



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

DZG DEUTSCHE ZENTREN
DER GESUNDHEITSFORSCHUNG

German Centre for Cardiovascular Research

ANNUAL REPORT



2017

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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Preface

For six years, DZHK researchers have been working at seven partner sites and thirty different institutions to develop new therapies for heart attack, heart failure and abnormal heart rhythms.

The heart and cardiovascular system are immensely complex. Diseases can develop in various parts of the system in very different ways. Moreover, the role of risk factors, like high blood pressure, too little exercise and poor diet, are becoming ever more apparent. Genetic causes of cardiovascular diseases are also increasingly the focus of research. These diverse, and seemingly opposed, issues provide a complex portfolio of research at the DZHK, briefly highlighted in Chapter 5.

For this research, we require experts from various specialties - from physics to psychology, from nutritional sciences to genetics, from molecular biology to heart surgery and cardiology - all working closely together. And our success supports our model. DZHK researchers were involved in nearly 3,000 scientific publications in the last five years, with more and more papers arising from collaborations between the DZHK partner institutions. Further partnerships are in the making.

In the reporting year of 2017, the German Centres for Health Research (DZGs) – also as a result of the recommendations of the German Council of Science and Humanities (Wissenschaftsrat) – have intensified the process of collaboration among themselves. Since diseases cross organ systems, so must the research. The DZGs see potential for collaboration in many areas, for example in research infrastructure, Big Data and prevention.

With these cooperative plans, and taking in to consideration the exciting clinical studies we have in the pipeline and international partnerships, like the one with the British Heart Foundation, we have reached the limit of our

financial scope. The fact that we have had to economise with a fixed budget for several years only exacerbates the problem – inflation and pay increments year-on-year, in effect have led to a steady budget decrease each year. We would strongly recommend an increase in funding, similar to that historically received by other research institutions, in accordance with the Pact for Research and Innovation.

We have built foundations on a strong organisational structure but the current financial plan for project funding is limiting us. We are convinced that we could better implement our core aim – the translation of research results into clinical application – if the administrative and funding-related frameworks better corresponded to our needs. In keeping with the German Council of Science and Humanities, we are therefore calling for the direct funding of our centre. We also require a funding framework that better suits a centre like ours, in order to be able to more efficiently forward funds to our supported scientists and offer them the best, most efficient conditions.

We hope you have an interesting read!



Thomas Eschenhagen
Sprecher des Vorstands



Gerd Hasenfuß
Vorstand



Thomas Sommer
Vorstand

The DZHK – Focus on Translation



1st DZHK Conference on Translational Medicine in January 2017 in Berlin

Innovations in cardiovascular medicine are needed for longer and healthier lives

Despite considerable advances in the last two decades, cardiovascular diseases are still the number one cause of death in Germany, and they are also responsible for the greatest loss of healthy years of life. Heart and circulatory diseases burden our healthcare system more than any other group of diseases, including cancers.

Although we are now living longer, we are also spending a larger proportion of our lives ill and cardiovascular diseases are the biggest driver of this.

People born in 2010 have a life expectancy of around 80 years but they will only be healthy for 69 of those years. Their unhealthy later life is more likely to be blighted by heart failure, heart valve diseases and abnormal heart rhythms than ever before.

Healthcare and heart research must work together to face to this growing challenge.

Due to advances in treatment, more people are surviving heart attacks than ever before, but they are left with permanently damaged hearts that can go on to develop heart failure. The number of people admitted to hospital for heart failure in Germany has nearly doubled in the last 20 years (445,000 in 2017). Heart failure impacts the whole body, so illnesses involving the brain, kidneys, muscle and skeletal systems, and the digestive organs can also be expected to rise.

There has also been a clear surge in heart valve disorders and abnormal heart rhythms in the last two decades.

High blood pressure and lipid metabolism disorders, which can be caused by an unhealthy lifestyle, also cause long term heart damage.

The DZHK will target this growing burden of cardiovascular diseases by reducing the number of people dying and improving the quality of life of those affected.

More information:

www.dzhk.de/en/dzhk/

www.dzhk.de/en/research/

Mission and Goals

The DZHK has a clear mission: We want to develop new therapies and diagnostic procedures for the benefit of people who are suffering from cardiovascular diseases. This can only be accomplished if we succeed in transferring the results of laboratory research into application in the real world (known as 'translation'). In order to do this, the DZHK unites excellent researchers and research clinicians from seven partner sites in Germany. It promotes

co-operation between them, with the aim of developing synergies and thereby accelerates the process of translation. Above all, the DZHK invests its funds in previously identified weak spots of the translation process. This is ensured through a coordinated research strategy and tightly allocated funding.

The DZHK is one of six German Centres for Health Research (Deutsche Zentren der Gesundheitsforschung, DZGs) that are dedicated to the improvement of the prevention, diagnosis and treatment of widespread diseases. It was founded in 2011 by the German Federal Ministry of Education and Research (BMBF) and is jointly funded by the Federal Government (90 percent) and the German state governments where each Centre is located (10 percent). The goal of the six German Centres for Health Research is to accelerate the progress of early research into clinical application.

Where Do We Stand?

The German Centre for Cardiovascular Research has a coordinated research strategy focused on translation. It has developed excellently in the six years since its inception, and has made the leap from a virtual research network to Germany's largest cardiovascular research centre. It has established efficient structures to translate results from basic research into application.

A variety of multicentre clinical studies were launched, some of which will produce initial results soon. For capturing and processing data from these studies, there is a common clinical research platform which is used by all DZHK partners and numerous external study sites.

The first study, TORCH-DZHK1, reached its goal of recruiting 2,300 participants in 2017. The data shall provide fundamental new insights into the development of non-ischaemic cardiomyopathies and thus enable new therapies to be developed.

The DZHK is on the way to creating Germany's largest whole genome collection (OMICs Resource) from healthy participants. From 2018, the data will be available to researchers in Germany and beyond in the search to look for key genes responsible for disease.

Research at the DZHK is very successful: Our last 2,909 DZHK publications are in tenth place globally – measured against the mean citation rate (SciVal database) in the cardiovascular field. We have made breakthroughs in the identification of genetic causes of heart attack, mechanisms of atherosclerosis, significance of non-coding regulatory RNAs for cardiovascular diseases, using stem cells to create models of disease and heart regeneration, how heart muscle changes during heart failure, the development of heart disease and in heart imaging.

In 2017, we were able to launch and fund a variety of clinical and preclinical projects but it is becoming apparent that funding further high-quality projects, worthy of support, will exceed our financial resources. In the reporting year, we spent € 3 million more than we obtained in contributions, largely due to costs accrued from projects funded in previous years.

The German Council of Science and Humanities is the most important advisory body to the Federal Government and German states. They have deemed the DZGs as a suitable model for advancing translational research in specific disease areas and we are proud to have been recognised for our successes. The Council acknowledges the important role of the six centres in the German scientific system and recommends their further development.

The institutional alliance of non-university and university research, in particular, was considered vital to successful translation. It is important that the potential of these collaborations be advanced long term and be used efficiently for the treatment and prevention of cardiovascular disease.

We especially welcome the Council's suggestions on governance and appreciate their explicit recommendation, in accordance with our own views, for institutional, permanent and reliable direct funding.

Alongside long-term projects, we try to consistently think innovatively and, with the guidance of our Scientific Advisory Board, we ask ourselves:

- What are the unsolved problems in cardiovascular medicine?
- What new directions can we take?

With this in mind, we launched the "Ideenwettbewerb" in 2017 as a way to inspire DZHK researchers to think laterally. All scientists registered at the DZHK were able to submit research ideas independent of our previous funding schemes. The ideas were meant to be for 'lighthouse projects' that could have a big impact into the future, involving multiple partner sites and, ideally, other German Centres for Health Research. In an open and transparent procedure, in which everyone could see and comment on the submitted suggestions, even choosing their favourite, three new projects were established after discussion in the Research Coordinating Committee (RCC).

The final, winning project has not been determined but we expect this to be addressed in the annual report for 2018.

Research at the Partner Sites



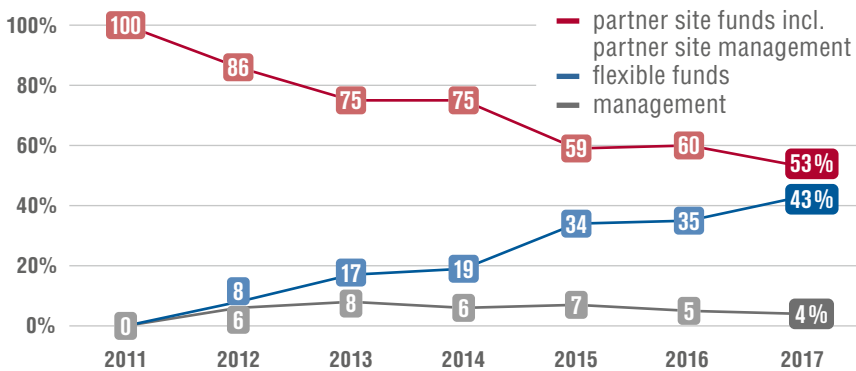
Partner Site Projects

In 2017, the DZHK invested approximately 53 percent of its funds in around 110 scientific partner site projects. The projects are often committed to issues of basic research, however, they might also be concerned with clinical studies, investments for large equipment, or financing of DZHK professorships. With these projects, the DZHK furthers the scientific focus areas of its partner institutions. For this reason, the projects have very different core themes. For example, the partner institutions focus on subjects like imaging techniques, prevention, epidemiology, microRNAs, genome analyses, artificial heart tissue, vascular diseases or cardiac arrhythmias. Within the scope of their partner site projects, clinicians are committed to finding solutions to very clearly defined clinical problems, which occur, for example, in stent implantations, heart transplantations or the diagnosis of heart attacks.

Since a new funding phase starts in 2019 for partner site projects (previous phase 2015-2018), the partner sites were asked to re-design and reapply for their site projects in the reporting year. The partner sites used this for extensive strategic discussions on their focuses for the next five to ten years. Within the scope of these discussions, the principal investigators (PI) of the partner sites were also newly appointed or confirmed. Through new appointments, the number of female PIs rose from 19 to 23 percent (see section Facts and Figures, chapter Finances and Staff). Applications for new partner site projects are made for the years 2019 and 2020. Subsequently, there is once again a funding phase of five years. The partner sites presented the results of their discussions to the RCC in autumn 2017.

An overview of all current ongoing partner site projects can be found on our projects database on the Internet:

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



DZHK funding types from 2011 to 2017:

The finance strategy of the DZHK budgets for the proportion of partner site funds to be limited to approx. 45 percent (incl. funds for partner site management) in order to allocate approx. 50 percent of the annual budget to flexible funds. As the funding requirement of the especially cost-intensive clinical studies and TR projects starkly increased as expected in 2017, we clearly drew closer to this goal in 2017.

DZHK Professorships

The DZHK professorships are a part of the partner site projects. They are appointed by the partner sites for strategically important subjects. At the close of 2017, there were 16 DZHK professorships, four of which were added in 2017. Until 2020, a total of 22 DZHK Professorships are planned. In their role as programme committee of

the annual DZHK Retreat, the DZHK Professors organised a successful retreat in Rostock-Warnemünde in the reporting year. A further focus was the development of a strategy paper for the parameters of a DZHK Professorship. This was not yet concluded by the end of the reporting year.

Holger Gerhardt (Berlin) is the new spokesperson for the professors, Tanja Zeller (Hamburg) is the deputy.

These are the new DZHK Professors:



In April 2017, **Jens Fielitz** took up the DZHK W2 Professorship for molecular cardiology at the Greifswald partner site. His research addresses molecular mechanisms of cardiac hypertrophy and its transition to heart failure. He focuses on the regulation of protein homeostasis in cardiomyocytes under stress. Among the main research areas of his group is the study of the pathophysiology of inflammation-mediated myocardial and skeletal muscle damage in patients with heart failure and critically ill patients. His aim is to develop new diagnostic and therapeutic approaches for patients with heart failure.



In July 2017, **Oliver Müller** took up the new DZHK W2 Professorship for “Epigenetics in Cardiac Hypertrophy” at the Faculty of Medicine of Kiel University. He will study the role of epigenetic mechanisms in the formation and progression of heart failure and cardiomyopathy.

His translational research activities also focus on developing efficient vectors for cardiovascular gene transfer as well as identifying and validating new target structures for the treatment of acquired or congenital cardiomyopathies. The overriding aim of his work is to develop new approaches for the therapy of cardiovascular diseases that are as of yet insufficiently treatable.



Michael Joner took up the new DZHK W3 Professorship for “early clinical studies” at the German Heart Centre Munich at the Technical University of Munich in October 2017.

The focus of his scientific work is in the translational evaluation of innovative research approaches of

cardiovascular diseases with the aim of conducting early clinical studies. His work focuses on the study of the progression of atherosclerotic changes in coronary arteries as well as on their examination using innovative molecular imaging methods. Novel approaches are tested in an animal model and subsequently investigated in specially designed clinical studies. A further focus is the initiation of early clinical studies on the development of innovative approaches for structural heart diseases.



Christoph Knosalla of the German Heart Center Berlin (DHZB) was appointed as the DZHK W2 Professor for heart failure surgery at Charité – Universitätsmedizin Berlin in February 2017. His work focuses on the translational research of severe heart failure with the aim of

advancing organ-preserving procedures and supporting myocardial recovery. In the last few years, he coordinated the creation of the DZHK Biobank at the DHZB. Prof. Knosalla also continues to be significantly involved in the preparation and conduct of the DZHK study “Early versus emergency left ventricular assist device implantation in patients awaiting cardiac transplantation (VAD)”. Numerous other research projects are ongoing or being prepared within the framework of the DZHK at the DHZB and its partners.

Investment Programme 2014–2017

In the reporting year, all equipment from the Investment Programme (see Annual Report 2016, page 11) was purchased and connected to the IT structures of the partner institutions as planned. As a result, the Investment Programme was successfully completed.

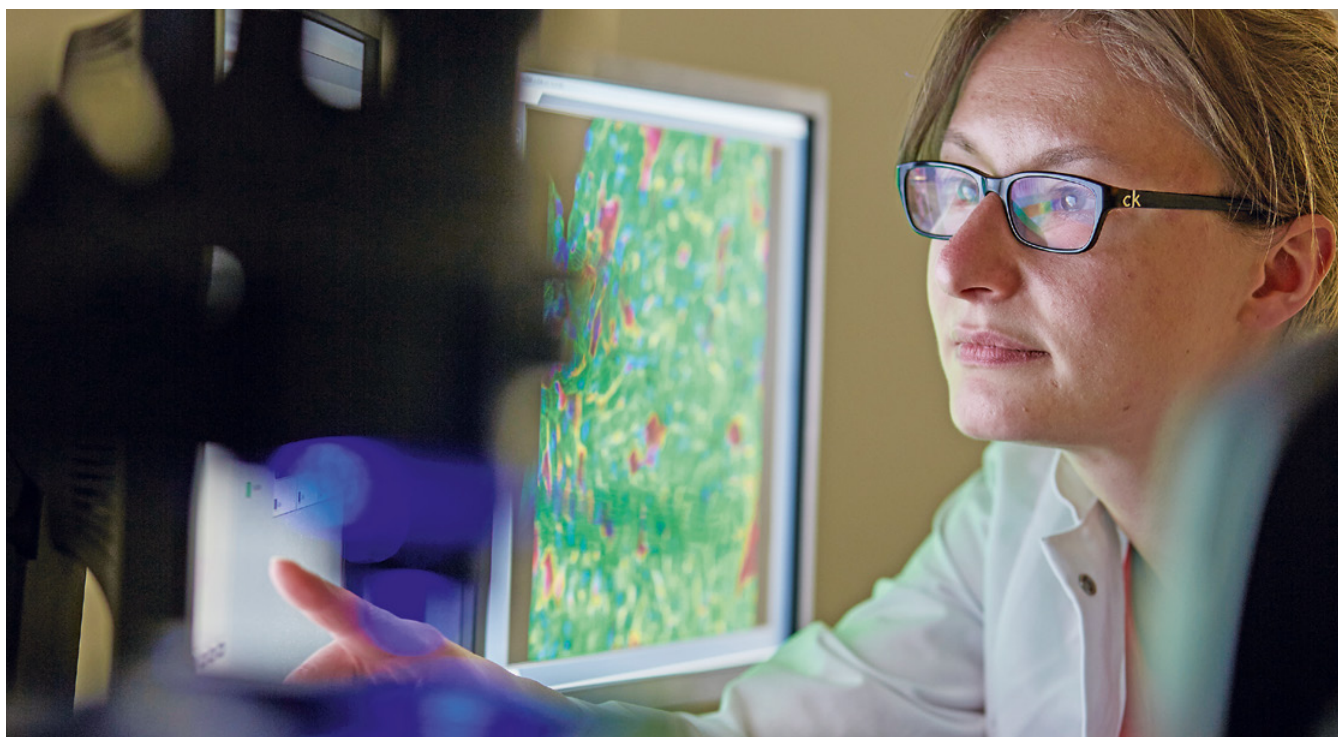
Achievements in 2017

- ✓ Two further DZHK Professors appointed
- ✓ All equipment of the Investment Programme approved within the scope of the Investment Programme 2016/17 purchased
- ✓ 100 percent outflow of partner site project funds freshly approved for 2017

Goals for 2018

- Appointment of two further DZHK Professors
- 100 percent outflow of partner site project funds approved for 2018
- Further increase in the percentage of female PIs

Preclinical Research



Connecting Basic Research and Clinical Application

Preclinical research in the broadest sense comprises all research work which takes place before clinical research. More specifically, we see it as research that bridges the gap between basic research and the first clinical studies. This stage generally constitutes a weak spot in the translational research chain, which is the reason why the DZHK gives it special attention.

In 2017, the DZHK allocated € 5.5 million of its flexible and competitive funds to the area of preclinical research. Translational Research Projects and co-operation projects by means of Shared Expertise as well as co-operations with external partners belong to the preclinical field.

Translational Research Projects

Until last year, Translational Research Projects (TRP) were called High Risk High Volume Late Translational Projects (HRHV). Associated with the name change, there is also a broadening of what this funding line focuses on. The aim of TRPs is still to support research work that immediately precedes the first application of new therapies or diagnostic methods in humans (first-in-man) or provides the necessary foundations for it. The Scientific Advisory Board and also the German Council of Science and Humanities had however recommended that we use the great potential of the DZHK in the preclinical field to a greater extent. This is seen, for example, in the area of structural optimisation of potential active agents. For this reason, in addition to the previous focuses, projects can now be funded that have lead development and optimisation as their aim.

The name change also takes into account the fact that not only risk-laden projects with a large financing volume should be worthy of application, but also smaller projects that champion substantially very good preclinical approaches. A further change is that the applicants may first submit a project outline in order to receive advice from the members of the Translational Research Group (TRG). We thereby want new applicants to benefit from the expertise acquired at the DZHK in this challenging sector with the aim of fielding projects of high-standing scientific quality that are important for translation.

The TRG consists of six external and four internal experts. They held four meetings in 2017 and evaluated and advised new projects. In 2017, the milestone-based

controlling of ongoing projects required increasingly more time.

Last year, we set ourselves the goal of (once again) increasing the application numbers of TRPs, which we succeeded in doing (2015: 6, 2016: 3, 2017: 8). This year, we were yet unable to reach the goal “accelerate the selection procedure”, since the DZHK moved its financial decisions to April and October, which did not coincide with the dates of the TRG meetings. The dates of the TRG meetings will be adjusted in the upcoming year in order to avoid delays.

For already ongoing and newly started TRPs, the DZHK has allocated € 2.5 million in the reporting year.

Translational Research Projects (TRP)

Applicant/ Coordinating investigator	Partner Site	Title	Start	Budget [Euro]
Stefanie Dimmeler	Goethe University Frankfurt	Development of miR-92a inhibitors for the treatment of cardiovascular disease	01.02.2015	2,843,120
Georg Lutter	Christian Albrechts University Kiel	Off-pump transapical mitral valved stent implantation	01.01.2016	337,290
Stefan Luther	Max Planck Institute for Dynamics and Self-Organisation, Göttingen	Low-energy termination of ventricular fibrillation in a porcine heart failure model	01.04.2016	1,023,000
Thomas Eschenhagen, Arne Hansen	University Hospital Hamburg-Eppendorf	IPSC-EHT transplantation for cardiac repair – towards first-in-patient	01.09.2016	1,411,921
Lucie Carrier	University Hospital Hamburg-Eppendorf	Gene therapy for neonatal sarcomeric cardiomyopathies: towards first-in-patient	01.10.2016	446,893
Christian Schulz	Hospital of the Ludwig-Maximilians-University (LMU) Munich	Generation and functional characterization of macrophage cell lines from yolk sac precursors	01.04.2017	256,655
Christian Weber Esther Lutgens Dorothee Atzler	Hospital of the Ludwig-Maximilians-University (LMU) Munich	Late pre-clinical development of CD40-TRAF6 inhibitors (TRAF-STOPs)	01.07.2017	613,230
Markus Schwaiger	Klinikum rechts der Isar (TUM) Munich	In vivo characterisation of the chemokine receptor CXCR4 for the detection of inflammation in atherosclerotic plaques by PET/MR	01.09.2017	333,401
Hugo Katus Patrick Most	Heidelberg University Hospital	A novel inotropic/lusitropic peptide drug against decompensated chronic heart failure	01.01.2018	377,683
Wolfram Zimmermann	University Medical Center Göttingen	GMP-production of engineered human myocardium for heart failure repair	09.01.2018	1,824,600

Translational Research Projects approved and/or started in 2017:

GMP-production of engineered human myocardium for heart failure repair

Duration: from 2018 to 2019

Budget: 1.8 million €

Aim: Irreversible and progressive loss of cardiomyocytes is the underlying cause of heart failure. Remuscularization of the failing heart can be achieved by epicardial implantation of tissue engineered myocardium. A major procedural challenge for the translation of cell based therapies is the set-up and validation of a cGMP-production process. This should be done early during the translation process to reduce costs and variability/inconsistency already in preclinical studies and facilitate clinical translation into first-in patient studies. We have developed a versatile protocol for the construction of engineered human myocardium from ESCs and iPSCs to meet cGMP demands. The objectives of this project are to now set-up a GMP production pipeline and obtain a manufacturing authorization from the local competent authority for the preparation of EHM for a first in patient safety study with an anticipated number of 10 patients with end-stage heart failure.

Involved scientist: Wolfram H. Zimmermann

A novel inotropic/lusitropic peptide drug against decompensated chronic heart failure

Duration: from 2018 to 2019

Budget: 378,000 €

Aim: The objectives of this proposal are the preclinical development of a cardiac-targeted peptide drug with inotropic and lusitropic effects for the short-term intravenous treatment of decompensated chronic heart failure (CHF) and its clinical translation into a first-in-human clinical trial. The life-threatening complication of the clinical syndrome presents a significant unmet medical need given its high mortality and severe adverse effects of clinical drugs to reconstitute cardiac performance. The proposed therapeutic innovation seeks to exploit a novel regulatory principle to improve cardiac contraction and relaxation by the molecular factor S100A1 and utilizes cell-permeable peptide technology that is derived from the molecule's C-terminal domain. The translational research project originates from comprehensive preclinical data showing the ability of S100A1ct peptide for a reversible short-term improvement and protection of cardiac performance in vivo and in vitro. In its funded first developmental module, the project seeks to define the therapeutically effective dose-range of S100A1ct in clinically relevant large animal disease models as well as demonstration of toxicological and immunological safety to conclude regulatory steps on ultimate GMP/GLP pre-clinical and clinical development.

Involved scientists: Hugo Katus, Patrick Most

Late pre-clinical development of CD40-TRAF6 inhibitors (TRAF-STOPs)

Duration: from 2017 to 2019

Budget: 613,000 €

Aim: Blocking the co-stimulatory CD40L-CD40 dyad reduces atherosclerosis. We found that the interaction between CD40 and TNF-receptor-associated factor 6 (TRAF6) is the driving force for atherosclerosis. Using virtual ligand screening, we identified several small molecule inhibitors termed TRAF-STOPs that were modeled to bind to the CD40-binding domain of TRAF6. Two TRAF-STOPs significantly reduce existing atherosclerosis, improve glucose tolerance and insulin sensitivity in mice, and ameliorate multiple sclerosis. Here we pursue the hypothesis that these TRAF-STOPs are candidates to pass the translational pipeline towards a clinical application to treat chronic inflammatory diseases, including atherosclerosis.

Dose finding studies, toxicity and pharmacological safety studies as well as pharmacodynamic studies will be performed, the pharmacological properties will be improved and the proof of the specificity of these small molecule inhibitors will be established

Involved scientists: Christian Weber, Esther Lutgens, Dorothee Atzler

Scientific Co-operations by means of Shared Expertise (SE)

In this funding line, the DZHK partners provide each other with laboratory methods and other scientific expertise mainly derived from the field of preclinical research. This way the knowhow of individual DZHK partners will benefit other DZHK partners. 27 co-operations by means of Shared Expertise were approved in 2017 (2016: 66). In the reporting year, 7 young scientists (26 percent) were applicants for SE Projects (2016: 21; 32 percent). The TOP 10 Shared Expertise were requested in approx. 41 percent of applications. The total funding amount for these projects was 2 million euro.

In order to reduce the administrative effort for the evaluation and approval of applications, the Board of Directors decided to reduce the number of projects and increase the average size of projects for a limited period. The average size of projects thus already increased to 43,000 euro in 2016. In 2017, it was 72,300 euro. For the years 2018 and 2019, we have decided to also reduce the total amount available for Shared Expertise and co-operations with external partners from 3 to 2 million euro per year. For the subsequent years, we plan to increase the funding amount and reduce the average project size again.

Regarding the satisfaction with this funding line, we carried out a survey in the first half of the year with all previous applicants since 2012. The survey's response rate was 70 percent. All projects had been started at the time of the survey, 67 percent of projects had been completed. 35 percent stated that the projects are not running or did not run according to the original schedule. In addition to scientific reasons, the administrative delay for the project's funding approval is stated as a reason for this, but so too are organisational reasons of the laboratory or communication problems between the co-operation partners. Overall, 88 percent are very satisfied or satisfied with the co-operation. Only 4 percent are unsatisfied or very unsatisfied.

The survey comprised 287 co-operation projects, which have so far resulted in 52 publications. 23 percent of these were published in highly regarded scientific journals (impact factor > 10).



Co-operations with External Partners

Certain expertise needed by DZHK researchers can only be found outside the DZHK. For this reason, similar to co-operations by means of Shared Expertise, there is the funding line called “Co-operations with external partners”.

These are smaller bilateral projects that belong to pre-clinical research. In 2017, 13 (2016: 21) co-operation projects with external partners were approved.

The total funding amount was € 1 million (2016: € 0.7 million). As already explained in Shared Expertise, we also reduced the number of projects and increased the sum for each individual project in this funding line.

Achievements in 2017

- ✓ Brief web presentation (Intranet) of the TRP projects
- ✗ Selection procedure for HRHV projects accelerated
- ✓ Number of applications for HRHV projects increased
- ✓ Shared Expertise project evaluated internally

Goals for 2018

- Elaborate concept for the utilisation of Shared Expertise by external scientists
- Accelerate selection procedure for TRP projects

Co-operations with external partners in 2017

Institution	Number of co-operations	DZHK funding project	DZHK funding external partners
Leibniz Institute for Analytical Sciences - ISAS - e.V.	1	205,173 €	75,000 €
University of Cologne, CECAD Research Center	2	136,418 €	66,680 €
University of Münster, Faculty of Medicine	1	136,300 €	78,300 €
University Hospital Aachen, Department of Gastroenterology, Metabolic Diseases and Internal Intensive Medicine	1	95,000 €	45,000 €
Leibniz University Hannover, Faculty of Engineering	1	74,564 €	35,351 €
University Hospital Essen, Clinic for Cardiology at Westdeutsches Herz- und Gefäßzentrum (WHGZ)	1	70,660 €	33,408 €
University of Bonn, Faculty of Medicine	1	69,720 €	32,220 €
University of Potsdam, Institute of Biochemistry and Biology	1	66,301 €	33,301 €
University of Würzburg, Institute for Clinical Epidemiology and Biometry	2	52,550 €	44,100 €
University Hospital Cologne, Department I of Internal Medicine	1	50,000 €	25,000 €
Justus Liebig University Giessen, Department of Internal Medicine	1	28,700 €	23,000 €

Clinical Research



4.1. Clinical Studies

Clinical studies are a focus of the DZHK's research strategy. Corresponding to our research strategy, we promote, for one, early clinical studies that test an innovative therapy or diagnostic procedure in humans for the first time. A further focus lies in guideline-relevant studies.

Their results are incorporated into treatment guidelines and are thus an immediate benefit to patients.

In the reporting year, 6.2 million euro went into clinical studies. At the end of the reporting year, the DZHK was conducting 17 clinical studies, 12 of which were recruiting patients. Four of the studies were in the preparation

phase, and one study had completed recruitment (table on p. 17). The two studies partially funded by the DZHK, ISAR-REACT5 and Revaccept-PCI in CAD, were recruiting in the reporting year as scheduled. Two DZHK-associated studies without DZHK funding, CULPRIT-Shock and FIX-HF-5C, completed recruitment in 2017. They are in the evaluation phase or have already published an initial analysis (CULPRIT-Shock, *New Engl J Med* 2017).

In the reporting year, further early clinical studies were recommended for funding. Since they are starting in 2018, they will be described in more detail in the annual report for the upcoming year.

**DZHK studies (shaded in red) and DZHK-associated studies (shaded in grey)
(the studies of the Competence Networks are shown in the table on page 40)**

Acronym	Disease/treatment/ diagnostics	Study type	Responsible chief investigators (DZHK partner site)	Study participants planned	Study participants recruited*
TORCH-DZHK1	Myocardial diseases	Registry	Katus (Heidelberg/Mannheim), Hoffmann (Greifswald)	2,300	2,309
TransitionCHF-DZHK2	Cardiac insufficiency	Cohort	Hasenfuß, Wachter (Göttingen), Edelmann (Berlin)	1,500	330
VAD-DZHK3	Severe heart failure, heart transplantation	GRS	Falk, Knosalla (Berlin), Hasenfuß, Friede (Göttingen)	200	36
TOMAHAWK-DZHK4	Cardiac arrest	GRS	Desch, Thiele (Hamburg/Kiel/Lübeck)	558	53
FAIR-HF2-DZHK5	Heart failure and iron administration	GRS	Karakas (Hamburg/Kiel/Lübeck), Anker (Berlin)	1,200	158
DEDICATE-DZHK6	Aortic valve stenosis	GRS	Blankenberg, Seiffert (Hamburg/Kiel/Lübeck)	1,600	80
APPROACH-ACS-AF- DZHK7	Circulatory disorders of the heart in combination with atrial fibrillation	GRS	Wakili, Massberg (Munich)	400	143
SPIRIT-HF-DZHK8	Heart failure	GRS	Pieske, Edelmann (Berlin)	1,300	-
SMART-MI-DZHK9	Sudden cardiac death after myocardial infarction	ECS	Bauer, Käbb, Massberg (Munich)	400	87
CAVA-ADHF-DZHK-10	Heart failure	ECS	Jobs (Hamburg/Kiel/Lübeck)	388	22
Ex-VAD-DZHK11	Exercise with a ventricular assist device	ECS	Edelmann, Pieske, Falk (Berlin), Halle (Munich)	66	2
Decipher HFpEF- DZHK12	Heart failure, MRI	ECS	Nagel (Rhine-Main)	170	-
DYNAMIC-MR- DZHK13	Cardiac valve insufficiency, mitral valve reconstruction	ECS	Pieske (Berlin)	150	-
CTSN-TVR-DZHK14	Mitral valve insufficiency	GRS	Falk (Berlin)	400 (int.)	11
SCREEN-AF-DZHK15	Early detection of atrial fibrillation	GRS	Wachter, Hummers-Pradier (Göttingen)	405 (in D)	12
CLOSURE-AF- DZHK16	Atrial fibrillation	GRS	Landmesser, Endres, Boldt, Skurk, Pieske (Berlin) Eitel, Thiele, Wegscheider (Hamburg/Kiel/Lübeck)	1,512	-
HFpEF-stress-DZHK17	Heart failure	ECS	Schuster (Göttingen)	70	18
SFB/TR19plus [#]	Myocarditis	Cohort	Felix (Greifswald)	500	87
ISAR-REACT 5	Circulatory disorders of the heart	GRS	Kastrati, Schüpke (Munich)	4,000	3,689
CULPRIT-Shock (DZHK-assoc.)	Myocardial infarction with cardiogenic shock	GRS	Thiele (Lübeck)	706	706
FIX-HF-5C (DZHK-assoc.)	Heart failure	GRS	Hasenfuß (Göttingen)	160	n.d.
Revacept-PCI in CAD	Coronary heart disease	ECS	Kastrati, Massberg (Munich)	332	17

TORCH-DZHK1 Registry Has Completed Recruitment

In the reporting year, the first DZHK study, TORCH-DZHK1, reached the recruitment goal of 2,300 patients. It is now in the completion phase of the data sets (1-year follow-up and data entries or monitoring).

TORCH-DZHK1 is a registry for capturing data and biosamples of patients with myocardial diseases that are not the result of a vascular constriction (non-ischaemic cardiomyopathies). This affects around 500,000 people in Germany: Approximately 40 percent of all heart failure cases are attributable to non-ischaemic cardiomyopathies. Diseases captured in the TORCH Registry include dilative cardiomyopathy (DCM), left ventricular non-compaction cardiomyopathy (LVNC), hypertrophic cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy (ARVC), myocarditis and amyloidosis. According to a preliminary data analysis, around 70 percent of the enrolled patients are male and 30 percent female. With 56 percent of patients, DCM appears the most frequently. The registry shall help with gaining a better understanding of the molecular causes and progression of cardiomyopathies, and it acts as recruitment hub for DZHK precision medicine studies with national and international partners.

Patient Recruitment and Study Sites

By the end of the reporting year, 3,543 patients in total were enrolled in DZHK studies (excluding associated and Competence Network studies), 671 of which were enrolled by the end of 2015, 1,194 in 2016 and 1,677 in the reporting period. The figure at the top of page 19 shows patient inclusion per quarter, which increased and was the highest in the last quarter. We also see this as a result of our efforts to implement the recommendations

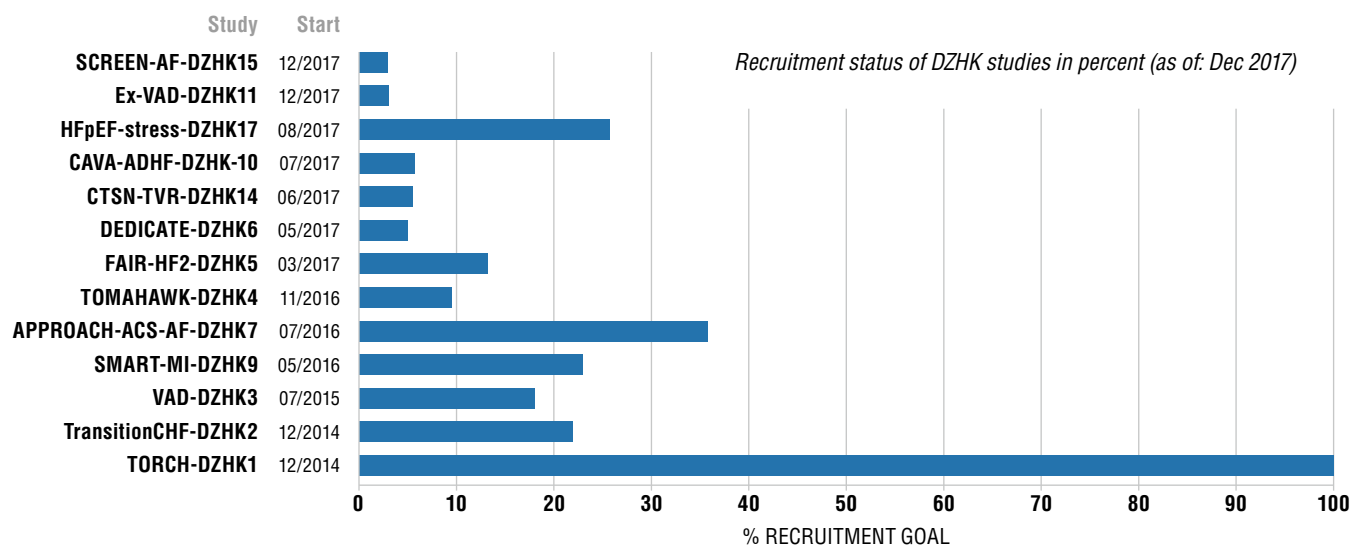
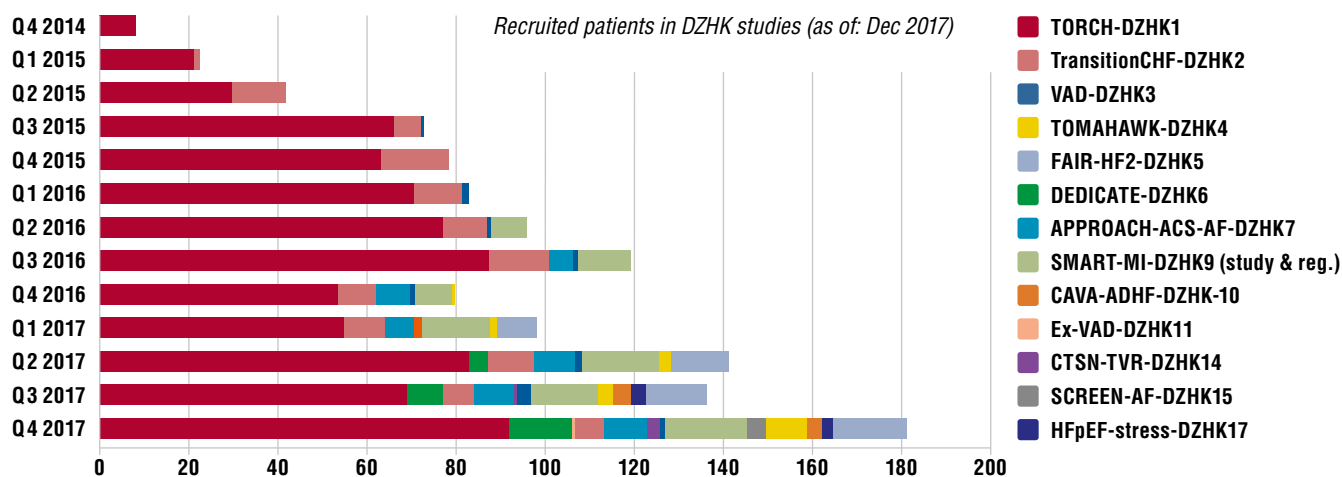
of the Scientific Advisory Board to improve recruitment performance. After the recruitment for TORCH is completed, a challenge for 2018 will be to increase recruitment in all other studies in a way that the total number of enrolled patients does not decline.

We have introduced comprehensive controlling that shows the actual state of recruitment of all DZHK studies and study sites, and enables us to quickly counteract in case of problems.

This procedure has already contributed to reducing the preparation period of the studies that started recruitment in 2017 to an average of 6 months. In order to boost competition between the 17 clinical sites of the DZHK, we introduced a recruiting score. It is published monthly on the intranet and compares the recruitment performance of the DZHK sites. The points are calculated from the weighted number of patients that a site recruited in the respective previous month and are added up to an overall score. The clinical staff funding for each DZHK site will depend on this overall score from 2019 onwards.

These three sites had the top recruiting score at the end of the reporting year (31.12.2017):

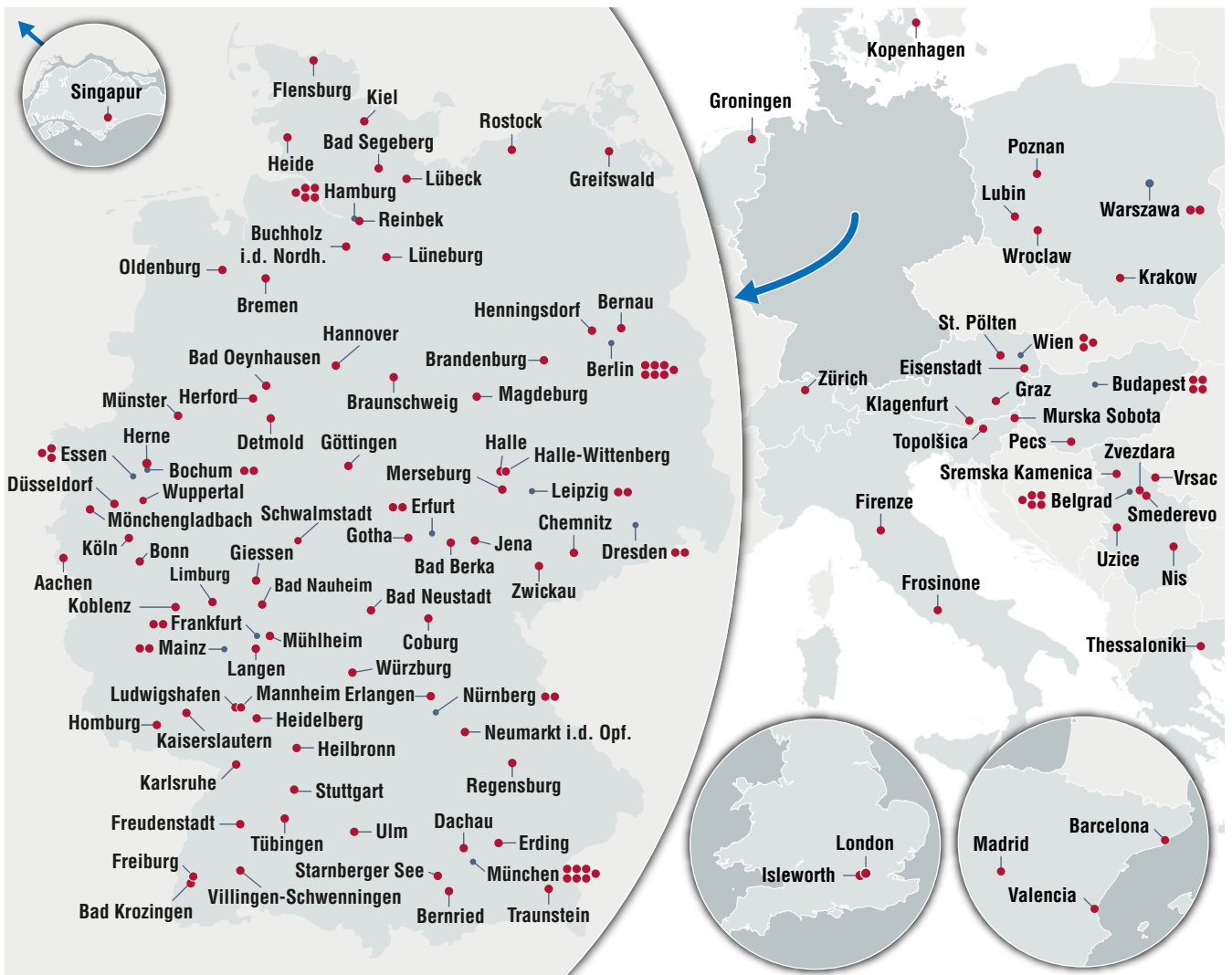
- University Heart Center Hamburg (UHZ): 337 points
- Charité - Universitätsmedizin Berlin, Campus Benjamin Franklin: 308 points
- Charité - Universitätsmedizin Berlin, Campus Virchow: 273 points



By means of our Investment Programme (see Annual Report 2016), we established “Clinical Study Units” at the 17 DZHK study sites and equipped them with standardised devices. The units commenced routine operation as examination centres for study patients in the reporting year. In order to ensure that all devices are operated in proper form and research is carried out in accordance with DZHK rules and regulations, we prepared the internal auditing of the

study units at the end of 2017, which will take place in the first quarter of 2018. By the end of the reporting year, we counted a total of 150 national and European sites that have committed to recruiting patients in one or more of the DZHK studies. Of these, 61 sites were actively recruiting patients at the end of the reporting year, including all 17 DZHK sites. The chart on page 21 provides an overview of the sites.

Involved in clinical DZHK studies



A total of 150 sites in Germany and Europe have committed to participating in clinical studies of the DZHK or are already enrolling patients

Committees and Working Groups

The second three-year term of office of the **Clinical Study Group (CSG)** began in the reporting year. Some members were newly appointed. A new aspect is that the group now also has three external members. Their

task is still in the preselection and internal assessment of applications for clinical studies as well as in advising the applicants and chief investigators. In 2018, they shall also assume controlling responsibilities.

Moreover, the ongoing DZHK studies will be given support by the newly founded **Working Group Clinical Research (WGCR)**, which is composed of representatives from study management, infrastructure co-operation partners and enrolling sites (clinical staff). All questions regarding a study's workflow can and shall be discussed among all members of this committee so that challenges can be countered effectively at operational level and support and learning effects can be generated.

In the reporting year, 15 study doctors and coordinators and 13 study nurses counted as **clinical staff**. These individuals are employed at the DZHK study sites and have the task of coordinating patient recruitment into the DZHK clinical studies in accordance with the rules and specifications of the clinical research platform. They therefore also play a key role in the identification of recruitment constraints and in the processes' improvement. In the reporting period, the DZHK allocated € 1.9 million for clinical staff. From 2019 onwards, the funding amount for clinical staff at a study site for a period of two years will depend on its position in the above-mentioned recruitment score on 31.03.2018.

This incentive scheme for good recruitment performance was developed in 2017 and has already led to a recruitment increase at individual study sites.

4.2. Clinical Research Platform

The clinical research platform, which we created in the last five years, is one of the outstanding structures in the DZHK. It is the only academic infrastructure of its kind in Germany for the conduct of multicentre clinical studies. A big challenge for us was and is operating this structure as a common activity of various DZHK partner sites. This requires a lot of coordination and an unrestricted motivation for working together.

In order to ensure and improve the quality of the clinical study staff's work, the funding line "Clinical Studies Training Programme" started in 2017 enables the professional development of clinical staff as well as other clinical employees involved in or with DZHK studies.

Achievements in 2017

- ✓ Recruitment goals for TORCH-DZHK1 (2,300 patients) achieved
- ✓ Recruitment for Culprit-SHOCK study completed
- ✓ Average study preparation time (from funding contract to enrolment of the first patient) decreased to six months
- ✓ 1,400 patients recorded in Central Data Management in 2017

Goals for 2018

- Capture at least 1,700 patients on the clinical research platform in 2018
- Complete auditing of the 17 DZHK study sites
- Successfully certify at least 90 percent of the DZHK study sites as "DZHK Clinical Study Units"
- Successfully complete recruitment in the study ISAR-REACT5 partially funded by the DZHK (n = 4,000 international study participants)

All data and biosamples of patients in our 17 current studies are captured and managed in a structured manner with standardised software systems: The clinical data are centrally stored at the Göttingen partner site in the eCRF system (secuTrial). Information on biosamples are managed in the Laboratory Information Management System (LIMS) in Greifswald and image data are managed in the Image Data Management System (IDMS) in Frankfurt. The framework for the capturing and processing as well as the eventual release of data is provided for

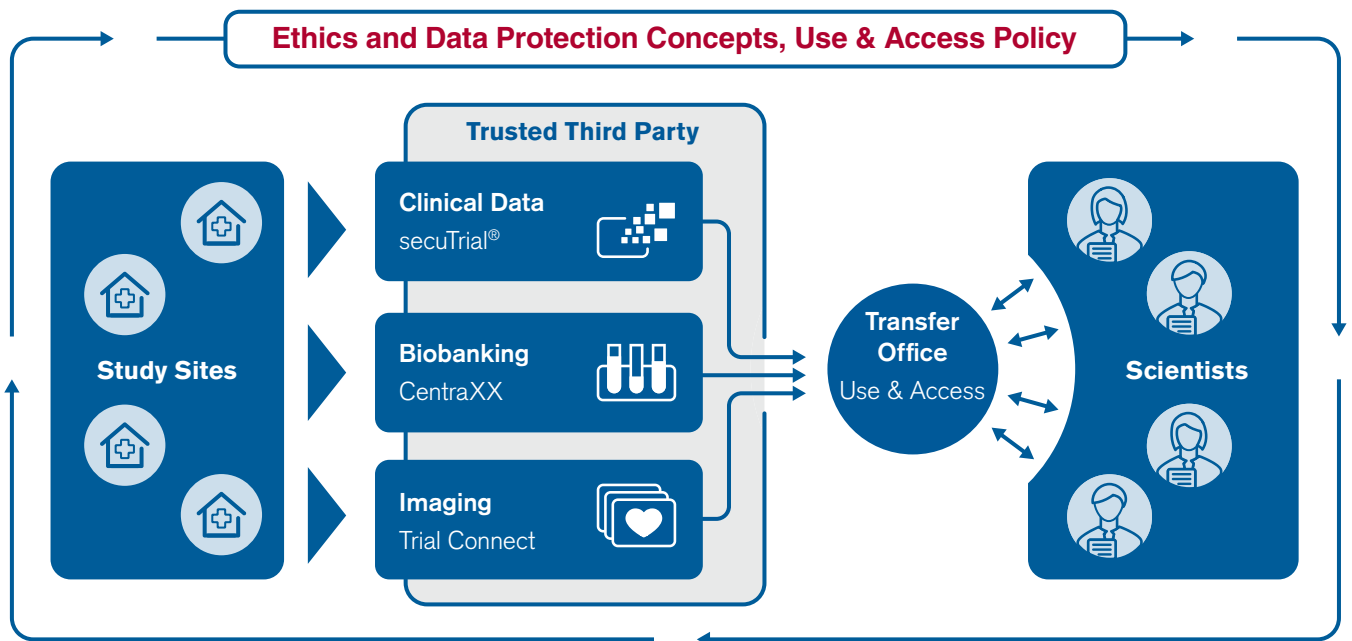
by an ethics and data protection concept developed specifically for and by the DZHK. An independent Trusted Third Party at the Greifswald partner site ensures that personal data are pseudonymised and that medical data cannot be linked to personal data at any time. The Trusted Third Party also continuously monitors compliance with the informed consent forms of patients. All our components fulfil the highest international standards in terms of ethics, as well as IT and data security.

61 study sites in total are meanwhile capturing clinical data with the software secuTrial and biosamples with our Laboratory Information Management System. In addition, we also implemented an Image Data Management System (IDMS) in the reporting year. It enables the central storage and evaluation of image data, such as echocardiographies, which often have a high informative value when it comes to cardiovascular diseases. With the introduction of the IDMS, sending data carriers to the respective evaluation site (CoreLab) is no longer required.

The CoreLab system of the DZHK ensures that image data are evaluated within an hour by experienced experts in a standardised manner. This increases the quality and scientific significance of the results.

DEDICATE-DZHK6 and CLOSURE-AF-DZHK16 are the first two DZHK studies to use the IDMS, together with all the sites involved in them. For 2018, we are planning to link at least 5 studies to the IDMS.

By the end of 2017, the data of 3,543 patients across studies were captured in the research platform. For every patient, hundreds of parameters (e.g. laboratory test, echocardiography, medical history, medication, etc.) are collected in a structured manner and subsequently quality assured. The ever-expanding database already comprises more than 1 million entries.



Involved in clinical DZHK studies

The data collection meanwhile is also a model for other consortia. So for example, the SFB 1002 uses the DZHK basic data set and a minimum data set based on the DZHK basic data set was created at the German Biobank Alliance. Interested scientists may request biosamples and data from the collection for their own research (see “Secondary use of data and samples”, p. 24).

In addition to the technical infrastructure, operating the platform also requires smooth and quality-assured processes that are continuously improved through user feedback. Furthermore, a great deal of effort is required for the technical integration of new studies and study sites as well as for user training and support. For instance, seven new DZHK studies and 94 enrolling sites were connected to the IT infrastructure in the reporting year. Around 750 applications for setting up or changing user permissions were processed by the Data Handling Unit.

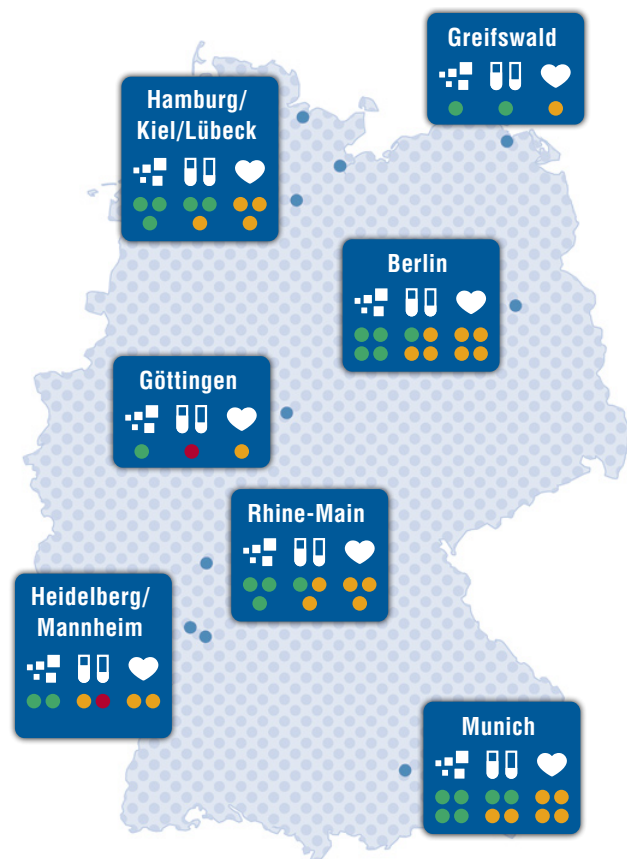
 **Clinical data:** secuTrial®

 **Biobanking:** CentraXX

 **Imaging:** Trial Connect

● In preparation
● In final preparation
● In full use

The DZHK invested 1.5 million euro for the clinical research platform in the reporting year..



The integration of the 17 clinical DZHK sites into the IT components of the clinical research platform.

Successful International Review

The current project phase of the clinical research platform ends at the close of 2018, so the decision on its extension is due. We therefore had the platform undergo an international review organised by the project management agency PT-DLR in the reporting year. The panel of experts positively evaluated the structure and recommended its further funding. In addition, the experts also gave suggestions for optimisation in some areas. They

recommended the further standardisation of processes to increase efficiency and verify the quality of data and biosamples. As a result, further synergies could be exploited and redundancies could be avoided. Furthermore, it was recommended that the secondary use of collected data and samples should now already be taken into account more intensively and that the interests of users should be considered during the further development of the system.

Next year, the clinical research platform will particularly focus on quality assurance and the further implementation of components, as well as the standardisation of processes recommended by the experts. Possibilities for the scientific use of data and samples will increasingly be the subject of strategic discussions at the DZHK next year.

Secondary Use of Data and Samples

The standardised capturing and processing of data and samples across studies brings with it great advantages for secondary use (Use & Access). We have already carefully prepared this process, but it will only really start once the first studies are completed. The Transfer Office located in Göttingen provides the Use & Access procedure with organisational and technical support. Interested scientists can already read about the sample and data pool ("Data Catalogue") that can be applied for and check their availability ("Feasibility Explorer") on the DZHK website.

Whether there is a sufficient number of the required data and biosamples can thus be ascertained before a potential submission of an application.

Access to the data and biosamples is regulated by the Use & Access Policy of the DZHK. The Transfer Officer receives usage applications from the scientific community and generates an initial availability statement on the number of data and biosamples. Subsequently, this is given to the Use & Access Committee together with the usage application. The Committee evaluates applications in terms of their compliance with ethical and legal standards and scrutinises the scientific significance of the research question. Following this, the Committee gives a recommendation on the requested access. Moreover, under the Use & Access Policy, usage applications

must be shown on the DZHK website with an abstract and the current status of the project. Chief investigators who want to use data or samples from their own project beyond the original research question must notify the Use & Access Committee of this usage. In the reporting year, we received four usage notifications relating to the TORCH Registry.

Over the next few years, strategies that improve the visibility of the DZHK's valuable collection of data and samples in the scientific community beyond the DZHK must be developed and implemented.

Achievements in 2017

- ✓ At least half of the clinical DZHK institutions are using LIMS
- ✗ The first studies are documenting image data using IDMS
- ✓ Feasibility Explorer installed
- ✗ Several usage notifications for data and samples received and processed

Goals for 2018

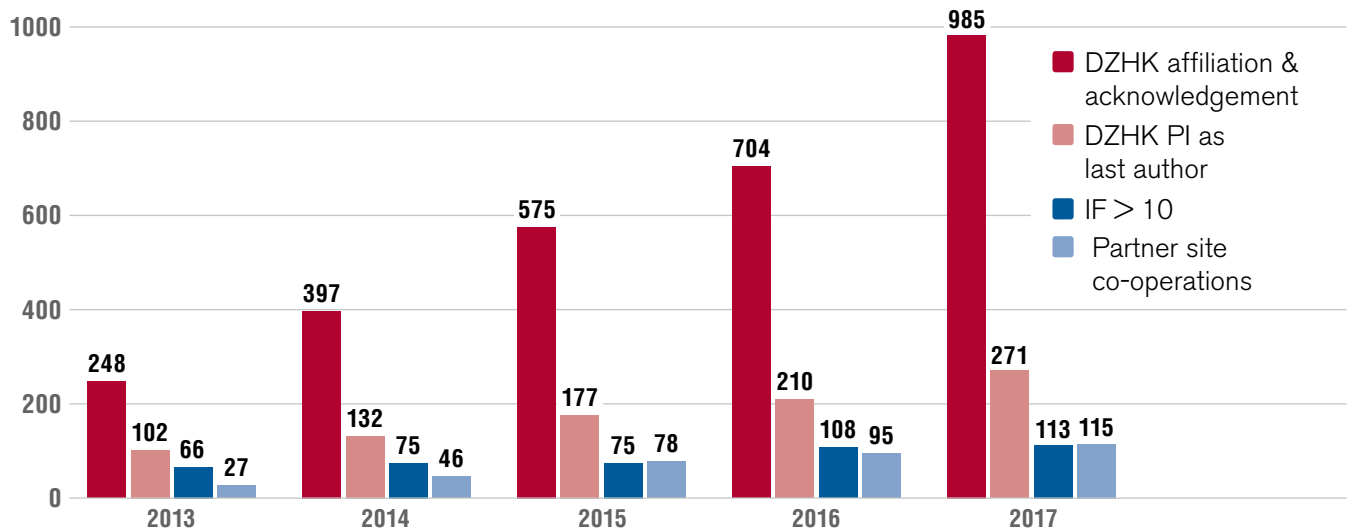
- All DZHK sites are connected to LIMS
- Five studies are connected to IDMS
- Use & Access processes are tested and improvements started to be implemented
- Several usage applications for data and samples received and processed
- Scientific publication on clinical research platform submitted
- Infrastructure and studies are working in conformity with the EU GDPR

Scientific Highlights and Publications

Research at the DZHK is very successful. This is evident in the number of scientific publications – most of which to date still originate from partner site projects. However, smaller bilateral or trilateral co-operations (Shared Expertise projects and co-operations with external partners) also increasingly result in scientific publications.

The number of publications is continually increasing per

annum; at the end of 2017, a total of 2,909 publications with DZHK affiliation or acknowledgement were counted. Please find more information about publications on page 56 of this report.



Paper of the Month 2017

Every month, the DZHK's Board of Directors selects a paper of the month, which is then announced in the DZHK Newsletter and published online on the DZHK website.

January

Abu-Taha, I. H. (University Medical Centre Mannheim) et al.: **Nucleoside Diphosphate Kinase-C Suppresses Camp Formation in Human Heart Failure.** *Circulation*. Involved DZHK partner sites: [Heidelberg/Mannheim](#), [Hamburg/Kiel/Lübeck](#), [Göttingen](#)

February

Kossmann, S. (University Medical Centre Mainz) et al.: **Platelet-Localized Fxi Promotes a Vascular Coagulation-Inflammatory Circuit in Arterial Hypertension.** *Science translational medicine*. Involved DZHK partner site: [Rhine-Main](#)

March

Jungen, C. (University Medical Center Hamburg-Eppendorf) et al.: **Disruption of Cardiac Cholinergic Neurons Enhances Susceptibility to Ventricular Arrhythmias.** *Nature communications*. Involved DZHK partner site: [Hamburg/Kiel/Lübeck](#)

April

Wild, P. S. (University Medical Centre Mainz) et al.: **Large-Scale Genome-Wide Analysis Identifies Genetic Variants Associated with Cardiac Structure and Function.** *The Journal of clinical investigation*. Involved DZHK partner sites: [Rhine-Main](#), [Berlin](#), [Göttingen](#), [Greifswald](#), [Hamburg/Kiel/Lübeck](#), [Munich](#)

May

Kessler, T. (German Heart Centre Munich) et al.:

Functional Characterization of the Gucy1a3 Coronary Artery Disease Risk Locus. *Circulation*. Involved DZHK partner sites: [Munich](#), [Hamburg/Kiel/Lübeck](#)

June

Tiburcy, M. (University Medical Center Göttingen) et al.:

Defined Engineered Human Myocardium with Advanced Maturation for Applications in Heart Failure Modelling and Repair. *Circulation*. Involved DZHK partner site: [Göttingen](#)

July

Leisegang, M. S. (Hospital of the Johann Wolfgang Goethe University) et al.:

Long Noncoding Rna Mantis Facilitates Endothelial Angiogenic Function. *Circulation*. Involved DZHK partner sites: [Rhine-Main](#), [Munich](#)

August

Meyer, I. S. (Heidelberg University Hospital) et al.:

The Cardiac Microenvironment Uses Non-Canonical Wnt Signaling to Activate Monocytes after Myocardial Infarction. *EMBO molecular medicine*. Involved DZHK partner site: [Heidelberg/Mannheim](#)

September

Jobs, A. (University Medical Center Schleswig-Holstein) et al.:

Optimal Timing of an Invasive Strategy in Patients with Non-St-Elevation Acute Coronary Syndrome: A Meta-Analysis of Randomised Trials. *Lancet*. Involved DZHK partner sites: [Hamburg/Kiel/Lübeck](#), [Munich](#)

October

Borchert, T. (University Medical Center Göttingen) et al.:

Catecholamine-Dependent Beta-Adrenergic Signaling in a Pluripotent Stem Cell Model of Takotsubo Cardiomyopathy. *Journal of the American College of Cardiology*. Involved DZHK partner sites: [Göttingen](#), [Hamburg/Kiel/Lübeck](#), [Heidelberg/Mannheim](#)

November

Wilck, N. (Max Delbrück Center for Molecular Medicine Berlin) et al.:

Salt-Responsive Gut Commensal Modulates Th17 Axis and Disease. *Nature*. Involved DZHK partner site: [Berlin](#)

December

Lehmann, L. H. (Heidelberg University Hospital) et al.:

A Proteolytic Fragment of Histone Deacetylase 4 Protects the Heart from Failure by Regulating the Hexosamine Biosynthetic Pathway. *Nature medicine*. Involved DZHK partner site: [Heidelberg/Mannheim](#)

Translational Research Highlights

Why Some Blood Thinners Increase the Risk of Heart Attack

Blood thinners are supposed to prevent platelets from forming clots that can clog blood vessels and cause strokes and heart attacks. In the laboratory, Munich-based DZHK researchers were able to find out why some blood thinners still lead to heart attacks.

People with atrial fibrillation have an increased risk of stroke, because their blood can clump together in the fluttering atria. They therefore receive blood thinners as a preventative measure. However, a new group of blood thinning agents, the so-called oral thrombin inhibitors (OTIs), slightly increase the risk of heart attacks. This was revealed in meta-analyses with around 10,000 people. "We wanted to follow this observation and ascertain why people have more heart attacks if they receive certain blood thinners, even though they are protected from strokes and deep vein thromboses", says Dr Tobias Petzold of the Hospital of LMU Munich.

Using flow chambers to mimic blood vessels, the researchers were able to recreate the effect in the laboratory. They coated the internal surfaces of the chambers in different ways, including with the von Willebrand factor and samples obtained from human blood vessel plaques. The flowing blood actually clotted more when it contained OTIs, particularly in the flow chambers that already contained plaques. This effect did not occur in static tests carried out by other research groups. From this, Petzold and his team concluded that OTIs change the way the coagulation factor thrombin bonds to platelets. The von Willebrand factor receptor is also involved in this process, but is only activated when blood is flowing. The researchers were also able to show that certain antibodies block thrombin from bonding, and thus also prevent the clumping of platelets and blood clot formation.



Although they protect against strokes, some blood thinners can increase the risk of myocardial infarction in patients suffering from atrial fibrillation.

"This mechanism could contribute to more heart attacks for people prescribed OTIs", explains Petzold. The Munich-based physicians conclude that before administering OTIs an individual's heart attack risk should be considered, i.e. by checking the level of plaque build-up in their coronary blood vessels. "However, if there is no risk of heart attack, the benefits of OTIs clearly outweigh the risks", emphasizes Petzold. In his opinion, in the coming years the focus will be to determine the ideal blood thinner for different patient groups with the help of clinical studies.

These findings are from the DZHK partner site project "Clinical Platelet Therapy Research" (81Z1600214).

Oral Thrombin Inhibitor Aggravates Platelet Adhesion and Aggregation During Arterial Thrombosis. Petzold et al. *Science Translational Medicine* (2016)

Blood Pressure in Germany Is Decreasing – Yet There is Room for Much More Improvement

An evaluation of seven large population-based studies reveals that blood pressure in Germany has decreased in the last two decades. The greatest decrease was seen in 55 to 74-year olds. Despite the decrease, blood pressure in Germany is still too high, particularly in men.

The Konsortium zur Blutdruckepidemiologie (Consortium for Blood Pressure Epidemiology), founded by DZHK scientists, analysed data from two national health surveys and five regional population-based studies conducted between 1997 and 2012. According to these, the blood pressure of both men and women has decreased nationwide, most notably among people aged 55 to 74. There were also regional differences: In the North East, blood pressure decreased the most compared to the national average. The previously observed gender differences have not changed: In women, high blood pressure is still recognised earlier, treated more often, and thus lowered more successfully.

The scientists also found that treatment for high blood pressure has increased in recent years and this could be behind the improvements seen in the nation's blood pressure health, but they also suggest that prevention efforts such as healthier diets, more exercise and giving up smoking have contributed to the positive development.

Despite recent improvements, Germany's blood pressure is still too high and the overall number of people with high blood pressure has only slightly changed. The researchers even suggest that diagnosis of the condition will only become more frequent due to our ageing society. However, there are real options for prevention and treatment in many cases.

"Using the example of North East Germany, we see how much can be achieved in a decade", says



"Preventing high blood pressure from occurring in the first place must remain the primary goal."

PD Dr Hannelore Neuhauser of the Robert Koch Institute. "However, preventing high blood pressure from occurring in the first place must remain the primary goal." The current threshold for a diagnosis of high blood pressure is 140/90mmHg, but Neuhauser points out that action should really be taken when readings reach around 120-140/80-90mmHg. In this range, drugs are not usually prescribed, but lifestyle changes can reduce blood pressure, or at least stop it rising further, and lower the risk of cardiovascular diseases. In other words: losing weight, exercising more, drinking less alcohol, eating a lot of fruit and vegetables, and stopping smoking can have dramatic positive effects.

These data were evaluated within the scope of the DZHK project group "Blood Pressure Epidemiology".

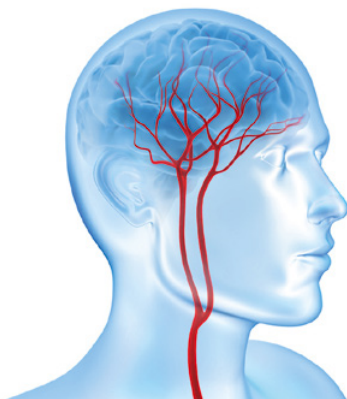
Hypertension in Germany - data from seven population-based epidemiological studies (1994–2012). Neuhauser et al., Deutsches Ärzteblatt

A New Therapy for Narrowed Carotid Artery

A rupture of a deposit in the carotid artery is responsible for around one in ten strokes. While stable deposits are less harmful, ruptured deposits can form blood clots and reach the brain. Prof Dr Lars Mägdefessel of the DZHK Munich partner site is searching for agents that make these deposits more stable.

Deposits on the blood vessel walls, also called plaques, are covered with a layer of tissue, the so-called fibrous cap. The thicker this layer is, the more stable and thus less harmful, the deposit is. Lars Mägdefessel is a DZHK Junior Research Group leader and has discovered a regulatory RNA molecule that can possibly stabilise the fibrous cap.

“Traditionally, physicians try to reduce the size of the plaques in vessels in order to widen the narrowed section”, says the researcher. In the carotid arteries, plaque rupture is much more dangerous than narrowing, so the idea of just stabilising, rather than reducing, the plaques is becoming ever more popular.



If deposits in the carotid artery rupture, it can lead to a stroke.

Mägdefessel and his team compared material from people with stable and unstable plaques in the carotid artery. They were able to show that a molecule called microRNA-210 is found in the fibrous caps of plaques, and is

more prevalent in stable plaques than in unstable ones. microRNA-210 stops the APC gene from being read, which means that smooth muscle cells in the fibrous cap live longer and the cap becomes more stable. Moreover, the animal model showed that administering microRNA-210 leads to fewer plaques rupturing.

However, APC is a tumour suppressor gene that inhibits the growth of tumours. Any existing tumour cells could multiply in the presence of microRNA-210, when APC is inhibited, so the team is currently researching how microRNA-210 can be administered locally, to avoid adverse side effects. For that reason, the researchers are testing coated stents or balloons that are inserted directly into the carotid artery in pigs. “For this step, we also rely on collaboration with companies that develop soft balloons that cause minimal friction and thus make the procedure safer”, says Mägdefessel. “Only in this way can our results reach those in need as effective therapies.”

These results are from the Junior Research Group “Non-coding RNA-based therapeutics and biomarkers for treatment and detection of vascular diseases” (81X3600604).

MicroRNA-210 Enhances Fibrous Cap Stability in Advanced Atherosclerotic Lesions. Eken et al. *Circulation Research* 2017

Gut Bacteria Are Sensitive to Salt

Berlin-based DZHK researchers together with an international team found that common salt reduces the number of certain lactic acid bacteria in the gut of mice and humans. This has an impact on immune cells which are partly responsible for autoimmune diseases and hypertension. Probiotics lowered the symptoms of disease in mice.

Too much salt in food can encourage high blood pressure and might even have a negative impact on the course of the autoimmune disease multiple sclerosis. Prof Dr Dominik Müller of the Max Delbrück Center for Molecular Medicine and his team have now demonstrated in mice that excess salt reduces lactobacilli in the gut, while blood pressure rises and the number of Th17 helper cells increases. These immune cells are associated with high blood pressure and autoimmune diseases like multiple sclerosis.

Even when mice were given the probiotic lactobacilli, alongside a high salt diet, the frequency of Th17 helper cells decreased and blood pressure still dropped. The probiotics also alleviated the neurological symptoms of experimental autoimmune encephalomyelitis, a disease model for multiple sclerosis. The researchers thus identified the gut bacteria, also called microbiome, as an important factor in diseases affected by salt.

The researchers also investigated the bacteria present in the gut of twelve healthy men who were given six extra grams of salt every day for a fortnight. As the study participants otherwise maintained their usual eating habits, this roughly doubled their daily intake of salt. The lactobacilli responded sensitively here, too. Most of the bacteria were no longer detectable after 14 days of increased salt intake. Blood pressure and the number of the Th17 helper cells also increased.

However, the new findings have not yet confirmed



Probiotics can help with the regeneration of gut bacteria damaged by salt.

whether lactobacilli have a therapeutic effect. Among other things, the researchers are planning a placebo controlled study in humans, which could show how probiotics in food affect blood pressure.

These results are from a research collaboration between the Max Delbrück Center for Molecular Medicine, Charité – Universitätsmedizin Berlin, the Berlin Institute of Health, the DZHK (partner site project 81Z1100101) and further international partners.

Salt-responsive gut commensal modulates TH17 axis and disease. Wilck et al., Nature (2017)

How Exercise and High Blood Pressure Affect the Heart

When the heart is put under stress during exercise, it is considered healthy. Yet stress due to high blood pressure is bad for the heart. Why? And is this always the case? DZHK researchers of Heidelberg University Hospital have discovered a new signal pathway that can protect against, or cause, heart failure – depending on the type of stress.

The researchers headed by DZHK Professor Johannes Backs examined a chain of metabolic processes in the heart, controlled by an epigenetic switch. Epigenetics investigates how environmental influences regulate our genes. The newly-discovered signal transmission pathway can be turned up or down in mice depending on stress. The researchers identified that, at the end of the same signalling pathway, one chemical fragment of the switch is more prevalent in mice subjected to 'healthy heart stress', like exercise, than those with 'unhealthy heart stress', like high blood pressure.

The researchers aimed to investigate the effect more closely so produced genetically modified mice that are not able to generate the important chemical fragment on the switch. The animals were subjected to physiological stress and, surprisingly, exercise no longer had the healthy effect on them. Instead, they developed temporary heart failure after the intensive workout which led to a distinctly reduced performance. This heart failure, however, regressed again.

It seems that this particular fragment on the switch protects the heart from damage caused by temporary physiological stress. But why not also from stress caused by high blood pressure or other kinds of 'unhealthy' stress? "Breaks make all the difference", says Backs. During exercise, there are frequent rest periods for the heart. An enzyme called protein kinase A recovers during the break periods and then ensures that the healthy path, via the activation of the fragment, is followed in the metabolic chain.

Even from an evolutionary perspective, the mechanism seems plausible to the researchers. Our ancestors, the gatherers and hunters, often had to be physically active



It's important to take a short breather, because extreme endurance sports without rest periods can damage the heart.

for many hours to find food and bring it home. The newly discovered signal pathway could have protected the heart. The results also explain why extreme endurance sports without rest periods can damage the heart. "We all intuitively know that breaks are important. Perhaps we have now found the molecular causes for this", states Backs.

These research projects were funded within the scope of Johannes Backs's DZHK Professorship (partner site project 81Z2500103).

A proteolytic fragment of histone deacetylase 4 protects the heart from failure by regulating the hexosamine biosynthetic pathway. Lehmann et al., Nature Medicine 2017

Promotion of Junior Scientists – the Young DZHK



Translational cardiovascular researchers that are working at the interface between research and treatment are becoming ever more important. For this reason, the promotion of young scientists is one of the most important objectives of the DZHK. In the reporting year, the DZHK provided € 2.5 million for the promotion of young scientists. In addition, the DZHK supports the Young DZHK, the self-organised union of all young scientists of the DZHK.

The Young DZHK counted 928 members at the end of the reporting year.

In 2017, the focus of the **Young DZHK Postdoc Committee** was on intensifying collaborating with other national and international junior scientist networks and enhancing international visibility in cardiovascular research (Chapter 8).

Training Programme

The DZHK Training Programme is made up of a range of modules. To a great extent, their allocation can be decided by each DZHK partner site themselves. The total number of funding measures in this area has increased in 2017 relative to the previous year (cf. table).

The DZHK Mentoring Programme is realised centrally. For this reason, mentee selection is done within the scope of a process organised by the Main Office. In 2018, the Mentoring Programme will be carried out in English for the first time. The call for the programme was thus done in English in the reporting year. With 24 applications, the number was a third higher than in previous years, which shows that the English-language offer was the right decision. 14 participants were selected and the programme starts in March 2018.

Funding initiatives for Young DZHK members from the Training Programme in 2017 (in parentheses 2016):

Travel grants for high-ranking conferences	289 (211)
Doctoral scholarships	38* (23)
Visiting Scientist Programme	20 (38)
Attendance of external workshops	63 (67)
Mentoring (Call 2017)	14 (14)

*financed by Training Programme and other partner site funds

Promotion of Excellence

The DZHK Excellence Programme is also made up of several modules. New in 2017 was the “**Clinician Scientist Programme**”. This programme is aimed at young physicians at the start of their specialist medical training. The participants will be exempted from patient care for two and a half years to intensively dedicate themselves to research during this time.

They can manage this time flexibly over eight years. The DZHK programme promotes four clinical scientists per year. There were ten applicants in the first call.



There were four applications for the **DZHK Junior Research Group** in the reporting year – However, the selection decision will only be made in 2018. The call was revised and application eligibility was broadened – from four to six years following the completion of their doctorate for natural scientists and from six to eight years following their state examination for physicians. We thereby give the applicants a longer Postdoc phase, which increases the size of the applicant cohort.

For the other four modules, the number of grants remained similar to the previous year – However, since the number of applications rose, the funding quota decreased overall (13/54, previous year 15/41). There were no applications for the Research Grant (release from teaching) and the Reintegration Grant in 2017. We are therefore considering discontinuing the Reintegration Grant and introducing a programme for the advancement of women in science. More specifically, the funding quotas were as follows:

- Rotation Grant for physicians: 3/9 (2016: 5/11)
- Research Grant (release from teaching): 0/0 (2016: 2/3)
- Reintegration Grant: 0/0 (2016: 3/3)
- Postdoc Start-up Grant: 15/45 (2016: 5/24)

Promotion of Excellence in 2017

Name	Institution	Funding Line	Title
Arash Haghikia	Charité – Universitätsmedizin Berlin	Rotation grant	The role of the gut-microbiome for the development of vulnerable coronary plaque
Mathias Orban	Hospital of the Ludwig- Maximilian-University Munich	Rotation grant	Mechanisms of early thrombopoiesis and the role of embryonic platelets in vasculogenesis
Cordula Wolf	German Heart Centre Munich	Rotation grant	Molecular pathways of right heart failure in patients with complex congenital heart disease
Baptiste Coxam	Max Delbrück Center for Molecular Medicine in the Helmholtz Association	Postdoc start-up grant	Decoding genetic and functional endothelial heterogeneity in vascular regeneration
Reiner Jumpertz- von Schwartzberg	Charité - Universitätsmedizin Berlin	Postdoc start-up grant	Metabolic and cardiovascular consequences of the human gut microbiota in gnotobiotic mice
Ibrahim El-Battrawy	University Hospital Mannheim	Postdoc start-up grant	Modelling short QT syndrome using human-induced pluripotent stem cell derived cardiomyocytes: Drug screening and carnitine as a therapeutic target
Agnieszka Anna Gorska	University Hospital Heidelberg	Postdoc start-up grant	Cand2 involvement in mTOR-dependent myocardial hypertrophy
Andrea Lang	Technical University of Munich	Postdoc start-up grant	Sympathetic control of resident macrophages in the adult heart
Sebastian Clauss	Hospital of the Ludwig- Maximilian-University Munich	Postdoc start-up grant	Evaluation of ZFH3 in the pathogenesis of Atrial Fibrillation
David Jochheim	Hospital of the Ludwig- Maximilian-University Munich	Postdoc start-up grant	Prevention of bioprosthetic heart valve dysfunction - a multimodal approach
Harmandeep Kaur	Max Planck Institute for Heart and Lung Research, Bad Nauheim	Postdoc start-up grant	GPCR signaling in smooth muscle dedifferentiation: from single-cell expression to new therapeutic strategies
Emiel van der Vorst	Hospital of the Ludwig- Maximilian-University Munich	Postdoc start-up grant	The calcium-sensing receptor, a crucial link between obesity and atherosclerosis?
Matthias Leisegang	University Hospital Frankfurt	Postdoc start-up grant	Identification of the endothelial function and the molecular mode of action of the lncRNA HIF1 -AS1

Achievements in 2017

- ✓ Clinician Scientist Programme launched
- ✓ Call for Junior Research Group revised in order to get more applicants
- ✗ Reintegration Grant revised
- ✓ Mentoring Programme prepared in English

Goals for 2018

- Develop funding line for the promotion of female scientists
- First clinician scientists selected

Scientific Exchange and Co-operation

Research results can only find their way into application if they are talked about and others learn about scientific breakthroughs and innovations. The DZHK encourages the internal and external exchange between its scientists in many ways, and thus enables continuous networking between them. The highlights of 2017 were the DZHK Conference on Translational Medicine organised for the first time and the annual DZHK Retreat. Furthermore, the DZHK co-funded several scientific events of its member institutions and organised three internal DZHK symposia.

1st DZHK Conference on Translational Medicine

In January 2017, the DZHK held the DZHK Conference on Translational Medicine in Berlin for the first time. With the involvement of top international scientists from various disciplines, industry representatives and representatives from public funding bodies as well as regulatory authorities, translation was discussed over two days with roughly 200 participants from various perspectives and current trends in international research were presented. Developments in the cardiovascular field were not the sole subject, but rather innovative, translational approaches beyond the disciplines were discussed.

The 2nd DZHK Conference on Translation Medicine will again be held in Berlin on 9 and 10 January 2019.

DZHK Retreat and Young DZHK Retreat

The DZHK Retreat, our most important internal exchange platform, was held for the fifth time in 2017. For this anniversary, we went to a particularly beautiful venue: the Baltic Sea. From 14 to 16 September, 250 DZHK scientists from all partner sites met in Rostock-Warnemünde. Beside the four paper sessions on the subjects heart failure & cardiomyopathies, vascular



disease, arrhythmias and clinical science & infrastructure organised by the DZHK Professors, there were two excellent keynote papers by Christine Seidman (Harvard) and Matthias Tschöp (Helmholtz Zentrum München). Furthermore, diverse working group and committee meetings were organised in Warnemünde, including the DZHK General Assembly of Members. The success of the retreat is also reflected in the results of the satisfaction survey. Overall, 98 percent of the survey participants stated that they were very satisfied or satisfied with the retreat (2016: 86 percent).

The preceding retreat of the Young DZHK was also very popular. There were many more registrations than available places again this year.

For this reason, there will be an additional 30 places for young scientists in the coming retreat. In the form of a permanent poster exhibition as well as the inclusion of papers by the Young DZHK in the main retreat, our junior scientists were again given the opportunity to present their work to established scientists.



Awardees at the Young-DZHK Retreat 2017: Kerstin Wöltje, Michael Molitor, Eva Riechert, Lavanya Iyer.

DZHK Symposia

Titel	Ort und Datum	Organisatoren
1 st Joint DGK / DZHK Translational Workshop: microRNA and long non-coding RNAs: Clinical relevance as biomarker and therapeutic target in cardiovascular medicine	16.02.-17.02.2017, Berlin	Johannes Backs (Heidelberg/Mannheim), Friederike Cuello (Hamburg/Kiel/Lübeck)
Reverse Translation: How to get Mechanistic Insights from Clinical Trials?	01.09.2017, Berlin	Ulrich Kintscher, Vera Regitz-Zagrosek (Berlin)
Metabolism and Cardiovascular Disease	26.10.-27.10.2017, Heidelberg	Johannes Backs (Heidelberg/Mannheim), Stefanie Dimmeler, Michael Potente (Rhine-Main)

Co-financed conferences at DZHK partner sites

Titel	Ort und Datum	Organisatoren
International Symposium on BioMedical Applications of X-Ray Phase Contrast Imaging (IMXP) 2017	26.01.-7.01.2017, Garmisch-Partenkirchen	Maximilian Reiser (Munich)
15 th Dutch-German-Joint-Meeting 2017	16.03.-18.03.2017, Münster	Friederike Cuello (Hamburg/Kiel/Lübeck)
34 th Meeting of the European Section of the International Society for Heart Research (ISHR)	24.07.-27.07.2017, Hamburg	Lucie Carrier (Hamburg/Kiel/Lübeck)
Scientific Symposium – Opening of the Heart Research Building Göttingen	11.09.2017, Göttingen	Wolfram-H. Zimmermann (Göttingen)
Göttingen Channels 2017 – Of Benches and Beds	22.09.-23.09.2017, Göttingen	Niels Voigt (Göttingen)
Peaks in Vascular Biology der Gesellschaft für Mikrozirkulation und Vaskuläre Biologie	05.10.-07.10.2017, Garmisch-Partenkirchen	Christian Kupatt (Munich)
6. Sportkardiologisches Symposium	02.12.2017, Munich	Martin Halle (Munich)

Project Groups

A total of 17 project groups existed at the DZHK by the end of 2017. These independent and relatively loose associations are composed of scientists from different partner sites with the aim of developing new project ideas on specific subjects. The project group “Konsortium zur Blutdruckepidemiologie (Consortium for Blood Pressure Epidemiology)” was able to publish novel findings on the development of high blood pressure (see also page 28). The project group eHealth was also particularly active. It met three times in 2017 and also organised two telephone conferences with the participation of numerous representatives from clinical application, IT and the field of public relations. In a draft paper, the aim of developing a DZHK app for various terminals (Android, iOS) and the related back-end for integration in the clinical research platform of the DZHK was described. With the development of such an app, the DZHK could take a leading role.

Internal Communication

The internal communication of roughly 1,500 scientists registered at the DZHK is still a big challenge. The most important instrument for this is the internal monthly newsletter, which had roughly 1,800 recipients at the end of the reporting year. In addition to the registered scientists, administrative employees of the partner institutions and the DZHK management are among the recipients. Among other things, the 2016 employee survey revealed that all internal communication should increasingly be carried out in English. In 2017, we have therefore started to communicate scientific subjects in the newsletter in English. We are planning to do this for the whole newsletter in 2018.

In the reporting year, we continued evaluating our employee survey by breaking down the results to partner site level. The partner sites are using this evaluation for internal discussions on the improvement of information and involvement within the partner sites.

Achievements in 2017

- ✓ Satisfaction of the DZHK Retreat participants increased
- ✓ Number of retreat participants increased
- ✓ At least two DZHK symposia carried out
- ✓ Administrative simplification of DZHK symposia
- ✓ Project group work produced concrete results

Goals for 2018

- Planning and organisation of the 2nd DZHK Conference
- Increase the number of participants at the Young DZHK Retreat
- At least two DZHK symposia carried out
- Internal newsletter now in English

Co-operations with Partners outside the DZHK



Successful translation will only be achieved with an interdisciplinary and cross-institutional network. It is therefore natural for the DZHK to co-operate with external partners that play an important role in the translation process.

In the field of cardiology and cardiovascular research, in Germany the DZHK works closely with the German Cardiac Society (DGK) and the German Heart Foundation. We held several talks with the latter in the reporting year and agreed on a closer collaboration in patient care and the promotion of young scientists, which will take effect in 2018.

Seeking advice from regulatory authorities for translational research projects has meanwhile become usual (see Chapter 3). The applicants normally have at least one consultation appointment at the Paul Ehrlich Institute (PEI) or the Federal Institute for Drugs and Medical Devices (BfArM) and may apply for separate funds for this.

External Co-operations with Science

DZHK researchers co-operate with scientific partners all over the world. In the reporting year, the DZHK commenced a new partnership with the British Heart Foundation. Both organisations want to invest half of a total of € 12 million each in order to fund pioneering research and promote the international collaboration between German and British cardiovascular researchers. One or several co-operation projects may be chosen per year which have up to € 2 million available to them per partner per year for a duration of several years. The first call for funding is in spring 2018.

In the field of preclinical research, we collaborated with 11 partners from all over Germany in 2017 within the scope of bilateral projects (see also Chapter 3). € 491,000 went to these external partners in total.

Within the scope of its clinical studies, the DZHK collaborates with university hospitals in Germany and Europe (see also Chapter 4). They recruit patients in DZHK studies and receive a patient fee in return. By the end of the reporting year, 59 sites of our external clinical partners were enrolling patients in studies fully funded by the DZHK. Some of our studies have started or have already finished paying patient fees to external sites.

The DZHK entered into a co-operation with the German Cancer Research Center (DKFZ) within the scope of its 1,000 Genomes Project (OMICs Resource). The DKFZ sequenced the genomes of 1,200 healthy control persons which will then serve as the basis of clinical research projects (see also Chapter 9).

Industry Co-operations

Consulting our principal investigators revealed that there were 14 ongoing industry co-operations in the reporting year. Many of our partner site projects as well as the studies and preclinical projects funded with flexible funds co-operate on an individual basis with industry partners. We were unable to enter into additional co-operations organised by the DZHK.



The idea of a broad comprehensive co-operation was carefully reviewed. However, we came to the conclusion that a co-operation of this kind is currently not useful, also in view of the decentralised structure of the association with its various member institutions.

External Co-operations for the Promotion of Young Scientists

As a comprehensive measure for the training and further development of the young scientists of all six German Centres for Health Research (DZG), the German Center for Diabetes Research (DZD) ran the first joint workshop for young scientists in the reporting period. The workshop on the subject “Translating Science into Clinical Practice” was held from 29 November to 1 December 2017 in Munich. Further workshops that will be organised by all DZGs in turn shall follow this first DZG workshop. Within this context, the DZHK is planning a workshop titled “Planning and designing a good clinical study” for 2018.

Together with the German Cardiac Society (DGK), we also organised three workshops as part of the series “Fundamentals of Cardiovascular Research” again this year:

- Finding one’s feet in the laboratory – Methods in cardiovascular basic research, 19 April 2017
- Drug development – The long journey to medication 28 June 2017
- Basic mechanisms of cellular biology 13 October 2017

From 2018, the respective summer workshop organised by the DZHK from the promotion of young scientists funding line will be held in English. This shall also enable the participation of non-German-speaking young scientists.

The **Young DZHK Postdoc Committee**, the advocacy for Postdocs at the DZHK, placed its focus in the reporting year on intensifying the collaboration with national and international early career researcher organisations:

- Early Career Section Academic Working Group of the American College of Cardiology
- Young DGK, the early career researcher organisation of the German Cardiac Society
- Scientists of Tomorrow, the early career researcher organisation of the European Society of Cardiology
- ATVB Early Career Committee (American Heart

Association)

- Young@Heart, the early career researcher organisation of the Netherlands Heart Institute

In collaboration with these organisations, the Young DZHK organised joint sessions at conferences, made the measures for the promotion of young scientists of the DZHK known, and invited speakers from the other organisations to the Young DZHK Retreat.

The Cardiological Competence Networks

Clinical studies of the Cardiological Competence Networks which are partially funded by the DZHK (DZHK-associated studies)

Acronym	Disease/ Study Goal	Study Type	Competence Network	Study participants, planned	Recruitment status
AFNET-EORP	Atrial fibrillation and clinical treatment	Registry	AFNET	3,500	3,500
AXAFA – AFNET 5	Atrial fibrillation, anticoagulation with NOACs, catheter ablation	Guideline-relevant study	AFNET	630	674
EAST – AFNET 4	Atrial fibrillation and stroke prevention	Guideline-relevant study	AFNET	2,745	2,676
DIAST-CHF	Heart failure	Cohort	KNHI	1,400 (number of 10-year follow-up examinations)	1,253
KNHI – TP 9a	Myocarditis	Guideline-relevant study	KNHI	120 (number of 10-year follow-up examinations)	78
KNHI – TP 9b	Heart failure	Guideline-relevant study	KNHI	650 (number of 10-year follow-up examinations)	1,682
CIBIS-ELD Trial	Beta-blockers in elderly patients with heart failure	Guideline-relevant study	KNHI	500 (number of follow-up examinations)	822
NRAHF	Congenital heart defects	Registry	KNAH	(open)	53,653
INH-Study	Chronic heart failure	Guideline-relevant study	KNHI	400 (number of follow-up examinations)	915
NOAH-AFNET 6	Atrial fibrillation, stroke prevention	Guideline-relevant study	AFNET	3,600	370

Competence Network for Congenital Heart Defects

The DZHK has been funding the Competence Network for Congenital Heart Defects (KNAHF) since 2015. The National Register for Congenital Heart Defects (NRAHF) is the core project of the collaborative research network supported by the cardiological professional associations DGPK, DGK and DGTHG. The NRAHF supports research activities all over the world with its powerful database infrastructure. The NRAHF has registered 52,000 patients, and the NRAHF's own biobank furthermore comprises approximately 7,000 gene and tissue samples. The KNAHF thus disposes of one of the largest research bases in the field of congenital heart defects.

Acting in a continuous exchange with patient and parent associations, organised in the action alliance Congenital Heart Defects, the KNAHF supervises clinical, epidemiological and genetic studies on congenital heart defects in all age groups and on cardiovascular diseases acquired during childhood. The nationwide association of physicians and scientists plans and realises these studies. Project-related, the NRAHF compiles the respective database and ensures legal security and the quality of data and samples.

Also in 2017, together with the DZHK, KNAHF realised research projects which are already finding their way into guidelines and hence into clinical practice. Pulsoxymetry screening was thus successfully included in the catalogue of postnatal routine examinations.

Based on the blood oxygen measurement, a series of severe congenital heart defects can be excluded with high certainty or alternatively treated promptly. With the help of the patient organisations organised in the action alliance Congenital Heart Defects (ABAHF), the Bundesverband Herzkrankte Kinder e.V. submitted an application for this at the competent Federal Joint Committee (G-BA) in September 2012. Since January 2017, the screening is compulsory as part of the check-ups U1/U2 immediately following birth.

In the future, a lot will continue to depend on the successful prevention, diagnostics and treatment of congenital heart defects and on the transfer of knowledge into the field of acquired cardiovascular diseases. The significant worldwide increase of patient numbers in both areas requires multicentre research on a permanent basis which moves the interests and needs of individual patients deliberately into the focus of medical and scientific action. KNAHF, sponsored by the German Heart Foundation, the Fördergemeinschaft Deutsche Kinderherzzentren e.V., and the Friede-Springer-Herz-Stiftung, will therefore dedicate itself to research and its effectual translation in the future in an even more broadly networked context under the roof of the DZHK.

 <http://www.kompetenznetz-ahf.de/en/home/>

Atrial Fibrillation Network

The Competence Network for Atrial Fibrillation e.V. (AFNET) is an academic research organisation that has set itself the aim of improving the life of patients with cardiovascular diseases. Scientists and physicians from hospitals and medical practices work together in AFNET in order to research new treatment methods for atrial fibrillation in particular. To this end, AFNET conducts science-initiated clinical studies and registries at a national and international level.


In 2017, the DZHK continued funding the three international clinical studies EAST – AF- NET 4, AXAFA – AFNET 5 and NOAH – AFNET 6, for which AFNET bears the overall responsibility as the sponsor, and the nationwide patient registry AFNET-EORP. Measures to enhance patient recruitment and support a study-specific biobank, as well as parts of the AFNET infrastructure, particularly project management in the branch office in Münster, were funded.

The AFNET-EORP registry (treatment of atrial fibrillation in Germany) and the EAST – AFNET 4 study (early rhythm control treatment) are currently in the follow-up

observation phase. The AXAFA – AFNET 5 study (anticoagulation during catheter ablation) has meanwhile been completed. The recruitment goal was reached in April 2017 and the results were published in March 2018. Patients have been enrolled in the NOAH – AFNET 6 study (anticoagulation in atrial high rate episodes) since June 2016.

The ongoing AFNET studies were funded by the DZHK and also supported by joint activities, e.g. with a stand at the annual conference of the German Cardiac Society (DGK).

AFNET is collaborating on the CLOSURE-AF-DZHK 16 study (atrial appendage closure in atrial fibrillation). Here, it is involved in project management and filling positions in committees. The study started patient recruitment in March 2018. Moreover, AFNET co-operates with the DZHK in the SMART-MI – DZHK 9 study (implantable monitor following myocardial infarction). AFNET supports the DZHK with the recruitment of study sites.

 <https://www.kompetenznetz-vorhofflimmern.de/en/home>

Competence Network for Heart Failure

The Competence Network for Heart Failure (KNHI) is a nationwide alliance for the research on heart failure. It has set itself improving prevention, early detection and treatment as its aim. Insights into the mechanisms of

heart failure and treatment options are gained through research. The aim is to integrate the acquired findings into medical care and thereby further improve the treatment of patients with heart failure.

Within the scope of the KNHI, the DZHK funds five studies, which were already initiated 10-15 years ago. The long-term follow-ups are currently in progress. Approximately 2,800 visits were realised and three of the five funded studies were completed by the end of 2017; the last visits of the follow-up phase will be realised next year.

Moreover, the KNHI itself is involved in two DZHK studies as a study site. In 2017, the Transition-CHF study was initiated and recruitment commenced; the CAVA-ADHF study will be initiated next year.

In order to directly improve patient care, the KNHI closely collaborates with the network of cardiologists “Heart Failure Bavaria”. With them, a quality assurance project was conducted and the outpatient/inpatient care model HeartCareBavaria was planned. In addition, a national curriculum for the further training of medical assistants for heart failure is being developed in agreement with the DGK and the certification committee for so-called Heart Failure Units. A high-level further training of this professional group will thereby be ensured in the future, which will thus contribute to strengthening the outpatient care of patients with heart failure.

 <http://knhi.de/en>

Achievements in 2017

- ✘ Development of framework conditions for individual co-operations with industry in the scope of HRHV projects and clinical studies
- ✓ Funds paid to external hospitals for patient fees
- ✓ Atrial Fibrillation Network: AXAFA – AFNET 5 and AFNET-EORP recruitment completed

Goals for 2018

- Decide on the further funding of competence networks
- DZHK-BHF co-operation tendered

Resources and Research Infrastructures



Clinical Research Platform

The DZHK is establishing resources long-term that may be used by all partners and also frequently by external scientists.

When creating resources in the DZHK, the focus lies in clinical research. The clinical research platform, including the collection of data and samples, is the most important and largest scientific infrastructure in the DZHK. It is described in more detail in Chapter 4.2.

Further resources and infrastructures will be briefly outlined below. We published the project database mentioned in the previous reporting year online. It is updated biannually. Our clinical standard operating procedures (SOPs) are also available online. They serve as models for many other consortia for their own processes.

OMICs Resource

With the “OMICs Resource”, the DZHK has created Germany’s largest control resource containing whole genomes of healthy individuals. The resource will contain DNA and RNA data sets of 1,200 individuals once data processing is completed. The samples are from six epidemiology cohort studies of our partner sites and are thus from all over Germany. Whole genome sequencing of DNA was conducted in Heidelberg at the German Cancer Research Center (DKFZ). RNA sequencing was carried out at the Max Delbrück Center (MDC) in Berlin. Both were able to be completed in the reporting year.

The successive data transfer of raw DNA data to Lübeck and Munich for data processing and storage started at the end of 2017.

Raw RNA data are processed in Berlin at the MDC. Data processing means that they are being edited for scientific analyses. This very time-consuming and computationally intensive process shall be completed in 2018. The data will subsequently be available for research purposes. Researchers from all medical specialties may use them as comparison data when searching for morbid changes in the human genome. The DZHK will therefore not only use the data for cardiovascular issues, but also make them available to external researchers from all over the world.

The DZHK invested a total of € 2.2 million in this valuable resource.



Shared Expertise

The DZHK summarises special know-how and specific laboratory methods of the DZHK partner institutions under the term “Shared Expertise”. All DZHK researchers may use Shared Expertise in the scope of bilateral small research projects. A total of 165 Shared Expertise were offered in the reporting year (2016: 155). Shared Expertise have been among the most popular and best known funding options in the DZHK from the beginning (see also Chapter 3)

➔ www.dzhk.de/research/preclinical-research/shared-expertise/

Stem Cell Registry

The Biobank Registry contains data pertaining to the induced pluripotent stem cells existing at the DZHK. The data sets can be filtered according to various features and thus allow researchers to make targeted requests to use the cells. At the end of the reporting year, the registry contained 179 data sets from the Göttingen, Hamburg and Munich partner sites. Further data sets from other partner sites shall be added. Usage requests have been received from working groups in Göttingen and Munich.

➔ <https://dzhk.de/resources/stem-cell-registry/>

Achievements in 2017

- ✓ OMICs Resource: whole genome and RNA sequencings completed
- ✓ OMICs Resource: processing generated raw data started
- ✓ Online publication and biannual update of project database

Goals for 2018

- OMICs Resource: Complete processing of raw data
- OMICs Resource: first usage applications received

The DZHK in the Public



Public Relations

We had planned to increase the output of public relations work and therefore, in the reporting year, published 24 press releases in German (2016: 13). 20 of those were also in English. In 2017, we quantitatively measured what response the online press releases had for the first time, and will continue to do so. According to this, the German press releases led to 341 mentions on websites, including many online presences of renowned newspapers and journals as well. This corresponds to an average of 14 mentions per press release. The English press releases led to only 2.5 mentions per press release, some of which were even in Arabic. We see scope for improvement in the international dissemination of our press releases.

Facebook, Twitter & Co

In 2017, we expanded our social media activities. For instance, there is now a LinkedIn profile and a Twitter account for the DZHK, which already had 200 followers by the end of the year. With regular Facebook posts aimed at the general public, we were able to increase our followers from 400 to 757 in 2017. This corresponds to a growth of 80 percent (2016: 29). Increased interactions with the posts (likes, link clicks, comments and sharing the content) showed that our followers are fans and truly interested in the matter.

YouTube: "Mit herzlichen Grüßen"

A highlight of 2017 was the release of our hip-hop video "Mit herzlichen Grüßen". Since going live in September, it was viewed 4,567 times on Facebook and 6,562 times on YouTube by the end of 2017.

The video was shared 81 times on Facebook, including by Eckart von Hirschhausen. The video yielded the biggest response from a younger target audience (25-34 year-olds), such as students. With 410 Facebook likes and 94 likes on YouTube, it is the most successful DZHK video to date, and positively contributes to public awareness and a community spirit of the DZHK. The popularity of the video rubbed off on the whole YouTube channel. The number of hits increased here overall too.

We also released another video from the series "Elevating Science". In it, Prof. Stefanie Dimmeler explains how the DZHK is developing new innovative therapies. All Elevating Science videos had 3,834 views by the end of the reporting period.

Website: The Number of Users Is Increasing

The number of hits online has further increased and was at 210,000 visits in 2017. Particularly the hits for

the areas of clinical research have increased, which accounts for the focus of our research strategy on this subject. We have added further subdomains to our website, including for the 1st Conference on Translational Medicine and our Retreat. In addition, further study websites as well as study logos and flyers have been developed. Further newly started studies were added to the Proband Information Platform (PIP) and the first uses of data and biosamples were displayed there. We are aiming for a greater awareness of the PIP next year. This coincides with the website relaunch and the first usage notifications. How we will present the usage projects in a readily comprehensible and up-to-date manner for study patients will also be a focus next year.

We have also started to develop a slide deck that shall move the importance of cardiovascular research into the focus of multipliers and decision-makers, and to highlight the special role of the DZHK in this context.

Meeting/Conference	Date/Place	In co-operation with
46 th Annual Meeting of the German Society of Thoracic and Cardiovascular Surgery (DGTHG) and the 49 th Annual Meeting of the German Society of Paediatric Cardiology (DGPK)	11 - 14 February, Leipzig	Competence Network for Congenital Heart Defects
83 rd Annual Meeting of the German Cardiac Society (DGK)	11 - 22 April, Mannheim	Cardiological Competence Networks
16 th GAIN Annual Meeting (German Academic International Network)	25 - 27 August, San Francisco	DZG

Achievements in 2017

- ✘ Public awareness of the Proband Information Platform (PIP) increased
- ✓ Publication of at least 24 press releases per year
- ✓ Publication of all press releases in English as well
- ✓ Social media activities intensified
- ✓ Project database of scientific DZHK projects published online
- ✓ Press responses increased

Goals for 2018

- Soft relaunch of the website
- Create DZHK patient videos for our study participants
- Create DZHK patient flyers for our study participants
- Create explanatory videos for users of the clinical research platform
- Increase response to the English press releases

Indicators for the Success of Translational Research



Indicators for the success of translation

Indicator	Definition	2017 (2016)
Short and medium term indicators		
1. Physician Scientists	Percentage of scientifically employed (licenced) physicians among the 1,433 researchers registered at the DZHK	49% (51 %)
2. Co-operations between partner sites	a. Number of Shared Expertise Projects (year)	27 (66)
	b. Number of publications with at least two DZHK authors from different partner sites	116 (95)
	c. Number of current major multicentre projects (recruiting DZHK studies and HRHV) (31 Dec.) in which multiple DZHK partner sites are involved	15 (7)
	d. Number of cooperative project groups (31 Dec.)	17 (16)
	e. Number of visiting scientist sojourns at other DZHK partner sites (year)	8 (10)
3. Communication with regulatory authorities	Consultation appointments (e.g. PEI, BfArM) in the scope of recruiting DZHK studies, HRHV projects and partner site projects (year)	1 (2)
4. Co-operation with industry	Co-operations with industrial partners in the scope of recruiting DZHK studies, HRHV projects and partner site projects (31 Dec.)	13 (17)

Indicators for the success of translation

Indicator	Definition	2017 (2016)
Short and medium term indicators		
5. Cooperative structures in clinical research	a. Type (quality) of cooperative structures (31 Dec.)	Central clin. res. infrastructure (Data Handling Unit, Trusted Third Party, Laboratory Information Management System, Image Data Management System and Ethics Project, Use & Access), Stem Cell Registry, OMICs Resource
	b. Number (quantity)	
	- of patients registered in the ZDM (31 Dec.)	3,543 (1,913)
	- SOPs (31 Dec.)	21 (15)
	- usage applications/notifications for data and biological materials (year)	0/4 (0/1)
	- approved usage applications/notifications (year)	0/1 (0/0)
6. High-ranking publications	All publications with DZHK affiliation and an impact factor >10 (year)	112 (108)
7. Preclinical projects and clinical studies	a. Number of HRHV projects and recruiting DZHK studies (31 Dec.)	23 (11)
	b. Publications resulting from HRHV projects and clinical studies (year)	13 (1)
Long-term success criteria		
8. Revised medical guidelines	Number of guidelines which have been revised as a result of DZHK studies and DZHK-associated studies (total)	1 (0)
9. New therapeutic and diagnostic principles	Number of new therapeutic and diagnostic principles which have been developed within the scope of DZHK projects and reached clinical application (total)	0
10. Patients treated according to new therapeutic and diagnostic principles	Number of patients who were treated according to new therapeutic or diagnostic principles developed by DZHK researchers (total) (measurability is questionable)	0

Comments regarding the table:

- *Definition of DZHK studies: financed with competitive/flexible funds; predominately or fully financed by the DZHK; study uses the infrastructure for clinical studies of the DZHK.*
- *All indicators are related exclusively to projects which are financed with DZHK funds; no indicator is related to the research of DZHK member institutions financed otherwise. For simplified documentation, the indicators 2a, 2c, 2e, 5, 7 and 8 refer exclusively to competitive/flexible DZHK funds and not to DZHK partner site projects.*

Facts and Figures

The German Centres for Health Research

With the German Centres for Health Research (DZG), the German Federal Ministry of Education and Research (BMBF) started to establish structures in 2009, the main objective of which is to optimise the translation process from research result to patient application, i.e. bringing new medical research results into application more quickly in order to improve the prevention and therapy of widespread diseases.

📄 <https://www.bmbf.de/en/pooling-research-to-tackle-common-diseases-2592.html>

Researchers and physicians from all over Germany join forces in the six German Centres of Health Research (DZG) so that patients can benefit from the results of research studies more quickly. They united in order to fight major widespread diseases, such as diabetes, cardiovascular diseases, cancer, neurodegenerative diseases, infections and lung diseases with the latest scientific knowledge.

Collaboration between the DZGs was coordinated by the DKTK in 2017. The DZHK Board of Directors and the DZHK Managing Director met in July at Frankfurt Airport in order to prepare the DZG-wide development paper, which was given to BMBF on 3 November 2017 and was discussed on 27 November at the DZG Discussion Forum. It was also decided to pool competence in the field of medicinal chemistry and start a DZG-wide initiative.

The members of the expert group support and advise from the planning phase onwards and during the conduct of the project in the field of medicinal chemistry, particularly in the identification of lead structures and the optimisation of low molecular weight agents towards clinical development candidates. For a pilot phase of three years, one to two projects per DZG can be conducted.

In the reporting period, the six DZG managing directors/administrative directors corresponded via monthly telephone conferences and prepared, among other things, the first joint appearance of all DZGs at the GAIN meeting (German Academic International Network), which took place in August 2017 in San Francisco. Prof. Eschenhagen and Prof. Kroenke introduced the six DZGs in a workshop and all six DZGs ran a stand together at the GAIN talent fair. The six DZGs held an event as part of the World Health Summit in October 2017 for the first time jointly with the Helmholtz health research centres. The focus was on a comparison between translational research in Germany and other countries or research systems.

In the reporting period, work on a common DZG research magazine started with a kick-off event at the layout agency. The commissioned editor created a project schedule, according to which the first issue's publication is planned for mid-2018. The DKTK has provided a sharepoint as a platform for the collaboration within the scope the project. Furthermore, on behalf of all DZGs, the DZHK successfully campaigned for the DZGs' inclusion on the online platform "Research in Germany". Implementation is planned for 2018.

DZG DEUTSCHE ZENTREN
DER GESUNDHEITSFORSCHUNG

Finances and Staff



Finances of the DZHK

In the reporting year of 2017, the DZHK had at its disposal for the third time the full annual funding amount promised since its foundation of about 41 million euros of new funds plus a carry-over from 2016 totalling 13.8 million euro. From this amount, funds totalling 44.1 million euro were drawn (2016: 39.9 million euro).

In 2017, the DZHK has thereby once again increased its spending by 10 percent compared to 2016. The funds that it has not spent have been carried over to 2018. Speaking in relative figures, the outflow of funds relative to the respective new funds (annual budget without a carry-over from previous years) was at 74 percent in 2015, 97 percent in 2016 and 108 percent in 2017.

The outflow of funds was not even higher in 2017, primarily because clinical studies and clinical infrastructure projects were further delayed.

Reasons for this are to some extent real delays resulting from the complexity of multicentre studies, but also to some extent the lack of experience at the time these projects were applied for and approved – the required funds had not been distributed realistically enough over the years of the respective project periods. For this reason, we will continue to approve funds for clinical studies closer to the end of the project period.

With a great number of projects newly started in 2017, among other things, we are working on maintaining the outflow of funds at a high level in 2018 and thus continue reducing the funds carried over from previous years.

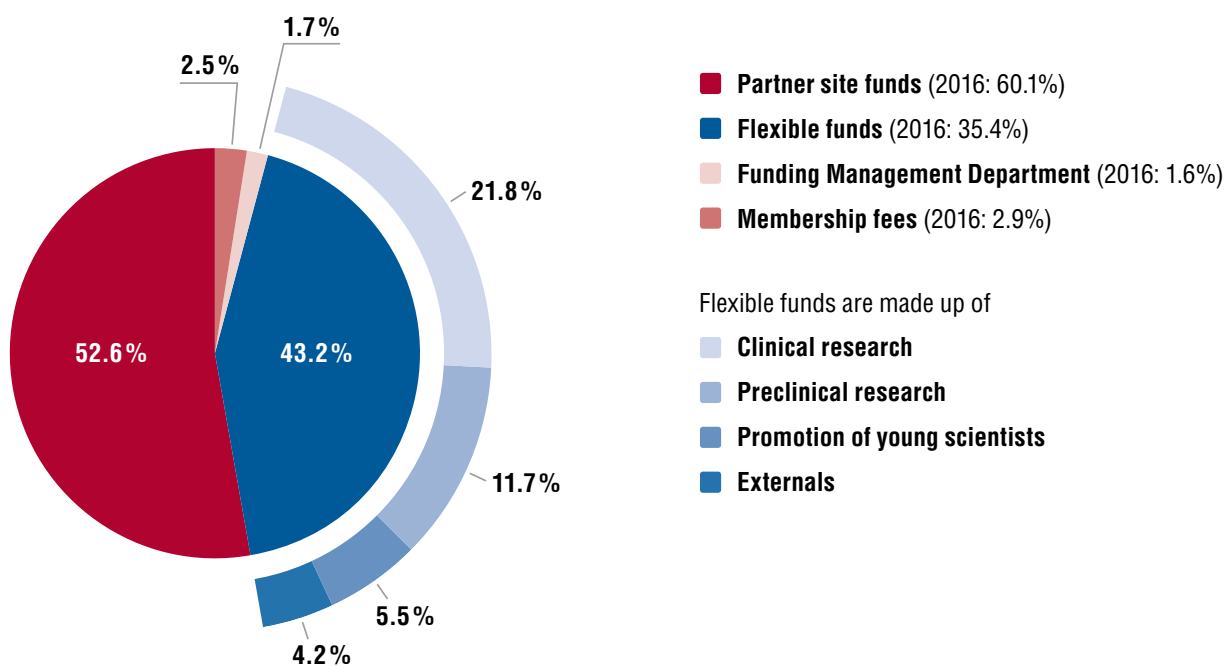
With the initiatives that have meanwhile been started, the DZHK is now clearly for the coming years. More projects have been approved and are in the planning phase than we actually have funds for. If the budget remains the same, we can only start new projects from 2018 onwards when old projects end – even though we have a substantially higher number of applications that were reviewed and found to be excellent.

We are therefore emphatically striving for an increase and an inclusion in the “Pact for Research and Innovation”, which would mean a regular budget increase at currently 3 percent per year. The transition from the phase of being concerned about a sufficient outflow of funds to a phase of having to economise with scarce funds will preoccupy the Funding Management Department, the Main Office and the partner site managements in 2018.

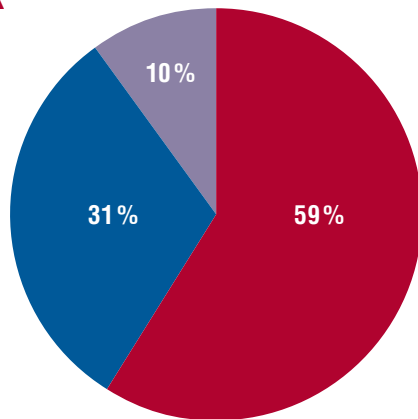
The drawn (expended) funds for 2017 amounting to 44.1 million euro break down as follows:

- **Partner site funds:** 23.2 million euro
- **Flexible funds:** 19 million euro (this includes 9.6 million euro for clinical research, 5.2 million euro for preclinical research, 2.4 million euro for the Training Programme and 1.8 million euro for externals (including 1.5 million euro for Competence Networks and 300,000 euro for co-operations with externals))
- **Membership fees:** 1.12 million euro (Predominantly contributions for the Main Office budget for 2018 amounting to 1.14 million euro)
- **Funding Management Department:** 700,000 euro

Allocation of DZHK funds expended in 2017 to areas of planned funding



Staffing costs/material costs/investment resources of the DZHK



- **Staffing costs: 29.5 million euro**
(2016: 22.9 million euro)
- **Material costs: 15.6 million euro**
(2016: 8.6 million euro)
- **Investments: 5 million euro**
(2016: 8.4 million euro)

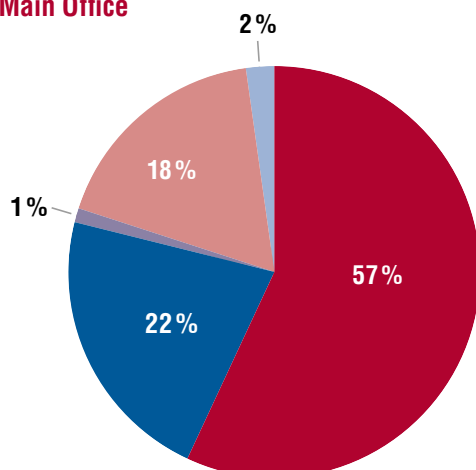
DZHK Main Office Budget

In 2017, the budget of the DZHK e.V. Main Office, which is financed by membership fees, amounted to 1.1 million euro (2016: 1 million euro). Of this total, 1.05 million euro were membership fees and 58,000 euro were carried over from the budget year 2015 to 2017.

1.02 million euro (2016: 0.98 million euro) of which were expended; the miscellaneous revenues amounted to 18,000 euro. The General Assembly of Members of the DZHK shall decide on the use of the resulting surplus amounting to 100,000 euro in September 2018.

Schomerus & Partner Berlin (tax counsellors, attorneys, financial auditors) were commissioned to prepare the annual financial statement of the association.

Staffing costs/material costs/investment resources of the Main Office



- **Staffing costs: 570,000 euro**
(2016: 560,000 euro)
- **Material costs: 230,000 euro**
(2016: 240,000 euro)
- **Investments: 10,000 euro**
(2016: 10,000 euro)
- **Public relations: 186,000 euro**
(2016: 151,000 euro)
- **Contributions (TMF e.V.): 20,000 euro**
(2016: 20,000 euro)

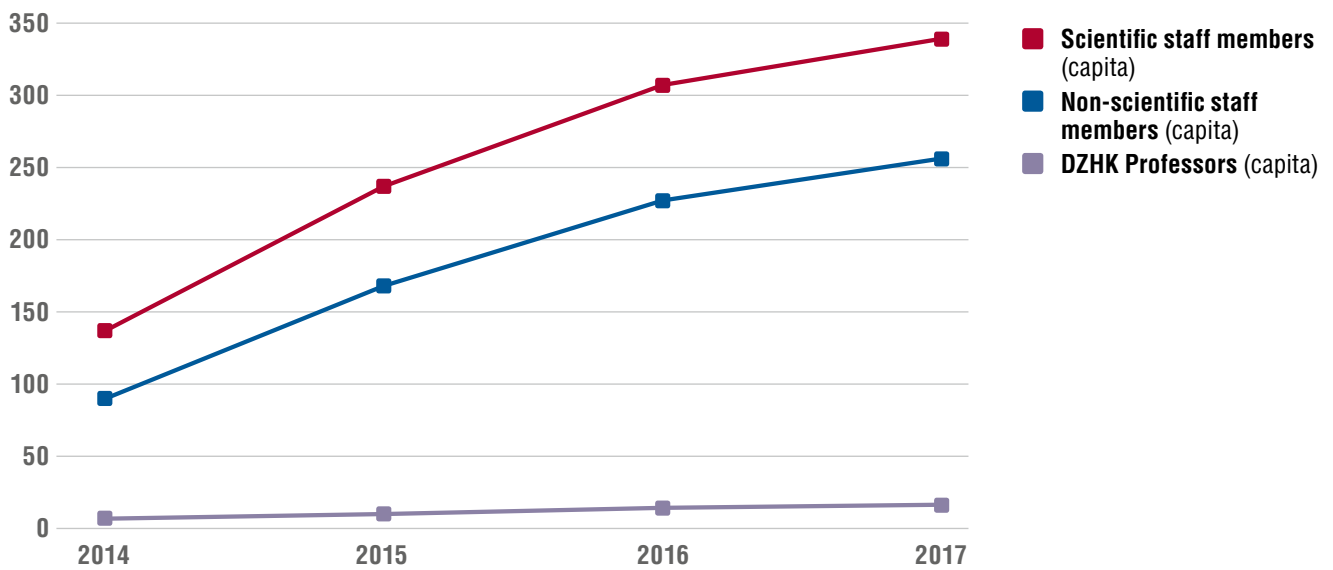
Staff

As of the reporting date, 31 December 2017, 431.13 (2016: 403.58) full-time equivalents (FTE), or 610 (2016: 532) persons or “capita” were financed by DZHK funds. This also included 16 employees of the DZHK Main Office, 12 employees of the Funding Management Department and 23 employees in the Competence Networks.

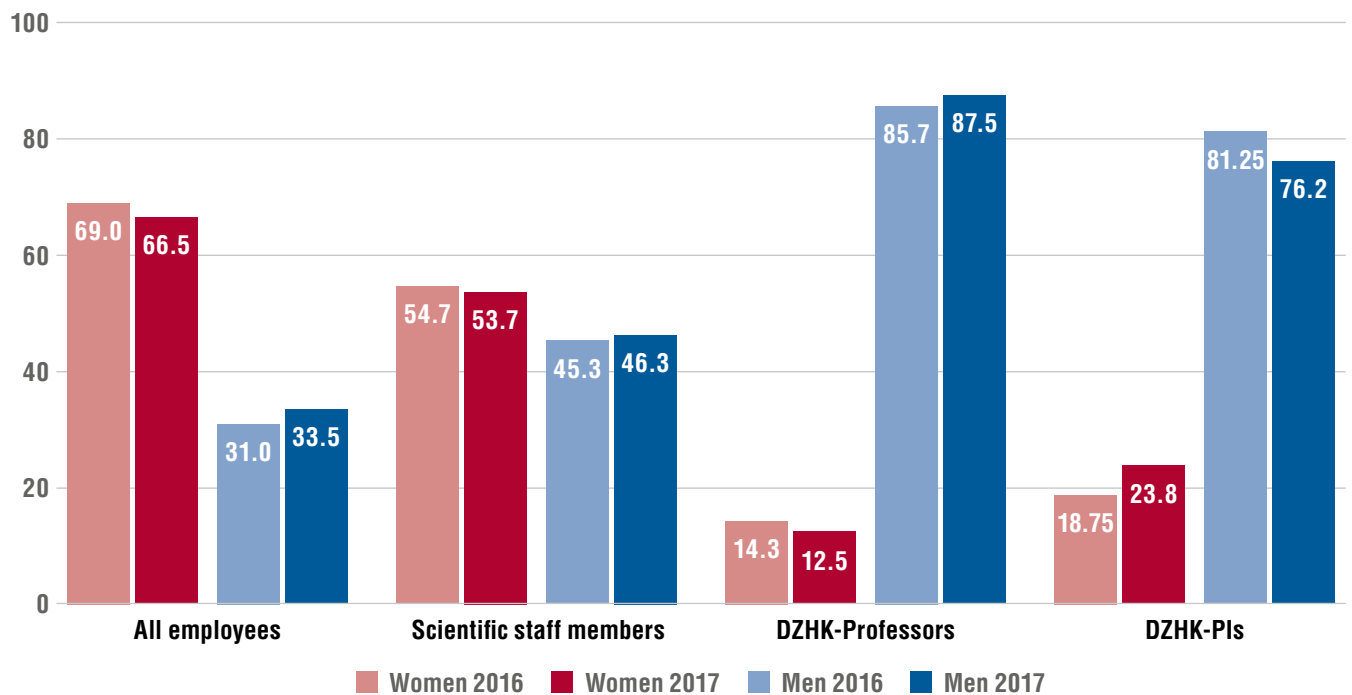
Number of employees financed by the DZHK 2014-2017

	2014	2015	2016	2017
Number of employees (as of 31 December) FTE	165.77	286.5	403.58	431.13
Number of employees (as of 31 December) capita	234	415	532	610
of which are male	78	130	165	207
of which are female	156	285	367	403
Number of scientific staff members (FTE)	96.54	154.39	220.76	237.23
Number of scientific staff members (capita)	137	237	307	339
of which are male	58	98	139	157
of which are female	79	139	168	182
Number of non-scientific staff members (FTE)	62.23	122.11	168.82	179.50
Number of non-scientific staff members (capita)	90	168	227	255
of which are male	15	26	27	36
of which are female	75	142	200	219
Number of DZHK Professors (FTE)	7	10	14	14.40
Number of DZHK Professors (capita)	7	10	14	16
of which are male	5	8	12	14
of which are female	2	2	2	2
For information only: additionally planned professorships	0	14	9	5

Development of DZHK employees 2014–2017



Gender distribution at the DZHK in percent – 2016/2017 comparison



Principal Investigators (PIs), DZHK Scientists, Young DZHK Members

In addition to the scientists funded by the DZHK, principal investigators (PIs) are of central importance to the DZHK. In most cases, the PIs are not funded by the DZHK. However, they contribute their ideas and expertise in the co-operation within the DZHK and thus provide the basis of our success. In the reporting year, the DZHK had 151 PIs (2016: 144). PIs are appointed by the partner sites and confirmed by the General Assembly of Members. Each partner site disposes of a maximum of 20 PI positions, whereby at each site there are additional positions for each DZHK Professor appointed with the help of DZHK funds at the partner site. The following PIs were newly appointed in autumn 2017 at the General Assembly of Members:

Göttingen Partner Site:

Lutz Ackermann, Susann Boretius, Sarah Köster, Stephan von Haehling (simultaneously DZHK Professor), Bernd Wollnik

Greifswald Partner Site:

Jens Fielitz (simultaneously DZHK Professor)

Hamburg/Kiel/Lübeck Partner Site:

Ingo Eitel, Inke König, Christian Meyer, Oliver Müller (simultaneously DZHK Professor), Renate Schnabel, Edzard Schwedhelm

Heidelberg/Mannheim Partner Site:

Gergana Dobрева, Dirk Grimm, Jörg Heineke, Florian Leuschner, Martina Schnölzer, Lars Steinmetz, Mirko Völkers, Joachim Wittbrodt

Munich Partner Site:

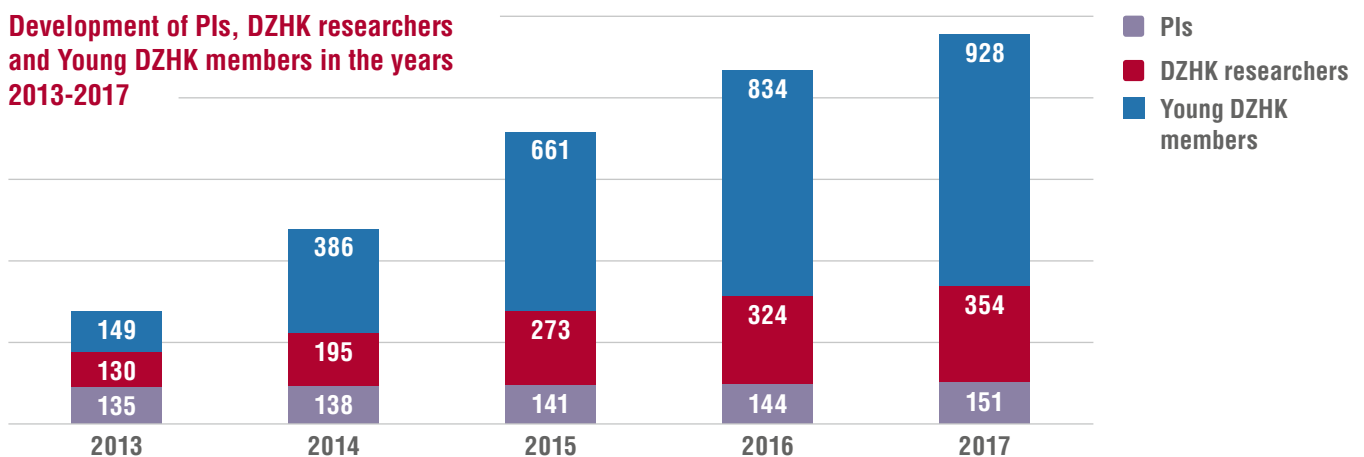
Michael Joner (simultaneously DZHK Professor), Christian Schulz, Sabine Steffens

Rhine-Main Partner Site:

Holger Nef, Thomas Walther

In order to assign scientists who are not PIs to the DZHK, there are two statuses: “Young DZHK member” and “DZHK researcher”. Both statuses must be applied for. Prerequisites are a defined commitment within the DZHK and the possibility of being assigned to one DZHK PI working at a partner institution. In the reporting year, the DZHK had 354 DZHK researchers (2016: 324) and 928 Young DZHK members (2016: 834).

Development of PIs, DZHK researchers and Young DZHK members in the years 2013-2017



Scientific Achievements, Prizes and Awards



The DZHK has had rules for a joint DZHK affiliation and a DZHK acknowledgement since 2012.

Here, we present the figures of the respective publications (see also Chapter 5). A complete list of the publications with DZHK affiliation or DZHK acknowledgement can be found online:

<https://dzhk.de/en/research/publications>

In addition, every month the DZHK Board of Directors selects a Paper of the Month, which is subsequently announced in the DZHK Newsletter and published online via the DZHK website (see p. 25).

Publications in 2017

	Anzahl 2017	(2016)
DZHK affiliation	951	(670)
DZHK acknowledgement	34	(34)
First authorship of a DZHK PI	46	(28)
Last authorship of a DZHK PI	271	(210)
First authorship of a Young DZHK member	196	(142)
First authorship of a DZHK researcher	104	(not recorded)
Last authorship of a DZHK researcher	204	(not recorded)
Co-operation with another DZHK partner site (PI)	115	(95)
Journals by Nature Publishing Group	30	(31)
Journals by Cell Press	5	(8)
NEJM, Lancet, JAMA	10	(8)
Circulation, Circ Res, EHJ, JCI, JACC	66	(56)
Science	2	(5)

Prizes, Grants, Personalia 2017

Name	Prizes, Grants, Personalia
Backs, Johannes (Heidelberg/Mannheim)	Arthur Weber Award 2017
Dimmeler, Stefanie (Rhine-Main)	Willy Pitzer Award
Frahm, Jens (Göttingen)	Jacob Henle Medal for his life's work
Friedrich, Matthias G. (Heidelberg/Mannheim)	President of the Society for Cardiovascular Magnetic Resonance (SCMR)
Gerhardt, Holger (Berlin)	6 million US dollars from the Fondation Leducq for the project "ATTRACT: Arterial flow as attractor for endothelial cell migration"
Heeger, Christian-H. (Hamburg/Kiel/Lübeck)	Eric N. Prystowsky Fellow Clinical Research Award 2017
Hinkel, Rabea (Munich)	Starting Grant of the European Research Council (ERC)
Hitz, Marc-Phillip (Hamburg/Kiel/Lübeck)	Science Award 2017 of the German Society of Paediatric Cardiology
Hoff, Kirstin (Hamburg/Kiel/Lübeck)	Young Investigator Award 2017 of the German Society of Paediatric Cardiology
Jobs, Alexander (Hamburg/Kiel/Lübeck)	AGIK Publication Prize
Katus, Hugo (Heidelberg/Mannheim)	President of the German Cardiac Society e.V.
Kayvanpour, Elham (Heidelberg/Mannheim)	Science Award of the Dresdener Herz-Kreislauf-Tage 2017
Kelle, Sebastian (Berlin)	Appointed as W2 Professor for "Molecular and Functional Coronary MRI Imaging" at the Charité – Universitätsmedizin Berlin
Lauten, Alexander (Berlin)	Dr. Rusche Research Project Award
Mägdefessel, Lars (Munich)	DFG Heisenberg Professorship
Meder, Benjamin (Heidelberg/Mannheim)	Wilhelm P. Winterstein Award 2017 of the German Heart Foundation
Nikolaev, Viacheslav (Hamburg/Kiel/Lübeck)	Albert-Fraenkel-Preis 2017

Name	Prizes, Grants, Personalia
Oehring, Robert (Greifswald)	Kaltenbach Doctoral Stipend of the German Heart Foundation
Petzold, Tobias (Munich)	Franz Maximilian Groedel Science Award 2017
Sager, Hendrik (Munich)	Starting Grant of the European Research Council (ERC)
Pokorny, Saskia (Hamburg/Kiel/Lübeck)	Sick Advancement Award 2017 of TU Hamburg for best dissertation
Schellinger, Isabel N. (Göttingen)	Rainer Greger Doctoral Thesis Award of the German Society of Nephrology
Schmidt, Constanze (Heidelberg/Mannheim)	August Wilhelm and Lieselotte Becht Science Award
Schrepfer, Sonja (Hamburg/Kiel/Lübeck)	2.6 million dollar research funding from the Center for the Advancement of Science in Space (CASIS)
Sedaghat-Hamedani, Farbod (Heidelberg/Mannheim)	Winner of the Young Investigator Award at the DGIM 2017
Sibbing, Dirk (Munich)	Pro Merito Award and nomination as an honorary member of the Hungarian Cardiac Society
Söhnlein, Oliver (Munich)	ESC Outstanding Achievement Award 2017 Visiting Professor of “Inflammation Research” at the Karolinska Institute in Stockholm, Sweden
Stellos, Konstantinos (Rhine-Main)	Starting Grant of the European Research Council (ERC) Oskar Lapp Science Award 2017
Toischer, Karl (Göttingen)	August Wilhelm and Lieselotte Becht Science Award
Trembinski, Dorotée-Julia (Rhine-Main)	Young Investigator Award beim Dutch-German Joint Meeting of the Molecular Cardiology Groups
Wang, Dong (Hamburg/Kiel/Lübeck)	Young Scientist Award of the German Society of Thoracic and Cardiovascular Surgery (DGTH)
Zeiber, Andreas (Rhine-Main)	President-Elect of the German Cardiac Society e.V.
Zeller, Tanja (Hamburg/Kiel/Lübeck)	Spokesperson of the e:Med Project committee

Facts and Figures

Administration

DZHK Administration

The employees of the Main Office, the Funding Management Department and the seven partner site managements together constitute the scientific administration of the DZHK. In 2017, their collaboration was once again close and cooperative, including within the scope of 31 weekly video conferences and four face-to-face meetings held either at the partner sites or the DZHK Main Office. In addition to the exchange on the respective current DZHK funding procedures and all administrative operations from filing applications to business reporting, a focus in 2017 of the joint work efforts was set on organising the first DZHK idea contest.

Main Office

In the reporting year, 16 employees including the managing director were working in the Main Office (14 FTE on 31 December 2017). The Main Office primarily supports the association's Board of Directors in coordinating scientific co-operation in the DZHK.

In the reporting year, this included in particular:

- Organising regular calls as well as the selection and evaluation procedures in the three cooperative areas: preclinical research, clinical research, and promotion of young scientists
- Organising the Mentoring Programme
- Connecting the first institutions to the Laboratory Information Management System and managing the co-operation between the central clinical-scientific infrastructure and DZHK studies
- Organising the Young DZHK Retreat and the DZHK Retreat
- Developing the co-operation with the British Heart Foundation (BHF)
- Controlling the outflow of funds together with the Funding Management Department and the partner site managements
- Organising, preparing and following-up all committee sessions
- Managing press and PR work as well as internal communication of the DZHK



Employees of the DZHK Main Office

Funding Management Department

The Funding Management Department (FMM) as part of Max Delbrück Center for Molecular Medicine in the Helmholtz Association (MDC) is entrusted with the administrative realisation of the funding of the DZHK partner institutions and external co-operation partners. It is authorised to review applications on their compliance with grant legislation as well as to inspect the use made of the funds in accordance with the DZHK provisions and the conditions of grant use of the German Federal Ministry of Education and Research (BMBF). The Funding Management Department also compiles controlling reports for the partner sites in order to support them with an effective budget management.

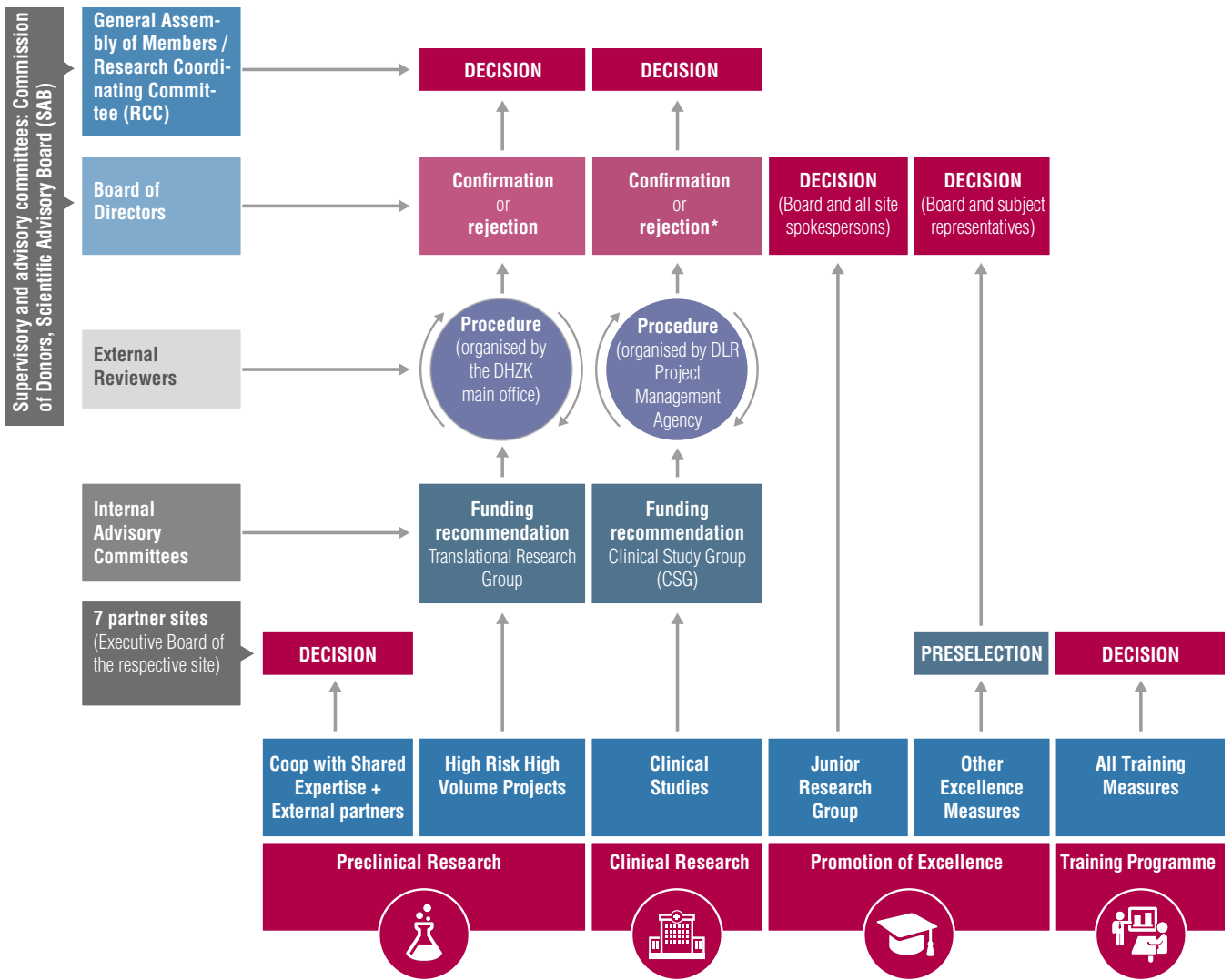
In the reporting year of 2017 the FMM was again responsible for forwarding funds for project funding to 28 of the 32 partner institutions of the DZHK. The five partner institutions to which the FMM does not forward any funds are: Robert Koch Institute (since it is a government research facility), University of Göttingen (funding only goes to the University Medical Center Göttingen, which is a member itself), University of Heidelberg (funding only goes to Heidelberg University Hospital, which is a member itself), Max Planck Institute for Experimental Medicine Göttingen (no funding so far), Max Delbrück Center for Molecular Medicine in Berlin-Buch (no 'forwarding' of funds). In addition, funds are forwarded to external co-operation partners, amounting to 41 in 2017 (70 in 2016), among which the three Competence Networks are funded. Altogether, 617 projects were funded in the reporting year (2016: 634 projects).

The FMM counted 10.3 FTE (12 capita) as of 31 December 2017. A position in the area finances/contract preparation was subsequently filled on 1 January 2018. The FMM positions, thus totalling 13, include management, scientific evaluation, review of applications and confirmation of use, controlling, secretariat and contract management.

Partner Site Management

By the end of 2017, one full-time or part-time employed scientist funded by the DZHK (partner site manager) and one full-time administrator funded by the DZHK worked at each of the seven decentralised partner site managements. Since the end of 2016, we have increased the originally low staffing ratio by adding a part-time position for a scientist at most of the partner sites in order to manage the marked increase in science-related tasks. The partner site managements are the interfaces between the scientific projects, partner site speakers, third-party funding administrations, human resources departments, deaneries of the research offices, legal departments, the DZHK Main Office and the FMM. The partner site managements coordinate all activities of the partner site. They organise partner site retreats, PI meetings and the work of the partner site's board of directors. In addition, each one carries out decentralised finance controlling for its respective site and coordinates the application and reporting system. They develop the procedures and processes at the DZHK together with the Main Office and FMM.

Procedural organigram of the DZHK for making funding decisions



*By Selection Board (2 board members, 2 SAB members, 2 CSG-representatives)

Partner Sites



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

Partner site Berlin

Partner site Spokesperson: Vera Regitz-Zagrosek, Director of the Institute for Gender Research in Medicine (GiM), Charité – Universitätsmedizin Berlin

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

Partner site Management: Carola Schubert (Partner site Manager), Mariam Abou-Saleh (Partner site Clerk), Charité – Universitätsmedizin Berlin

Partner Institutions at the DZHK Berlin site

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

Research Focus within the DZHK

The member institutions at the Berlin partner site focus on the clinical and translational investigation of heart failure, vascular and metabolic diseases as well as gender aspects in clinical application, research and academic teaching (Charité). Researchers at the MDC are primarily concerned with basic and translational research in the field of genomics, vascular biology, molecular cardiology and myocardial function, whereas the DHZB focuses on surgery in cases of cardiac insufficiency, transplantation and assistance systems as well as cardiovascular diseases in children. The RKI and DIfE (Federal State of Brandenburg) also belong to the member institutions where researchers are concerned with epidemiological studies and with the subjects of nutrition and metabolism. In 2017, the studies CTSN-TR with its main study centre at DHZB and Ex-VAD with its main study centre at Charité - Campus Virchow started recruiting at the Berlin partner site. In addition, the CLOSURE-HF study, currently the largest clinical study worldwide on the best possible therapy in patients with atrial fibrillation, started at Charité - Campus Benjamin Franklin. Furthermore, four new studies were released for funding by the RCC and were formally applied for. The studies concerned are METRIS-HF, DYNAMIC-MR, COLIMA (all three main study centres are at Charité) and PRAISE, which is funded together with the DZNE.

Among young scientists, it was not only the new training measure “Clinical Studies Training Programme” that proved highly popular. In the second half of the year, six measures for the professional development of medical staff working in clinical studies were already carried out.

In February 2017, Prof. Christoph Knosalla of the DHZB was appointed as the DZHK W2 Professor for heart failure surgery.



Max Planck Institute for Biophysical Chemistry

Partner site Göttingen

Partner site Spokesperson: Wolfram H. Zimmermann, Director of the Institute for Pharmacology at the University Medical Center Göttingen

Vice Partner site Spokesperson: Eberhard Bodenschatz, Director of the Max Planck Institute for Dynamics and Self-Organisation

Partner site management: Axel Kaul (Partner Site Manager), Uschi Hübner (Scientific Project Manager) since November 2017, Sylvia Vann (Partner Site Clerk), University Medical Center Göttingen

Partner Institutions at the DZHK Göttingen site

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

Research Focus within the DZHK

The focus of the Göttingen DZHK partner site is research on heart failure with the subjects “Mechanisms of the transition from clinically asymptomatic cardiac insufficiency to symptomatic heart failure as well as heart regeneration in case of heart failure”. At the Göttingen partner site, the focus lies on infrastructure support across eleven partner site projects and three DZHK Professorships (Anker, Luther, Uecker). 2017 was particularly focused on the strategic planning for 2019 and 2020 and beyond. The General Assembly of Members at the Göttingen partner site decided on ten partner site projects, the continuation of DZHK Professorships (Luther and Uecker), and the establishment/new appointment of DZHK Professorships for innovative clinical studies (successor Anker), metabolic cardiology (von Haehling) and paediatric cardiovascular genetics and developmental biology (call in 2020). Three clinical studies and two high risk high volume studies are currently being coordinated by the Göttingen DZHK partner site.

After two years of construction, the DZHK research facility of the UMG was inaugurated on 12 September 2017.

The scientific focus of the working groups based there is ultra-high resolution imaging and electrophysiology. In order to further strengthen the relationship between heart and brain research in Göttingen, a Heart and Brain Center Göttingen (HBCG) will be established following the approval of the “Joint Science Conference (GWK)” of the Federal Government and Federal States on 4 April 2017. Interdisciplinary scientific studies shall be conducted there in close co-operation with the DZHK and DZNE in the future.



University Medicine Greifswald

Partner site Greifswald

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

Vice Partner site Spokesperson: Ulrich John, Director of the Institute for Epidemiology and Social Medicine at University Medical Centre Greifswald (since January 2018: Marcus Dörr, University Medical Centre Greifswald)

Partner site Management: Stefan Groß (Partner site Manager), Anne-Kathrin Beiersdorf (Partner site Clerk) [since July 2017: Susanne Franck], University Medical Centre Greifswald

Partner Institutions at the DZHK Greifswald site

University Medical Centre Greifswald

Research Focus within the DZHK

Special expertise of the Greifswald partner site is in conducting population-based epidemiological and clinical

studies with comprehensive cardiovascular phenotyping, research on the prevention of systolic/diastolic heart failure or dilative cardiomyopathy, high-throughput multi OMICs analyses, telemedicine, biobanking and data management/analysis in large patient cohorts. In 2017, the three additional projects established within the scope of the 2016/2017 top-up programme were completed and the corresponding publications were prepared. In 2017, the University Medicine Greifswald was involved in the clinical DZHK studies TORCH, TransitionCHF, Culprit-SHOCK, TOMAHAWK, SMART-MI as enrolling study site. The initiation of the studies APPROACH-ACS, FAIR-HF2, CLOSURE-AF, CAVA-ADHF and SPIRIT-HF is scheduled for the first quarter of 2018. Patients have been enrolled in Culprit-SHOCK since 2014 and recruitment ended in the second quarter of 2017. Patients have been enrolled in TORCH and TransitionCHF since 2015. Recruitment for TORCH will end at the beginning of 2018 so that the one-year follow-ups will then be carried out. Within the scope of the ESC-EORP registry for cardiomyopathies, approx. 90 study participants have been enrolled since 2015, and in 2018, too, further cases of myocarditis shall be enrolled. In the field of clinical research, the Trusted Third Party of the Central Data Management (collaborative project together with the Göttingen partner site and the Main Office in Berlin) is established in Greifswald. The partner site will continue to assume patient management in the TORCH study. Furthermore, the Greifswald partner site coordinates DZHK basic and study biobanking and operates the Laboratory Information Management System of the DZHK. The appointment procedure for the W2 Professorship in "Molecular Cardiology" was completed in 2017 and was filled by Prof. Jens Fielitz of the Max Delbrück Center for Molecular Medicine Berlin in the second quarter of 2017. The appointment procedure for "Cardiovascular Prevention" was completed in 2017 to the extent that PD Dr. Sabina Ulbricht of the Institute of Social Medicine and Prevention Greifswald will fill the post in the first quarter of 2018.



University Medical Center Schleswig-Holstein, Campus Kiel

Partner site Hamburg/Kiel/Lübeck

Partner site Spokesperson: Thomas Eschenhagen, Director of the Institute for Experimental Pharmacology and Toxicology at University Hospital Hamburg-Eppendorf

Vice Partner site Spokesperson: Norbert Frey, Director of the Cardiology and Angiology Clinic at University Hospital Schleswig-Holstein

Partner site management: Doreen Stimpel (Partner Site Manager), [since November 2017: Christiane Neuber], Monika Glimsche (Partner Site Clerk), University Medical Center Hamburg-Eppendorf

Partner Institutions at the DZHK Hamburg/ Kiel/Lübeck site

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

Research Focus within the DZHK

The four partner institutions at the site combine their individual expertise to pursue the common goal of finding the potential causes of cardiovascular diseases and developing new treatment concepts. In particular, the scientific focus is on identifying genetic risk factors and biomarkers of cardiovascular diseases, stem cells and tissue engineering, as well as on mechanisms and therapies of congenital and acquired cardiomyopathies. In 2017, the partner site linked its basic research disciplines with clinical research even more. Together with partners of the DZHK, UKE is testing innovative therapy approaches with specific regard to clinical application (gene and myocardium replacement therapy) within the scope of two projects of the Translational Research Projects (TRP) funding line. The partner site is currently heading four clinical studies fully funded by the DZHK. The guideline-relevant studies DEDICATE and FAIR-HF2 in Hamburg and the early clinical study CAVA-ADHF in Lübeck have successfully started recruitment. Within the scope of the 2016/2017 top-up programme, the spectrum of experimental methods was extended by various investments and the locally shared scientific infrastructure was further consolidated. In order to support scientific exchange and networking, various series of seminars, symposia (1st Joint DGK/DZHK Translational Workshop) and conferences were endorsed in 2017. A highlight was the successful organisation of the international 34th Meeting of the European Section of the International Society for Heart Research (ISHR) in Hamburg. The W2 Professorship for “Epigenetics in Cardiac Hypertrophy” has been filled by Prof. Dr. med. Oliver Müller since July 2017, and an endowed professorship is being finalised. The DZHK thus funds four professorships at the partner site (Prof. Jeanette Erdmann, Lübeck; Prof. Arne Hansen and Prof. Tanja Zeller, both Hamburg).



University Medical Centre Mannheim

Partner site Heidelberg/Mannheim

Standortsprecher: Hugo A. Katus, Ärztlicher Direktor der Abteilung Innere Medizin III des Universitätsklinikums Heidelberg

Partner site Spokesperson: Hugo A. Katus, Medical Director of the Department of internal Medicine III of the Heidelberg University Hospital

Vice Partner site Spokesperson: Martin Borggreffe, Director of Medical Clinic I of the University Hospital Mannheim (since May 2017: Thomas Wieland, University Medical Centre Mannheim)

Partner site management: Tanja Weis (Partner Site Manager), Claudia Marquart (Scientific Project Manager) [since August 2017: Annabell Skarabis], Ines Schneider (Partner Site Clerk) since March

Partner Institutions at the DZHK Heidelberg/Mannheim Partner Site

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

Research Focus within the DZHK

The scientific focus of the Heidelberg/Mannheim partner site is the investigation of genetic and inflammatory cardiomyopathies and arrhythmias.

Cardiomyopathies are investigated in an integrative and translational approach in order to develop new diagnostic procedures and innovative treatment concepts. Genetic, epigenetic and electrophysiological analyses, imaging diagnostics, ps-iPS cells as well as model systems from cell culture to zebrafish, mouse and rat, all the way to the human-relevant porcine model are being used in order to identify new diagnostic and therapeutic target structures as well as for the functional analysis of molecular signal pathways. Methodical platforms (next generation sequencing, AAV platform, zebrafish platform, large animal platform, path clamp) are available to the entire DZHK, just like a state-of-the-art biobank with fully-automated sample processing. With the translational pipeline, new associated genetic loci and variants, epigenetically modified candidate genes, miRNAs and important signalling molecules could be identified as potential targets, which could subsequently be functionally investigated on their diagnostic and therapeutic potential. Heidelberg/Mannheim is involved in clinical and preclinical research in many ways. Among other things, the TORCH Registry, as the first clinical DZHK study, could reach its recruitment goal under the management of Heidelberg University Hospital. Moreover, the Heidelberg/Mannheim partner site is involved in eight further clinical DZHK studies as an enrolling study site. In preclinical research, a total of 14 co-operations with Shared Expertise or external partners were successfully carried out. In 2017, two further Postdoc Start-up Grants and a Rotation Grant were obtained for the partner site within the Excellence Programme. In September 2017, the second DZHK partner site retreat was held with over 70 participants. The focus of the event was on scientific strategy, networking and scientific exchange on all levels, as well as the promotion of young scientists.



Helmholtz Zentrum München – German Research Center for Environmental Health

DZHK Munich Partner Site

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

Vice Partner site Spokesperson: Christian Weber, Director of the Institute for Prophylaxis and Epidemiology of Cardiovascular Diseases at Ludwig Maximilian University Munich

Partner site Management: Sandra Rauser (Partner site Manager), Sissy Künzel (Partner site Clerk), Technical University of Munich

Partner Institutions at the DZHK Munich site

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

Research Focus within the DZHK

The scientific focus at the Munich partner site (“Munich Heart Alliance”, MHA) of the DZHK is the investigation of so far unknown molecular mechanisms of cardiovascular diseases, the development of new therapy approaches based on these and their translation into clinical studies.

With the harmonisation of ethics applications and the Central Image Data Management System for clinical studies, Munich is involved in clinical initiatives across the DZHK. In addition, the main study centres of the DZHK studies “ISAR-REACT 5” and “Revacept-CAD” are located at the German Heart Centre Munich and the main study centres of “APPROACH-ACS-AF”, “SMART-MI” and the “AFNET-EORP Atrial Fibrillation Registry” are at the Hospital of LMU Munich. In preclinical research, a HRHV project by Prof. Christian Schulz (“Generation and functional characterization of macrophage cell lines from yolk sac precursors”) and one by Prof. Christian Weber (“Late pre-clinical development of CD40-TRAF6 inhibitors (TRAF-STOPs)”) were released for funding in 2017. Particularly encouraging is the successful integration of the young researchers within the scope of the DZHK Promotion of Excellence. In 2017, two applications for the Rotation Grant for physicians and four applications for the Postdoc Start-up Grant, two each for “early career” and “late career”, were awarded to Munich-based young researchers.

The W3 Professorship for “Early phase of clinical studies in cardiology” at the German Heart Centre Munich was taken up by Prof. Michael Joner in September 2017. With Prof. Christian Schulz and Prof. Sabine Steffens, two DZHK PI positions were newly filled.

Two meetings with papers and poster presentations on the status of Munich’s DZHK projects again supported scientific exchange and the connection of research activities at the partner site in 2017.



Goethe University Frankfurt

Partner site Rhine-Main

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

Vice Partner site Spokesperson: Stefanie Dimmeler, Director of the Institute for Cardiovascular Regeneration of the University Hospital Frankfurt

Partner site management: Angelika Bonauer (Partner Site Manager), Julia Dahlhaus (Partner Site Clerk) [since October 2018: Linda Sulzmann], University Hospital Frankfurt

Partner institutions at the DZHK Rhine-Main site

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

Research Focus within the DZHK

The focus of the Rhine-Main DZHK partner site is in the identification of epigenetic signatures and mediators of

cardiovascular diseases in order to be able to use these as either biomarkers or as potential 'targets' for the repair and regeneration of vessels and myocardial tissue.

The MyoVasc study in Mainz, which was specifically designed to better understand the mechanisms in humans, has already enrolled over 3,000 patients and started the four-year follow-up examinations. A new platform for high-throughput protein profiling using PEA technology was implemented for analysing the biological material. At the Kerckhoff-Klinik, over 13,000 patients have so far been included in the Kerckhoff Biomarker Registry. Here, the collection of long-term follow-up data is currently taking place.

The Frankfurt-based Institute for Experimental and Translational Cardio Vascular Imaging was further expanded with the commissioning of the CAT scanner. Furthermore, the main study centre for the DZHK study Decipher HFpEF was established and the first patient was enrolled at the end of 2017.

Within the scope of the partner site project, a workflow for phosphoproteome analysis was implemented at the MPI, which enables a clear reduction of the sample quantity. As a result, substantially more sensitive phosphoproteomics can be done within the DZHK.

For the purpose of the identification and therapeutic manipulation of non-coding RNAs in the cardiovascular system, light-activated microRNA inhibitors could be further developed in Frankfurt. The toxicological studies of the preclinical HRHV project on the inhibition of mirR-92a were successfully completed. Based on the promising results, a phase I study is planned for 2018. In addition, the long non-coding RNA "Mantis" was identified, which could be a potential biomarker for endothelial dysfunction.

Furthermore, new lipid mediators that play a central role in diabetic retinopathy were discovered (Nature 2017).

Acronyms

AFNET	Arterial Fibrillation Competence Network
IDMS	Image Data Management System
CSG	Clinical Study Group
DZG	German Centres for Health Research
DZHK	German Centre for Cardiovascular Research
FMM	Funding Management Department
KdZG	Commission of Donors
KNAH	Competence Network for Congenital Heart Defects
KNHI	Competence Network for Heart Failure
LIMS	Laboratory Information and Management System
PI	Principal Investigator
RCC	Research Coordinating Committee
SE	Shared Expertise
SOP	Standard Operating Procedure
TRG	Translational Research Group
U&AC	Use & Access Committee
ZDM	Central Data Management
✓	Goal reached
✓	In progress
x	Goal not reached

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In the interest of better readability and lack of space feminine forms will not always be mentioned separately in this publication. Of course, these terms refer to female as well as male persons.

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