

## Cardiovascular Research in Germany

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### Introduction: Development of Cardiovascular Research

German academic cardiovascular medicine has been traditionally rigidly separated into clinical cardiology, where the top clinicians had some early career basic science exposure but practiced exclusively clinical medicine, and classic basic science departments, that is, physiology, pharmacology, and pathology, where the chair had a cardiovascular focus. The institutional funding by the universities, which are, with few exceptions, state institutions in Germany, was sufficient to provide budget/resources for personnel, equipment and consumables to conduct basic research, and was in the range of 1 to 2 Mio € per year for such institutions. This situation has changed progressively but profoundly during the past 3 decades: almost all university clinics of cardiology now practice not only clinical cardiology but perform also basic science studies. They find it, however, increasingly difficult to recruit young physicians to a clinician scientist path of career. Basic cardiovascular science is no longer restricted to the classic university departments of physiology, pharmacology, pathology, but many chairs for experimental cardiovascular medicine under a variety of names/designations have been founded (>10 chairs in the past decade). Here, it has become extremely difficult to recruit young physicians into such basic science departments, and their personnel has now mostly a natural sciences rather than a medical background. Institutional funding for a basic cardiovascular research department has been restricted and now rarely exceeds 300 000 € to 600 000 € per year. Thus, there is an increasing pressure for competitive external funding. Along with these changes, the rigid hierarchical system of German academic medicine with a single professor and chair has become more flexible and more similar to the Anglo-American system where many professors with a different specialization coexist in the same department. Such more flexible system has in part evolved because many clinicians and researchers have had exposure to the Anglo-American system in the form of international postgraduate training or fellowships.

Quantitative data on the number of scientists working in Germany is not available to us. We assume, though, that the number of researchers organized in the German Cardiovascular Research Center (DZHK) provides a reasonable estimate.

Currently, the DZHK has 1353 members, of whom 143 are principle investigators, 344 scientists (>7 years after PhD, >10 years after medical exam), and 866 PhD students or researchers ≤7 years after PhD or 10 years after medical exam. Assuming that the DZHK represents ≈40% of total cardiovascular science in Germany, the numbers would amount to 3383/358/860/2165.

German scientists are traditionally organized in societies. The German Society for Circulation Research is the oldest cardiovascular society in Europe. It was founded in 1927 and initially had an academic and scientific focus. In the past decades, it has coevolved with the above discussed changes in German cardiovascular medicine and has been extended to clinical and public health-related interests. The German Cardiac Society (renamed 1994) is currently among the largest cardiovascular societies with >10 000 members. Still, the German Cardiac Society is a scientific stronghold, and its well-attended annual meeting in Mannheim remains an important forum for basic and translational cardiovascular research. Even though basic scientists make up <4% of all members, 6/29 Working Groups focus on basic and translational research and ≈20% (372 of 1880 accepted abstracts in 2017) were categorized as basic/translational research. The German Cardiac Society also publishes 2 prestigious journals, that is, *Basic Research in Cardiology* (IF 5.3) and *Clinical Research in Cardiology* (IF 4.7).

### Funding of Cardiovascular Research in Germany

Globally across all sciences, the fraction of third-party funding of German Institutions of Higher Education increased from 3352 Mio € (19% of total) in 2003 to 6760 Mio € (28% of total) in 2012 (DFG Förderatlas 2015, [http://www.dfg.de/sites/flipbook/foerderatlas\\_2015/files/assets/basic-html/page6.html](http://www.dfg.de/sites/flipbook/foerderatlas_2015/files/assets/basic-html/page6.html); Figure 2–4), with a clear trend to further increase since then. Thus, the dependency on competitive funding has seen a major increase, and this also applies to cardiovascular funding. At present, the total funding of cardiovascular research in Germany can be estimated at 253 Mio €/y (Figure 1A) and a third-party contribution of 31%. The most frequently addressed and internationally recognized research questions supported in Germany by third-party funding regard

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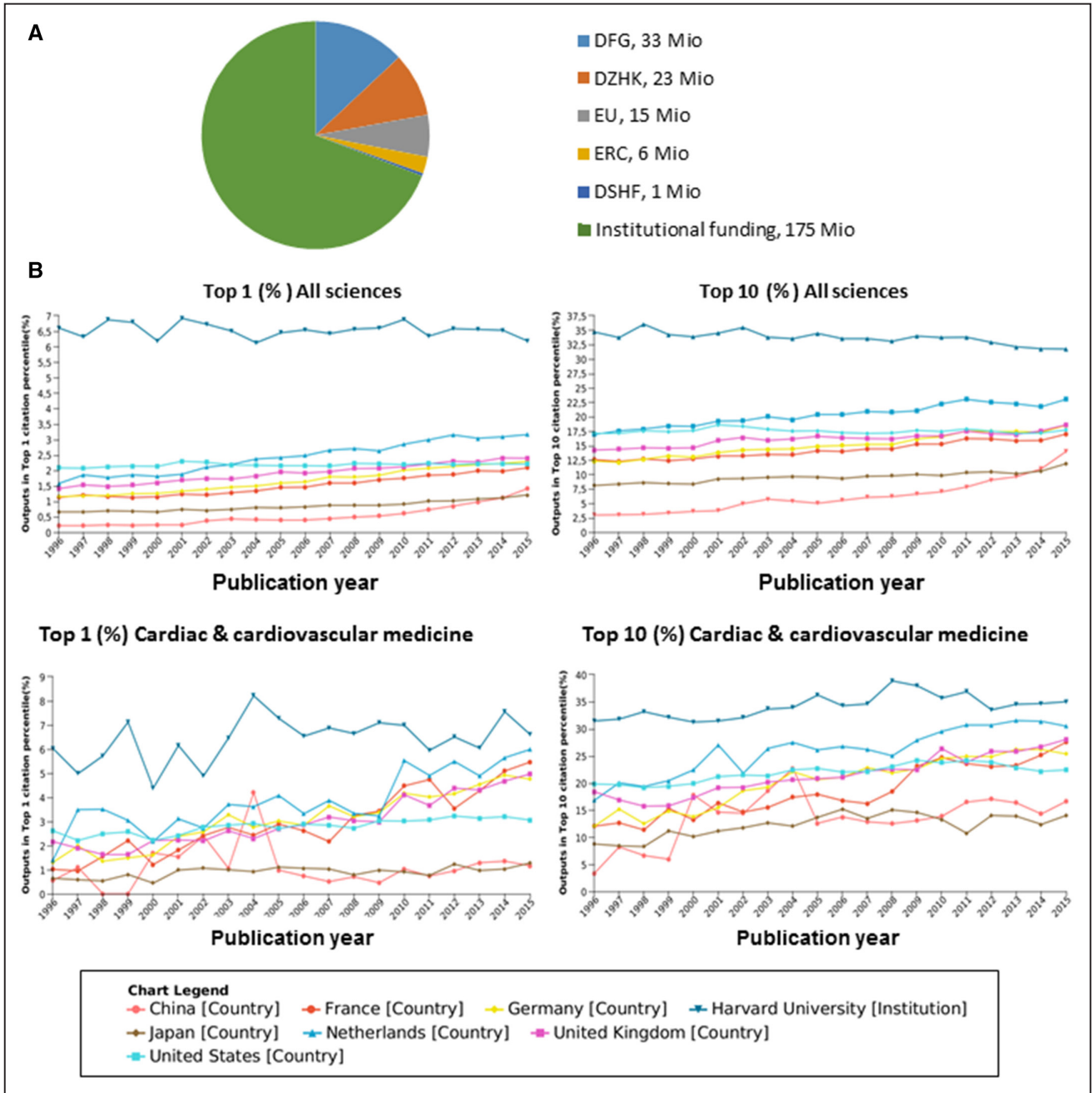
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**Figure.** A funding of cardiovascular research in Germany. Numbers are mean yearly budgets in 2012 to 2016. Note that numbers for DFG (German Research Foundation), DZHK (German Center for Cardiovascular Research), EU (European Union), ERC (European Research Council), and DSHF (German Heart Research Foundation) funds for cardiovascular research are exact, EU and core funding is an estimate, based on the assumption that the fraction of cardiovascular research funding at the level of the EU and institutional funding equals that at the DFG (mean 1.18%) or the ERC (1.42%). **B**, SciVal analysis of publication in all disciplines (**top**) and in the field cardiology and cardiovascular medicine (**bottom**). The ordinate shows the percent of papers that belong to the top 1 (left panels) or top 10 (right panels) best cited papers in the field; the abscissa gives the publication year.

mechanisms of vascular dysfunction and atherosclerosis,<sup>1-3</sup> heart failure and remodeling,<sup>4-6</sup> cardiovascular imaging,<sup>7-9</sup> stem cells and regeneration,<sup>10-12</sup> cardioprotection and conditioning,<sup>13-15</sup> and genetics and biomarkers<sup>16-18</sup>; along with these topics, the 3 most frequently cited German original articles from the past 5 years are listed.

The German Research Foundation (DFG) is the most important funding organization in Germany. It is an independent organization governed by scientists, who are nominated by the

universities and elected by all active scientists including post-doctoral fellows. It distributes money, which is contributed by the federal state (70%) and the individual states of Germany (30%), that is, tax payers' money (total budget 2015, 2840 Mio €). It funds individual projects and scientists, but—with the exception of junior investigators—the allocated budget covers mostly consumables and personal costs for PhD students and postdocs but not the personal salary of the applicant. The acceptance rate by the DFG has been between 20%

and 30%. With 45% of total spending, single ROI-like grants make up the largest funding program, open to the entirety of science. The DFG also supports networks within universities or clusters of universities and institutes, with the greater aim that universities commit themselves to special research areas. Depending on the size of the network, small (around 6–9 projects) or larger consortia (around 15–10 projects) are supported by Research Units or Collaborative Research Centers, respectively. Total funding of cardiovascular research amounted to a mean of 33 Mio €/y (1.2% of total).

A Research Unit (Forschergruppe or FOR) is made up of a team of researchers working together on a research project, which, in terms of thematic focus, duration, and finances, extends beyond the funding options available under the individual grants and has a medium-term perspective—generally 6 years—with annual budgets of around 0.6 to 0.9 Mio € per year. Clinical Research Units (KFO) provide similar opportunities in the field of disease- or patient-oriented clinical research. One hundred ninety-six research and clinical research units are currently funded, among them 3 with a cardiovascular focus.

Larger networks are supported by Collaborative Research Centers (CRC), with the scope of a 12-year funding perspective and an annual budget of around 2 to 3 Mio €. Transregio-CRCs (TRR) are networks of  $\leq 3$  universities. Out of 268 currently funded CRCs with a total volume of 630 Mio €, 8 CRCs (2.9%) have a cardiovascular focus (Table). Cardiovascular researchers also participate in CRCs, which are not exclusively focused on cardiovascular disease and are interdisciplinary.

In addition, a special program to support excellence in research in Germany, the Excellence Initiative, was announced in 2005. The Excellence Initiative aims to promote top-level research and to improve the quality of German universities and research institutions in general, to make Germany a more

attractive research location, make it more internationally competitive, and focus attention on the outstanding achievements of German universities and the German scientific community. This Initiative has been renewed in 2012 but will end in 2017 with a completion of funding in 2018. Of the 37 current projects, 2 have a cardiovascular focus, namely, the excellence cluster Cardiopulmonary Systems with a cardiovascular and pulmonary focus (Frankfurt/Giessen) and Rebirth pursuing regenerative approaches in different organ systems including the heart and lung (Hannover).

A new program, the Excellence Strategy will start in 2019 and is designed to continue the development of German universities, which has successfully begun with the Excellence Initiative in 2005 by supporting research of the highest standard, enhancing research profiles, and facilitating cooperation in the research system. It is expected that around 45 to 50 clusters with a yearly budget of 3 to 10 Mio € and a perspective of 14 years will be supported.

The German Federal Government promotes health research by supporting 5 German Health Centers, which are German-wide networks of focusing on specific diseases: cardiovascular, neurodegenerative, infections, pulmonary, and diabetes mellitus. The DZHK has been founded in 2011 on the basis of a competitive evaluation by an international review board and comprises 32 institutions organized in 7 partner sites all across Germany. It is dedicated to promote translation of novel diagnostic and therapeutic concepts to clinical practice and training of translational scientists.

European funding significantly contributes to funding of cardiovascular research in Germany. This includes funding of collaborative networks but also excellence programs for individual funding by the European Union's Research Framework Program Horizon 2020. Funding of European networks is possible for specific research questions, which are announced by calls, whereas individual funding is supported by the European Research Council (ERC). The ERC supports investigator-driven frontier research across all fields, solely on the basis of scientific excellence. Funding is available for researchers of any nationality, for early career investigators with 2 to 7 years (start-up grants) or 8 to 12 years (consolidator grants) since completion of their PhD, as well as for senior investigators (advanced grants). Since its start 2007, 106 of 7485 ERC grants were classified as cardiovascular. In Germany, of the 1104 funded grants, 19 were cardiovascular.

**Table. Current Support of Collaborative Cardiovascular Research Grants in Germany**

Title of Program	Acronym	Start	Sites
Pulmonary Hypertension and Cor Pulmonale	CRC 1213	2016	Giessen
Master Switches in Cardiac Ischemia	CRC 1116	2015	Düsseldorf
Atherosclerosis: Mechanisms and Networks of Novel Therapeutic Targets	CRC 1123	2014	München
Modulatory Units in Heart Failure	CRC 1002	2012	Göttingen
Endothelial Signaling and Vascular Repair	CRC 834	2010	Frankfurt
Mechanisms and Imaging of Cell-Cell-Interactions in the Cardiovascular System	CRC 688	2006	Würzburg
Molecular Cardiovascular Imaging (MoBiI) - From Mouse to Man	CRC 656	2005	Münster
Vascular Differentiation and Remodeling	TRR 23	2005	Mannheim/ Heidelberg/ Frankfurt

### Perspectives and Challenges of Cardiovascular Research in Germany

The increasing competitiveness of German research funding and the support of networks have changed the research landscape in Germany. But did this lead to more productivity and excellence? It may be too early to measure the impact of the last years' changes, but at least bibliometric measures of success indicate that Germany's contributions to the top 10 of cardiovascular research are increasing in the past years, similar to that of the United Kingdom and France and exceeding that of the United States (Figure 1B). Whether this also relates to major break-through discoveries and clinically relevant new therapies or promotes economy would be interesting to know.

The support of collaborative networks certainly improved interactions among researchers and stimulated the complementary development of technologies and sharing of resources. However, in the field of investigator-initiated clinical trials (IIT), Germany is still far behind other countries with a strong tradition of collaborative clinical studies. One of the major investments of the DZHK was, therefore, to establish a nationwide clinical study infrastructure.

Finally, despite the fact that research in general is currently well funded, cardiovascular research is competing with other disciplines. There is a risk of general underestimation of the importance of cardiovascular disease, particularly because the society is largely under the impression that cardiac diseases are treatable and most problems are already solved. Cancer, neurodegenerative diseases, and antibiotic resistance are seen as more severe threats. We need to further educate the lay audience and politicians about this misconception because cardiovascular disease remains the number one reason for death. The up to 2-fold higher mortality for ischemic heart disease in East compared with West German States (Herzbericht 2016, <https://www.bvmed.de/download/herzbericht-2016.pdf>, Tables 2/7) is another challenge. Importantly, frequent and severe cardiovascular diseases such as the many facets of heart failure increase with age and remain a therapeutic challenge. Thus, ample challenges, but also exciting chances of cardiovascular research lie in front of us.

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G. Heusch has been president of the German Cardiac Society and speaker of the DFG medical panel. He is member of the executive board of SFB 1116 and currently supported by the DFG and EU. T. Eschenhagen is Chairman of the Board of Directors of the DZHK, is a member of the Senate Commission for CRCs of the DFG, and is currently supported by the DFG, DZHK, EU, and the ERC. S. Dimmeler is board member of the TRR 23, CRC834, CRC902, and the DZHK and is Co-Spokesperson of the Excellence Cluster Cardiopulmonary Systems. She is supported by the DFG, DZHK, EU, and the ERC.

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