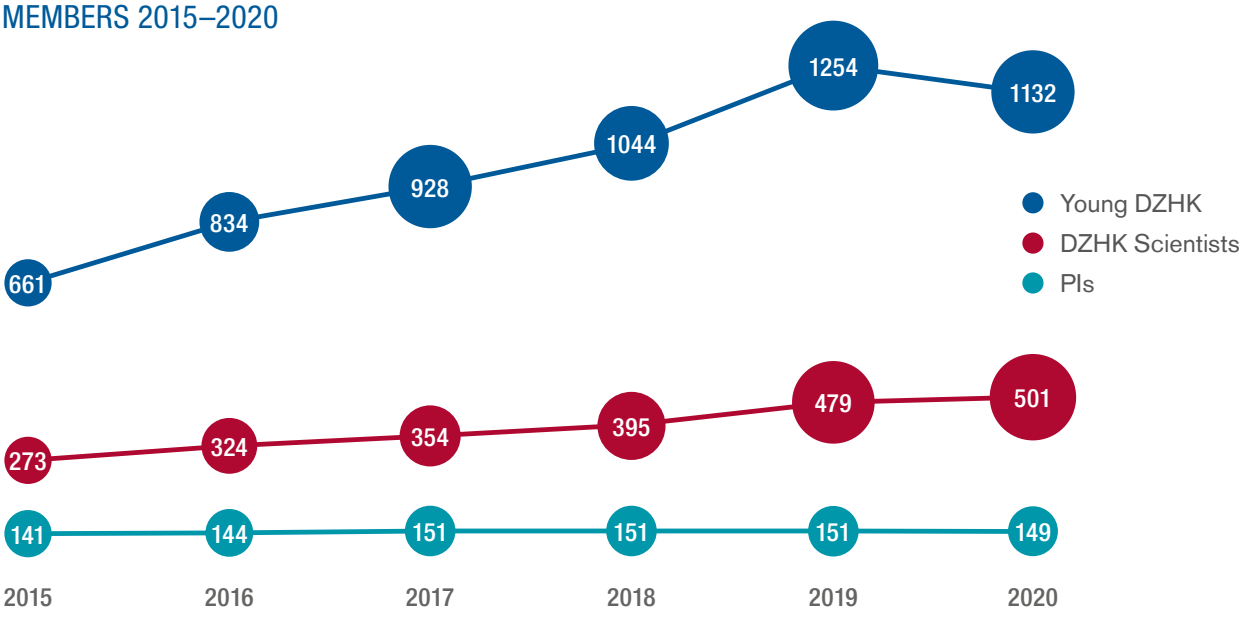
In 2020, 149 Principal Investigators (PI), 501 DZHK Scientists (2019: 479) and 1,132 Young DZHK members (2019: 1,254) were affiliated with the DZHK.

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 using DZHK funds.

The excellence of the DZHK is closely linked to its PIs - outstanding scientists in cardiovascular research. In the year under review, the 149 PIs shaped research at the seven partner sites and were involved, for example, in the work of the DZHK's committees. Each partner site can appoint a maximum of 20 PIs. DZHK professorships that were established at the partner sites with DZHK funds are counted separately. PIs are not usually funded by the DZHK.

In 2021, the General Assembly will decide again who will receive DZHK PI-status or whether the current status will be extended. The PIs were last appointed in 2017. From 2021 onwards, each member institution is to appoint at least one PI. Thirty percent of the PIs at each partner site are to be women.

NUMBER PIS, DZHK SCIENTISTS AND YOUNG DZHK MEMBERS 2015–2020



RESEARCH MANAGEMENT

The employees of the association management, the funding management department (FMM) and the seven partner site management teams make up the DZHK's research management. The joint head office of the association management and the FMM is in Berlin. The partner site managements are decentralised branches of the association management and are located at each of the seven partner sites.

Association Management

In the year under review, 19 employees (15.54 FTE as of 31/12/20) were working in the association management (in previous annual reports: head office), including the managing director. Together with the Board of Directors of the DZHK, the association management is responsible for the strategic alignment of the collaborative research, the allocation of available funding, and press and public relations work.

In September 2020, the General Assembly appointed Dr Katharina Eulenburg as the new DZHK Managing Director as of 1 January 2021. For eight years Dr Eulenburg was responsible for strategic questions and headed the Preclinical Research Group. She succeeds Joachim Krebser, who held the position for nine years and was the first Managing Director since the founding of the DZHK.

In 2020, these tasks were new and of particular relevance for the management of the association:

- Conducting and follow-up of internal review in January 2020 (see p. 5)
- Restructuring of the team and tasks, as the DZHK is temporarily providing its Clinical Research Platform to the national Covid-19 research network of the university medicine (NUM/NAPKON) (see p. 34)
- Pandemic-related adjustments in the processes and funding of projects and studies
- Auditing of the DZHK centres with Clinical Study Units (see p. 32)
- Start of the development of a short- and medium-term DZHK strategy
- Finalisation of a funding concept for the re-use of data and samples from the DZHK collection, preparation of the versioning of the DZHK usage regulations (see p. 35)
- Internal and external communication of Covid-19 measures and projects (see p. 46)

Funding management department

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

A total of 456 ongoing projects were approved for funding in the reporting year (2019: 514). The total number of DZHK projects to date is 1,593. The FMM had 10.71 FTEs (12 heads) as of 31 December 2020. One assistant position in the area of finance was unoccupied as of the reporting date. The FMM's staff positions are distributed among the areas of management, scientific review, review of applications and where-used lists, controlling, team assistance and contract management.

Partner site management

The partner site management teams are an interface between scientific projects, partner site speakers, third-party funding administrations, HR departments, deans' offices, legal departments, the DZHK association management and FMM. As a rule, the DZHK usually provides funds for one full-time position for a scientist acting as the partner site manager and one full-time position for an administrator. They organise partner site retreats, PI meetings, and coordinate the work of the executive board and the application and reporting system. They also carry out decentralised financial controlling for their partner site. Together with the DZHK association management and FMM, they also develop procedures and processes at the DZHK.

Partner Sites

DZHK PARTNER SITE BERLIN

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

Highlights 2020

The DZHK partner site Berlin expanded its expertise by recruiting outstanding new scientists in various research fields. The DZHK-funded Junior Research Group on Heart Failure with Preserved Ejection Fraction (HFpEF), led by Gabriele Schiattarella, started in October 2020 at the partner institutions Charité and MDC. Michael Potente was appointed to a BIH professorship at Charité. As the new DZHK PI at the Berlin site, he further expands the research focus “Translational Vascular Biomedicine” at Charité, MDC, and BIH. Furthermore, DZHK scientist Claudia Langenberg has been appointed BIH professor for computational medicine and brings her expertise to the field of data-based medicine.

Alexander Meyer, who was already actively involved in Berlin research as a member of the Young DZHK, received a W2 professorship for "Clinical Applications of Artificial Intelligence (AI) and Data Science" at the Charité - Universitätsmedizin Berlin. The focus of his professorship is the application of AI and data science in clinical cardiovascular medicine. Furthermore, a new W3 professorship in anesthesiology focused on cardioanesthesia was established at Charité. Benjamin O'Brien was appointed as the head physician of the Clinic for Cardioanesthesiology and Intensive Care Medicine at the German Heart Center Berlin.

DZHK scientist and head of the Quantitative Developmental Biology Laboratory Jan Philipp Junker (MDC), and his collaborator Maria Colomé-Tatché at Helmholtz Zentrum München, have received a Helmholtz Artificial Intelligence Grant of €200,000 to improve and better understand big data processing.

MDC researchers Norbert Hübner and Nikolaus Rajewsky received a Chan Zuckerberg Initiative grant totaling approximately €1.2 million. The scientists in the two research groups will analyse the entire spectrum of heart cells and their genetic activity, and then compare it to existing data from Europeans. This project is part of the international "Human Cell Atlas" (HCA) initiative.

BIH opened the Käthe-Beutler-Haus on the Berlin-Buch research campus, expanding the campus into a "Vascular Biomedicine" focus area. The Käthe-Beutler-Haus provides state-of-the-art office and laboratory space for translational research groups, including several DZHK research groups (including groups led by Holger Gerhardt and Michael Potente) and the OMICS technology platforms.

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 the Laboratory Animal Science Unit 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); Max Planck Institute for Biophysical Chemistry, Max Planck Institute for Dynamics and Self-Organisation (MPIDS); Max Planck Institute for Experimental Medicine; German Primate Centre, Leibniz Institute for Primate Research (DPZ)

Highlights 2020

For DZHK projects, a state-of-the-art image analysis system has been available since Autumn 2020, enabling targeted structure-agnostic phenotyping of iPSC collectives and cardiac-derived cells. The CV8000 HCA system from Yokogawa, which was acquired as part of the DZHK investment program, offers the possibility of analysing 2D and 3D cultures automatically in live culture and after fixation. This will further expand the stem cell platform regarding analytical capacities, using and developing artificial intelligence-based methods.

On 19 November 2020, the cornerstone for the new Heart and Brain Center Göttingen (HBCG) was laid. The building creates a joint research infrastructure to investigate cross-organ causes of the cardiovascular and nervous systems' common diseases. This interdisciplinary interaction is unique and does not exist at any other research location in Germany. The cost of the new research building is around €38 million and completion is scheduled for December 2022.

The Collaborative Research Center SFB 1002 "Modulatory Units in Heart Failure", which entered the third funding phase in July 2020 (speaker: Professor Gerd Hasenfuß), will sustainably support cardiovascular research at the Göttingen partner site. Professor Wolfram-Hubertus Zimmermann has coordinated a transatlantic network of excellence on the topic of "Genome editing in myocardial insufficiency" for five years and leads a BMBF-funded "INDI-Heart" collaborative project with the participation of Professor E. Bodenschatz and Professor R. Hinkel. With Professor Dr Karl Toischer, who received a Heisenberg professorship for the promotion of outstanding young scientists in 2020, and Professor Dr Michael Zeisberg, who received a W3 professorship for Experimental Nephrology in September 2020, the location has been strengthened both scientifically and clinically.

The TAVI bio/database established through SFB1002 will provide insights into the molecular pathophysiology of heart failure. Currently, this is being used to develop a personalised treatment for cardiac fibrosis. The Göttingen partner site enables DZHK members to use the bio/database as a resource for hypothesis generation and validation.

DZHK PARTNER SITE GREIFSWALD

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

Deputy spokesperson
Marcus Dörr and Jens Fielitz, Greifswald University Hospital

Partner site management
Stefan Groß (partner site manager), Susanne Franck (partner site administrator/controlling),
since 04/2020 Kornelia Sadewasser (partner site administrator/finances and parental leave replacement for Susanne Franck)

Partner institutions at the DZHK partner site Greifswald
Greifswald University Hospital (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)

Highlights 2020

A state-of-the-art laboratory animal house is nearing completion at the partner site. It is connected to the molecular biology research laboratories of cardiology and will be available to the DZHK projects for experimental animal work from autumn 2021. Intervention and examination rooms are planned, which will serve the phenotyping of cardiovascular diseases. For this purpose, a 4D small animal echocardiography device was purchased in 2020 with DZHK and EU funds (EFRE).

In 2020, the fourth follow-up study (20 years) of the Study of Health in Pomerania (SHIP-4: N = 1,200) was completed, and the recruitment of a third independent population-based cohort (SHIP-NEXT: N = 4,500) was prepared (recruitment start: May 2021). In addition to SHIP, SHIP-TREND and the NAKO Health Study, DZHK projects will have four population-based cohorts with a total sample size of > 220,000 available in the future. In SHIP-NEXT, researchers will use new innovative cardiovascular research methods such as non-contact pulse wave measurements or long-term tracking.

Local collaboration with other health centres such as the DZNE has been expanded e.g., through studies on the "Heart and Brain Axis" in SHIP-TREND. For example, echocardiographic parameters were associated with the cerebral cortex, with an effect size roughly equivalent to that of smoking. The Center for Innovation Competence - Humoral Immune Responses in Cardiovascular Diseases, established jointly with the Faculty of Mathematics and Natural Sciences, received additional BMBF funding of €2 million in 2020 to invest in equipment for biophysical diagnostics in the context of cardiovascular diseases, such as dilated cardiomyopathy. In a new DFG-funded project on the role of protein tyrosine phosphatases in inflammatory cardiac and skeletal muscle failure, we are collaborating with research groups at Charité Berlin and Monash University, Australia.

Scientists from the site were involved in numerous nationwide Covid-19 projects in 2020, and also leadership or spokesperson positions (e.g., steering committee of the National Pandemic Cohort Network [NAPKON], Use & Access Committee NAPKON, spokesperson FOSA Cardiology). In particular, the establishment of the NAPKON infrastructure, which was based on the existing DZHK structures, was accompanied by the Greifswald officers of the DZHK Trust Office and the DZHK-LIMS. Greifswald was the leading recruiting centre of the NAPKON cross-sector platform (SÜP cohort) and has also established several local Covid-19 cohorts, partly through state funding.

DZHK PARTNER SITE HAMBURG/KIEL/LÜBECK

Partner site spokesperson
Until 10/2020: Norbert Frey, Director of the Cardiology and Angiology Clinic at University Hospital Schleswig-Holstein, Campus Kiel
From 11/2020: Heimo Ehmke, Director of the Institute of Cellular and Integrative Physiology, University Hospital Hamburg-Eppendorf

Deputy spokesperson
Until 10/2020: Heimo Ehmke, Director of the Institute for Cellular and Integrative Physiology, University Hospital Hamburg-Eppendorf
From 11/2020: 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, and Jeanette Erdmann, Director of the Institute for Cardiogenetics at the University Medical Center Schleswig-Holstein (Lübeck)

Partner site management
Since 10/2020: Doreen Stimpel (Returning after parental leave, partner site manager), Monika Glimsche (finances at partner site)
Until 12/2020: Anna Gundler (parental leave substitute), 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)

Highlights 2020

Since April 2020, Professor Kirchhof (Clinic Director Universitäres Herz- und Gefäßzentrum Hamburg, together with Professor Blankenberg) at UKE has been strengthening DZHK research activities in the field of personalised medicine in cardiovascular and other chronic diseases. They have done this by integrating OMICs information and other large clinical datasets. Under Professor Kirchhof's scientific leadership, the EAST-AFNET-4 study database has been successfully finalised and biomarker and genomics data have been integrated.

In July 2020, Professor Spielmann took over the leadership of the Institutes of Human Genetics of UKSH at the Lübeck and Kiel campuses. The cross-campus combination of molecular genetic and clinical expertise will create a modern and competitive centre for human genetics. Professor Szymczak received a W2 professorship in Genetic Epidemiology at the Institute of Medical Biometry and Statistics at the University of Lübeck in September 2020. In the future, Professor Szymczak and the director of the institute Professor König, plan to further develop machine learning methods for precision medicine as part of the Center for Artificial Intelligence.

For the first time, Kiel University Medicine will have a research and teaching campus called the Quincke Research Center. This will provide DZHK scientists with a state-of-the-art research laboratory with analytical equipment of the latest technology since February 2020. On the Lübeck campus, the DZHK research groups of Professors Erdmann, Spielmann, and Langer were able to move into the new Biomedical Research building in July 2020. The new building is located directly next to the Center of Brain, Behaviour, and Metabolism (CBBM, speaker: Professor Schwaninger) and enables a more intensive interaction between the research areas

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), 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)

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

Highlights 2020

In the context of filling the position of Professor Hugo A. Katus as Medical Director of Heidelberg Cardiology, who represented the Heidelberg/Mannheim partner site as the spokesperson for many years, Professor Norbert Frey was recruited as his successor as of October 2020. The site was also able to advertise a DZHK W3 professorship for RNA biology at the Institute of Experimental Cardiology (Director Professor Johannes Backs), which is planned to be filled in 2021. In addition to personnel successes, important research funds were also acquired independently of the DZHK in the reporting year.

Under the leadership of Professor Florian Leuschner, who holds a Heisenberg professorship in Heidelberg, the transatlantic research network "Immuno-Fib" in the thematic context of immune cardiology was acquired from the renowned Leducq Foundation, together with Professor Robert Gropler from St. Louis and teams at seven international sites. Researchers working with Professor Johannes Backs and Professor Norbert Frey submitted a draft proposal for an SFB to the DFG in 2020. After the TORCH registry reached more than 2,000 successfully recruited patients, the TORCH-plus registry enrolled the first patient in Heidelberg in this reporting year.

DZHK PARTNER SITE MUNICH

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

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

Partner site management
Sandra Rauser (partner site manager), 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)

Highlights 2020

The scientists involved in the DZHK in Munich can refer to knowledge gained in the treatment of more than 45,000 cardiac patients annually at Munich University Hospitals. They are highly trained in coordinating and conducting large national and international clinical trials, which have already contributed significantly to international guidelines and therapies. A broad spectrum of methods is available for DZHK collaborative projects, such as state-of-the-art OMICS technologies, various imaging and phenotyping methods, and large animal, small animal, and iPSC platforms for human cardiovascular disease models. Another important resource is the nationwide unique KORA cohort (Cooperative Health Research in the Augsburg Area) with 18,000 participants and up to 30-year follow-up.

In 2020, investments were made in new and modern equipment for DZHK research at the partner site, especially in the area of imaging and cell analytical methods. Dr Konstantin Stark (ERC Starting Grant), Professor Hendrik Sager (Else Kröner Fresenius Foundation), and Dr Leo Nicolai and Dr Katharina Lechner (both Corona Program of the German Heart Foundation) were successful in acquiring third-party funding. Professor Martin Halle (MRI) has been the new president of the European Association of Preventive Cardiology (EAPC) since September 2020 and is a board member of the European Society of Cardiology (ESC). In addition, Dr Leo Nicolai was elected as a further spokesperson for the Munich Young DZHK and Professor Christian Weber as the new partner site spokesperson from January 2021.

DZHK PARTNER SITE RHINE MAIN

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

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

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

Partner institutions at the DZHK partner site Rhine Main
Goethe University Frankfurt; Max Planck Institute for Heart and Lung Research, Bad Nauheim; Kerckhoff Clinik, Bad Nauheim; Johannes Gutenberg University Mainz

Highlights 2020

In 2020, Professor Stefanie Dimmeler was elected as the new spokesperson of the DZHK Board of Directors. She also received the ESC gold medal in September for her outstanding cardiovascular research. DZHK Professor Eike Nagel and Young DZHK member Sebastian Cremer have obtained grants from the German Heart Foundation for Covid-19 research (€180,000).

As part of the Biomarker Research partner site project, the Kerckhoff Biomarker Registry was expanded to over 16,000 patients with well over 100,000 biospecimen samples. The biomarker register, which is now one of Germany's largest biobanks of patients with cardiovascular diseases, is integrated into the DFG Collaborative Research Center 1213 "Pulmonary Hypertension and Cor pulmonale" through the aspect of pulmonary hypertension. The SFB 1213 is funded by the DFG, with approximately €1.8 million for another four years until 2024, and comprises a total of seven projects at the Kerckhoff Clinic and the Max Planck Institute for Heart and Lung Research in Bad Nauheim.

At University Medical Center of the Johannes Gutenberg University Mainz, one of four BMBF research cores for mass spectrometry in systems medicine has been acquired under the co-leadership of Professor Philipp Wild and Professor Stefan Tenzer (approx. €18 million for six years). The DIASyM research consortium will analyse heart failure syndrome in a systems medicine approach based in-part on the MyoVasc biobank. As a contribution to pandemic control, an EU grant (ERDF; approx. €17.6 million) was obtained to conduct a large population-based study on Covid-19. The Gutenberg Covid-19 study (total volume approx. €2.5 million) has enrolled 10,250 participants since October 2020 and generated an extensive biobank and database. A particular scientific highlight is the associated population-based peripheral blood mononuclear cell (PBMC) bank. Furthermore, a new investigator-initiated clinical trial (MyoMobile) to understand the clinical and molecular effects of physical activity in heart failure with preserved pump function has been funded (approx. €2.1 million; funder: Bayer AG). This exciting trial involves the use of personalised, app-based activity coaching for participants with heart failure.

ACRONYMS

ACS	Acute coronary syndrome
ADP	Adenosine diphosphate
BDMS	Image Data Management System
BfArM	Federal Institute for Drugs and Medical Devices
BHF	British Heart Foundation
BIH	Berlin Institute of Health
BMBF	Federal Ministry of Education and Research
CAD	Coronary artery disease
DGK	German Cardiac Society
DFG	German Research Foundation
DHF	Dutch Heart Foundation
DHZB	German Heart Centre Berlin
DNA	Deoxyribonucleic acid
DZG	German Centers for Health Research
DZHK	German Centre for Cardiovascular Research
DZNE	German Center for Neurodegenerative Diseases
ECS	Early clinical study
EFRE	European Regional Development Fund
ERC	European Research Council
ESC	European Society of Cardiology
EU	European Union
FMM	Funding Management Department
FTE	Full-time equivalent
GCRFF	Global Cardiovascular Research Funders Forum
GRS	Guideline-relevant study
IF	Impact factor
iPSC	Induced pluripotent stem cells
IT	Information technology
LIMS	Laboratory Information and Management System
LMU	Ludwig Maximilian University of Munich
MDC	Max Delbrück Center for Molecular Medicine
miR-92a	MicroRNA-92a
MRI	University Hospital rechts der Isar
MRT	Magnetic resonance tomography
NAKO	NAKO Study = formerly The German National Cohort
NAPKON	National Pandemic Cohort Network
NUM	University Medicine Network
PEI	Paul-Ehrlich-Institut
PI	Principal Investigator
RCC	Research Coordinating Committee
RNA	Ribonucleic acid
SE	Shared Expertise
SFB	Collaborative Research Centres
SOP	Standard Operating Procedure
StM	Site Management
TAVI	Percutaneous aortic valve replacement
TRG	Translational Research Group
TRP	Translational Research Project
TUM	Technical University Munich
UKE	University Hospital Hamburg-Eppendorf
UKSH	University Medical Center Schleswig-Holstein
WGCR	Working Group Clinical Research
✓	Goal achieved
↻	In progress
–	Goal not reached

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