



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

DZG DEUTSCHE ZENTREN
DER GESUNDHEITSFORSCHUNG

German Centre for Cardiovascular Research (DZHK)

ANNUAL REPORT



2015



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

In 2015, the DZHK once again recorded an exceptional growth. About 1,200 people now belong to our network: physicians, pharmacologists, physiologists, biologists, chemists, physicists, biostatisticians, ethicists and many others. We incorporated the Cardiological Competence Networks. In the clinical partner institutions study physicians, nursing staff and health information managers collaborate with dedication on our clinical studies. The mission that unites everyone is translation in cardiovascular research, i.e., transferring research results into clinical practice. It is probably the first time in Germany that so many people are working together for this purpose. The fact that people's attention is drawn to the topic of translation in cardiovascular research and that they are motivated to make individual contributions in their field is considered to be a very special achievement and additional value of the DZHK. Among others, this involves the development of new measures for promoting junior scientists as well as establishing a unified study data management system that is not dependent on individual persons.

In 2015, our budget accrued to the planned sum of 41 million euro. Our network enables us to sensibly manage these funds and to specifically support excellence in translational approaches. Committees like the Translational Research Group and the Clinical Study Group discuss and review applications and advise applicants of clinical studies and large preclinical projects. The committees gain a lot of experience in the process, especially where the inclusion of regulatory authorities and industrial partners in early phases of research projects is concerned. This benefits the next applicant and eventually the whole of the DZHK. This kind of wealth of experience is an added value that can only emerge in a network like the DZHK and that can be established and shared in the long run.

And our efforts are starting to pay off: large multicentre clinical DZHK studies have successfully been initiated

and promise to provide new knowledge and treatment recommendations for important endemic diseases, such as heart failure and myocardial infarction. The cooperations between sites, between disciplines and even within institutions have been intensified. The collaboration with the Cardiological Competence Networks is bringing forward new ideas. The number of scientific publications continues to rise and their topics reflect the strategic focus of the DZHK. Publications with several DZHK partners have also risen. The appeal of the network is also shown not least by the large interest in our internal events, especially in our annual retreat, which is regularly overbooked.

We always have the patient in mind in all of that. The efforts of the DZHK shall benefit them. An important group for the DZHK are study participants – without them clinical research would not be possible. In order to ensure that they are well informed about what occurs with their data and biological samples, we have started to build an information platform for them that will go online in 2016.



*Thomas Eschenhagen
Chairman of the
Executive Board*



*Gerd Hasenfuß
Executive Board*



*Thomas Sommer
Executive Board*

The German Centre for Cardiovascular Research (DZHK)



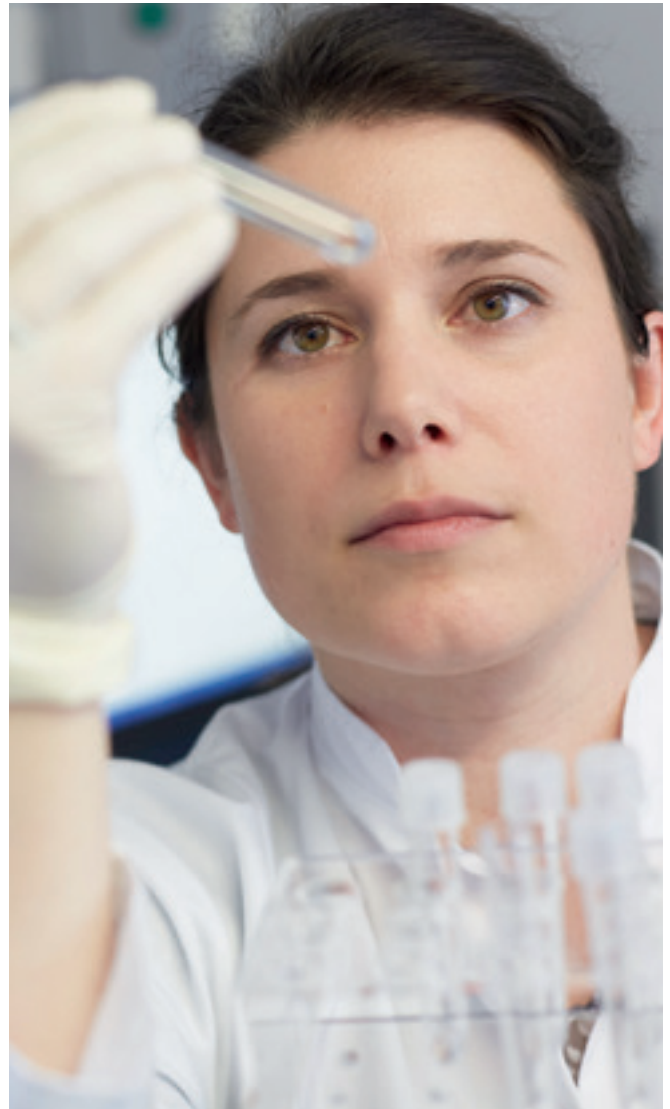
For its multicentre clinical studies the DZHK has invested in the latest diagnostic units

DZHK – a German Centre of Health Research

The German Centre for Cardiovascular Research (Deutsches Zentrum für Herz-Kreislauf-Forschung, DZHK) is among the six German Centres for Health Research (Deutsche Zentren der Gesundheitsforschung, DZG) that are dedicated to the improvement of the prevention, diagnosis and treatment of endemic diseases. It was founded in 2011 upon the initiative of the German Federal Ministry of Education and Research (BMBF) and is funded jointly by the Federal Government (90 percent) and the governments of those German states in which member institutions are headquartered (10 percent). The goal of the six German Centres for Health Research is to quickly bring results from basic research to clinical application.

Mission and goals of the DZHK

The DZHK focuses on translating new knowledge gained from cardiovascular research as rapidly as possible into clinical practice in order to improve the diagnosis, prevention and treatment of cardiovascular diseases. This mission is of utmost clinical and health economic importance, because in the future the incidence of cardiovascular diseases will increase further as a result of the rising incidence of metabolic disorders (obesity, diabetes) and due to demographic change. In order to be able to implement this mission, the DZHK unites excellent basic researchers and clinical researchers from seven sites in Germany. It promotes the cooperation between them with the goal to develop synergies and to thereby accelerate the process of translation. Above all, the DZHK invests its funds in previous weak spots of the translation process. This is ensured through a coordinated research strategy and specific funding instruments.



Where do we stand?

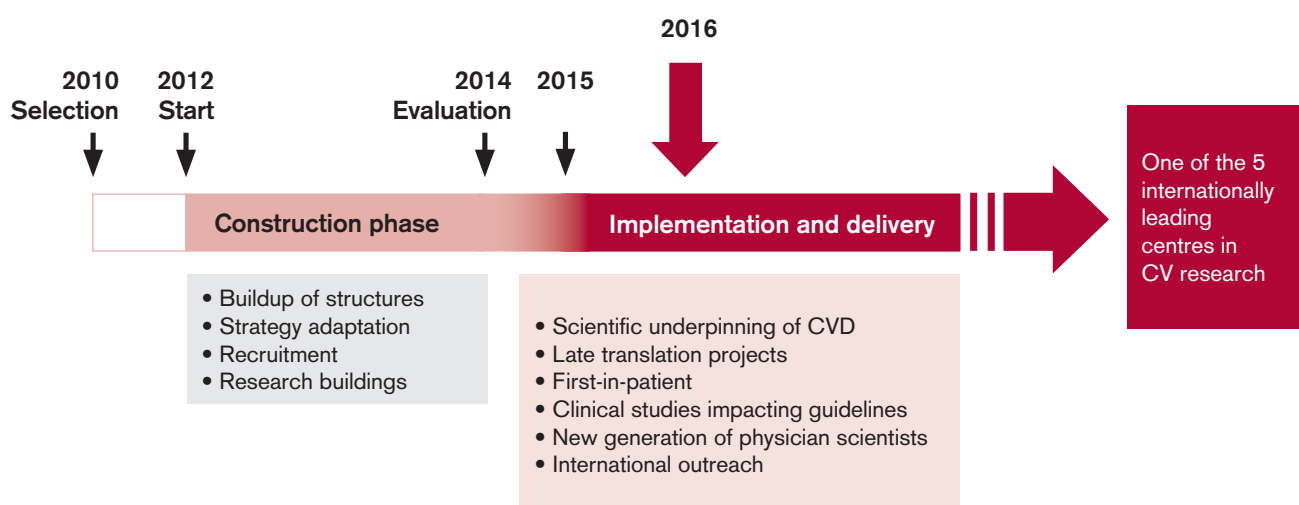
The DZHK completed its fourth year of business operations in 2015. Hence, after a successful start-up phase, the phase of realisation could begin. In 2015, for this first time and as scheduled, the centre had at its disposal the full budget of 41 million euro (2014: 14 million).

In 2015, the sites have once again made outstanding investments in order to strengthen their infrastructure and common resources (investment programme 2015). They purchased major instrumentation for basic research, clinical research and the DZHK Biobanking Project. In addition, the 17 clinical member institutions standardised their infrastructure with a view to the conduct of multicentre clinical studies. In the OMICs Resource Project the DZHK commissioned the sequencing of 1,000 genomes of healthy individuals (cf. Chapter 6). Within the scope of partner-site funding, additional DZHK tenured professorships were awarded, which is an important contributory factor to reinforce and stabilise the work of the DZHK at its various sites.

According to DZHK strategy, 55 percent of the research funds are flexible, which means that they

are awarded internally in the scope of application procedures and competition. Due to the increase of funds, we carried out a total of 11 application procedures in the funding lines Preclinical Research, Clinical Research and Promotion of Excellence in the reporting year (2014: 2 application procedures). We have launched the first major preclinical and clinical studies and were able to include the 500th patient in November 2015. In addition, the excellence programme to promote young translational researchers was initiated in 2015, here we were able to award 14 grants and sponsorships and recruit two excellent junior scientist group leaders from abroad.

It is our goal to rank among the five leading cardiovascular research centres in the world.

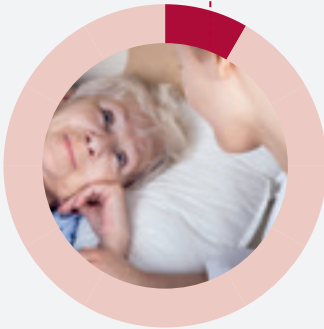


Development of the DZHK since 2010

Highlights in 2015

JANUARY

Start of supporting the Cardiological Competence Networks by the DZHK



APRIL

Joint fair stand with the Competence Networks at the 81st annual meeting of the German Cardiac Society



FEBRUARY

Parliamentary evening of the six German Centres for Health Research (DZG) in Berlin



MARCH

Opening of the new MRI building in Göttingen



JULY

Selection of two DZHK junior scientist group leaders



NOVEMBER

Twelve centres participate in the TORCH registry, the 500th patient is included



SEPTEMBER

3rd DZHK Retreat, focusing on clinical research



DECEMBER

Purchase of a cross-site laboratory information system for clinical studies



OCTOBER

DZHK symposium "The Noncoding Genome in Cardiovascular Diseases – Pathogenic Implications and Therapeutic Perspectives" in Berlin



Research Strategy – Focus on Translation



Innovative studies promote a rapid translation of research results into clinical practice

The DZHK has a clear mission: We want to develop therapies for the benefit of people who are suffering from cardiovascular diseases. This can only be accomplished if we succeed in translating the results from basic research into application, rapidly and purposefully (translation).

At this point, we would like to explain once again how we elaborated our translation strategy:

- We have defined disease categories on which we focus our efforts (1).
- We have identified weak spots in the translation of cardiovascular research (2).
- We have developed instruments and structures in order to counter these weak spots (3).

(1) Heart at risk – the three most important diseases

Anyone who pursues a specific objective needs to bundle all available resources. The DZHK consequently does not focus its attention on all diseases pertaining to the heart and the circulatory system, but on three major issues which are of particular importance to the patients and the healthcare system: the prevention and therapy of myocardial infarctions, the prevention and individualised therapy of heart failure and the prevention of sudden cardiac death. Why have we chosen these diseases?

Each year, 220,000 people in Germany suffer a **myocardial infarction**. The number of casualties is receding on account of the improvements made

in emergency care. Yet, approximately 50,000 people still die of a heart attack (in comparison: approx. 26,000 people die of colon cancer). People in their “best” years are often affected without warning. Survivors have to cope with the consequences and often develop **heart failure**. The circumstance that more people survive a myocardial infarction is one reason for the increasing incidence of heart failure. Roughly 400,000 patients were admitted to hospital with heart failure in 2013, 46,000 died. Another reason is the demographic change, because heart failure increases with age. Heart failure is not curable yet. A **sudden cardiac death** is a very tragic incident, as it often affects young people who have no recognisable pre-existing conditions. The cause is almost always a life threatening cardiac arrhythmia which resulted from an unidentified disease of the cardiac muscle. The diseases mentioned cause high costs and thus burden the healthcare system (all figures derived from: Deutscher Herzbericht 2015).

(2) Closing the gaps in the translation chain

It is a long way from the discovery of a biological principle to developing a therapy and the air gets progressively thinner if the path runs from basic research over preclinical and clinical research to application. From the numerous principles discovered by basic research and published in high ranking journals, only a small fraction finds its way to clinical studies. That research often gets stuck on the basic level is also a consequence of the gratification system prevailing in science. Research with cells or mice can be conducted in reasonable time frames and renowned journals like publishing articles about it, which ultimately makes up the currency of success for the researchers and their careers. Besides, it is easier to acquire research funds for a completely new approach than for the repetition of studies using a different animal model (e.g., pigs instead of mice).

And yet, it is a very important step in the translation chain of cardiovascular research to prepare initial studies with humans as much as possible. To this end, for example, extensive toxicity tests have to be carried out and therapies have to be tested with larger experimental animals. Such and similar research activities are summarised under the term of **late preclinical research**. They are laborious, time consuming and hardly acknowledged by academic research. Accordingly, only few researchers work in this field. The DZHK would like to change this and that is why late preclinical research constitutes one of the two main focuses of our research strategy.

The other main focus is clinical research. In the field of clinical studies we have identified two phases as main issues for the DZHK. **Early clinical studies** are one main focus at the DZHK, because they close the gap between applied basic research and practical application. On account of high regulatory and administrative obstacles early clinical studies have so far not been conducted often enough by academic researchers. And yet, because of their equipment and orientation, universities in particular are ideally suited to test specific questions in patients and apply their entire arsenal of clinical and basic research methods. **Guideline relevant studies** immediately contribute to patient treatment guidelines and can help to improve therapies. They often require huge case numbers which is made possible with the multicentre approach of the DZHK.

(3) Flexibility, cooperation, competition

We hold in reserve flexible funds for the translation steps mentioned above, which we award under conditions of fair competition. To this end, we have established the funding lines “High Risk High Volume Late Translational Projects (HRHV)”, “Early Clinical Studies” and “Guideline relevant Studies”. Once or twice a year all researchers of the DZHK are called to submit their



ideas for these funding lines. This allows us to ensure that only those research projects that comply with the DZHK strategy and are of high-standing scientific quality receive funding. In this context, the location of the individual site does not matter, instead, the best ideas prevail.

The projects we support with flexible funds also inspire cooperations. This applies particularly to the very popular funding line “Cooperations by means of Shared Expertise”. And finally, we employ flexible funds to individually support and qualify junior scientists, particularly if they are working in the field of translational research.

However, translation also needs basic research, because it provides the foundation for all medical innovation. For this reason, in the long run about 40 percent of all funds at the DZHK flows into the sites according to a pre-determined allocation key in order to extend their individual capacities even further.

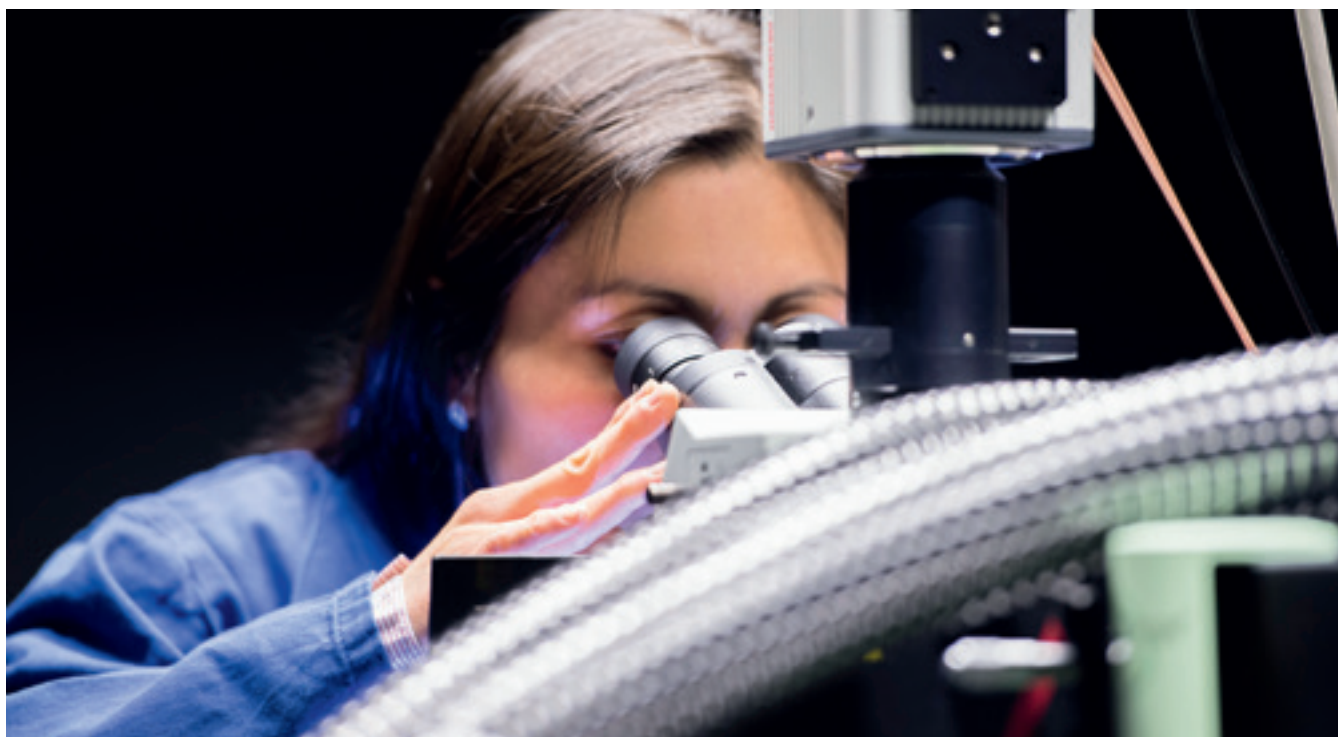
Cooperation and competition are balanced at the DZHK, which we regard as an important condition for a successful translation. The fixed site-allocated funds give the DZHK partners the long-term security they need for the establishment of important research infrastructures and the development of excellence in specialised fields. The competitive funds (up to 55 percent of the total budget) ensure that the best ideas are researched in the critical phases of translation and allows us to respond quickly to new research trends. Both sectors mutually depend on each other.

Start-up difficulties

This ambitious strategy brought with it start-up difficulties in 2015 that will extend into 2016. For example, the funds reserved for preclinical and clinical projects were not spent completely, as not enough projects could be started. Our selection processes with their intentional and reasonable interconnection of internal and external auditors and committees lead to a lot of work for the expert reviewers and also for the administration, which was due to the encouragingly high number of project applications.

Yet, we are convinced that the chosen approach, which consists in focusing strategically on certain phases of translation and allocating the funds competitively and flexibly, is the right one. It is already achieving successes and is expected to bear ample fruit in the years that lie ahead.

Preclinical Research



This chapter is concerned with preclinical research, which the DZHK finances with its flexible funds. In addition, the DZHK partners finance preclinical research with their site funds. The DZHK has established three funding procedures, which are applicable to the field of preclinical research: In the High Risk High Volume Late Translational Projects (HRHV), only a few albeit large and partially risk-laden projects located in the field of late preclinical research are funded. A prerequisite for funding is that proof of feasibility has been submitted and that the perspective of the clinical application is comprehensible. Cooperation projects by means of Shared Expertise and cooperation projects with external partners are smaller, mostly bilateral projects in greater number. Their purpose is to use synergies and link partner institutions together or get external expertise into the DZHK. The cooperation projects with industrial partners, originally planned as

a fourth funding procedure for the preclinical stage, have been integrated into the High Risk High Volume Projects.

High Risk High Volume Late Translational Projects (HRHV)

The DZHK holds 3 million euro per annum in reserve for large, high risk projects located in the field of late preclinical research. HRHV projects comprise research, which prepares the first application of new therapies or diagnostic methods in humans (first-in-man). These might consist in toxicological or dose-finding studies, the generation of human-relevant animal models or the reproduction of the proof of concept in a large-animal model.

Funds reserved for HRHV projects could not be spent



Zebra fish are used as model organisms for cardiovascular research. They are provided as Shared Expertise within the DZHK.

completely in the reporting year. Funding of HRHV projects was awarded by tender for the first time in 2014. Only one project from this first call was selected for funding and then launched in 2015. For two further project applications in 2014, the Translational Research Group (TRG) of the DZHK recommended a revision (cf. chapter “Committees” for TRG).

Twelve applications for HRHV projects had then already been submitted in the reporting year. The TRG gave five applications to external reviewers for assessment. As a result, three applications will be funded as projects from 2016. The project “Development of miR-92a inhibitors for the treatment of cardiovascular diseases” (Dimmeler, Rhine-Main) started in 2015, has now run through its first year and reached the planned milestones.

Projects recommended for funding in 2015

Transapical mitral-valve stent implantation without using a heart-lung machine

Duration: from 2016 to 2017

Budget: 185,000 € in 2016; 152,000 € in 2017

Aim: The object of this project is the therapy of mitral-valve insufficiency by means of a transapical mitral-valve stent implantation in the beating heart without using a heart-lung machine. In this project, the design of the stent is supposed to be further developed for the mitral position, so that a greater match with the natural anatomy is attained with a new oval shape. In addition to the apical fixation, another fixation system shall also be developed. The additional anchorage shall ensure the correct anatomical position of the stent.

Involved scientists: Georg Lutter, Saskia Pokorny, Jessica Haupt, Klaas Loger, Hamburg/Kiel/Lübeck

Collaboration in the DZHK: Christian Kupatt, München

Low-energy defibrillation of ventricular fibrillation in pigs as an animal model for heart failure

Duration: from 2016 to 2017

Budget: 648,000 € in 2016; 375,000 € in 2017

Aim: In previous studies run by the working group led by Stefan Luther it was shown that the energy applied in cardiac arrhythmias could be reduced by 80 to 90 percent compared to conventional defibrillations. In order to translate these results successfully into clinical application, the necessary proof of efficacy in an animal model is to be produced in the scope of this project: the termination of ventricular fibrillation by means of a novel defibrillator compared to conventional defibrillation will be examined in pigs used as an animal model for heart failure. The results will constitute the foundation for preparing a study for a first-in-human application.

Involved scientists: Stefan Luther, Gerd Hasenfuß, Markus Zabel, Göttingen

Collaboration in the DZHK: Christian Kupatt, München

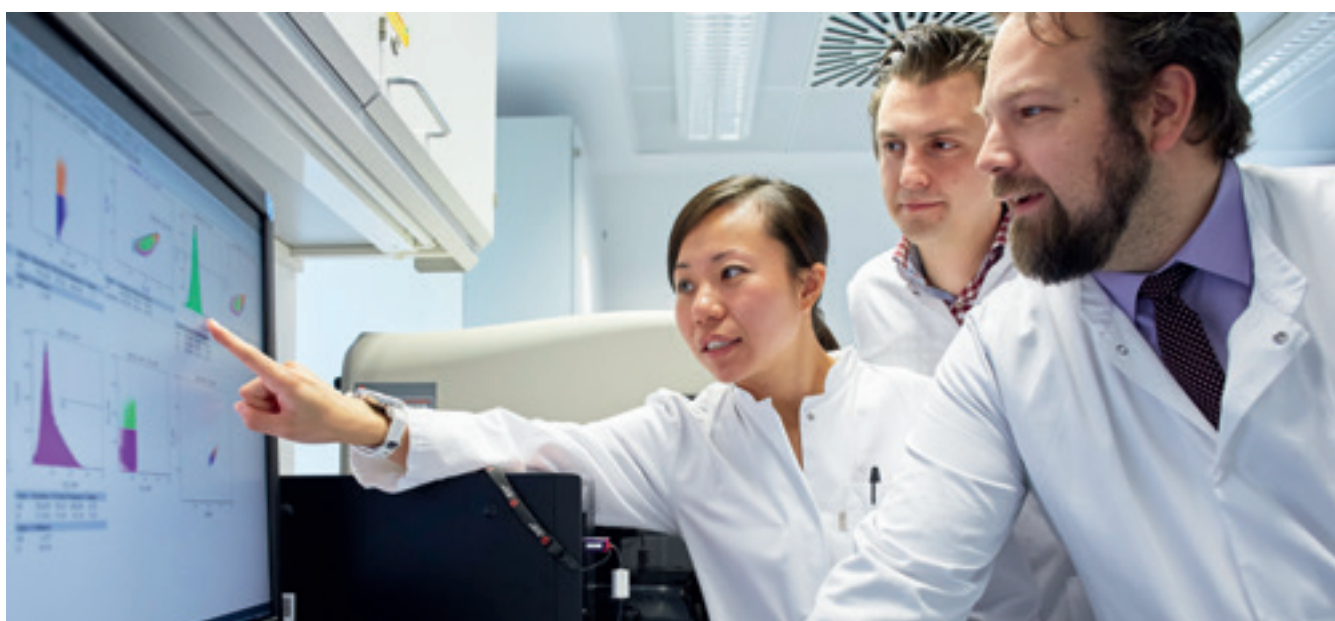
In vivo characterisation of the chemokine receptor CXCR4 to detect an inflammation in atherosclerotic plaques by means of PET/MR

Duration: from 2016 to 2017

Budget: 206,000 € in 2016; 231,000 € in 2017

Aim: It was demonstrated in preliminary studies with animal atherosclerosis models that the radionuclide ⁶⁸Ga-Pentixafor binds specifically to cells which mediate an inflammation process and thus enables a non-invasive assessment of an inflammation in atherosclerotic plaques. This project shall carry out the necessary toxicity and dose tests for an initial application in humans. If these tests are successfully completed, the proof of concept shall be demonstrated in patients, whereby it shall be determined whether the incorporated amount of ⁶⁸Ga-Pentixafor correlates with the expression of CXCR4.

Involved scientists: Markus Schwaiger, Stephan Nekolla, Yvonne Döring, München



Teamwork: Short distances and close consultations with colleagues are common practice at the DZHK

Cooperations by means of Shared Expertise (SE)

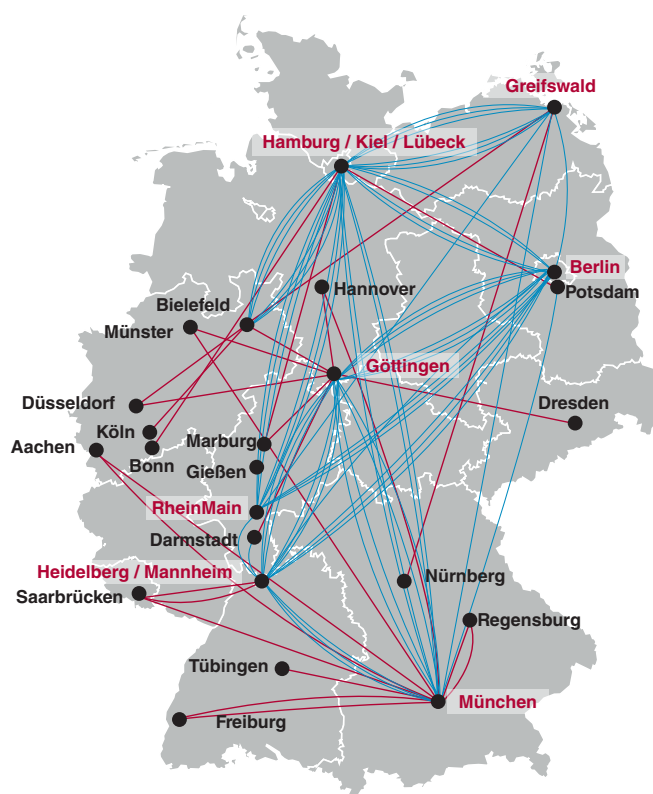
In this funding line, the DZHK partners provide each other with laboratory methods and other scientific expertise mainly from the field of preclinical research. This way all partners will benefit from the entire knowhow of the DZHK. The idea is to make available expertise accessible to all instead of re-establishing it at a different site. This year, the main emphasis of the utilisation of the SE was once again on basic technologies such as OMICs or the production of AV vectors. The continued strong utilisation of single SEs shows that the concept of a “market place” for core facilities does work and that the most coveted ones come out on top. Apart from increasing networking at the DZHK, this results in an efficient application of research funds, because redundant structures are prevented.

The budget for SE projects amounted to 1.5 million euro in the reporting year and was fully spent. Due to the popularity of this funding line, the Research Coordinating Committee (RCC) decided in the reporting year that the budget for cooperations by means of Shared Expertise should be increased to two million in 2016, and 2.5 million in 2017.

The DZHK partners offered 26 new Shared Expertise projects in the reporting year. In total, they counted 144 Shared Expertise projects at the end of the year (2014: 118). A total of 79 projects were applied for and approved (2014: 45). Hence, the total number has risen to some extent, which had not been defined as a goal, since the administrative effort increases as a result of many small projects. In the coming years we intend to reduce the number of new cooperation projects and increase their average funding amount. In 2015, the average funding amount of 29,000 euro was already some-

what higher than in the previous years. The total sum of all approved applications amounted to 2.3 million euro. The average duration of the projects was twelve months.

The number of junior researchers who applied for SE projects more than doubled in the reporting year. A total of 29 Young DZHK members were applicants and/or co-applicants for such projects (2014: 11). Hence, cooperation projects utilising Shared Expertise also have the important function of encouraging young researchers on their way toward scientific independence. We seek to further increase the percentage of junior researchers in this funding instrument in the years to come.



Cooperations with Shared Expertise (blue lines) and external partners (red lines)

Top 10 of the most frequently utilised Shared Expertise

SE	Name of Shared Expertise project	Since	Location	Uses applied for in 2015	Uses since 2012
SE006	Genomics/proteomics	Sep 12	Berlin	8	20
SE028	AAV Vector platform	Sep 12	Heidelberg/ Mannheim	8	15
SE001	Generation and cardiovascular phenotyping of transgenic rats	Sep 12	Berlin	6	19
SE019	Experimental and therapeutic stem cell bank and stem cell phenotyping	Sep 12	Göttingen	3	6
SE031	Next-generation sequencing platform (Heidelberg)	Sep 12	Heidelberg/ Mannheim	3	7
SE034	Cardiovascular in-vivo candidates screening platform	Sep 12	Heidelberg/ Mannheim	3	3
SE118	Measurement of caspase and proteasome activity	Dec 14	Göttingen	3	3
SE048	Large animal platform for ischaemic heart disease	Sep 12	Munich	2	3
SE092	Primary cardiac fibroblasts	Mar 14	Hamburg/ Kiel/Lübeck	2	3
SE097	Analysis of endothelial cell function	Apr 14	Rhine Main	2	3

Cooperations with external partners

This funding line will be explained in Chapter 9.

Industry cooperations

This funding line will be explained in Chapter 9.

Achievements in 2015

- ✓ Approval of three more HRHV projects
- ✓ Approval of 40–50 Shared Expertise projects (average value 20,000 -25,000 EUR)
- ✓ Successful completion of 40 Shared Expertise projects
- ✓ Share of young scientists in Shared Expertise projects: 30 percent

Goals for 2016

- Successful development of the HRHV project started in 2015 until the first briefing of the Federal Institute for Drugs and Medical Devices (BfArM)
- Launching the three HRHV projects approved in 2015
- Bringing three further HRHV projects to the fund-release stage
- Further increasing the share of young scientists in Shared Expertise projects
- Opening the funding line “Cooperation with external partners” for DZHK members and DZHK scientists (currently only for DZHK-PI)

Clinical studies represent an important cornerstone of the DZHK's research strategy. Only if new hypotheses or therapeutic approaches can be tested in patients will they have a chance to someday improve the clinical routine. In our 2013 strategy discussion, we identified guideline-relevant studies and early clinical studies as the challenges to translation in clinical cardiovascular research. Ever since, both study types have been the focus of the DZHK's funding activity with flexible funds. In addition, we also support registries and cohorts, which provide valuable information about the aetiology and course of cardiovascular diseases.

Focusing on: heart failure

In the reporting year, the DZHK funded and/or approved a total of 25 clinical studies, registries and cohorts (including studies of the Competence Networks) (2014: 8). The studies¹ are concerned with those cardiovascular diseases that are the most frequent and most relevant for the healthcare system and the population. Heart failure is currently the focus of DZHK studies. The incidence of heart failure has been increasing for years. In 2013, there were 396,380 incidences in Germany (source: Deutscher Herzbericht 2015). The studies of the DZHK on heart failure investigate the various types, courses, severity grades, therapeutic approaches and comorbidities. For example, the DZHK study FAIR-HF 2 will determine whether the administration of iron preparations increases the survival rate of certain patients with heart failure. The study KNHI-TP 9b of the Competence Network for Heart Failure (KNHI) is concerned with heart failure in HIV-infected patients. Most of the studies on heart failure are potentially guideline-relevant, which means that their results will have a direct impact on the treatment of patients who are suffering from heart failure.

The term "study" in this chapter denotes all research projects belonging to the clinical field, hence they also include registers and cohorts.

Clinical Research

Some studies of the DZHK are also concerned with a combination of diseases, for example, APPROACH-ACS-AF. This study seeks to determine the best treatment for patients suffering from an acute coronary syndrome and concomitantly from atrial fibrillation:

The clinical studies of the DZHK are concerned with these diseases.

Disease	Number of studies at the DZHK
Heart failure	12
Ischaemic cardiac diseases (myocardial infarction, angina pectoris)	3
Myocardial diseases (inflammatory and non-inflammatory)	3
Atrial fibrillation	3
Cardiac arrest, sudden cardiac death	2
Congenital heart defects	1
Valvular heart diseases	1



Surgery using a cardiac catheter at the DZHK partner site Munich

**DZHK studies (highlighted in colour) and DZHK-associated studies
(the studies of the Competence Networks are shown in table on page 25)**

Acronym	Disease/Treatment/ Diagnostics	Study Type	Responsible PIs (site)	Study Participants (planned)	Study Par- ticipants recruited*
TORCH	Myocardial diseases	Registry	Katus, Hoffmann (Heidel- berg, Greifswald)	2,300	564
TransitionCHF	Myocardial insufficiency	Cohort	Hasenfuß, Wachter, Edelmann (Göttingen)	1,500	106
VAD	Severe heart failure, heart transplantation	Guideline rele- vant study	Falk, Knosalla, Hasenfuß, Friede (Berlin, Göttingen)	500	1
TOMAHAWK	Cardiac arrest	Guideline rele- vant study	Desch, Thiele (Lübeck)	558	-
FAIR-HF 2	Heart failure and iron administration	Guideline rele- vant study	Karakas, Anker (Göttin- gen)	1,200	-
SMART-MI	Sudden cardiac death after myocardial infarc- tion	Early clinical study	Bauer, Kääb, Massberg (Munich)	400	-
APPROACH-ACS-AF	Circulatory disorders of the heart in combination with atrial fibrillation	Guideline rele- vant study	Wakili, Massberg (Mu- nich)	400	-
DEDICATE	Aortic valve stenosis	Guideline rele- vant study	Blankenberg, Seiffert (Hamburg/Kiel/Lübeck)	1,600	-
SPIRIT-HF	Heart failure	Guideline rele- vant study	Pieske, Edelmann (Berlin)	1,300	-
CAVA-ADHF	Heart failure	Early clinical study	Thiele, Jobs (Hamburg/ Kiel/Lübeck)	352	-
Ex-VAD	Exercise with cardiac support system	Early clinical study	Edelmann, Pieske, Halle, Falk (Berlin)	66	-
Decipher HFpEF	Heart failure, MRI	Early clinical study	Nagel (Rhine-Main)	170	-
SFB/TR19 plus	Myocarditis	Cohort	Felix (Greifswald)	500 ¹	37
ISAR-REACT 5	Circulatory disorders of the heart	Guideline rele- vant study	Kastrati, Schüpke (Mu- nich)	4,000	2,904
CULPRIT-Shock	Myocardial infarction with cardiogenic shock	Guideline rele- vant study	Thiele (Lübeck)	706	315
FIX-HF-5C	Heart failure	Guideline rele- vant study	Hasenfuß (Göttingen)	230 (n=80 in Germany)	n.d.

As of: 31.12.2015 | ¹Number of follow-ups

Comprehensive information on the studies at: <https://dzhk.de/forschung/klinische-forschung/aktuelle-studien>

“DZHK studies” and “DZHK-associated studies”

Studies fully or predominantly funded by the DZHK (we call them “DZHK studies”) constitute the heart of the DZHK's clinical research activity (cf. Table page 19). They use the Central Data Management System (ZDM) of the DZHK for the recording of patient data and biological samples. The data derived from the studies can thus also be subsequently consulted for scientific issues investigated across multiple studies. Usually, all 17 clinical DZHK partner institutions participate in the DZHK studies. In 2015, a total of three DZHK studies were active, two were in preparation (project had started, first patient had not yet been included) and seven were either newly approved or their funding application had received a positive answer from the RCC (the project had not started yet) in 2015. The VAD study was able to recruit its first patient in 2015, an achievement which had been formulated as an objective in the Annual Report of 2014. Furthermore, the study was extended with a registry (VAD registry).

In addition, clinical studies are able to apply for the status of “DZHK-associated study”, which can be associated with a partial funding by the DZHK. The application may also be made when a study is already in progress. In this way, the DZHK intends to give studies with exciting scientific questions and of relevance to the DZHK the opportunity to intensify the recruitment of patients or realise further scientific modules. A new associated study (SFB/TR19 plus) was added in the reporting year. This concerns the follow-up visits of the cohort “Inflammatory Cardiomyopathy” of the Collaborative Research Centre Transregio 19 located in Greifswald. The study does not receive any funding from the DZHK, however, patient data and biological materials from this study are recorded in the Central Data Management System of the DZHK.

Furthermore, we have been funding studies and registries of the Cardiological Competence Networks since 2015, as their main subjects heart failure, atrial fibrillation and congenital heart defects fit in very well with the DZHK's research strategy (cf. Page 25). They possess the character of DZHK associated studies.



Close cooperation with clinical DZHK partner institutions

Application procedure and approval

In the reporting year, DZHK members were invited to submit new ideas for guideline relevant studies and early clinical studies in two respective calls. In total, we received 50 brief and full applications for early clinical studies and 16 for guideline relevant studies. These applications passed through a two tiered procedure. The CSG Steering Committee (cf. Chapter “Committees”) first reviewed the brief applications received and invited 28 selected applications to submit a full application. All full applications were externally and internationally reviewed. In the event of a positive assessment, the Research Coordinating Committee recommends funding, whereupon the studies receive an official funding approval notice from the DZHK Funding Management Department. Ultimately, three guideline relevant studies, five early clinical studies and one cohort (DZHK studies and DZHK-associated studies) were approved in 2015 or received a positive answer for funding from the RCC. All these projects will start in 2016.

Recruitment, initiation of study centres, CSG staff

In the reporting year, the first DZHK studies began to recruit patients on a larger scale. With the inclusion of the first patients, the clinical-scientific infrastructure of the DZHK consisting of Central Data Management (ZDM) and the Trusted Third Party passed its baptism of fire. At the end of the reporting year, a total of 671 data sets were registered at the ZDM (also refer to Chapter 7). In addition, 16 out of 17 clinical DZHK partner institutions passed their initiation as a study centre, 14 of which have begun with the recruitment of patients. Besides, three external partner sites have also been initiated as study centres: the University Hospital of Jena, Hannover Medical School and the University Hospital of Aachen (goal for 2015: 2).



Employee of the CSG Staff



Hannover has been recruiting patients for TORCH since 2015.

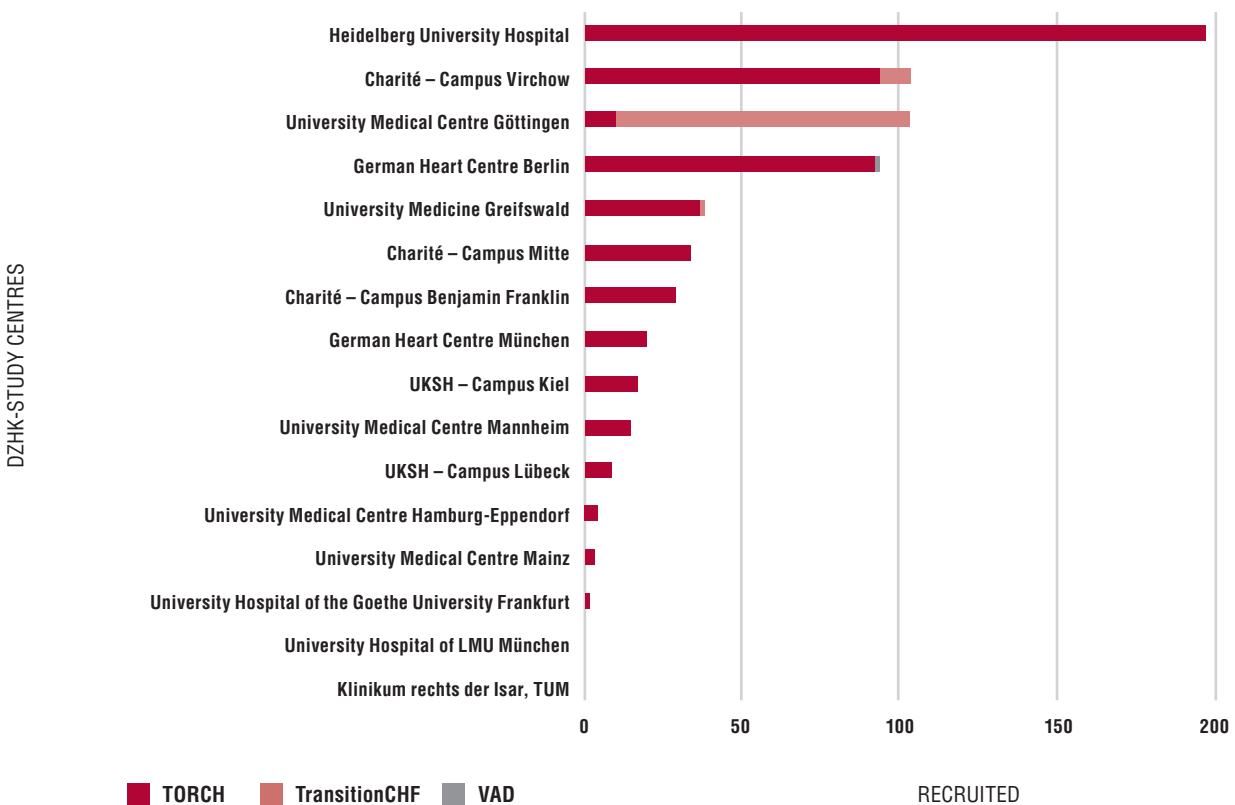
The staff members of the Clinical Study Group (CSG) are an important instrument when it comes to recruiting patients at the sites of the DZHK member institutions. They contribute a lot to the highly encouraging number of recruited patients. We were able to engage 12 study physicians (7 FTE) and 16 study nurses (16 FTE) for the DZHK. The CSG staff was then fully appointed in the reporting year, which we defined as a goal in 2014. At the member institutions, the CSG staff coordinate the recruitment for all DZHK studies, hence not only for studies that are carried out at their own institution or site. To be well equipped for this task, we organised two quality training sessions for study personnel in Berlin which was attended by the CSG staff and additional clinical personnel from the initiated study centres.

Proband information platform (PIP)

The DZHK has made available a first version of an information platform on its website for participants of the clinical studies of the DZHK. It contains information such as short and easily comprehensible descriptions of the DZHK studies currently in progress.

In addition, preparations for building a proficient internet-based patient information platform started in 2015. This platform will also provide information about research projects using biological materials and data derived from DZHK studies. Volunteers or patients previously involved in DZHK studies will not only be able to monitor the outcome of the study in which they took part, they will also be able to see what kind of research has been subsequently done with the data and samples from all the DZHK projects. This gives patients and volunteers a comprehensive transparency

Recruited study participants at DZHK study centres per study



As of 31.12.2015

about the contents and results of DZHK research. The media and editorial infrastructure of the platform will be developed in 2016.

Reports of the Cardiological Competence Networks

The DZHK has been supporting selected studies and structures of the Cardiological Competence Networks since 2015. Guideline relevant studies in the field of heart failure and atrial fibrillation and the promotion of the National Registry for Congenital Heart Defects are

priorities. In order to ensure close contact between the DZHK and the Competence Networks, the DZHK appointed a “representative” for each Competence Network. This person stands in a close contextual relationship with the respective Competence Network and is supposed to act as a contact and support in all matters concerning the DZHK. The DZHK representatives for the Competence Networks are Gerd Hasenfuß (Competence Network for Congenital Heart Defects), Heribert Schunkert (Competence Network for Heart Failure), and Martin Borggrefe (Atrial Fibrillation Network).

Competence Network for Congenital Heart Defects

With the core project National Register for Congenital Heart Defects, the Competence Network for Congenital Heart Defects provides an efficient database infrastructure complete with a biobank for networked research that, among other things, enables us to



Competence Network Congenital Heart Defects: interdisciplinary teams of specialists have to cooperate so that patients receive the best possible care

include under-aged patients. All over Germany, the registry comprises data and samples from people of all age groups who have all types of congenital heart defects. At the end of 2015, the register contained the data sets of a total of 49,582 patients. National researchers and an increasing number of international researchers benefit from this infrastructure. This is also reflected by an increase of the scientific output in 2015. The spectrum of topics includes studies with single patient groups as well as broadly designed analyses all the way to methodical issues. After funding by the German Federal Ministry of Education and Research ended in late 2014, this valuable resource continues to exist thanks to the funding of the DZHK since 2015.

A direct additional benefit resulted from the cooperation within the scope of the DZHK project group “Genetics of Congenital Heart Disease”, in which representatives of the Wellcome Trust Sanger Institute of Cambridge are involved next to scientists of the Competence Network and the DZHK. The group is dedicated to generating ideas for joint basic cardiovascular research. From this group, a position paper among other things has been brought forward containing guidelines on genetic diagnostics applicable to cardiovascular diseases. This paper is the first of its kind ever written in German and is being supported by both relevant German cardiological professional societies, the DGK (German Society for Cardiology) and the DGPK (German Society for Pediatric Cardiology).

Schulze-Bahr E, Klaassen S, Abdul-Khaliq H, Schunkert H, Gendignostik bei kardiovaskulären Erkrankungen: Positionspapier der Deutschen Gesellschaft fuer Kardiologie (DGK) und der Deutschen Gesellschaft fuer Paediatrische Kardiologie (DGPK), *Kardiologie* 9(3): 213-243 (2015-06).

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

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

Acronym	Disease/ Study Objective	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	227
EAST – AFNET 4	Atrial fibrillation and stroke prevention	Guideline relevant study	AFNET	2,745	2,409
DIAST-CHF	Heart failure	Cohort	KNHI	1,400 (number of follow-up examinations in 10 years)	1,936
KNHI - TP 9a	Myocarditis	Guideline relevant study	KNHI	120 (number of follow-up examinations in 10 years)	322
KNHI - TP 9b	Heart failure	Guideline relevant study	KNHI	650 (number of follow-up examinations in 10 years)	1,447
CIBIS-ELD Trial	Beta-blockers in elderly patients with heart failure	Guideline relevant study	KNHI	500 (number of follow-up examinations)	1,020
NRCHD	Congenital heart defects	Registry	KNAH	(open)	49,762
INH-Study	Chronic heart failure	Guideline relevant study	KNHI	400 (number of follow-up examinations)	1,022

Further information to the studies: <https://dzhk.de/forschung/klinische-forschung/aktuelle-studien>

Competence Network for Heart Failure

The DZHK promotes five long-term studies of the Competence Network for Heart Failure (KNHI) which were initiated eight to ten years ago and comprise a total of nearly 6,000 study participants. The cohorts encompass most of all heart phenotypes occurring in the clinical heart failure syndrome and, in addition, large groups of high-risk patients in whom heart failure might develop in the future. The continuation of these studies with long-term follow-ups after 10 to 15 years provides the unique opportunity to better evaluate the



Heart failure: one of the most urgent health problems of modern society.

predictive validity of early diagnoses and the effects of continually adjusted treatment. In all five studies, the follow-up examinations proceeded according to schedule in 2015 and amounted to nearly 1,000 out of 3,000 follow-up examinations.

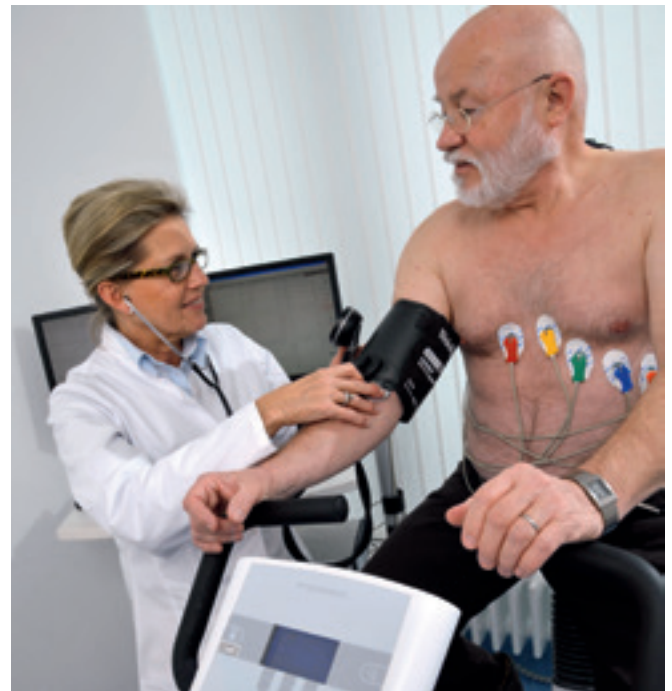
The DZHK profits directly from its access to all study data which the KNHI study centres have gathered so far and will continue to gather in the future. The DZHK members are entitled to use the study results of long-term analyses or cross project analyses to the same extent as the KNHI partners. The DZHK had a direct additional benefit from cooperating with the KNHI by using the KNHI basic data set containing nearly 150 parameters as the foundation for discussing the DZHK basic data set. Just how these comprehensive resources can be used to the benefit of joint projects shall be jointly determined at a conceptual study meeting of DZHK and KNHI scientists in 2016.

<http://knhi.de>

Atrial Fibrillation Network

The Atrial Fibrillation Network (AFNET) is an interdisciplinary research network in which scientists and physicians from hospitals and practices work together throughout Germany. The network endeavours to improve the treatment and care of patients suffering from atrial fibrillation in Germany, Europe and the United States by means of coordinated research. To this end, the Atrial Fibrillation Network conducts investigator-initiated clinical studies and registers on a national and international level.

Since January 2015, the DZHK has been cooperating with the AFNET in the scope of a strategic partnership. Two clinical studies, one patient register and parts of the AFNET infrastructure were funded by the DZHK in 2015. This funding permitted AFNET to

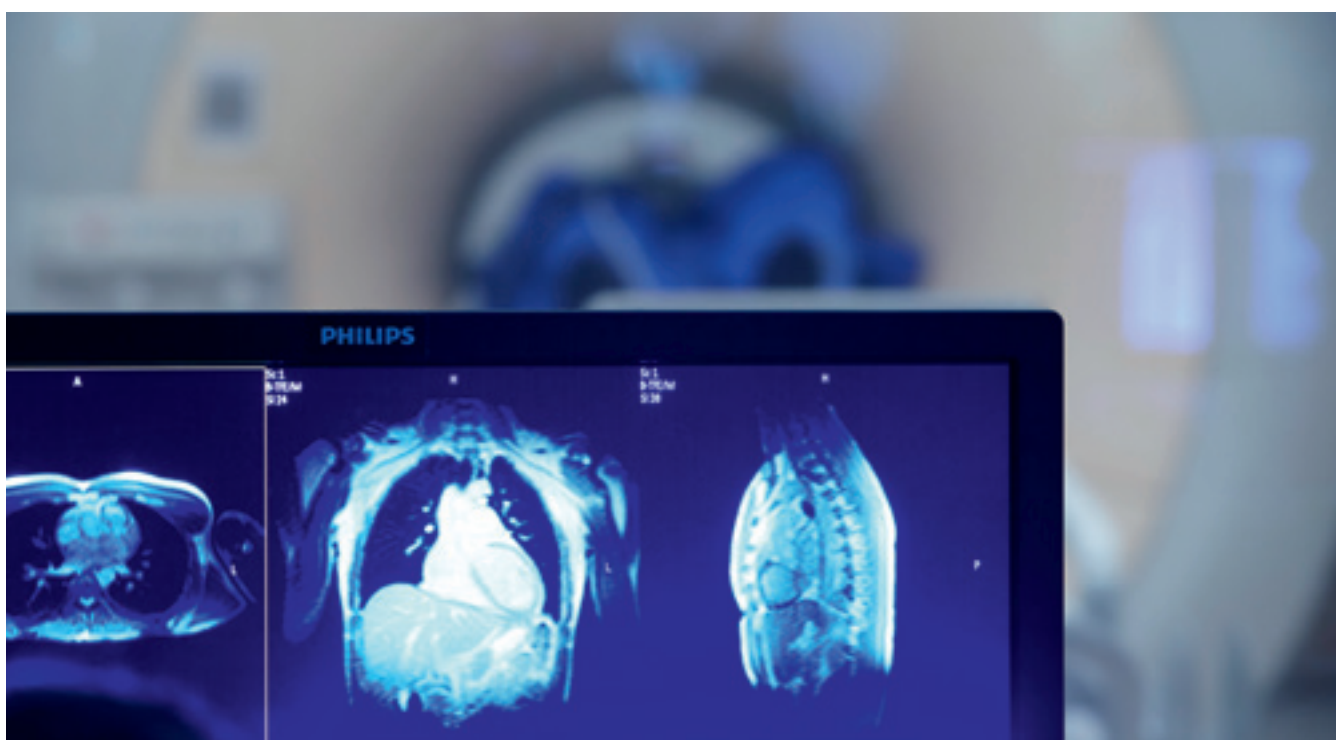


Clinical studies and register at the Competence Network Atrial Fibrillation

further expand its project management at its branch office in Münster. Measures to increase the recruitment of patients were funded within the scope of the current studies EAST – AFNET 4 and AXAFA – AFNET 5 and the AFNET EORP registry. In addition, preparations were made in 2015 for the launch of the Europe-wide NOAH – AFNET 6 study which will start in 2016. It will investigate the benefit of oral anticoagulation in patients with atrial high rate episodes.

AFNET bears the overall responsibility in the legal sense as a sponsor in international clinical studies. Furthermore, AFNET is involved in other national and international studies and projects as well as in one project application concerning a DZHK-funded clinical study on left atrial appendage occlusion in cases of atrial fibrillation.

<http://www.kompetenznetz-vorhofflimmern.de>



Achievements in 2015

- ✓ Approval of four new study applications in both programmes
- ✓ Begin of VAD recruitment
- ✗ Recruitment of patients at all 17 clinical partner institutions
- ✓ Inclusion of a minimum of 500 patients
- ✓ Initiation of at least two external study centres that recruit patients in DZHK studies
- ✓ Appointment of the entire CSG staff

Goals for 2016

- Approval of four new study applications in both programmes
- Recruitment of 2,500 patients
- Consolidation of the CSG staff as a group, election of a spokesperson
- Submission of one study application by each Competence Network

Research Highlights at the DZHK



How to prevent the occlusion of arteries

When it comes to atherosclerosis, various blood cells form a fatal alliance. DZHK professor Oliver Söhnlein from the Ludwig Maximilian University in Munich has discovered a method to prevent this. In the focus stands a small artificial protein for which he has already filed a patent.

The consequences of atherosclerosis are the most frequent cause of death in the western industrial countries (source: Wikipedia). Occluded blood vessels might result in circulatory disorders of the heart, myocardial infarction, thrombosis or stroke. For cardiovascular researchers, everything revolves around the narrowed coronary arteries of the heart. If they are entirely occluded, the result is a myocardial infarction. Oliver Söhnlein and his team have found out how a triad of blood cells – platelets, neutrophils and monocytes – are involved in the formation of such vascular occlusions.

Monocytes are white blood cells that the body summons into action whenever invaders must be expelled. In case of infections, they migrate to the scene of action, become activated and transform into macrophages in order to incorporate the harmful elements. Platelets (thrombocytes) are involved in blood coagulation and the neutrophils belong to the white blood cells. Their main purpose lies in the defence of pathogens.

Normally, this triad of blood cells works to the benefit of the organism. In case of atherosclerosis, however,

their interaction is fatal: platelets and neutrophils are activated at the same time when they attach to the plaques inside blood vessels. Thus, each releases a small protein. Both proteins unite and form a complex that adheres to the wall of the vessel and becomes an attachment site for monocytes. The monocytes adhere to the wall, which is followed by an undesired inflammatory reaction inside the vessel. If a great number of monocytes and their degradation products accumulate inside a coronary artery, it will occlude and cause a myocardial infarction.

To prevent the formation of the complex, researchers have rebuilt a slightly modified form of the neutrophil protein in the laboratory. This artificial protein called SKY displaces the natural neutrophil protein and forms a complex with the platelet protein, which no longer precisely matches with the monocyte attachment site. As a result, the monocytes do not adhere to the vascular wall and the inflammation does not occur. The researchers were already able to demonstrate that the method works in mice that suffer from myocardial infarctions. Oliver Söhnlein therefore filed a

patent for the SKY protein. However, what sounds so elegant at first glance has a snag: “Monocytes are not always bad. Therefore, we only want to interfere with the complex formation at sites where it is detrimental, which is in the arteries affected by plaques,” says Oliver Söhnlein. To achieve this, the researchers are currently searching methods which could allow their protein to be released with tissue specificity.

Oliver Söhnlein developed these results within the scope of his DZHK professorship and they were financed with DZHK site funds. Oliver Söhnlein conducted mechanistic research on the activation of monocytes in the scope of the DZHK funding line “Cooperations with External Partners” which included a cooperation with the University of Münster.

Recruitment of classical monocytes can be inhibited by disturbing heteromers of neutrophil HNP1 and platelet CCL5. DZHK authors: Bongiovanni, Horckmans, Paulin, Ng, Hinkel, von Hundelshausen, Stefens, Kupatt, Weber, Soehnlein, Science Translational Medicine 09 Dec 2015: Vol. 7, Issue 317, pp. 317ra196

Healing after a myocardial infarction?

After a myocardial infarction, the macrophages seem to take on the role of the “good guys” of the immune system. They migrate into the injured heart and help build a stable infarction scar. Cardiologists then speak of healing. The researchers from the Max Planck Institute for Heart and Lung Research in Bad Nauheim wanted to find out how exactly macrophages reach the damaged area.

Following a myocardial infarction, the tissue of the heart will either be damaged or die, because there is no longer blood perfusion. Thanks to very good emergency services, nowadays many patients survive a myocardial infarction. Everything would be fine if the injured heart tissue would just simply form a scar tissue afterwards. Unfortunately, this is not the case.

For many people affected, scar formation does not proceed as it should. As a result, the heart's pumping efficiency might become permanently impaired, which often gives rise to chronic heart insufficiency that ends with a fatal outcome.

Physicians and researchers know quite little about the

reason why scar formation is sometimes disturbed. It is certain that cells belonging to the immune system and their messengers are involved in the healing process. Even until ten years ago, it was assumed that their involvement was predominately a negative one. Monocytes, macrophages, neutrophil granulocytes, and their messengers, the cytokines, were suspected of disturbing the healing process by triggering inflammatory reactions. Today we know that this is not the whole truth: Especially the macrophages play a positive role in the healing of the heart. Studies were able to show that a more ordered scar formation occurs when more macrophages migrate into the damaged tissue. How the process of migration and activation is exactly controlled on the molecular level, however, still remains unclear.

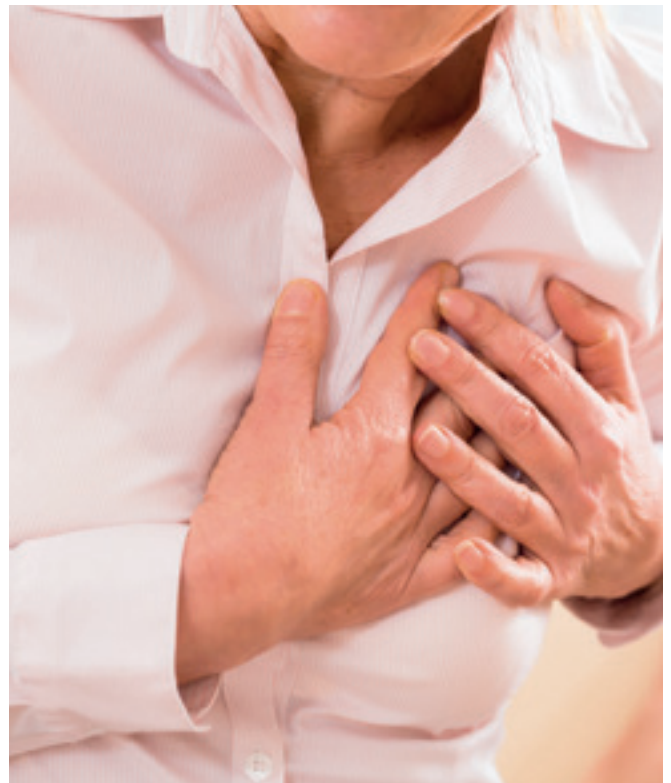
Researchers associated with Thomas Braun and Holger Lörchner at the Max Planck Institute for Heart and Lung Research in Bad Nauheim took a closer look at the complicated interactions between cells of the immune system and the damaged cells of the heart muscle. After an infarction, the affected heart muscle cells dispatch an armada of messengers. The researchers wanted to know exactly which ones attract the macrophages. Among dozens of candidates examined, they finally came across the factor Reg3 β , which enhanced the migration of macrophages into the damaged heart. The researchers were able to demonstrate the protective effect of the factor in mice that were incapable of producing this factor. After a myocardial infarction, these mice died at a higher rate than animals possessing Reg3 β . Once the researchers injected Reg3 β , they had rebuilt in the laboratory directly into the hearts of the mice that did not have the factor, more macrophages migrated into the heart once again and the healing processes went well.

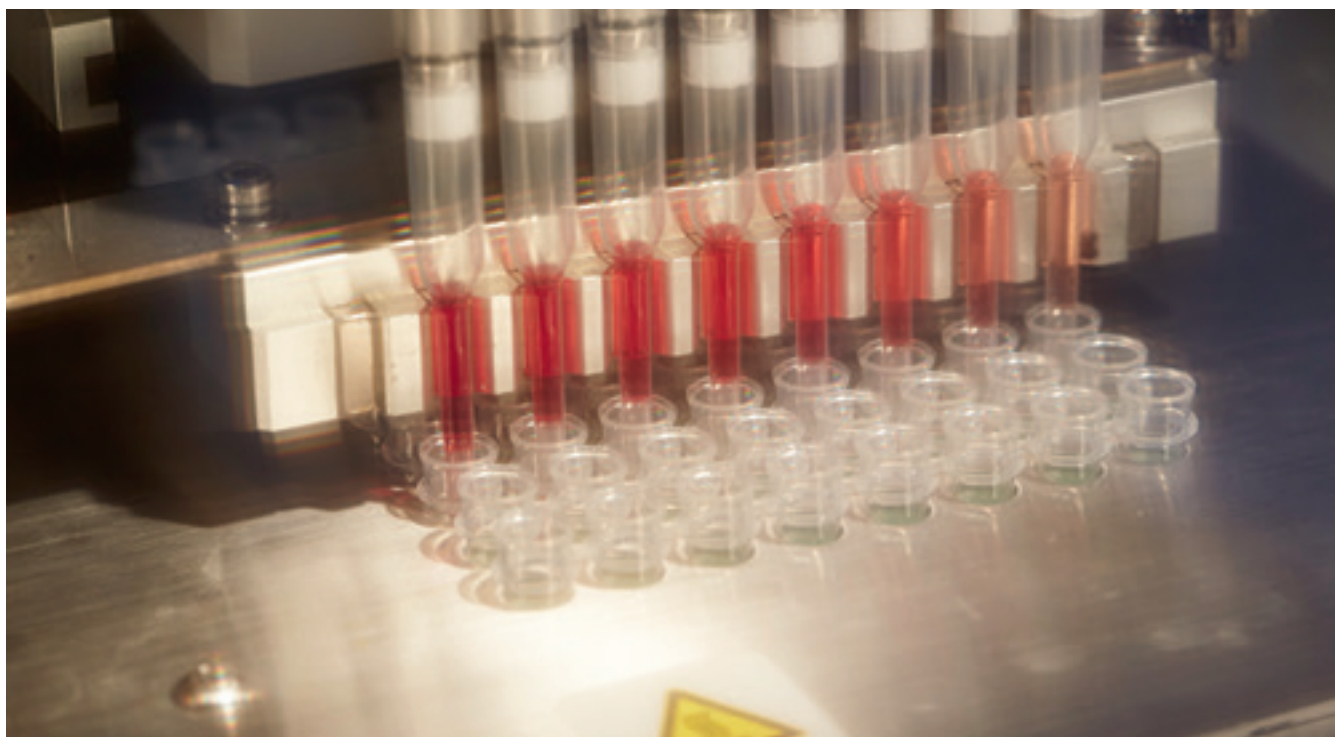
For Holger Lörchner, this is proof of the positive effects of immune cells after a myocardial infarction.

However, there is no doubt that the immune system elicits some unfavourable effects too. Understanding the interaction of the various components of the immune system when reconstructing the heart is therefore an important prerequisite for developing a therapy on these findings someday.

Lörchner, who is a member of Young DZHK, therefore submitted an application for postdoc start-up funding and his application was approved. He now wants to investigate how neutrophil granulocytes, another type of immune cells, interact with Reg3 β and whether they belong to the “good” or the “bad guys” of the reconstruction process.

Myocardial healing requires Reg3 β -dependent accumulation of macrophages in the ischaemic heart. DZHK authors: Lörchner, Braun, *Nature Medicine* 2015 Apr;21(4):353-62





Search operation inside the genome

Ten new gene locations associated with cardiovascular diseases were discovered by an international consortium in the course of the greatest “search operation” worldwide for genetic risk factors for cardiovascular diseases in the genome. Researchers of the DZHK sites Hamburg/Kiel/Lübeck and Munich were significantly involved.

Genome-wide association studies (GWAS) search for risk factors of diseases on the level of the hereditary substance DNA (genome). In such studies, the researchers search for typical alterations within the entire genome, the so-called SNPs (single nucleotide polymorphisms) and see whether these alterations are associated with certain diseases. If this is the case, it does not tell us whether there is a causal relationship between alteration and the disease. But it might tell us something about the statistical risk of a human suffering from a cardiovascular disease.

For many years, Prof Jeanette Erdmann (Lübeck) and Prof Heribert Schunkert (Munich) have been significantly involved in international studies on elucidating the genetic causes of cardiovascular diseases, for example, in the largest GWAS study conducted worldwide so far in cardiovascular research. The consortium CARDIoGRAMplusC4D, consisting of more than 150 partners from 20 countries, analysed nine million SNPs in the genomes of 60,000 patients with coronary heart disease or who had a myocardial infarction and compared them with 125,000 healthy control



patients. In the course of this study, the researchers were able to identify ten further previously unknown gene locations which are involved in the cardiovascular

process. The worldwide cardiovascular research community is now aware of about 60 gene locations which could be associated with diseases of the heart and its vessels. Researchers everywhere in the world are now able to take a closer look at these gene locations in order to identify the mechanisms of pathology. Ideally, these locations could be starting points for a therapy.

Despite the considerable number of nine million studied SNPs, the picture of genetic risk factors is not complete yet. In the future, researchers will have to study even more SNPs in even larger patient populations in order to get a picture as complete as possible. At the DZHK, an important resource for such future studies will be the “OMICS Resource Study” where, different to any previous GWAS study, the entire genome of 1,000 healthy patients will be sequenced for the first time. These analyses will then provide the basis for comparisons with groups of people carrying a disease.

The evaluation of data revealed that only about 20 percent of the SNPs have something to do with known risk factors such as high blood pressure or cholesterol metabolism. In addition, the researchers discovered that the gene modifications particularly affected locations with regulatory functions. These are areas of the DNA that do not contain the blueprint for the synthesis of proteins, but regulate the processes of switching the expression of encoded DNA on and off. These effects are not very obvious in detail. However, if a person is a carrier of several of such modifications, several genes will consequently be falsely regulated. As a result, this condition leads to an elevated risk of having a cardiovascular disease.

A comprehensive 1000 genomes–based genome-wide association meta-analysis of coronary artery disease. CARDIoGRAMplusC4D Consortium. Nature Genetics 47, 1121–1130 (2015).

Errors in the protein factory cause cardiovascular diseases

This text is about translation. This time, not the transfer of research results into clinical practice is meant, but the translation of genetic information into proteins at the site of the ribosomes, the protein factories in cells. If this process is falsely regulated, it might become the cause of cardiovascular diseases. This is what the results obtained by DZHK researchers in Berlin indicate.



Genes contain information about the structure of proteins, the basic building blocks of life. In other words, this means that if genes are defective, defective proteins and the outbreak of disease will be the consequence. If irregularities are registered in the genes of a great deal of people and these data are then related to the manifestation of diseases, one will obtain indications as to which genes might be involved in the diseases. Such so-called genome-wide association studies have already led to the identification of many genes suspected of being involved in cardiovascular diseases. However, often they cannot be identified, because the researchers do not know exactly how the genes cause the diseases.

Whether a protein is ultimately synthesised at the right time, in the right tissue, and in the right quantity also depends on how the genes are read (transcribed) and how gene copies are converted (translated) into proteins. Accordingly, a gene might be intact but the formation of a copy of the gene, the so-called messenger RNA, does not proceed as it should. The messenger RNA is at last translated into proteins at the site of the ribosomes. Here, again, something might go wrong.

Prof Norbert Hübner's team from the Max Delbrück Centre for Molecular Medicine has taken a closer look at the step of gene translation. As it takes place in the ribosome, the analytical method is referred to as "ribosome profiling". To this end, the researchers compared

the heart and liver tissues of two rat strains to each other. While one rat strain is healthy, the other spontaneously develops high blood pressure and is therefore frequently used in genetic research as a model for cardiovascular diseases.

First, the researchers measured the reading, i.e. the transcription, of all genes in both tissues. It was not a new finding that several hundred genes were read differently in healthy and disease-prone animals. Then they started searching in the ribosome and discovered how many messenger RNAs had been translated into proteins. The result was astonishing: twice as many genes displayed differences in the translation into proteins; differences which cannot be explained with transcription analyses.

Finally, the researchers even succeeded in identifying some of the “suspects”. They examined the genes which genome-wide association studies had brought

into connection with cardiovascular or metabolic diseases and used the equivalents of the respective genes known to be responsible for the disease in humans in the rats. And they succeeded: a major proportion of these genes in heart and liver tissues are regulated in the course of translation.

The researchers therefore think it is very likely that gene regulation on the level of translation also plays an important part in cardiovascular diseases of humans. They now intend to test this hypothesis in affected human tissues.

The text was written using sections of an article from MDC Insights by Elke Binder of 1st September 2015

Translational Regulation Shapes the Molecular Landscape of Complex Disease Phenotypes. DZHK authors: Adami, Kreuchwig, Fvan Heesch, Rajewsky, Hübner, N. *Nature communications* 6, 7200, (2015).

Scientific Infrastructures and Resources at the DZHK



Representatives of the DZHK and of the University Medical Faculty in Göttingen (UMG) at the ceremonial laying of the cornerstone of a new research building for translational cardiovascular research held in September 2015

As a research facility, the DZHK disposes of both central and decentral scientific infrastructures and resources. They are designed to survive time and serve the purpose of supporting basic research, clinical research and as the foundation for internal and external cooperations.

New buildings for the DZHK

In September 2015, the foundations were laid for a new research building dedicated to translational cardiovascular research at the DZHK site in Göttingen. With its 44 laboratories, the building will accommodate Göttingen's DZHK research groups and a Collaborative Research Centre for heart failure. Among others, works with the STED microscope developed by Nobel Prize winner Prof Stefan Hell from Göttingen are

planned to take place there. Hence, the foundations of the new research building have been built in such a manner that interfering oscillations are prevented. The first researchers are expected to move into the building in late 2016. The construction costs amounting to about 11.3 million euro are covered by the University Medical Centre Göttingen.

Beyond this, in March 2015, the University Medical Centre Göttingen has inaugurated a building designed for working with real-time magnetic resonance imaging (MRI). The real-time MRI used in the building is the only one of its kind which is being used for clinical application. Real-time MRI technology was invented in Göttingen and was developed by the research team led by Prof Jens Frahm, Max Planck Institute for Biophysical Chemistry. The technology enables a so



Cardiac diagnostic with an ergometric bicycle at the partner site Greifswald. In the meantime, all DZHK partner sites have been equipped with examination rooms

far unachieved temporal and spatial resolution of MRI in real time. An interdisciplinary and cross-institute working group, to which also researchers of the DZHK belong, is developing the technology for the clinical application in patients.

Examination rooms and instruments for clinical studies

In the reporting year, the DZHK has furnished examination rooms for clinical studies at the 17 university hospitals of its member institutions. These rooms were made available by the partner institutions and are the workplaces of the CSG staff funded by the DZHK. The clinical researchers within the DZHK had previously agreed on an identical pool of examination instruments with which the rooms were to be equipped. Therefore, identical ECG instruments, ultrasound in-

struments, spirometers and other pieces of equipment relevant to cardiovascular diagnostics worth 1.4 million euro were purchased. This ensures that the same conditions prevail in all clinical examinations, regardless of the location, and the collected data can be subject to cross-study and cross-site evaluation. The instruments and appliances solely serve research purposes and are not applied in clinical routine. The rooms are clearly identified as DZHK examination rooms and this way the visibility of DZHK research for patients and clinic staff is assured.

Central Data Management and Trusted Third Party

The Central Data Management (ZDM) for the clinical studies, consisting of the Trusted Third Party in Greifswald, the "ITLab" project for the coordination of

the IT infrastructure and the Biobanking Project at the main office in Berlin and Data Handling (DH) in Göttingen, took up regular operations late in 2014, when the first patient of the TORCH registry was enrolled. New studies and registers were started in 2015 and operations were further optimised. Late in 2015, four studies and registers (TORCH, TransitionCHF, VAD and SFB/TR19+) were already working with the systems of the ZDM and more than three further studies were in different states of preparation.

DZHK studies record data and biological materials according to standardised procedures. These harmonised data models and processes provide the basis for the sustainable use of data and biological samples. The regulations and the processes for data use were elaborated by the Use and Access Committee (U&AC), which was appointed in October 2015 and took up operations in January 2016 (cf. Chapter “Committees”). The ZDM has collaborated as an advisor in designing the process flows and will support the U&AC by means of a so-called transfer office in the future.

In the reporting year, the necessary interfaces and processes were also coordinated by the ZDM in order to enable the integration of the two new components of the clinical-scientific IT infrastructure, i.e. the Laboratory Information and Management System (LIMS) and the planned Image Data Management System (IDMS).

DZHK Biobank

The DZHK operates a decentralised biobank with central data handling. This means that the samples are stored under standardised conditions at the site of the partner institutions, but the data are stored centrally. A set of basic biological materials and, if applicable, a set of study-specific biological materials are taken



from each patient in every clinical study of the DZHK. Samples from approximately 500 patients were collected by late December 2015.

In 2015, the clinical partner institutions of the DZHK modernised and extended their biobank technology in order to process and store biological materials under standardised conditions. To this end, rack scanners, automatic sample processing stations and deep freezers were purchased.

In the reporting year, the tender and awarding of a contract for a Laboratory Information and Management System (LIMS) also took place. The system will enable the standardised and digitalised registration of biological materials and pertinent data. It will be implemented in 2016 and will then be available to all participating study centres. It constitutes the networking core of the decentralised DZHK Biobank.

OMICs project – 1,000 genomes for research

The DZHK OMICs resource was started in the reporting year. This is a representative random sample of the German population whose DNA and RNA shall be completely sequenced. This will enable us, for the first time ever in Germany, to register the entire information of the genome and analyse it for cardiovascular research issues. This resource permits us to achieve a considerable refinement of the genome-wide analyses, because now the information of the entire genome can be accessed, thus permitting us the study of genetic variants that seldom occur.

In addition, the data derived from healthy people serve as a control resource for research work in patients at the DZHK and for external partners as well. The samples come from six cohorts affiliated with the DZHK member institutions. The representativeness of the sample composition for the population living in Germany is assured by the fact that the cohorts are spread throughout the whole of Germany.

We succeeded in acquiring both the German Cancer Research Centre in Heidelberg (DKFZ) and the Max Delbrück Centre in Berlin (MDC) as partners for conducting sequencing. Sequence data are stored at the DZHK sites in Munich and Lübeck where comprehensive expertise is available in this field. The costs for the DZHK OMICs resource project amount to approximately 2.2 million euro, which includes the costs for sequencing the samples, as well as for expanding storage and computing capacities needed for the generated sequence data.

The sequencing work shall be carried out in 2016, following the negotiations and the closure of a cooperation contract between the DZHK and the DZHK member institutions that are involved in this project.



Stem Cell Registry

Induced pluripotent stem cells (iPSC) have developed into a central tool of translational research at the DZHK. For this reason, a cross-site Stem Cell Information Management-System (StIMS) has been established for the electronic documentation and archiving of laboratory processes spanning the entire life cycle of the samples. In addition, Standard Operating Procedures (SOP) defining standardised procedures of sample processing were created. A concept for the integration of the StIMS into the central infrastructure

was elaborated in agreement with the ZDM. It shall be implemented in 2016. This integration effort enables the combination of stem cell data with data derived from various DZHK studies.

Moreover, the DZHK Stem Cell Registry was established in the reporting year. The registry combines selected data related to stem cells with those related

to activities at the site of the DZHK members and thus serves as a central platform for the scientific exchange both within and outside the DZHK. The registry can be accessed on the DZHK website (<http://dzhk.de/resources/dzhk-stem-cell-registry>) and is thus also directly accessible to the international research community.



Achievements in 2015

- ✓ Completion of the DZHK research building at the Göttingen site (funded with university funds)
- ✓ Establishment of uniform minimum standards for equipment at the DZHK clinical study centres of the DZHK
- ✓ Phenotyping units established
- ✓ Use & Access Committee initiated
- ✓ Decision made for a laboratory information system
- ✗ All clinical study documents are also available in English

Goals for 2016

- External transparency of data and sample stock
- Systems for Use & Access established and first inquiry accepted
- Decision made in favour of an image data management system
- Clinical-scientific infrastructure also available in English

Cooperation and Scientific Exchange at the DZHK

The close cooperation between the individual partners is an important aspect of translation. For us, it is therefore a matter of great concern to employ all our measures and structures to promote the stable networking between partners of the DZHK as well as eligible external partners. Some of the cooperative measures at the DZHK shall now be presented below.

Project groups

Project groups within the DZHK are cross-site consortia of scientists who generate new ideas within a limited period of time. The objective of project groups is to submit applications for project funding in the medium term — regardless of whether they are for small experimental cooperation projects, high risk translational research projects, or clinical studies. Moreover, they contribute to reinforcing networks among clinically working scientists and basic scientists.

In 2015, three new projects groups were added to the ten already founded in 2014. These are concerned with congenital heart defects, gender medicine in cardiovascular research as well as inflammation, (auto) immunity and cardiomyopathies. The project groups are founded without any central content-related provisions made by the DZHK; instead, they are initiated independently by the scientists themselves. The foundation of a project group requires the approval of the Board of Directors.

In 2015, we enquired into the activities of the project groups for the first time since their foundation. The feedback we got made it clear that the project groups promote scientific exchange within the DZHK and that they clearly benefit from the various expertise available at the DZHK sites: Apart from organising DZHK symposia (2), workshops (4) and lectures (2) at DZHK retreats, the funding lines assignable to the preclinical field were primarily used (provider of Shared Expertise

projects: 2, experimental cooperations by means of Shared Expertise: 10, HRHV applications: 2). Five applications for clinical studies emerged from project groups. Moreover, the project groups collaborate with each other (2), as well as with the Cardiological Competence Networks funded by the DZHK (1), and with external scientists. So far, 29 DZHK publications have resulted from the work of the project groups.

Project groups are entitled to make a claim for expenses at the DZHK for costs incurred for project group meetings. The DZHK video conference system is also at their disposal. They do not have a budget of their own.

Symposia and conferences

DZHK symposia are events which serve the purpose of internal exchange on subjects which are of relevance to the entire DZHK. With the exception of individual external speakers, attendance at these cross-site events is reserved for the members of the DZHK. Each of the symposia held in 2015 were attended by scientists from at least five DZHK sites. The ideas for the symposia are developed by the RCC and originate, for example, from the project groups. For 2015, the RCC decided on organising the following three symposia:

-
- Non-Human Primates in Advanced Therapy Medicinal Product Development, 29 June 2015, Göttingen (106 participants from five DZHK sites)
 - Biological Imaging and Sensing, 1 to 2 October 2015, Greifswald (70 participants from six DZHK sites)
 - The Noncoding Genome in Cardiovascular Diseases – Pathogenic Implications and Therapeutic Perspectives, 16 to 17 October 2015, Berlin (100 participants from all DZHK sites)
-



200 scientists gathered at the DZHK Retreat 2015 in Potsdam

If a member institution of the DZHK organises a scientific conference whose subjects are of interest to the DZHK, it is possible to obtain funding for organising the event. However, it is conditional that a DZHK session is a part of the conference. In 2015, the DZHK supported six conferences of its member institutions with funding (2014: 2). Members of the Young DZHK receive a refund for their travel expenses from the DZHK if they attend.

DZHK Retreat and Young DZHK Retreat

The **DZHK Retreat** took place for the third time from 17 to 19 September. The day before, the members of the Young DZHK had the opportunity to meet for the second time at a retreat of their own. As in the years before, the number of applications exceeded the

number of available places. On the second day of the retreat, approximately 200 scientists met in Potsdam.

In the reporting year, the retreat programme predominantly covered scientific subjects, but strategic and administrative aspects were presented and discussed as well. Next to the three international high-class keynote lectures held by Jeffery Molkentin (Cincinnati), Garret FitzGerald (Philadelphia) and John McMurray (Glasgow), a highlight was the podium discussion about the central topic of the DZHK: translation. Moderated by Gerd Hasenfuß, member of the Board of Directors, the lecturers Garret FitzGerald, Jeffery Molkentin and the speakers of the Translational Research Group (TRG), Heimo Ehmke and Mat Daemen, discussed the progresses and challenges of translating research approaches into clinical practice. Furthermore, there were three parallel workshops focusing on the topics of RNA biology, fibrosis, and biobanking, as well as one session each to introduce the funded projects and studies of the preclinical and clinical fields. For industry perspectives, we were able to get representatives of Bayer HealthCare, Sanofi, Servier SAS and Biotronik, who gave insight into their late preclinical projects in a joint session.

The **Young DZHK Retreat** organised by the postdoc representatives enjoyed great popularity in its second year. A total of 94 junior scientists applied for the 54 available places. Each prospect was requested to submit an abstract and, if selected by the postdoc representatives, also attend the main DZHK Retreat. While the Young DZHK Retreat was in progress, the participants introduced their scientific work to each other on guided poster walks and in lectures. This year, the poster exhibition stayed up during the entire retreat period. Kindly supported by Bayer AG, the best three posters were once again awarded with a prize. Additionally, the organisers were also able to get two excellent keynote speakers: Vasan Ramachandran

(Boston), member of the Scientific Advisory Board of the DZHK, and Volker Adams from the University Hospital of Leipzig. The Young DZHK Retreat was also used to introduce the mentoring programme offered by the DZHK.

The DZHK Retreat is the most important network and exchange instrument of the DZHK. This is also reflected by its associated advance meetings. In 2015, the members of the OMCs project and the DZHK professors met in Potsdam prior to the event. The DZHK professors followed the proposal of the Board of Directors and agreed to function as the programme committee at the 2016 retreat in Bad Aibling. In the future, we would also like to connect the Young DZHK Retreat to the main DZHK Retreat even more. Apart from the lectures held by the Young DZHK prize winners, there shall also be lectures by junior scientists in the scope of the regular scientific programme of the retreat.

Internal communication

Most important channels for regular internal communication are the monthly e-mail newsletter and the Intranet. The newsletter informs all persons who are involved with the DZHK about important strategic committee decisions and about tenders, deadlines, scientific events, new Shared Expertise and job vacancies. It now has 1,300 subscribers. The Intranet serves as an internal information platform and download archive. This is where users can also find protocols issued by the most important DZHK committees (Board of Directors, RCC, CSG Steering Committee, Use & Access Committee, site manager meetings, Assembly of Members, Scientific Advisory Board) alongside current funding documents. In addition, the users can easily register for internal events. Internal communication at the sites is effected for the most part by means of mailings and annual or biannual site retreats.

In 2015, the internet-based video conference system was also frequently used and its application range extended. For example, the sites are able to independently call in online meetings, and committees are also increasingly switching from personal meetings to online meetings. The Use & Access Committee initiated in late 2015 exclusively holds online meetings. In the time from April 2015 to April 2016 a total of 503 video conferences (2014/2015: 357) with a total of 2,191 participants (2014/2015: 1,555) were held.

So that the funding processes are more transparent and efficient, we began revising and standardising our 12 funding guidelines including 18 funding measures in 2015. This process had not been concluded by the end of the reporting year.

Achievements in 2015

- ✓ At least three DZHK symposia
- ✓ Project groups with tangible results
- ✓ Ongoing: more transparent and structured design of the funding guidelines

Goals for 2016

- Project groups work with tangible results
- Two DZHK symposia
- Increase attendance numbers of the retreat
- Finalisation of the revision of the funding guidelines

External Cooperations



It is absolutely essential that various disciplines and institutions join forces when it comes to translation. The DZHK has therefore anchored cooperations with external partners in its research strategy and reserved ten percent of its funds for these cooperations. External cooperations occur within the DZHK Preclinical Research and Clinical research funding lines. In addition, the three Cardiological Competence Networks were supported with 1.68 million euro from these funds (cf. Chapter 4).

Cooperations with external partners (preclinical research)

In the scope of the Preclinical Research funding line, DZHK scientists can also cooperate with external partners — with the objective of bringing external expertise into the DZHK and giving external partners the oppor-

tunity to get involved with the DZHK. The cooperations follow rules similar to those that regulate cooperations by means of Shared Expertise (cf. Chapter 6). Similar to the latter, both partners obtain research funds for the joint project from the DZHK. In the reporting year, the DZHK conducted 30 of such cooperations (2014: 13), 27 with German universities and out of the remaining three, one with the Max Planck Institute, one with the Fraunhofer Institute and one with the German National Metrology Institute (Physikalisch Technische Bundesanstalt).

The projects are approved according to an internal selection process of the respective sites. In 2015, they were very diversified with respect to their issues and methods. In the cooperation projects, for example, the methylation status of heart muscle cells and their progenitor cells was examined, the interaction partners

of proteins were determined, and a zebrafish platform was developed in order to investigate the pathological mechanisms of atherosclerosis. Even a psychological mode of intervention was developed to influence the behaviour of a patient after a myocardial infarction.

Overview of cooperations with external partners

- Total of approved applications: €748,094
- Average project costs: €24,936
- Average share of cooperation partner I (DZHK): €11,873 (equals 48 %)
- Average share of cooperation partner II (external): €13,063 (equals 52 %)
- Average project duration applied for: 10 months

Cooperations with external partners

- 2013: 20 cooperations
- 2014: 12 cooperations
- 2015: 30 cooperations



Industry cooperations

The DZHK set itself right from the start the objective to enter into a larger strategic preclinical research cooperation with an industrial partner. This is the reason why talks with Bayer HealthCare took place during the past few years. In the reporting year, we pushed this process once again by submitting a list of approximately 50 target molecules for drugs derived from basic research to the company in order to review the possibilities of cooperation and further development. These target molecules concern molecular structures which are involved in the pathology of cardiovascular diseases and might represent potential target sites for new therapies. Ultimately, a structured cooperation could not be realised, since too few target molecules were within the field of interest of the industrial part-

ner. Subsequent to further talks, both parties agreed to abstain from this kind of cooperation for the time being.

As far as clinical research is concerned, the DZHK organised its first joint workshop with representatives from industry in Berlin in December. The goal was to inform each other about one's research activities and thus explore the possibilities for cooperations. Big Data and personalised medicine stood in the centre of the workshop which was also attended by representatives of Bayer HealthCare, SAP and representatives of other university hospitals alongside DZHK scientists. Building on this successful meeting, more contacts are planned for in 2016.



Apart from large strategic cooperations, the DZHK focuses its attention increasingly on individual, project-related cooperations, particularly in the scope of clinical studies and HRHV projects. For example, almost every HRHV project of the late preclinical stage has a partner who is a small start-up company that owns a patent for a method or technology the project needs. Each one of these cooperations must be designed and negotiated individually. For this to run as smooth as possible and to comply with the provisions of applicable funding and competition laws, we have started to work out fundamental rules for the funding of such cooperations.

Achievements in 2015

- ✓ Initiation of at least two external study centres which recruit patients in DZHK studies (cf. Chapter 4)
- ✗ Contract draft for a structured cooperation with an industrial partner (cf. text above for explanations)

Goals for 2016

- Elaboration of framework conditions for individual industry cooperations in the scope of HRHV projects and clinical studies
- Funds paid to external hospitals for patient fees

Promotion of Junior Scientists – the Young DZHK



The next generation of scientists at the DZHK is increasingly establishing itself as a platform for young researchers. For the promotion of junior scientists, the DZHK created a comprehensive sponsorship offer in the shape of the excellence programme, which is particularly for postdoctoral researchers. The mea-

asures for promotion of junior scientists were intensively advertised in the reporting year; including with a Young DZHK brochure and a supplement in the weekly newspaper “Die Zeit” (cf. Chapter 10). In total, the DZHK allocated 1.5 million euro for the promotion of junior scientists in 2015.

Report of the spokesperson of Young DZHK, Dorothee Atzler:

The Young DZHK has existed since 2013 and our core task is to build a network for young scientists, both basic researchers and clinical researchers, within the DZHK. We want to provide a cross-site platform for scientific and personal exchange and assistance in career planning and — while cooperating closely with DZHK principal investigators — the best possible qualification in the field of translational cardiovascular research.

Our core team, i.e. the “PostDoc Committee”, is composed of two members from each site who elect the spokesperson and the deputy spokesperson of the committee. Among our most significant successes within the last three years are the increase in the number of members to over 700, the full membership of the Committee in the RCC including the right to vote, and the realisation of a separate Young DZHK Retreat, which has already taken place twice as a satellite symposium in advance to the regular DZHK Retreat. A survey among the participants revealed a very high rate of satisfaction with both Young DZHK Retreats.

Thanks to the support rendered by the Board of Directors and the main office, we were able to further develop the DZHK excellence programme initiated in 2014. We particularly appreciate that two former members of Young DZHK have taken another step in their careers: Georgios Kararigas has been appointed to W1 DZHK professor at the Charité University Hospital in Berlin and Konstantinos Stellos to associate professor at the Goethe University in Frankfurt.

New in 2015: Young DZHK workshops

The Young DZHK has started developing its own workshop series. It considers itself a supplement to the DGK-DZHK workshop series and is supposed to give the members of the DZHK additional further training opportunities. The topic proposals come directly from the Young DZHK, whereas the workshops are organised by the Young DZHK PostDoc Committee. The first workshop was held in Berlin in November 2015 on the topic "Applied Regression Modelling". It was fully booked and rated very well by participants (83 percent "Course was great", 100 percent "Would suggest course to colleagues"). Another workshop entitled "Large Animal Models in Cardiovascular Research" is scheduled to take place in Hamburg in the autumn of 2016.

Training and mentoring

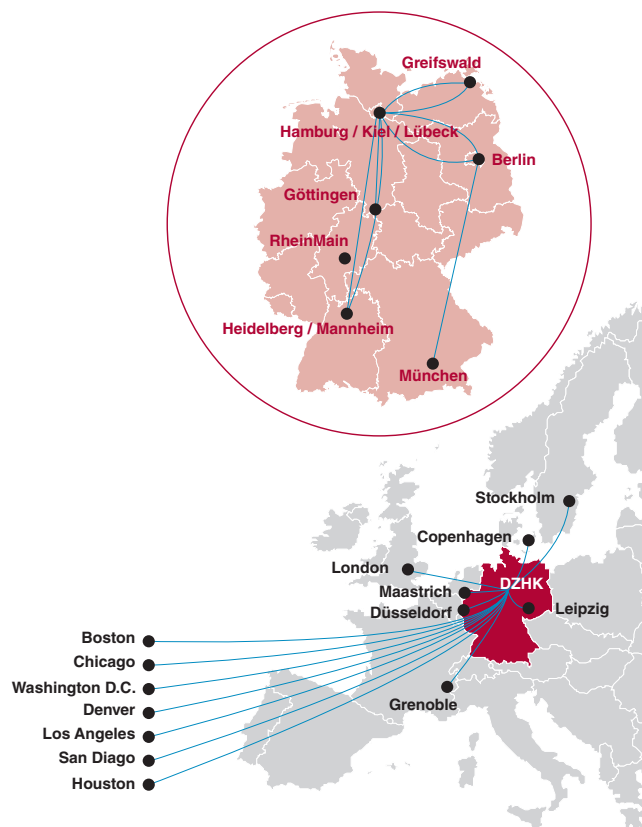
The cooperation of researchers across the boundaries of disciplines and institutions is encouraged at the DZHK at an early stage. To this end, the DZHK provides exchange and further training opportunities in the context of its training programme. Thus, with the mobility programme junior scientists may go to a laboratory of a DZHK partner institution (9) or an external laboratory (15) in order to learn or apply a method. Young physicians have the opportunity to dedicate themselves to their research full time for one year and during this time they will receive a doctoral fellowship in order to conduct an experimental doctoral thesis at the DZHK. The DZHK funds the young researchers' participation in high-ranking conferences in order to present their own research results to the national and international science community.

The mentoring programme has started its second year. It is for young physicians, life scientists and science managers. The goal is to qualify young academ-

ics from cardiovascular research for leadership assignments. This year, there have been 19 applications for 14 places.

A total of 272 applications were approved for staff training (2014: 200).

Travel grants for high-ranking conferences	180 (107)
Grants for doctorates	31 (25)
Mobility programme	24 (51)
Attendance of external workshops	24 (31)
Mentoring (call 2015)	14 (14)



The mobility programme permits to learn new research methods outside the own institution

Joint workshop series with the German Cardiac Society (DGK)

Since 2013, the DZHK has held the series “Fundamentals of Cardiovascular Research” jointly with the DGK. Three workshops are held each year. Two of them are held by the DGK during its spring and autumn conference and in the summer, a workshop designed and organised by the DZHK takes place in Berlin at the DZHK main office. The backdrop of the programme is to offer clinical scientists a type of curriculum similar to the one life scientists in graduate schools have.

Excellence Programme

The excellence programme was developed on the initiative and with the contribution of the Young DZHK PostDoc Committee. The programme is for Young DZHK members who have completed their doctorate. Selection proceeds according to scientific achievement. In addition, it takes into consideration the particular life situation of the researchers in this stage and therefore includes support for the return after family

leave and exemption from teaching and patient care in favour of research. The measures of the excellence programme are as follows:

DZHK Junior Research Groups

The objective of the DZHK Junior Research Groups is to acquire qualified and talented junior scientists at home and abroad for the DZHK and to support them on their journey to early scientific independence. In this regard, the funding measure is similar to the Emmy Noether Programme of the German Research Foundation (DFG). By leading a junior research group, but also by assigning teaching tasks in a reasonable scope, the junior scientist shall become more eligible for a professorship. A DZHK junior research group will be funded for up to five years; up to 250,000 euro per year may be applied for. The junior scientists can choose the DZHK member institution where they want to work themselves. The first invitations to tender for two junior scientist groups took place in 2015, whereupon eleven national and international applications were received, among them were several applications from exceptionally good candidates

Junior Research Groups approved for 2015:

Name	Member Institution	Project Title	Duration (months)
Shirin Doroudgar	University Hospital Heidelberg	Sarco/endoplasmic reticulum protein homeostasis and cardiac function	60
Lars Mägdefessel	Technical University of Munich	Non-coding RNA-based therapeutics and biomarkers for treatment and detection of vascular diseases	60



Shirin Doroudgar



Lars Mägdefessel

Postdoc start-up grant

Postdoctoral researchers who intend to apply at major project sponsors for their own research project may prepare this with the aid of this funding and generate first research data. The maximum amount is 60,000 euro and is approved for the duration of one year at most.

In 2015, 34 applications were received, 14 of which were preselected by the sites. A selection committee composed of site spokespersons and the Board of Directors finally approved five applications. After the first round, the procedure was discussed in the RCC and subsequently a modification of the tender process was decided.

Due to the great number of applications, the decision was made to increase the number of funded projects per annum from five to ten, however, distributing them

to two tender processes per annum. One of the two tenders is for junior scientists with a doctoral degree who are still at the beginning of their careers. The second tender is for experienced junior scientists. In addition, the decision was made to adopt a quota system for the funding to be awarded. A certain quota will be reserved for physicians depending on the number of applications they submit.



Postdoc start-up funding approved for 2015

Name	Member Institution	Project Title	Duration (months)
Jan Haas (PhD)	University Hospital Heidelberg	Dissection of molecular disease mechanisms in non-compaction cardiomyopathy	12
Holger Lörchner (PhD)	Max Planck Institute for Heart and Lung Research, Bad Nauheim	The regulatory role of Reg3β on neutrophil persistence and functionality after the onset myocardial infarction	12
Ryota Matsuoka (PhD)	Max Planck Institute for Heart and Lung Research, Bad Nauheim	The role of sympathetic and parasympathetic innervation in heart development and regeneration	12
Maliheh Nazari-Jahantigh (PhD)	Technical University of Munich	Role of miR-147 in macrophages in atherosclerosis	12
Yassine Sassi (PhD)	Technical University of Munich	The function of microRNA in cardiac arrhythmia	12



Beside their clinical work young researchers are granted time for research at the DZHK

Rotation grants for physicians

This programme is for physicians who are Young DZHK members and engaged in a DZHK research project. They may be exempted from patient care for one year and dedicate themselves to their research. Funds for human resources are raised in conjunction with this grant that will be used to finance the substitute. This measure serves the purpose of stabilising clinical research at the DZHK in the long term. In 2015, eight applications were submitted to the main office, six of which were approved by the selection committee.

Rotation grants approved in 2015

Name	Member Institution	Project Title	Duration (months)
Nadya Al-Wakeel	German Heart Centre Berlin	Heart failure in children and adolescents	24
Thorsten Kessler	German Heart Centre Munich	Functional characterisation of risk factor gene ADAMTS7 in vascular smooth muscle cells	12
Constantin Kühl	University Hospital Schleswig-Holstein, Campus Kiel	Characterisation of long non-coding RNAs as novel modulators of cardiac hypertrophy	12
Michael Schwarzl	University Heart Centre Hamburg	Pressure-Volume analysis in structural heart disease	12
Lisa Tilemann	University Hospital Heidelberg	Efficacy of ticagrelor after cardiopulmonary resuscitation in hypothermic patients with a myocardial infarction	12
Maura Magdalena Zylla	University Hospital Heidelberg	Catheter ablation for atrial fibrillation in heart failure with preserved ejection fraction	12

Research grant — release from teaching

With this grant, Young DZHK members who are engaged in teaching for more than four hours per week can be released from teaching for two semesters. During this time they can dedicate themselves more intensively to their research and, for example, finish their post doctoral qualification (habilitation). Funds for human resources are raised in conjunction with this grant which will be used to finance the substitute.

Reintegration grant

With this programme, the DZHK wants to facilitate the reintegration of young researchers after family leave. Persons whose contract expired while on parental leave are eligible to apply. The grant secures the financing of one's job for six months at most. In 2015, no applications for a reintegration grant were submitted.

Research grants approved in 2015:

Name	Member Institution	Project Title	Duration (months)
Nadine Althof	Charité University Hospital Berlin	Impact of immunoproteasomes on innate immune response to myocarditis	12



A total of 14 DZHK young researchers participated in the second class of the mentoring programme

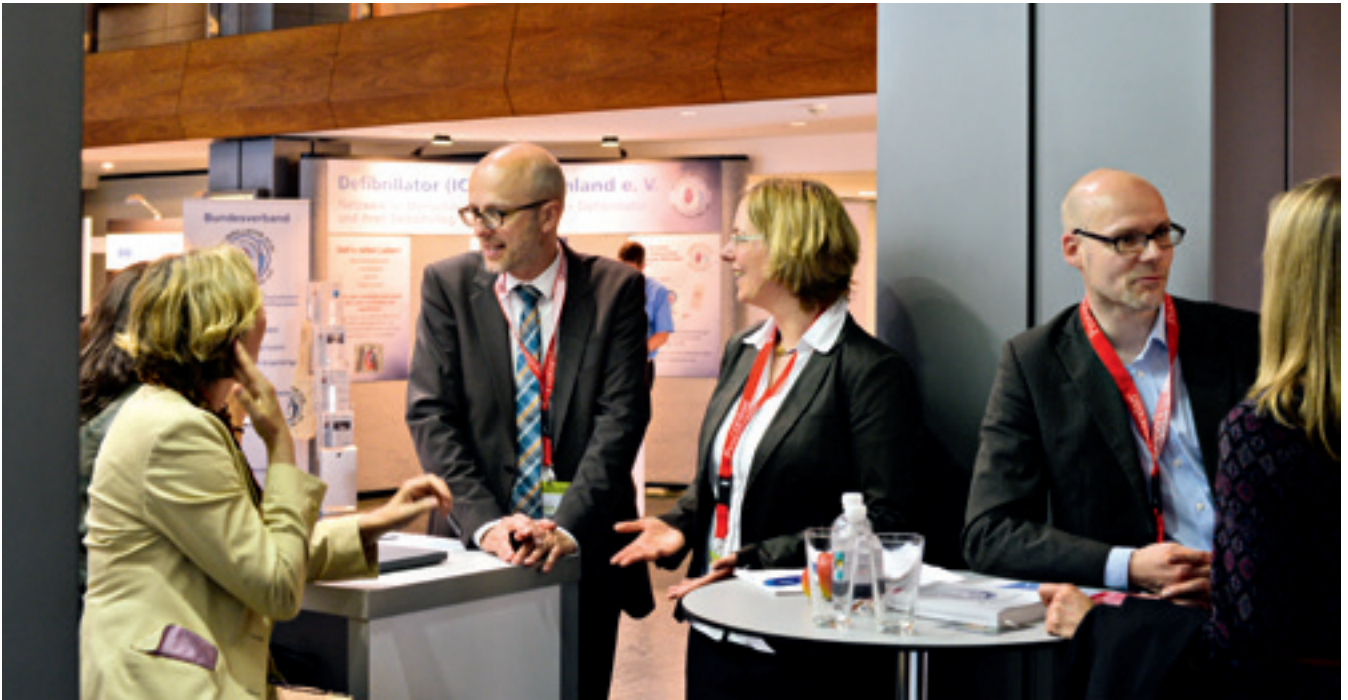
Achievements in 2015

- ✓ Documentation of a turnover rate of at least ten percent in the Young DZHK (entries/leaves)
- ✓ A minimum of 20 grants for doctoral theses for physicians
- ✓ Awarding five postdoc start-up grants
- ✓ Awarding five rotation grants
- ✓ Establishment of at least one Junior Research Group

Goals for 2016

- Increasing the awareness of teaching release and reintegration in order to obtain more applications
- Summary on how the measures are requested after two tender rounds
- Further development of the mentoring programme
- Publication of a mentoring alumni newsletter

The DZHK in the Public



The DZHK has become a brand name and presents itself at major events - as is the case here at the Annual Conference of the German Society of Vascular Surgery in Mannheim

In the reporting year, the DZHK set the focus of its public relations activities on the promotion of junior staff. In a bilingual brochure we introduced the measures of the training and mentoring programme as well as the newly established promotion of excellence. A half-page advertorial in a special research supplement in "Die Zeit" illustrated the attractiveness of the DZHK's promotion of young researchers by showing examples of young DZHK researchers and it had a very positive response. Together with the DGK, we produced a flyer for the DGK-DZHK junior staff promotion programme in a new design that particularly appeals to this young target group. We published the tenders for the DZHK Junior Research Groups on ResearchGate and in Nature online. In order to increase our international outreach and inspire an online career network, the DZHK started an online presence on LinkedIn in English.

For the first time, we organised a larger joint fair stand at the annual meeting of the German Cardiac Society in Mannheim, together with the Cardiological Competence Networks supported by the DZHK since 2015. This produced synergies in addressing the individual target groups and also promoted networking activities between the organisations. We also made arrangements for the joint public relations work of the DZHK and the Competence Networks. Funding by the DZHK will be referred to by logos and explanatory texts in all documents and online appearances of the Competence Networks. In the field of public relations we supported the Competence Networks with two press releases.

Internet and Intranet were extended by new modules in the reporting year as well. These platforms increasingly serve the purpose of exchange among scientists

and people who are involved in science projects. Thus, we established a database on the website with data derived from the Stem Cell Registry. Here, users from all over the world can search for certain cell lines and submit inquiries to the DZHK institutions storing the cell lines. A protected domain for people who are involved in clinical studies of the DZHK has been created on the website. It provides all the documents needed for the initiation of a study centre and the course of a clinical study. Some DZHK studies also offer specific documents and newsletters relating to their particular study. Apart from improving the transparency on work flows, these measures also function to make the DZHK more well known, as people who do not belong to a DZHK member institution also have access here.

We developed a signposting system for the new DZHK examination rooms at the partner institutions. Now the commitment of the DZHK in the field of clinical research at the sites is highly visible for study personnel and patients. For patients participating in the clinical studies of the DZHK, we developed the first version of a patient information platform on the internet (cf. Chapter 4).



DZHK exhibition stand at the German Society of Cardiology (DGK) 2015 in Mannheim

The first DZHK YouTube video went online in late 2015. In it, Thomas Eschenhagen, spokesperson of the DZHK Board of Directors, explains why translation is so difficult and the nature of the approach the DZHK pursues. Within a short time the video had a three-digit number of views and is a good start for a series which shall be continued with two to three videos in 2016.

On the subject of the DZHK research magazine we had intensive talks with the six DZG in order to clear up the modalities and participations. We further researched providers and prices. At the end of 2015, we had a concept which four DZGs approved. Two of the six DZGs either ruled out participating at this point in time or kept the issue open. Based on these conditions, a tender of a service provider may proceed in 2016.

Achievements in 2015

- ✓ Publication of a brochure on DZHK promotion of junior staff
- ✓ Increased visibility of the DZHK at partner institutions (DZHK professors and DZHK projects on website, signposting)
- ✓ Launch of DZHK video series
- ✓ Online patient information for study participants
- ✓ Development of a design for a DZG research magazine

Goals for 2016

- Construction of a comprehensive patient information platform
- Marketing of the DZHK clinical studies
- Production of two or three YouTube videos
- Publishing a project database of major DZHK projects on the internet
- Starting first approaches to address the broader public

Indicators of the Success of Translational Research at the DZHK



Whether an organisation is successful depends on many factors and is difficult to measure, especially during start-up. Indicators of success reveal how conditions that make the success of an organisation likely are fulfilled.

Ever since its establishment, the DZHK has been discussing how the success of translational research can be measured and evaluated together with the other German Centres for Health Research (DZG). As yet, generally acknowledged indicators of the success of translational research do not exist anywhere in the world. Customary research indicators such as high-ranking publications are only of marginal relevance for translational or clinically oriented research institutions, since they cannot be used to measure the progress from the patients' perspective.

In the preceding Annual Report (2014), we therefore proposed under the keyword "Benchmarks" indicators which we thought would at least be applicable to the

translational cardiovascular research of the DZHK. In 2015, the six German Centres for Health Research (DZG) finished their discussion on the development of common indicators and reported a number of indicators to the funding bodies, about which the supervisory boards shall be informed annually in the future. Among them are multiple indicator groups oriented to structures, e.g., management, personnel, further training, platforms and databases. We report about them, in principle, at the pertinent sites within the Annual Report. As far as the core area of translational research is concerned, the DZG indicators focus on stating publications and projects in the fields of basic research, preclinical research and clinical research, followed by indicators relating to patents, industrial cooperations and public relations.

In the future, beyond its report addressed to the funding bodies about joint DZG indicators, the DZHK will also present the development of some DZHK-specific indicators each year in its Annual Report.

Indicators for the success of translation		
Indicator	Definition	2015
Short and medium term indicators		
1. “Physician scientists” (physicians working in science)	Scientists at the DZHK who are working both clinically (in patient treatment) and scientifically (31 Dec)	Not yet registered in 2015
2. Cooperations between partner sites	a. Number of Shared Expertise projects (year)	79
	b. Number of publications with at least two DZHK authors from different sites (year)	78
	c. Number of major multicentre projects in progress (clinical DZHK studies and HRHV) (31 Dec)	3
	d. Number of cooperative project groups (31 Dec)	10
	e. Number of stays of visiting scientists at other DZHK sites (year)	9
3. Communication with regulatory authorities	Consultation appointments (e.g., PEI, BfArM) in the scope of in-progress clinical studies, HRHV projects and site projects (year)	2
4. Cooperation with the industry	a. Cooperations with industrial partners in the scope of clinical studies, HRHV projects and site projects (31. Dec)	8
	b. Structured DZHK workshops with industrial partners (year)	1
5. Cooperative structures in clinical research	a. Type (quality) of cooperative structures (31 Dec)	Central Data Management (ZDM) including Data Handling and Trusted Third Party, Stem Cell Registry, Central Ethics Project
	b. Number (quantity) of	
	- ZDM registered patients (31 Dec)	679
	- SOPs (31 Dec)	15
	- use applications for data and biological materials (year)	0
- Approved use applications (year)	0	

Indicators for the success of translation		
Indicator	Definition	2015
6. High-ranking publications	All publications with DZHK affiliation and an impact factor >10 (year)	76
7. Preclinical projects and clinical studies	a. Number of HRHV projects and DZHK studies (31 Dec)	4
	b. Publications of HRHV projects and clinical studies (year)	0
Long-term success criteria		
8. Revised medical guidelines	Number of guidelines which have been revised as a result of DZHK studies (total)	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 and diagnostic principles developed by DZHK researchers (total). (Measurability is questionable)	0

Annotations:

- Definition of DZHK studies: Relying on competitive/flexible funds; predominately funded by the DZHK; study uses the Central Data Management of the DZHK.
- Indicators 2 - 8 relate exclusively to projects that are funded with competitive/flexible DZHK funds. Indicators 1, 9 and 10 refer to these and additionally to DZHK-funded site projects. No indicator relates to research of the DZHK member institutions funded otherwise.

Facts and figures

The German Centres for Health Research

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

For, although an increasing number of people recover from cancer and increasingly fewer people die of cardiovascular diseases, the six major endemic diseases are still the cause of much suffering and very high healthcare costs — in Germany, one-hundred billion euro per year. Due to the ageing population, the incidences of people with dementia, diabetes, heart failure, cancer or lung diseases are still on the rise. Resistant strains of bacteria are becoming a threat in hospitals; infectious diseases still take the lives of many people, especially in developing countries.

Further successes in therapy and diagnosis can no longer be achieved single-handedly by individual research groups. Instead, more effective structures are needed in which all significant partners cooperate in a process of translation — university physicians and researchers from non-university institutes, the pharmaceutical industry, regulatory bodies, politics and patient associations.

With the German Centres for Health Research, the German Federal Ministry of Education and Research started to establish such effective structures in 2009. A main objective 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 endemic diseases. A total of 41 sites with more than 100 partner institutions now constitute the six German Centres for Health Research.

Under the motto “For patients to benefit from the results of research more quickly”, the DZG presented itself at a joint parliamentary evening in Berlin in February 2015 and gave an interim assessment: Their innovative structures are internationally acknowledged and suited to promote the translation of medical research. This successful event with an attendance of more than 100 people was organised by the German Centre for Cardiovascular Research (DZHK).

In October 2015, the DZG under the direction of the German Centre for Infection Research (DZIF) organised for the second time a joint workshop within the scope of the World Health Summit. The subject was “Education and training of clinical and translational scientists”.



Parliamentary evening of the DZG in Berlin

In November 2015, the DZG agreed on common indicators to evaluate the progress and success of translational research in the DZG. In addition, the DZHK initiated preparatory discussions for the release of a joint DZG PR research magazine in 2015.

Member institutions

In the reporting year, as in the previous year, the number of 28 association members remained constant. They represent 32 member institutions, which are shown in the following figure along with their respective geographical sites.

The German Centre for Cardiovascular Research



Member institutions by German states where headquarters are located

Federal state	Headquarters
Baden-Württemberg	German Cancer Research Centre (DKFZ) European Molecular Biology Laboratory (EMBL) Klinikum Mannheim GmbH Heidelberg University Heidelberg University Hospital
Bavaria	German Heart Centre Munich (DHM) Klinikum rechts der Isar (MRI) Hospital of the University Munich (KMU) Max Planck Institute of Biochemistry (MPI) Technical University of Munich (TUM) Helmholtz Zentrum München – German Research Centre for Environmental Health (HMGU) Ludwig Maximilian University Munich (LMU)
Berlin	Charité – University Hospital Berlin German Heart Centre Berlin (DHZB) Max Delbrück Centre for Molecular Medicine in the Helmholtz Association (MDC) Federal Republic of Germany, represented by the German Federal Ministry of Health, represented by the Robert Koch Institute (RKI)
Brandenburg	German Institute of Human Nutrition in Potsdam-Rehbrücke (DIfE)
Hamburg	University Medical Centre Hamburg-Eppendorf (UKE) Asklepios Klinik St. Georg
Hesse	Goethe University Frankfurt Kerckhoff Klinik GmbH, Bad Nauheim Max Planck Institute for Heart and Lung Research, Bad Nauheim
Mecklenburg-Western Pomerania	University Medicine Greifswald
Lower Saxony	German Primate Centre, Göttingen Max Planck Institute for Biophysical Chemistry, Göttingen Max Planck Institute for Dynamics and Self-Organisation, Göttingen Max Planck Institute for Experimental Medicine University of Göttingen University Medical Centre Göttingen
Rhineland Palatinate	University Medical Centre Mainz
Schleswig-Holstein	Kiel University University of Lübeck

Finances and Staff



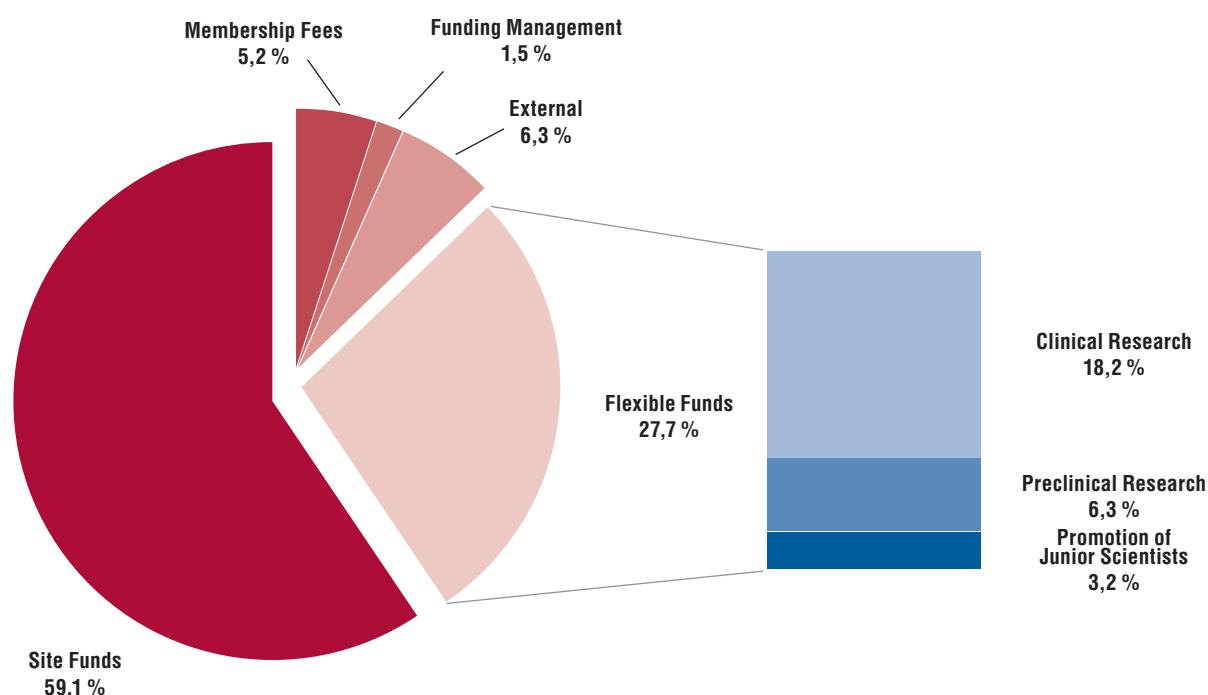
Finances

In the reporting year 2015, it was for the first time that the DZHK disposed of the EUR 41,021,000 new funds held out in prospect at the time of its foundation as the full annual funding amount (2014: EUR 14,632,000) plus a carryover of EUR 3,444,000 (2014: EUR 4,842,000) from 2014. From this amount, funds totaling EUR 30,393,000 (2014: EUR 15,786,000) were drawn.

In terms of absolute figures, the DZHK spent approximately twice as much in 2015 as in 2014. As the available funds had nearly tripled, a sum of EUR 14,072,000 could not be expended. These funds were carried over to 2016. Speaking in relative figures, the outflow of funds relative to the respective new funds (annual budget without a carryover from previous years) was at 73 percent in 2013, 108 percent in 2014, and

at 74 percent in 2015. That the outflow of funds was not higher in 2015 was particularly due to the fact that financially strong new projects, such as multicentre clinical studies, HRHV projects and infrastructure projects, such as the laboratory information system or the OMICs cooperation, are highly complex. This was the cause for some partly obvious and not always predictable delays in preparation, approval and start for these projects. In the case of clinical studies, there was a further delay in the outflow of funds even after the project had successfully started, because the invoices for the enrolled patients were issued only after a period of several months and the funds were only claimed then. Due to a great number of newly started projects, we will require distinctly more funds in 2016. We anticipate that the new funds will be completely expended in 2016 and that we can at least begin reducing the funds carried over.

Allocation of DZHK Funds Expended in 2015



The drawn (expended) funds for 2015 amounting to EUR 30,393,000 break down as follows:

- Site funds: EUR 17,963,000
- Flexible funds: EUR 8,442,000 (including EUR 5,546,000 for clinical research, EUR 1,921,000 for preclinical research and EUR 975,000 for the training programme)
- Externals: EUR 1,925,000 (including EUR 1,685,000 for Competence Networks and EUR 240,000 for cooperations with external partners)
- Membership fees: EUR 1,592,00 (including EUR 941,000 of the annual tranche for 2015 and EUR 651,000 as an instalment of the annual tranche for 2016)
- Funding Management Department: EUR 471,000

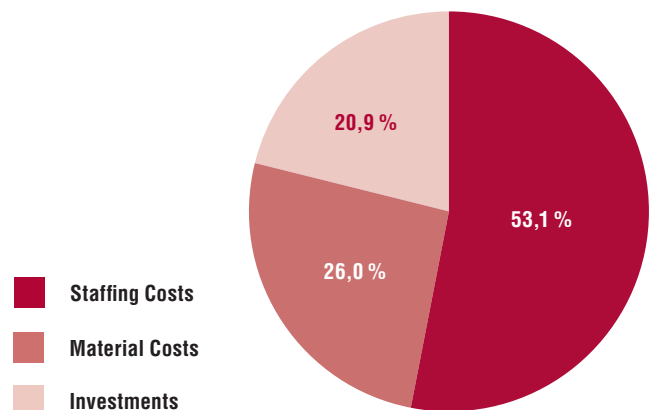
Comments: Due to the fact that the outflow of funds for site projects was markedly better than that of the flexible funds, the percentage of site projects in this representation turns out higher and the percentage of the flexible funds lower than had been stated in DZHK funds planning.

As the membership fees for 2016 were already due on 15 Jan 2016, not only the membership fees for 2015, but also a considerable proportion of the membership fees for 2016 were paid in 2015. According to funds planning, the membership fees are equivalent to approx. 2.5 percent of an annual budget. The main office is financed by membership fees (see page 63).



Staffing costs/material costs/ investment resources of the DZHK

- Staffing costs: EUR 16,707,000 (2014: 7,407,000)
- Material costs: EUR 8,174,000 (2014: 3,666,000)
- Investments: EUR 6,593,000 (2014: 2,199,000).

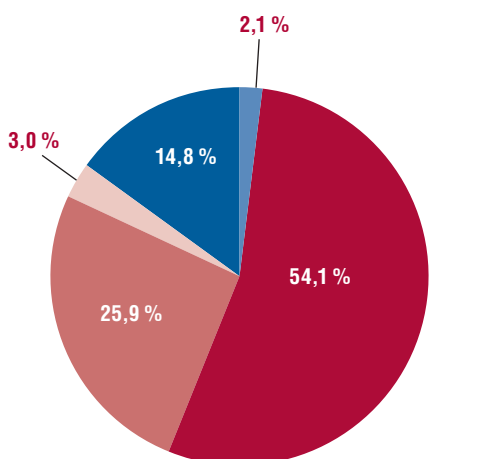


DZHK Main Office Budget

In 2015, the budget of the main office of DZHK e. V., which is financed by membership fees, amounted to EUR 998,000 (2014: EUR 843,000). Of this total, EUR 941,000 were membership fees and EUR 57,000 were carried over from the budget year of 2013 to 2015.

EUR 958,000 (2014: EUR 825,000) of which were expended; the miscellaneous revenues amounted to EUR 18,000. The remaining EUR 58,000 were carried over to 2017.

- Staffing costs: EUR 518,000 (2014: EUR 480,000)
- Material costs: EUR 248,000 (2014: EUR 205,000)
- Investments: EUR 29,000 (2014: EUR 16,000)
- Public relations: EUR 142,000 (2014: EUR 103,000)
- Membership fees (TMF e. V.): EUR 20,000 (2014: EUR 20,000)



In the reporting year 2015, the DZHK **Funding Management Department** (FMM) at the Max Delbrück Centre for Molecular Medicine in the Helmholtz Association (MDC) was again responsible for passing on funds for project funding to 26 of the 32 partner institutions of the DZHK¹. The six partner institutions to which the FMM did not forward any funds are: The RKI (because it is a governmental research facility), the University of Göttingen (funds only go to the University Medical Centre Göttingen, which is a member itself), Heidelberg University (funds only go to Heidelberg University Hospital, which is a member itself), the Max Planck Institute for Experimental Medicine in Göttingen (no funding until now), the Asklepios Klinik Hamburg (no funding until now), the Max Delbrück Centre for Molecular Medicine in Berlin-Buch (no “forwarding” of funds). In addition, contributions are made to an increasing number of external cooperation partners, amounting to 44 in 2015 (11 in 2014), among which the three Competence Networks are funded. Altogether, 679 projects were funded in the reporting year (2014: 454 projects).

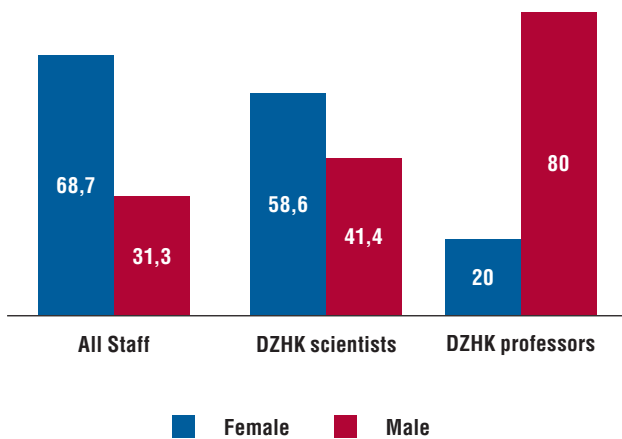
The FMM was extended by a second controlling position in October 2015 and hence now counts 7.5 FTE or 9 staff positions, which are assigned to the tasks of executive management, scientific evaluation, review of applications and confirmation of use, controlling and secretariat.

¹The DZHK e. V. has 28 members. The Max Planck Society as a member of the registered association accounts for five partner institutions. The main office of the DZHK e. V. is a recipient of contributions and therefore is also considered a partner institution.

Staff

In 2015, as of 31 December, 286.50 (2014: 165.77) full-time equivalents (FTEs) and/or 415 (2014: 234) "capita" were financed from DZHK funds. This also included 15 employees of the DZHK main office, 9 employees of the Funding Management Department and 30 employees in the Competence Networks. (cf. table page 66).

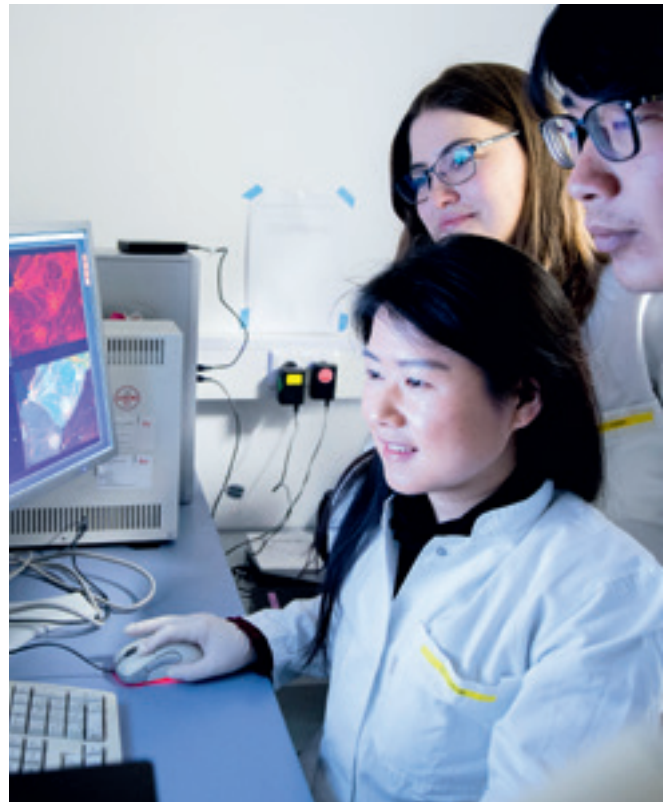
Gender distribution 2015 in %



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 cooperation within the DZHK and thus provide the basis of our success. In the reporting year, the DZHK had 141 PIs (2014: 138). PIs are appointed by the sites and confirmed by the General Assembly of Members. Each site disposes of a maximum of 20 PI

places, whereby at each site there are additional spots for each DZHK professor financed with DZHK funds. In the reporting year 2015, the General Assembly of Members confirmed the following 13 PIs: Till Keller (Rhine Main), Eike Nagel (Rhine Main, simultaneously DZHK professor), Wolfram Ruf (Rhine Main), Didier Stainier (Rhine Main), Viacheslav Nikolaev (Hamburg/Kiel/Lübeck), Dirk Westermann (Hamburg/Kiel/Lübeck), Tanja Zeller (Hamburg/Kiel/Lübeck, simultaneously DZHK professor), Daniela Panáková (Berlin), Wolfgang A. Linke (Göttingen), Martin Uecker (Göttingen, simultaneously DZHK professor), Volkmar Falk (Berlin), Georgios Kararigas (Berlin, simultaneously DZHK professor) und Christoph Dieterich (Heidelberg/Mannheim).



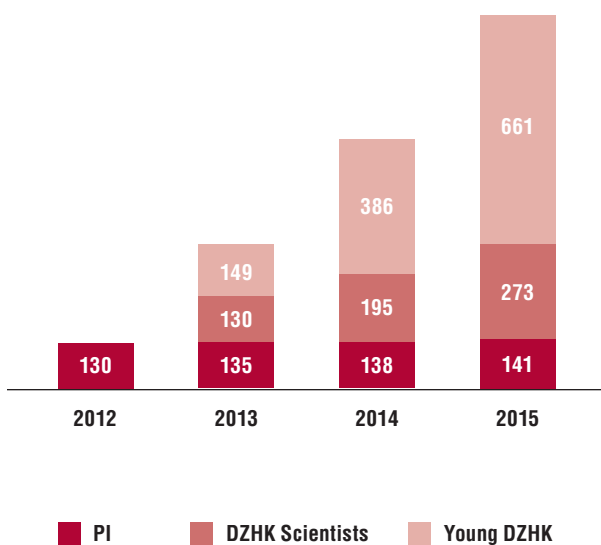
In total, far more women work at the DZHK than men

The affiliations of the 141 PIs are as follows:

- 61 from universities (basic researchers)
- 51 from universities (clinicians)
- 17 from the Helmholtz Association
- 9 from the Max Planck Institutes
- 3 from other, non-university research institutions (EMBL, DPZ, RKI)

There are two statuses, i.e. “Young DZHK member” and “DZHK scientist”, which allow us to assign scientists who are not PIs to the DZHK. Both statuses must be applied for. Prerequisites are a defined commitment within the DZHK and the possibility of an assignment to one DZHK-PI working at a partner institution. In the reporting year, the DZHK had 273 DZHK scientists (2014: 195) and 661 Young DZHK members (2014: 386).

Development of PI, DZHK Scientists and Young DZHK Members from 2012 to 2015



Number of staff financed by the DZHK categorised by the respective German state in which the member institution has its headquarters (incl. Competence Networks, main office and Funding Management Department).

DZHK-financed staff in 2015	BB	BE	BW	BY	HE	HH	MV	NI	RP	SH	KNe	GSt.	FMM	Total	2014
Number of staff (as of 31.12 / FTE)	0,35	55,20	31,63	31,16	22,05	19,10	36,96	25,66	9,77	14,48	19,78	12,86	7,50	286,50	165,77
Number of staff (as of 31.12 / capita)	2,00	68,00	48,00	43,00	33,00	25,00	51,00	60,00	11,00	20,00	30,00	15,00	9,00	415,00	234,00
male	0,00	28,00	16,00	9,00	7,00	3,00	17,00	23,00	2,00	7,00	15,00	2,00	1,00	130,00	78,00
female	2,00	40,00	32,00	34,00	26,00	22,00	34,00	37,00	9,00	13,00	15,00	13,00	8,00	285,00	156,00
Number of scientific staff members (FTE)	0,35	34,66	18,95	19,16	9,08	10,70	23,06	15,30	3,33	9,18	4,90	5,72	0,00	154,39	96,54
Number of scientific staff members (capita)	2,00	45,00	31,00	29,00	14,00	14,00	29,00	42,00	4,00	14,00	7,00	6,00	0,00	237,00	137,00
male	0,00	25,00	13,00	8,00	3,00	3,00	13,00	21,00	2,00	6,00	4,00	0,00	0,00	98,00	58,00
female	2,00	20,00	18,00	21,00	11,00	11,00	16,00	21,00	2,00	8,00	3,00	6,00	0,00	139,00	79,00
Number of non-scientific staff members (FTE)	0,00	18,54	11,68	11,00	11,97	6,40	13,90	8,36	6,44	4,30	14,88	7,14	7,50	122,11	62,23
Number of non-scientific staff members (capita)	0,00	21,00	16,00	13,00	18,00	9,00	22,00	16,00	7,00	5,00	23,00	9,00	9,00	168,00	90,00
male	0,00	1,00	2,00	0,00	3,00	1,00	4,00	0,00	0,00	1,00	11,00	2,00	1,00	26,00	15,00
female	0,00	20,00	14,00	13,00	15,00	8,00	18,00	16,00	7,00	4,00	12,00	7,00	8,00	142,00	75,00
Number of DZHK professorships (FTE)	0,00	2,00	1,00	1,00	1,00	2,00	0,00	2,00	0,00	1,00	0,00	0,00	0,00	10,00	7,00
Number of DZHK professorships (capita)	0,00	2,00	1,00	1,00	1,00	2,00	0,00	2,00	0,00	1,00	0,00	0,00	0,00	10,00	7,00
male	0,00	2,00	1,00	1,00	1,00	1,00	0,00	2,00	0,00	0,00	0,00	0,00	0,00	8,00	5,00
female	0,00	0,00	0,00	0,00	0,00	1,00	0,00	0,00	0,00	1,00	0,00	0,00	0,00	2,00	2,00
Information: additionally planned professorships	0,00	2,00	2,00	2,00	2,00	0,00	2,00	2,00	1,00	1,00	0,00	0,00	0,00	14,00	

BB: Brandenburg, Berlin site
 BE: Berlin, Berlin site
 BW: Baden-Württemberg, Heidelberg/Mannheim site
 BY: Bavaria, Munich site
 HE: Hesse, Rhine Main site
 HH: Hamburg, Hamburg/Kiel/Lübeck site

MV: Mecklenburg-West Pomerania, Greifswald site
 NI: Lower Saxony, Göttingen site
 RP: Rhineland-Palatinate, Rhine Main site
 SH: Schleswig-Holstein, Hamburg/Kiel/Lübeck site
 KNe: Competence Networks
 GSt: Main Office
 FMM: Funding Management Department

Facts and figures

Scientific Achievements

The DZHK has had rules for a joint DZHK affiliation and a DZHK acknowledgement since 2012. Here, we present the figures of the corresponding publications. A complete list of the publications with DZHK affiliation or DZHK acknowledgement can be found on the Internet at: <http://dzhk.de/en/research/publications>



Virtually every month the DZHK Board of Directors selects a **Paper of the Month**, which subsequently is announced in the DZHK newsletter and published on the Internet via the DZHK website.

On the one hand, publications are the hard currency of research; on the other, they are not equivalent to the actual mission of the DZHK, which is the promotion of translation. Moreover, they are always the result of many factors and research promotion measures, of which the DZHK is but one. However, publications are one way to assess the productivity of scientists involved in the DZHK and to get an impression of which topics the DZHK is working on. In 2015, the DZHK published 574 papers (2014: 404), in which authors with DZHK affiliation or DZHK acknowledgement were involved. The majority of the publications (344) concerned superior cross-cutting issues, such as epidemiology, genetics, genome-wide association studies, diagnostic imaging, pharmacotherapy and biomarkers of cardiovascular diseases as well as different types of clinical studies. The strategic focus of the

Publications

Publications in 2015	Number in 2015	(2014)
DZHK affiliation	536	(368)
DZHK acknowledgement	38	(36)
First authorship of a DZHK-PI	38	(11)
Last authorship of a DZHK-PI	177	(130)
First authorship of a Young DZHK	126	(-)
Cooperation with another DZHK site (PI)	78	(40)
Journals by Nature ² Publishing Group	15	(11)
Journals by Cell Press ³	6	(4)
NEJM, Lancet, JAMA	6	(9)
Circulation, Circ Res, EHJ, JCI, JACC	49	(51)
Science	1	(-)

² includes Nature, Nat Med/Nat Cell Biol/Nat Immunol/Nat Genet | ³ includes Cell, Cell Metabolism, Cell Stem Cell, Molecular Cell

DZHK is reflected more specifically in the disease-oriented papers (168). The majority of the papers researched the mechanisms of heart failure, congenital and inflammatory cardiomyopathies, stem cells and regeneration (82), mechanisms of atherosclerosis and vessel dysfunction, i.e., of myocardial infarction (60), as well as of cardiac arrhythmia as the cause of atrial fibrillation and sudden cardiac death (26). Papers on high-blood pressure, stroke, kidney diseases or congenital heart defects (62 in total) were not represented as much. Systematic reviews (81) on topics from all subject areas demonstrate that the DZHK authors express their views on cardiovascular research topics in a way that assures international attention. With 13.9 percent of all publications, the proportion of systematic reviews corresponded to approximately what is common in cardiovascular research (13.5 percent of the total, 2011-2015).

The amount of papers that were published in journals cited statistically often (impact factor >10), was at 13.4 percent (77). This is indicative of an overall high scientific level. However, perhaps how the papers are perceived in science is even more important. This is expressed in the so-called field-weighted citation index, which compares the citation rate of individual publications with the worldwide average in that field. This is set at 1. A value of 2 thus means that the paper is cited twice as much as the worldwide average. Fortunately, the value for the DZHK papers published in 2015 was on average over 3 and 2.5 for all DZHK papers since its foundation (Germany as a whole 1.8; evaluation on 01 Aug 2016 with the database SciVal)

Paper categories	
Theme	Number
Epidemiology/health system research	55
Genetics/GWAS	48
Atherosclerosis/vascular remodelling + inflammation	46
Imaging	38
Pharmacotherapy/pharmacology	30
Heart failure/remodelling/hypertrophy	29
Biomarkers	27
Basic mechanisms/myocyte function	27
Stem cells/iPSC/tissue engineering	27
Arrhythmias	26
Cardiomyopathies (genetic, toxic, inflammatory)	22
Hypertension	17
miRNAs/lncRNAs	17
Clinical intervention studies	17
Prevention/exercise/lifestyle	17
Technologies	16
Gender medicine	15
Endothelial cells/vascular function	14
Cardiac surgery/LAD	14
Clinical observation studies	14
Other	13
Stroke	12
Case report/interventional therapy	9
Developmental biology	6
Kidney	5
DNA /RNA based/protein based therapy	5
Ischaemia/reperfusion	4
Congenital heart defects	4

Facts and figures

Personalia, Prizes and Awards

Personalia, Prizes and Awards	
Name	Prize
Prof. Dr. Johannes Backs (Heidelberg/Mannheim)	Outstanding Early Investigator Award of the Basic Cardiovascular Science Council of the American Heart Association (AHA)
Prof. Dr. Michael Bader (Berlin)	Gold medal of the E.K. Frey - E. Werle Foundation
Prof. Dr. Felix Berger (Berlin)	Prize of the University Heart Centre Freiburg
Dr. Mihaela Delcea (Greifswald)	ERC Starting Grant
Prof. Dr. Stefanie Dimmeler Rhine Main	ERC Advanced Investigator Grant
Prof. Dr. Christoph Herrmann-Lingen (Göttingen)	Elected President of the American Psychosomatic Society (APS)
Dr. Rabea Hinkel (Munich)	Franz Maximilian Groedel Research Award 2015
Dr. Mahir Karakas (Hamburg/Kiel/Lübeck)	- Moderated Posters Award 2015 of the European Society of Cardiology - Werner Otto Prize
Prof. Dr. Adnan Kastrati (Munich)	Paul Morawitz Prize
Prof. Dr. Christian Kupatt (Munich)	Moderated Posters Award 2015 of the European Society of Cardiology
Dr. Florian Leuschner (Heidelberg/Mannheim)	Publication award of the AG "Chronic Heart Failure" of the German Cardiac Society
Prof. Dr. Lars Maegdefessel (Munich)	ERC Starting Grant
Prof. Dr. Patrick Most (Heidelberg/Mannheim)	Albert Fraenkel Prize 2015
Dr. Uwe Raaz (Göttingen)	Jörg Vollmar Prize 2015
Prof. Dr. Sonja Schrepfer (Hamburg)	Paul Martini Prize
Dr. Farbod Sedagat-Hamedani (Heidelberg/Mannheim)	Scholarship of the German Cardiac Society
Prof. Dr. Konstantinos Stellos (Rhine Main)	Young Investigator Award of the "Council on Functional Genomics and Translational Biology" of the AHA
Dr. Nina Henriette Uhlenhaut (Munich)	Friedmund Neumann Prize 2015
Dr. Mirko Völkers (Heidelberg/Mannheim)	Emmy Noether Programme of the German Research Foundation (DFG)
PD Dr. Antje Voigt (Berlin)	Klaus Georg and Sigrid Hengstberger Research Scholarship Award 2015
Dr. Christoph Zehendner (Rhine Main)	ATVB Early Career Investigator Award of the "Council on Arteriosclerosis, Thrombosis and Vascular Biology"

DZHK professorship appointments within the reporting period



*Eicke Nagel,
University Hospital Frankfurt*

On 1 January 2015, the site Rhine Main appointed **Eicke Nagel** (formerly King's College, London) as DZHK W3 professor for cardiovascular imaging at the Goethe University in Frankfurt. He works intensively on the translation of new diagnostic methods into clinical routine, especially in the areas of coronary heart disease, cardiomyopathy and heart failure (HF-REF, H-PEF). The research is conducted locally in close cooperation with the departments of cardiology, radiology and nuclear medicine and translated as widely as possible into multicentre studies.



*Martin Uecker,
University Medical Centre Göttingen*

In September 2015, **Martin Uecker** (formerly University of California, Berkeley, USA) accepted a DZHK-W2 professorship for real-time magnetic resonance imaging (MRI) at the Göttingen site. His research activities are centred in the field of new computer-aided MRI methods and reach from the basic development of new MRI methods over their practical realisation and integration into commercial MRI systems to translation into clinical practice.



*Georgios Kararigas,
Charité – University Hospital Berlin*

Since November 2015, **Georgios Kararigas** holds a DZHK-W1 professorship for translational gender research in medicine with a focus on cardiac insufficiency at the Charité – University Hospital Berlin. His major research topics comprise the mechanisms of gender differences in cardiovascular (patho)physiology, endocrine actions in the heart as well as gene expression and regulation. In particular, he is concerned with the analysis of heart-specific regulatory functions of oestrogen, applying a combination of computational and genome-wide methods.

Facts and figures

Committees and Governance of the DZHK

Board of Directors

The Board of Directors manages the DZHK strategically and operatively and represents the Centre externally. It is elected by the General Assembly of Members for a period of office lasting three years and in the reporting year was composed of Thomas Eschenhagen, University Medical Centre Hamburg-Eppendorf (UKE) as Chairperson of the Board, Gerd Hasenfuß, University Medical Centre Göttingen, and Thomas Sommer, Max Delbrück Centre for Molecular Medicine in the Helmholtz Association. The Board of Directors usually convenes twice a month, during the reporting year the Board met 18 times altogether.

Research Coordinating Committee (RCC)

In the RCC, the Board of Directors, the site spokespersons and the representatives of the member institutions as well as the representatives of the Young DZHK exchange views on all principle DZHK topics. In addition, the RCC makes a wide range of important decisions, including the majority of funding decisions, whereby this committee is authorised either by the Board of Directors or the General Assembly of Members. The RCC meets once a month and permits the presence of several permanent guests who represent significant DZHK activities, e.g., Central Data Management. It can be considered as an extended Board of Directors or a small General Assembly of Members, but it also has the character of a DZHK parliament. The most important RCC issues in 2015 were accompanying discussions and funding decision-making for clinical studies and three High Risk High Volume projects; comprehensive presentation of each DZHK site in one of the sessions with a subsequent discussion.

General Assembly of Members

The highest organ of the DZHK e. V. is the General

Assembly of Members, which convenes twice a year at the main office in Berlin. It is composed of the representatives of the 28 member institutions of the association. All members of a site have a common voice in the General Assembly of Members. The General Assembly of Members establishes the guidelines for the work of the association and answers questions of fundamental significance, e.g., about the strategic alignment, changes to the structure of the association, acceptance of new DZHK-PIs and the business plan and investment plan of the Centre. In 2015, it also extended the duration of the main office project "Training Programme" and infrastructure projects in the field of clinical research, decided on the 2015 investment programme and on a revision of the bylaws.



Scientific Advisory Board

The association is supported by a Scientific Advisory Board consisting of internationally renowned experts in the field of cardiovascular research. The Scientific Advisory Board advises the Board of Directors and the General Assembly of Members on all scientific and programmatic queries. It convenes once a year chaired by Garret FitzGerald and supports the DZHK in continuously defining its strategy more precisely. The most significant recommendations made in the 2015 session were related to the DZHK's structural and

thematic focus as well as to the definition of a “Grand Challenge”. In addition, the board recommended better connections between the DZHK projects and an improved decision-making process in the DZHK for funding clinical studies.

Commission of Donors (KdZG)

The Commission of Donors assists the DZHK in securing exchange with the donors. Donors of the DZHK are the German Federal Government (90 percent) and the governments of the federal states (10 percent) in which the headquarters of the member institutions are located. Each donor posts one representative in the commission. The chair of the commission is the representative of the German Federal Government. In strategic as well as essential financial, organisational and personnel matters, the Board of Directors and the General Assembly of Members are required to obtain the approval of the Commission of Donors. In 2015, the body convened once at the DZHK main office and once at the DZHK site in Heidelberg/Mannheim. Topics focused on in these meetings were, among others, the definition of an allocation key for federal state shares starting in 2015, discussions about a potential modification of the financing procedure of the DZG and about key figures of DZHK development, as well as the adoption of the 2016 business and investment plan and the medium-term financial planning for the years 2017–2019.

Donors of the DZHK are:

- German Federal Ministry of Education and Research (BMBF); the federal states of Baden Württemberg; Bavaria; Berlin; Brandenburg; Hamburg; Hesse; Mecklenburg-Western Pomerania; Lower Saxony; Rhineland-Palatinate; Schleswig-Holstein.

- 90 percent of the DZHK funds are provided by the German Federal Government and 10 percent by those federal states in which the headquarters of the member institutions are located.

Translational Research Group (TRG)

The TRG supports the DZHK in building expertise in the area of late translational research. It audits and evaluates applications for High Risk High Volume Late Translational Projects and gives recommendations for the eligibility for funding of the applications to the Board of Directors and the RCC. In addition, it advises the applicants about regulatory affairs, protective rights and aspects of commercialisation. DZHK internal members are scientists with experience in late preclinical research and with experience in conducting clinical studies. DZHK external members possess specific knowledge in matters of regulatory proceedings, protective rights, translational research and in biostatistics. Timm Jessen und Harald Petry resigned from the TRG in the reporting year. Martin Bechem could be acquired to succeed Timm Jessen. The TRG held three sessions in the reporting year.

Clinical Study Group (CSG) – Steering Committee

The CSG Steering Committee is an internal body, which is composed of preclinical and clinical researchers, biostatisticians, and one representative of the DZHK's clinical infrastructure. It was appointed in 2014 by the General Assembly of Members for three years and convened seven times in the reporting year. The Committee advises the Board of Directors and the RCC in all matters of clinical research. Furthermore, it discusses the applications for clinical studies in the DZHK and considers, in addition to their scientific quality, whether they comply with the research strategy of the DZHK. Moreover, it advises the applicants,

submits proposals for improvements and requests the submission of full applications. In 2015, it supervised a total of four calls for clinical studies, among which were the two initial calls for the funding line “Early Clinical Studies”. After completion of the multi-tiered process, which also includes external reviewers, the RCC issued nine funding recommendations in 2015 at the suggestion of the CSG Steering Committee or the Selection Board.

Use & Access Committee (U&AC)

The Use and Access Committee (U&AC) was appointed by the General Assembly of Members in October 2015. It evaluates use applications for the secondary use of basic data and basic biological materials derived from clinical studies in accordance with the DZHK's Use and Access Policy. The U&AC is composed of representatives from each DZHK site, experts in biobanking, ethics and statistics, one representative of the technology transfer units and one external advisor. It holds monthly video conferences and is supported by the Transfer Office of the DZHK.

DZHK Professors

DZHK professorships are financed at the sites by DZHK site funds. In 2015, the DZHK professors met



DZHK professors at the DZHK Retreat in Potsdam (September 2015)

for the first time. In September, Tanja Zeller and Holger Gerhardt were elected spokesperson and deputy spokesperson of the representative body of DZHK professors. As such, they have permanent guest status in the RCC where they represent the interests of the DZHK professors. In the reporting year, the DZHK professors agreed that they would constitute the programme committee for the DZHK Retreat 2016. At the end of the reporting year there were ten professorships funded by the DZHK.

PostDoc-Committee of the Young DZHK

Cf. Chapter 10

DZHK Administration

The employees of the main office, the Funding Management Department and the seven site management offices together constitute the science administration of the DZHK. In 2015, their collaboration was close and cooperative, including within the scope of 47 weekly video conferences and five personal meetings at the sites or at the main office of the DZHK. In addition to the exchange on the respectively current DZHK funding procedures and all administrative operations from filing applications to business reporting, a particular focus in 2015 of the joint work efforts was set on the revision and standardisation of all funding guidelines.

Main Office

In the reporting year, 15 employees including managing director were working in the main office (12.86 FTE on 31 December 2015). The main office primarily supports the association's Board of Directors in coordinating the scientific cooperation in the DZHK. In the reporting year, this included in particular:

- Organisation of regular calls as well as the selection and evaluation procedures in the three cooperative areas preclinical research, clinical research and promotion of junior scientists
- Organisation of the mentoring programme
- Execution of the Europe-wide tender procedure for a DZHK laboratory information system
- Preparation and execution of the 2015 investment programme
- Controlling of the flow of funds together with the Funding Management Department and the site management offices
- Organisation, preparation and follow-up activities for all committee sessions,
- Press and public relations as well as internal communication within the DZHK (cf. Chapter 11)



Staff of the DZHK main office in May 2016

An intermediate management level was introduced in 2015 as part of the job growth at the main office decided in 2014, (Strategy Group, Preclinical Research & Training Group, Clinical Research Group, and Administration & Communication Group).

Funding Management Department

The Funding Management Department (FMM), as part of the Max Delbrück Centre for Molecular Medicine in the Helmholtz Association (MDC), is entrusted with the administrative realisation of funding of the DZHK partner institutions and external cooperation partners. It is authorised to review applications on the 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 the controlling reports for the sites in order to support them with an effective budget management.

Partner site Management

In 2015, one 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. The partner site managements are the interfaces between the scientific projects, partner site directors, third-party funding administrations, human resources departments, deans of the research offices, legal departments, the main office and the FMM. The site managements coordinate all activities of the site. They organise site retreats, PI meetings and the work of the 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. Together with the main office and Funding Management Department, they develop the procedures and processes at the DZHK.

Panel members can be found on the DZHK website under:
<https://dzhk.de/das-dzhk/gremien>

Facts and figures

Sites



Charité – University Hospital Berlin

DZHK Berlin site

Site spokesperson: Vera Regitz-Zagrosek, Director of the Institute of Gender in Medicine (GiM), Charité – University Hospital Berlin

Vice site spokesperson: Roland Hetzer, German Heart Centre Berlin (DHZB) [since 12/2015: Holger Gerhardt, Max Delbrück Centre for Molecular Medicine in the Helmholtz Association (MDC)]

Side management: Carola Schubert (Site manger), Patrick Cochanski (Site clerk) [since 4/2016: Mariam Abou-Saleh], Charité – University Hospital Berlin

Partner institutions at the Berlin DZHK site

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

Research focus within the DZHK

The focus of the member institution at the Berlin site is the clinical and translational investigation of cardiac insufficiency, vascular and metabolic diseases as well as gender aspects in hospital, research and academic teaching (Charité). The researchers at the MDC are primarily concerned with basic research and translational research in the area of genomics, vascular biology, molecular cardiology and myocardial function, whereas the focus of the DHZB is 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. The 2015 investment programme enabled the fund raising for the field of clinical and experimental infrastructure and biobanking in order to significantly improve clinical studies and basic research. For example, the MDC acquired a new STED microscope, as well as exercise machines for ongoing and future clinical studies at Charité. In 2015, in the field of preclinical research, a total of seven Shared Expertise (SE) cooperations of the Berlin site were used by other sites. Twenty further cooperations between other sites developed from these seven SE cooperations. In the field of clinical research, the recruitment for the DZHK studies TORCH and TransitionCHF was successfully continued at all clinical institutions in the reporting period. Enrolment of patients in the studies partially funded by the DZHK or DZHK-associated studies ISAR-REACT 5 and Culprit-SHOCK also commenced. Georgios Kararigas was appointed to the junior professorship in “Translational gender research with a focus on cardiac insufficiency” advertised in December 2014.



University Medical Centre Göttingen

DZHK Göttingen site

Site spokesperson: Wolfram H. Zimmermann, Director of the Institute of Pharmacology at the University Medical Centre Göttingen

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

Side management: Axel Kaul (Site manager), Sylvia Vann (Site clerk), University Medical Centre Göttingen

Partner institutions at the Göttingen DZHK site

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

Research focus within the DZHK

The research focus of the Göttingen DZHK site is cardiac insufficiency research with the subjects “Mechanisms of the transition from clinical asymptomatic myocardial weakness to symptomatic heart insufficiency as well as heart regeneration in case of cardiac insufficiency”. The 2015 investment programme was used to strengthen the clinical study infrastructure on site and build a biobank for the purpose of a long-term and secure archive and storage of study materials. The funds for cooperative initiatives were used comprehensively using cooperations with Shared Expertise (SE) and cooperations with external partners. The SE offered by the Göttingen DZHK site in 2015 were utilised six times, whereas Göttingen utilised SE projects offered by other sites at 15 opportunities. In clinical research, the focus in the second half of 2015 was placed on an intensified, successful patient recruitment for the clinical DZHK studies TransitionCHF and TORCH as well as the initiation of further study centres for TransitionCHF. The new MRI centre at the German Primate Centre (2,400m²) took up operations and was formally opened on 20 April 2015. The international masters programme “Cardiovascular Science”, unique in the whole of Germany, was accredited in August 2015 and the foundations of the new DZHK research and laboratory building at the UMG were laid on 22 September 2015. Prof. Dr. Martin Uecker accepted the DZHK-W2 professorship “Real-time MRI”; Prof. Dr. Stefan Luther was appointed DZHK-W2 professor for “Optical Imaging and Numerical Simulation”. Prof. Dr. Wolfgang Linke (professor for cardiac mechanotransduction at the Heart Centre Göttingen, UMG) was appointed to the position of DZHK-PI.



University Medicine Greifswald

DZHK Greifswald site

Site spokesperson: Stephan B. Felix, Director of the Clinic of Internal Medicine at University Medicine Greifswald

Vice site spokesperson: Ulrich John, Director of the Institute for Epidemiology and Social Medicine at University Medicine Greifswald

Site management: Stefan Groß (Site manager), Anne-Kathrin Beiersdorf (Site clerk), University Medicine Greifswald

Partner institutions at the Greifswald DZHK site

University Medicine Greifswald

Research focus within the DZHK

Special expertise of the Greifswald site is in conducting population-based epidemiological and clinical studies with comprehensive cardiovascular phenotyping, research on the prevention of systolic and diastolic cardiac insufficiency or dilatory cardiomyopathy, high-throughput OMICs analyses, telemedicine, biobanking and data management/analysis. The clinical infrastructure of the DZHK Examination and Training Centre was extended with the aid of the 2015 investment programme, including for additional diagnostic opportunities as well as exercise machines for prevention studies. At present, pilot studies on the prevention of cardiovascular diseases are being conducted. Since 2014 subjects have been recruited for the HOMEX-HF pilot study on sports activities in cases of cardiac insufficiency. Furthermore, the IBEKO study on reducing sitting behaviour as an independent cardiovascular risk factor was started in 2015. The University Medicine Greifswald also participates as an enrolling study centre in the clinical studies TORCH, TransitionCHF, Culprit-SHOCK and soon also in TOMAHAWK, DEDICATE and SPIRIT-DHF. Patients have been enrolled in Culprit-SHOCK since 2014 and in TORCH and TransitionCHF since 2015. In the field of preclinical research, a total of five Shared Expertise (SE) projects of the site were used by other sites in 2015. Seven further cooperations between other sites developed from these five SE projects. In the field of clinical research, the Trusted Third Party of the Central Data Management (collaborative project together with the Göttingen site and the main office in Berlin) is established in Greifswald. In addition, the site takes responsibility for patient management in the TORCH study. Moreover, DZHK basic and study-related biobanking is coordinated by the Greifswald site. At the end of 2015, the site was chosen to operate the future central laboratory information system of the DZHK.



University Medical Centre Hamburg-Eppendorf

DZHK Hamburg/Kiel/Lübeck site

Site spokesperson: Thomas Eschenhagen, Director of the Institute for Experimental Pharmacology and Toxicology at the University Medical Centre Hamburg-Eppendorf

Vice site spokesperson: Norbert Frey, Director of the Clinic of Cardiology and Angiology at UKSH

Site management: Doreen Stimpel (Site manager), Monika Glimsche (Site clerk), University Medical Centre Hamburg-Eppendorf

Partner institutions at the Hamburg/Kiel/Lübeck DZHK site

University Medical Centre Hamburg-Eppendorf, Kiel University, University of Lübeck, Asklepios Klinik St. Georg

Research focus within the DZHK

The scientific focuses at the Hamburg/Kiel/Lübeck site are the research of genetic risk factors and biomarkers of cardiovascular diseases, the regenerative and biomedical utilisation of pluripotent stem cells and tissue engineering, the identification of molecular mechanisms of pathological hypertrophy and the development of individualised treatment concepts of cardiac insufficiency, in particular genetically caused cardiomyopathies. In the scope of the 2015 investment programme the spectrum of experimental methods at the site was extended and, locally, a common clinical infrastructure for DZHK studies and for DZHK-wide study biobanking was established. In the field of preclinical research, a total of ten Shared Expertise (SE) projects of the site were used by other sites in 2015. From this use, eleven further cooperations with other sites developed. Frequently utilised SE projects of the site were the micro-RNA platform in Lübeck, cellular stretch models in Kiel and cardiometrics in Hamburg. In the second half of 2015, a new project of the funding instrument “High Risk High Volume Late Translational Project” on the subject of valve stent implantation has been approved in the field of late preclinical research (Kiel). Besides, with four big hospitals, the site disposes of a highly diversified medical expert knowledge and conducts clinical studies in all major fields of cardiology. At present, the site coordinates the nationwide clinical studies FAIR-HF2 (Hamburg) and TOMAHAWK (Lübeck) which are fully funded by the DZHK. Further clinical studies funded by the DZHK – CAVA-ADHF (Lübeck) and DEDI-CATE (Hamburg) – are planned for 2016/2017. So far, the DZHK funds three professors at the site (Prof. Erdmann, Lübeck; Prof. Hansen and Prof. Zeller, both Hamburg). The tenure procedure for a further W2 professorship on the subject “Epigenetics in cardiac hypertrophy” at Campus Kiel has been initiated.



Heidelberg University Hospital

DZHK Heidelberg/Mannheim site

Site spokesperson: Hugo A. Katus, Medical Director of the Department of Internal Medicine III of the Heidelberg University Hospital

Vice site spokesperson: Martin Borggrefe, Director of the Internal Medicine Clinic I of the University Medical Centre Mannheim

Site management: Tanja Weis (Site manager), Claudia Marquart (Scientific project manager), Matthias Knüll (Site clerk), Heidelberg University Hospital

Partner institutions at the Heidelberg/Mannheim DZHK site

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

Research focus within the DZHK

The scientific focus of this site is the research of hereditary and inflammatory cardiomyopathies. In the context of a translation pipeline, the cardiomyopathies are being worked on scientifically from genetic and molecular diagnostics all the way to innovative molecular therapy concepts. For this, genetic, epigenetic and electrophysiological analyses, imaging diagnostics, ps-iPS cells as well as model systems of cellular systems including zebrafishes, mice and rats all the way to the human-relevant porcine model for the functional analysis of molecular signal pathways and the identification of new diagnostic and therapeutic targets. Methodical platforms (next generation sequencing, AAV platform, zebrafish platform, platform for human-relevant disease models) are available to the entire DZHK, just like a modern fully-automated biobank with automated sample processing. As part of the investment programme, the clinical facilities in Mannheim and Heidelberg were equipped with innovative echocardiography scanners. Furthermore, the implementation of a production line based on the baculovirus insect cell expression system for the AAV platform and a laboratory information management system for Heidelberg's CardioBiobank were also enabled. In the field of preclinical research, seven Shared Expertise (SE) projects were used by other sites in 2015. Especially the AAV platform and the next generation sequencing platform were in high demand. Sixteen additional cooperations with other sites resulted from the offered SE projects. In the field of clinical research in 2015 it is important to note the successful patient recruitment in Heidelberg's TORCH register. A total of 564 patients from 13 centres were enrolled. In addition, the Heidelberg/Mannheim site was involved in three further DZHK studies as an enrolling centre and thus holds a leading position in patient recruitment in the DZHK. In matters concerning personnel planning, the appointment of a second DZHK professorship "Functional Genomics of Cardiomyopathies" has been postponed to the first half of 2016.



German Heart Centre Munich

DZHK Munich site

Site spokesperson: Stefan Engelhardt, Director of the Institute for Pharmacology and Toxicology at the Technical University of Munich

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

Site management: Sandra Rauser (Site manager), Sissy Künzel (Site clerk since 09/2015), Technical University of Munich

Partner institutions at the Munich DZHK site

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

Research focus within the DZHK

The scientific focus at the Munich site (“Munich Heart Alliance”, MHA) is the identification of new therapy targets and the development of innovative and optimised processes for the treatment of cardiovascular diseases. In this, the entire medical translation chain from basic research via experimental studies, the examination of clinical samples all the way to conducting clinical studies is represented. In the scope of the 2015 investment programme, the infrastructure of the three cardiology hospitals in Munich was harmonised to enable the conduct of DZHK studies. In the field of preclinical research, the focus was set on instruments for the application of experimental therapy methods in model organisms. In preclinical research, one HRHV project under the leadership of a MHA-PI, and another in which an MHA-PI is involved, have been approved for funding. Six Shared Expertise (SE) projects were used by other sites in 2015, resulting in seven further cooperations with other sites. In the field of clinical research, the harmonisation of ethics applications proceeded in the scope of one project at the HMGU. The main study centres of the studies partially funded by the DZHK ISAR REACT 5 and APPROACH-ACS-AF are located at the DHM or KUM, whereas the main study centre of the AFNET-EORP register for atrial fibrillation is located at KUM. The guideline-relevant study APPROACH-ACS-AF and the early clinical study SMART-MI, both initiated by the Medical Hospital and Policlinic I at KUM, were released for funding by the RCC. The same applies to the establishment of a central image data management system, in which Munich is one of the four DZHK sites involved. Two meetings with lectures and poster presentations on the status of Munich's DZHK projects as well as the “MHA Lecture on Experimental Cardiovascular Medicine” support the scientific exchange and the connection of research activities at the site. So far, one DZHK professorship (Prof. Söhnlein) in Munich is being funded, appointment procedures for two others are in progress.



Goethe University Frankfurt

DZHK Rhine Main site

Site spokesperson: Andreas Zeiher, Medical Director of the Department of Cardiology at the University Hospital Frankfurt

Vice site spokesperson: Stefanie Dimmeler, Medical Director of the Institute for Cardiovascular Regeneration at the University Hospital Frankfurt

Site management: Angelika Bonauer (Site manager), Alexander Schwarz (Site clerk), University Hospital Frankfurt

Partner institutions at the Rhine Main DZHK 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 research focus of the Rhine Main site is the identification of epigenetic markers and mediators of cardiovascular diseases in order to stimulate the repair and regeneration of vessels and cardiac muscle tissue. Another focus is the identification and therapeutic influence of non-coding RNAs in the cardiovascular system. In the scope of the biomarker project of the Kerckhoff Klinik, samples from more than 10,000 patients could be entered into the biomarker database up to the end of 2015. The MPI in Bad Nauheim focuses on the representation of global protein modifications in complex biological samples. The University Medical Centre Mainz started the second follow-up in February in the MyoVasc study and enrolled the 2,000th patient with cardiac insufficiency in September. In Frankfurt, the imaging facility directed by Professor Nagel was put into operation. Thanks to the 2015 investment programme the infrastructure for the participation in studies financed by the DZHK at the three clinically operating institutions, namely the Kerckhoff Klinik in Bad Nauheim, the University Medical Centre Mainz and the University Hospital in Frankfurt, could be extended or created. The first patients were enrolled for TORCH in Frankfurt and Mainz at the end of 2015. In the field of preclinical research, a total of five Shared Expertise (SE) projects were used by other sites in 2015. Seven cooperations with other sites resulted from these projects. In Mainz and Frankfurt, an appointment procedure for a W3 professorship "Vascular and Myocardial Interactions" (Prof. Dr. Tommaso Gori) and a W2 professorship "RNA Therapeutics" (Dr. Reinier Boon) were completed in the reporting period.

Acronyms

AFNET	Atrial Fibrillation Network
BDMS	Image Data Management System
CSG	Clinical Study Group
DZG	German Centre for Cardiovascular Research
DZHK	Deutsches Zentrum für Herz-Kreislauf-Forschung
FMM	Funding Management Office
HRHV	High Risk High Volume Late Translational Projects
KdZG	Commission of Donors
KNAH	Competence Network for Congenital Heart Defects
KNHI	Competence Network for Heart Failure
LIMS	Laboratory Information 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
✓	Goals reached
✓	Goals in process
x	Goals not reached

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Reference for use of gender equitable language:

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

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