Comprehensive
Heart Failure Center
Würzburg

10 YEARS

of RESEARCH
TREATMENT
PREVENTION

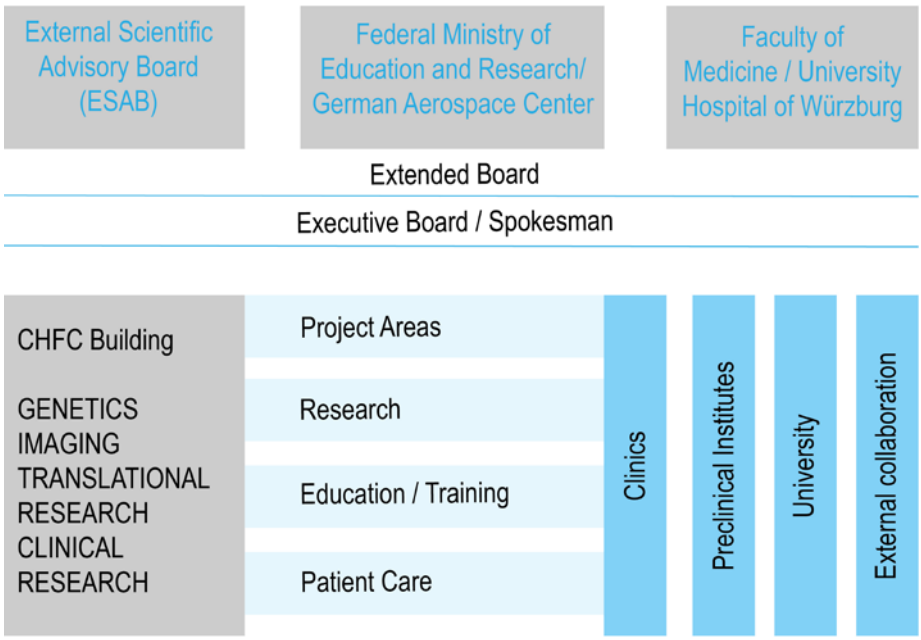
A HISTORY OF SUCCESS

VERSATILE
inside and out

Close network between departments and the outside world
The new research building of the CHFC houses the four research professorships for Genetics, Translational Research, Imaging and Epidemiology, who closely collaborates with the clinics and departments of the University Hospital of Würzburg (Universitätsklinikum Würzburg, UKW) and the Julius Maximilian University of Würzburg as well as with external cooperation partners in various interdisciplinary project areas.

Education, patient care, information
The members of the CHFC are also partners for educating young researchers and clinicians, for providing patient care and for educating the public on prevention.

Unique interdisciplinary approach
The organizational structure of the CHFC embodies the interdisciplinary approach undertaken by the CHFC as a guiding principle, which is unique in Germany, Europe and even worldwide. The Board of Directors elects the Executive Board, which in turn elects a spokesperson. An external scientific advisory board (ESAB) advises and reviews the work of the CHFC and gives strategy and funding recommendations to third-party sponsors, in particular the Federal Ministry of Education and Research (Bundesministerium für Bildung und Forschung, BMBF) and the German Aerospace Center (Deutsches Zentrum für Luft- und Raumfahrt, DLR), as well as the Faculty of Medicine and the University Hospital of Würzburg.



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DEAR READERS,

Heart failure is the most common cause for hospitalization in Germany, and its incidence continues to rise. Four percent of the German population already suffers from heart failure. Since the prevalence increases with age, patients often also suffer from diseases affecting other organ systems that have a negative impact on the progression of heart failure. Conversely, patients with heart failure have a higher risk of developing diseases of the brain, kidney, lung, metabolism or even cancer. We therefore no longer regard heart failure as a disease of an isolated organ, but as a systemic disease requiring interdisciplinary research and treatment approaches.

Therefore, the Comprehensive Heart Failure Center (Deutsches Zentrum für Herzinsuffizienz) – hereafter referred to as the CHFC – was founded with the concept to to study the interaction of the heart with other organ systems in greater detail. The three main languages, wiith which the heart communicates with other organs ,are neurohormonal activation, inflammation and metabolism. For more than ten years, the CHFC and its interdisciplinary teams of basic research scientists, physicists, engineers and clinicians from various disciplines have been investigating these interfaces between the organ systems in particular, in order to develop new therapeutic and preventive methods that will benefit our patients' medical care. Internationally visible successes have already been achieved in the first ten years, particularly concerning the interplay between the heart, brain and psyche, but also concerning the roles that metabolism and inflammatory processes play in the development of heart failure.

The center also focuses on research into hereditary diseases of the cardiac muscle, so-called cardiomyopathies. We analyze how gene mutations impair the motor function of the heart, which is often associated with inefficient use of energy. This subject area also benefits from the close interdisciplinary collaboration being realized under the roof of a new and modern research building, which opened its doors for the first time in 2017.

The long-term vision of the CHFC is to execute excellent interdisciplinary research and patient care with national and international visibiltiy. We are very grateful for the substantial funding we have received from the German Federal Ministry of Education and Research (BMBF), which has catalyzed innovative research structures and projects over the past ten years. We also extend our gratitude to the University of Würzburg's Faculty of Medicine for their long-standing and sustained support and to the Free State of Bavaria, which has invested not only in the new research building, but also in the sustainability of the structure for the period after the BMBF funding expired. We will continue to pursue our involvement in research associations at the federal level so that other research locations can also benefit from the added value of our center.

Christoph Maack
CHFC Spokesperson

Heart failure, also called cardiac insufficiency, is one of the most common diseases in Germany. Heart failure related mortality is higher than of many types of cancer. Nevertheless, its causes are poorly understood, and the disease itself is hardly curable. Major research efforts are therefore needed to improve prevention, diagnosis and therapy, as well as multidisciplinary approaches that take a holistic view of the disease – including all its concomitant and secondary diseases.

More than ten years ago, the Comprehensive Heart Failure Center (CHFC) at Würzburg was founded as one of eight Integrated Research and Treatment Centers (in German: Integriertes Forschungs- und Behandlungszentrum, IFB) for precisely this reason. Würzburg has been highly successful in establishing cutting-edge clinical research while at the same time creating an attractive environment for patient-oriented research and the advancement of young scientists. The IFBs are role models for innovation in the German university medicine landscape, and are sustainably integrated into their respective locations. The Federal Ministry of Education and Research (BMBF) has contributed to this success story with its funding totaling more than 370 million euros.

As a unique institution in Germany, the CHFC combines indispensable basic research, excellent clinical research, and efficient patient care under one roof. Different scientific disciplines work hand in hand, which has already produced impressive results. For instance, the STAAB cohort study, for example, in which 5,000 residents of the city of Würzburg were examined, yielded important findings for future research, prevention and treatment. Risk factors for developing heart failure were found in almost 60 percent of the participants, including a striking number of young people. Even if, fortunately, not all patients develop symptomatic heart failure later on in life, research will keep this finding in mind in order to get to the bottom of the causes of heart failure in an even more targeted manner in the future.

Such an excellent research infrastructure pays off especially in the current COVID-19 pandemic. The STAAB cohort is now employed to elucidate highly relevant issues about the spread of the virus and antibody status. All of you working at the CHFC have already achieved a lot in the past years, and this brochure provides impressive evidence of this. I thank you for your hard work and wish you continued success in the future.

Veronika von Messling,
Head of the Life Sciences Division,
Federal Ministry of Education
and Research

Following its extremely ambitious and visionary foundation, the Comprehensive Heart Failure Center at Würzburg has experienced a sustainable and excellent development and today stands for cutting-edge research that is highly recognised on a national and international level. From research into fundamental mechanisms contributing to the development of heart failure and novel methods for diagnosing this widespread disease towards clinical management and specialized patient care programs – the CHFC has an established place in the global research landscape. With its interdisciplinary concept and organization, it contributes significantly to Bavaria‘s ability to set standards in the field of cardiovascular research.

All those involved – including scientists from medicine, psychology, physics and computer science, specialized nursing staff, and all employees, who keep the CHFC running on a day-to-day basis – have succeeded in bringing both research and teaching as well as patient care to the highest level through integrative cooperation. As a result, the departments, research groups and junior groups have delivered impressive results in recent years. This development and the strategies for future sustainability have fully convinced the Bavarian Government of its value.

For this reason I am very pleased that we have found a way to continue supporting the CHFC in the future as well. Let‘s continue the success story together!

Bernd Sibler,
Bavarian State
Minister for
Science and the
Arts

An interdisciplinary approach, innovative translational research and the advancement of young academics: These are the core characteristics of the Würzburg Faculty of Medicine, which are quite significantly reinforced and shaped by the scientific and structural concept of the Comprehensive Heart Failure Center. With the CHFC, the research location Würzburg has become considerably more attractive as a research location, and several internationally renowned scientists have found their way to the CHFC in recent years.
A visible expression of the interdisciplinary collaboration and the advancement of young scientists in the field of cardiovascular research is the CHFC research building, which was opened in 2017, it provides scientists with more than 5000 m2 of space to study heart failure along the entire translational chain, from early preclinical and clinical research towards healthcare research. This infrastructure provides a unique opportunity for young and advanced scientists to develop new ideas how to prevent and cure heart failure. The concept developed at the CHFC for supporting young scientists has significantly promoted the establishment of clinician scientist programs at the Faculty of Medicine. I am very grateful to the initiators of this center, but also to all colleagues and employees for their commitment to the founding and successful development of the center over the past ten years. They have all made an outstanding contribution to the profile and international reputation of the University of Würzburg's School of Medicine.

Matthias Frosch, Dean of the Faculty of Medicine at the University of Würzburg

Georg Ertl, Founder and former CHFC spokesperson

The Integrated Research and Treatment Center (IFB) for the Prevention of Heart Failure and its Complications developed consistently at the Würzburg campus. As early as the beginning of the 1980s, there were already multiple individual grants from the German Research Foundation for projects on remodeling processes, such as remodeling of the heart, examining the role of the immune system in the development of heart failure, and the effect of heart failure on the kidneys. These projects and the countless other interdisciplinary and interdepartmental projects formed the basis for the development of the Collaborative Research Center SFB 355, the "Pathophysiology of Heart Failure", whose collaborations were also very important for the founding of the CHFC later on.

During the early 2000s, the research spectrum was decisively expanded in the direction of clinical research. The Interdisciplinary Heart Failure Network (INH) initially was launched as a registry and was later expanded into a randomized trial as part of the Heart Failure Competence Network (Kompetenznetz Herzinsuffizienz, KNHI). It showed that a new medical care program for patients with heart failure was superior to the usual care provided in the health care system in every respect, and it established health services research at the Würzburg site. These studies were also used as the foundation of the so-called heart failure units (HFU), networks which coordinate the care of patients with heart failure between university clinics, non-university clinics and cardiologists and general practitioners in an ambulatory setting, certified by the German Cardiac Society (DGK).

The name given to the center by the BMBF when the BMBF's application was submitted captures the essence of our mission: "Integrated Research and Treatment Center". It underscores the requirement that research should present itself in patient treatment. "The Prevention of Heart Failure and Its Complications," in turn, considers not only the syndrome but also the specifics of underlying diseases, other organs, and complications. It has always been important to us to take a comprehensive view on heart failure. While the English name of our center, "Comprehensive Heart Failure Center", reflects our approach, the short, ambitious acronym for the German name, DZHI, has become well-established in Germany.

I still admire the foresight of the reviewers regarding the future development of the CHFC as an integrated research and treatment center. The success story of the CHFC shows that structures for research should ideally be based on the research itself and that it should not be the other way around, i.e., where prescribed structures are the basis for the research conducted. Of course, structures must change and be open to new science and new generations of scientists. This is exactly what the DZHI has been able to demonstrate.

The CHFC is a flagship for excellent, internationally visible and interdisciplinary research, teaching and research transfer at the Julius-Maximilians-University (JMU) of Würzburg. From the very beginning, cardiologists and clinicians have cooperated with basic researchers and scientists from a wide range of disciplines at the university to fundamentally understand the causes of heart failure and improve treatment. This approach is internationally unique, and has produced ground-breaking research results. For example, interdisciplinary teams of cardiologists, psychiatrists, psychologists, physicists and computer scientists have worked to understand, why and through which mechanisms psychological problems worsen the progression of heart failure and how to intervene preventively. An important result of this research was the first demonstration that moderated, six-week internet-based training prevented the development of anxiety and depression after implantation of a cardioverter defibrillator. This new approach is ground-breaking, because it allows for organizing large-scale, low-threshold implementation of care pathways for inpatients and outpatients alike. The JMU is proud of the CHFC‘s achievements and of its beeing a successful model for future interdisciplinary research projects.

Paul Pauli, president of Julius-Maximilians-University Würzburg, Chair of Psychology I

The CHFC has passed its litmus test. The Integrated Research and Treatment Center and its associated departments and clinics are now in an excellent position to focus on its novel research areas in an interdisciplinary manner. The advancement of young researchers as well as the numerous activities to convey knowledge about symptoms and relevant prevention measures should also be continued in a similar way in the future.

Huibert Pols, former Rector of Erasmus University Rotterdam, Chairman of the External Scientific Advisory Board (ESAB) of the CHFC

HEART FAILURE at a glance

DISEASE

- Cardiovascular diseases are the most common causes for death in Germany, account for about 35% of fatalities.
- Almost 4 million people in Germany suffer from heart failure –and the numbers are still increasing.
- Heart failure is the most common cause for hospital admissions in Germany and is associated with higher mortality risk than most malignant diseases.
- Heart failure is increasingly diagnosed in people younger than 50 years of age, mainly caused by overweight and diabetes.
- More than half of the patients with heart failure have seven or more comorbidities.

COSTS

Heart failure care requires 46 billion euros per year in Germany, representing 14% of all medical expenses.

CAUSES

42% of the participants in the STAAB study (p. 24) have at least one cardiovascular risk factor and are thus at increased risk to develop heart failure later in life (i.e., precursor stage A). The most important risk factors are:

- Severe obesity, with a BMI ≥ 30 kg/m2
- Raised blood pressure
- Diabetes mellitus
- Lipid metabolism disorders
- Smoking

HOW TO PREVENT HEART FAILURE

- ✅ Get at least 30 minutes of endurance training five times a week. This also includes walking and biking to work!
- ✅ Eat a healthy diet with plenty of vegetables, fruit and fish, but little meat and salt.
- ✅ Achieve and maintain a normal weight.
- ✅ Consume no or only moderate amounts of alcohol.
- ✅ Stop smoking, preferably today.
- ✅ Avoid permanent stress and ensure regular relaxation.
- ✅ Have a regular health check-up with your family doctor.

THE CHFC IN FIGURES

- Concept: interdisciplinary research, treatment and prevention of heart failure. In the state-of-the-art building at the University Hospital site, 5000 m² of space is availabe for this purpose, 90% of which is used for research.
- The construction of the CHFC cost 56 million euros. 45% was paid by the Free State of Bavaria, 45 % by the German state and 10% by the University Hospital and the Faculty of Medicine of the University.
- More than 3,500 patients are cared for each year during more than 8,000 visits in the CHFC's outpatient clinics. About half of these visits are study-related visits, in line with the concept of integrated research and treatment.
- The number of study-related visits at the CHFC has tripled since the new building opened in 2017.
- The CHFC was and is a National Study Center in six global studies.
- More than 100 clinical studies were conducted from 2015 to 2020.
- The BMBF has funded the CHFC with 45 million Euros from 2010 and 2020.
- Mission: prevention of heart failure and its complications.

How the SUCCESS STORY began

"The University Hospital of Würzburg has placed its focus on heart failure research and providing medical care to heart failure patients for decades. This was the breeding ground that led to the development of the CHFC."

Stefan Frantz, Director of the Medical Clinic I and co-founder of the CHFC

After a competitive two-year application process, the founders of the CHFC – Georg Ertl, Christiane Angermann, Martin Lohse, Stefan Frantz, and Stefan Störk – finally succeeded in winning the Federal Ministry of Education and Research (BMBF) over. In November 2010, the CHFC began operations as an Integrated Research and Treatment Center (IFB). This was the beginning of a success story of interdisciplinary work aimed at preventing heart failure and its complications.

"Research in Würzburg focused on heart failure very early on," says Stefan Frantz, referring to Collaborative Research Center SFB 355, in which preclinical researchers investigated the pathophysiology of heart failure in interdisciplinary and interdepartmental projects from 1993 to 2006. A particular focus of the SFB 355 was imaging and in vivo biochemical measurements using 31P magnetic resonance spectroscopy (MRS). SFB 688 then focused on mechanisms and imaging of cell-cell interactions in the cardiovascular system from 2006 to 2017. This SFB also included projects on heart failure.

Clinical heart failure research also took hold in Würzburg in the beginning of the 2000s. Christiane Angermann and Stefan Störk set up a cardiology-oriented clinical study group at the Medical Polyclinic, which decisively expanded the research spectrum in the direction of clinical research.

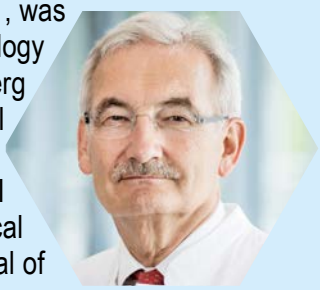
"At the beginning of the new millennium, there was a spirit of optimism in the field of heart failure. Clinical research on heart failure was gaining momentum, and there were more and better drugs and clinical devices on the market. The previously inevitable progression of heart failure became treatable and the prognosis of patients improved dramatically," explains Stefan Störk.

Another milestone was the founding of the Heart Failure Competence Network (KNHI) in 2003, with an office initiially set up in Berlin and later in Würzburg. "The prominent role that the Würzburg site played in the KNHI and its comprehensive biomaterial bank and clinical database, which is unique in Europe, were trend-setting," remarks Georg Ertl. The KNHI was funded for twelve years by the BMBF and for another three years by the German Center for Cardiovascular Research e.V. (Deutsches Zentrum für Herz-Kreislauf-Forschung e.V., DZHK). Leading scientists in the field of heart failure from 30 university hospitals, five research institutes, seven heart centers, 17 cardiovascular clinics, more than 200 medical practices, and four rehabilitation clinics, as well as other organizations and associations were involved in this collaborative network. Synergies were to be used to make progress in research and iimplement the findings in medical care. This source of funding was replaced by the BMBF's call for the establishment of Integrated Research and Treatment Centers (IFBs). The IFBs were intended to refine the idea of the competence network by focusing on local excellence and funding specific sites.

"Crucial for the final steps to the CHFC having a successful outcome in the application procedure was the integration of subjects and their protagonists, who primarily did not have heart failure in their spectrum," reflects Georg Ertl. He cites the interaction between cardiology and psychiatry as a notable and particularly successful example. Yet again, it was another study that laid the foundations for long-term intensive cooperation. The MOOD-HF study, which showed that the antidepressant escitalopram did not provide any benefit to patients with heart failure, was disappointing from a therapeutic standpoint but extremely important scientifically and clinically. "Ultimately, it was the collaborations that had developed over many years, which resulted in the joint application for an IFB. What is more, they also became its unique, international selling point," summarizes Georg Ertl. Of the 59 applications submitted, eight made it to the funding stage, one of which was from Würzburg.

FOUNDER

Georg Ertl, who hast been working at the University Hospital of Würzburg since 1981, was appointed to the Chair of Cardiology at the Mannheim / Heidelberg School of Medicine and Hospital in 1995. He was Director of the Medical Clinic and Polyclinic I from 1999 to 2017, and Medical Director of the University Hospital of Würzburg from 2017 to 2020.



Stefan Frantz replaced Georg Ertl as Director of the Medical Clinic and Polyclinic I. He completed his internship, worked as a resident physician and qualified as a professor at UKW. He became Director of the University Clinic and Policlinic for Internal Medicine III at the University of Halle/Wittenberg in 2014. Since 2017, he has been Director of the Medical Clinic and Policlinic I at the University Hospital of Würzburg. Frantz has been researching inflammatory processes in the heart since the 1990s.

Christiane Angermann moved from the City Center Campus of Ludwig Maximilian University (LMU) in Munich to Würzburg in 2000. Here, the Professor of Internal Medicine and Cardiology participated in many studies within the scope of the KNHI. She was instrumental in the development of the HeartNetCare-HF™ care program and its testing in the randomized INH trial.

Stefan Störk came to Würzburg in 2001 as a resident physician and currently works as a cardiologist and epidemiologist at the CHFC. In 2010, he became Scientific Director of the CHFC. He heads the Department of Clinical Research and Epidemiology at CHFC. His main focus is the development and implementation of scientifically based concepts to improve the medical care of heart failure patients.

Martin Lohse has been Professor of Pharmacology and Toxicology at the University of Würzburg since 1993, where he founded the Rudolf Virchow Center in 2001. He was one of the initiators of the biomedicine degree program in 2001 and one of the founders of the graduate schools at the University of Würzburg. From 2016 to 2019, he was chairman of the Max Delbrück Center in Berlin and headed the Berlin Institute for Health Research for two years. He studies receptors for hormones and neurotransmitters, which are essential targets for drugs. He has received numerous awards for his research, including the Leibniz Prize, the Jacob Henle Medal and the Bavarian Order of Merit.

IMAGING for Life

To visualize the invisible, and to measure what could not be measured before: These are Laura Schreiber's goals.

The physicist joined the CHFC in November 2014 and has created a sophisticated and visionary infrastructure for experimental and clinical imaging procedures in the new research building. Due to this infrastructure, results from experimental research can be rapidly transferred to human applications. The centerpiece is Germany's newest ultra-high-field whole-body MRI system with a field strength of seven tesla.

Looking deep inside the body with the help of magnetic resonance imaging already fascinated Laura Schreiber while she was pursuing her doctorate degree at the German Cancer Research Center in Heidelberg. Since 1997, she has dedicated herself to the organ that she considers most difficult to image: the heart.

At the CHFC, she and her team, as well as scientists inside and outside the Faculty of Medicine, are further developing ultra-high-field MRI to obtain better images of the beating heart. MRI is an important tool in the diagnostic process as well as in research, where it can contribute to the understanding of how heart failure develops. It provides information not only on the morphology and anatomy of the heart, but also on tissue and cell functions, microstructure, blood flow, metabolism and more. Since using the 7-Tesla MRI to take images of the heart still poses outstanding technical and physical challenges to the researchers, there are only a handful research centers worldwide which are willing to face the challenge and work with this system. Other experimental imaging devices such as PET and SPECT/CT are used at the CHFC to investigate a variety of functional and molecular processes in the study of heart failure and its concomitant diseases.

Laura Schreiber is particularly proud of the coil laboratory, where engineer Ibrahim Elabyad is developing and building his own coils that are close to the chest and thus to the heart. As a result, the magnetic field is optimally irradiated and received in humans or test animals of different sizes and thoracic shapes.

The work of doctoral candidates Johannes Martens and Tim Jedamzik is also unique worldwide.. Johannes Martens has developed a methodology to simulate fluid flows and transport processes in the coronary arteries to predict blood flow in the myocardium as well as delivery of substances to different regions of cardiac tissue. The scientists believe that the distribution of drugs can also be calculated in this way. Tim Jedamzik is examining the application of these methods to patients with coronary artery disease.

Another emerging application in the characterization of heart tissue is Cardiac Diffusion Tensor Imaging, or cDTI. Here, David Lohr is investigating how microscopic organization of the muscle fiber bundles in the heart can be depicted non-invasively by means of this imaging system. The analysis of these images makes it possible to draw conclusions about regular or altered arrangements of the cardiac muscle fibers in diseases, such as cardiomyopathies, myocardial infarction or rare diseases such as amyloidosis.

Since cDTI images would require a patient to remain in the MRI for an unacceptably long time, this is where artificial intelligence comes into play. Laura Schreiber and the Computational Imaging group are working on automatic analysis techniques that significantly reduce the measurement time. This involves creating an artificial neural network from many different MRI images, which is then applied to the patient's images to automatically identify different parts of the heart as well as normal and abnormal tissue. In another project, a combination of MRI images and other data such as ECG, blood tests and genetic analyses will be used to predict the progression of the disease or even the risk of sudden cardiac death.

MANY COMPETENCIES, ONE FOCUS: the best possible images of the heart

In addition to Laura Schreiber's department, other imaging working groups are developing and using innovative imaging methods:

- Cardiologist and physicist **Wolfgang Bauer**, senior physician at the Medical Clinic and Polyclinic I, does clinical imaging on the 3-tesla MRI scanner and conducts experimental studies.
- **Caroline Morbach** heads the echo laboratory at the CHFC and specializes in recording the dimensions and function of the heart using ultrasound.
- **Takahiro Higuchi**, Head of Nuclear Cardiology at Andreas Buck's Department of Nuclear Medicine, focuses on positron emission tomography (PET) – a nuclear medicine procedure that can be used to diagnose heart diseases at an early stage.
- **Peter Jakob** of the Chair of Experimental Physics V at the Department of Physics specializes in the field of basic physics-based research in nuclear magnetic resonance.
- **Herbert Köstler** heads Experimental Radiology in Thorsten Bley's Department of Radiology. His MRI expertise is in image reconstruction technology and clinical measurements, including MR spectroscopy.

"Our vision is to provide unique and innovative imaging methods to understand heart failure better, to diagnose the disease earlier, to monitor patients with heart failure and comorbidities, and over the long-ter, to prevent heart failure."

Laura Schreiber

THE POWER PLANTS of the cells

Mitochondria play an important role in heart failure and are potential targets for new drugs. The Department for Translational Research focuses on mitochondrial function and its interplay with cardiac mechanics.

Through his work in emergency medicine during his social service year, Christoph Maack became fascinated with cardiovascular medicine. After finishing medical school and obtaining his doctorate on the role of beta blockers in patients with heart failure, he moved from Cologne to Homburg with his longtime mentor Michael Böhm. During his three-year post-doc period at Johns Hopkins University in Baltimore, U.S.A, he shifted his research focus from beta blockers to mitochondria. These organelles are the key to a cell's life and death decisions, as they provide vital energy but can also cause cell death through oxidative stress. An excellence grant (Emmy Noether Program) and later a professorship from the German Research Foundation (DFG) enabled him to establish an independent working group after his return to Homburg. Some of the people he worked with in the lab early on, such as Michael Kohlhaas, Alexander Nickel and Michelle Gulentz, joined him, when he moved to Würzburg..

"We can offer the whole range of interaction between the mechanics of the heart and metabolism."

Christoph Maack

It has been Christoph Maack's goal to be clinically active while simultaneously conducting basic and translational research in his specialized field of heart failure. In the summer of 2017, he accepted the CHFC's offer to join the CHFC team, which approaches heart failure from various methodological and topical angles. Maack is board-certified in internal medicine, cardiology and intensive care medicine and is a DGK-certified heart failure specialist. He works in the outpatient clinic, heads the Translational Research Department, and is the CHFC spokesperson.

Bringing energy balance into equilibrium

To this day, his research has focused on mitochondria. They are where the cell's fuel, ATP, is produced. In a sense, they are the power plants of the cells, with calcium providing the ignition. A disturbed calcium balance impairs the function of the mitochondria, which in turn causes an energy deficit and oxidative stress. This ultimately weakens the heart.

Christoph Maack and his translational

research team want a better understanding of the processes involved in energy production in order to develop therapies that prevent oxidative stress and bring everything into balance. Drugs that directly target mitochondria and thereby delay or even prevent heart failure are already undergoing experimental and clinical trials.

Today, Christoph Maack no longer sits on the laboratory bench. But he is proud of his team, which consists of top-class experts from the fields of medicine, physiology and biochemistry who think in interdisciplinary terms and work autonomously. He gives new impetus to his team members who then further develop his ideas.

Deciphering disease mechanisms

An important focus is on the disease mechanisms of hypertrophic cardiomyopathy (HCM). The gene mutation of this disease substantially increases the energy demand of the heart. The members of the translational research team have discovered that this leads to more oxygen radicals in the mitochondria and these trigger arrhythmias. In model systems, therapies that attack mitochondria have already been able to prevent arrhythmias. The CHFC now plans to conduct clinical studies enabling the HCM team to investigate in interdisciplinary cooperation whether catheter ablations and drug therapies reduce energy demand and thereby improve heart function and the patient's symptoms. Another important focus of the department is the pathophysiology in Barth syndrome, a genetic disorder that leads to pathological changes in the cardiac muscle. A specialist in this field is Jan Dudek, who heads a junior group within the department. Maack and his team have found that the impaired energy production of the cardiac muscle cells due to the genetic defect is related to calcium imbalance. Both energy production and the detoxification of oxygen radicals depend on the uptake of calcium. The team was able to observe the calcium defect only in the mitochondria of cardiac muscle cells and not in the mitochondria of skeletal muscle or brain. Thus, regulation of impaired calcium uptake may be a promising therapeutic target for the treatment of this disease.

The Department of Translational Research collaborates with many other research institutions within and outside Würzburg as well as with various funding organizations, in particular the German Research Foundation (Deutsche Forschungsgemeinschaft, DFG) and the Barth Syndrome Foundation.

FASCINATED BY THE CODE of life

Even as a doctoral candidate, Brenda Gerull studied how genetic changes influence hereditary heart diseases. At the Max Delbrück Center for Molecular Medicine in Berlin, she discovered that mutations in the giant protein titin can lead to a specific form of chronic heart failure called dilated cardiomyopathy. Since then, the cardiologist has been fascinated by the huge impact that a single altered letter in the "code of life" can have on the body.

In February 2016, the Berlin native accepted the CHFC's offer to become a Research Professor for Cardiovascular Genetics and moved from Calgary, Canada, to Lower Franconia. In Würzburg, she realized her dream of working as both a clinical physician and researcher and founded the Center for Genetic Cardiac and Vascular Diseases. Together with a highly motivated team, she conducts research on the genetic causes and molecular mechanisms of various forms of heart failure.

Vision of personalized medicine

Currently, only about half of the genetic causes of cardiomyopathies are known and many of the underlying molecular mechanisms are still unclear. Brenda Gerull's goal is personalized medicine: The vision of one day being able to offer every patient an individualized and effective concept for prevention, diagnosis and treatment motivates her day by day. She focuses her research on the mechanistic pathways caused by the gene mutations. How do the mutated genes disturb cardiac structure and function? How do they lead to heart failure? And what can we do against it?

Using advanced DNA technologies such as next-generation sequencing, the Cardiovascular Genetics team can quickly and accurately determine known genetic variants in known genes, as well as discover new ones. In the cellular and molecular studies, genetic variants are introduced into the genome of model systems using gene-editing technologies such as CRISPR-Cas9. Zebrafish or mice and human inducible pluripotent stem cells serve as models.

Transparent fish and contracting cardiac muscle cells

Brenda Gerull is particularly proud of the establishment of the zebrafish facility and stem cell technology. Zebrafish are particularly well suited for studying the heart at the embryonic stage. In the first three to four days, they are still transparent so that the heartbeat and

the way the blood is pumped through their body can be followed under the microscope. The fish are therefore an ideal model for characterizing developmental defects, heart failure and arrhythmias. Another excellent model system for personalized medicine includes human induced pluripotent stem cells. Skin cells from patients with genetic cardiomyopathies are reprogrammed, differentiated into cardiac muscle cells and mechanistically studied.

Finding the missing puzzle piece

One focus is on the LEMD2 gene, which was discovered by Brenda Gerull and her team. A mutation in this gene leads to changes in the structure and function of the nuclear envelope and can cause arrhythmias and heart failure – similar to a group of rare disorders known as laminopathies. Brenda Gerull hopes her research will provide the missing puzzle piece so that the disease mechanisms behind this particular form of arrhythmic cardiomyopathy can be understood and therapeutic approaches can be found in the overall complex of these proteins.

In another project, mutations in cell-cell connection proteins are being examined. Changes in so-called desmosomes result in arrhythmogenic cardiomyopathy (ACM). Brenda Gerull is particularly interested in how genetic changes interact with environmental factors to cause the disorder. For example, the influence of metabolism, inflammatory processes, age or gender on cardiomyopathies is being investigated within the scope of the Heart Failure Interfaces concept. This concept involves many research groups which work together gainfully not only at the DZHI, but also on the entire campus.

What roles do genes play in heart failure, and where might new therapies start? The Cardiovascular Genetics team is looking for answers to these questions.

"We are providing the missing puzzle piece in order to understand disease mechanisms and to find novel therapeutic approaches."

Brenda Gerull

WHOLEHEARTEDLY for better patient care

Transferring evidence-based medicine into practice in a standardized way and thus providing better care for heart failure patients: That is the goal of Stefan Störk and his team.

Stefan Störk is a passionate physician and researcher. After obtaining his doctorate degree on the topic of "Effect of intravenous molsidomine administration on nitrate tolerance in heart failure patients with coronary heart disease" in Berlin, he became resident physician at the LMU Hospital of Munich and began his career in the Preventive Cardiology study team. In 2001, he moved to the University Hospital of Würzburg after completing his training in Clinical Epidemiology at the Universities of Utrecht and Rotterdam, which he undertook before becoming a specialist in cardiology. This epidemiological subfield deals with the application and development of methods for clinical research.

With foresight, patience, and perseverance

Since then, he has focused on healthcare services research in the field of heart failure. With foresight, patience and perseverance, he and his team are looking for ways to transfer evidence-based diagnostics and therapy to everyday practice in a standardized manner, where it is adapted to the needs of patients and the medical profession. This includes technical advancements in the field of cardiac ultrasound, studies on the efficacy and safety of drugs or implantable devices, the establishment of modern IT structures and the structured collection of data and biomaterials.

Stefan Störk is in charge of the CHFC outpatient clinics, which are affiliated with Medical Clinic I. In addition to the general cardiology outpatient clinic, they offer treatment with special consultation hours for patients with terminal heart failure, genetic heart disease, rare diseases such as amyloidosis and hypertrophic cardiomyopathy (HCM), obesity and treatment-resistant hypertension. Treatment data are processed in such detail that they can be immediately used for research. Ideally, this is seen in the large disease registries that map the natural history of a disease. The CHFC has a pioneering role in registry research. The exemplary integration of research into everyday clinical treatment is the guiding principle that has driven Stefan Störk's work since the CHFC was founded: "The best-researched patient is the best-cared-for patient."

Echocardiography is part of almost every examination and clinical study. Caroline Morbach has taken over Stefan Störk's former pet project. With the Academic Core Lab, the cardiologist ensures that the cardiac ultrasonographies performed at the medical campus have consistent high quality so that the measured values can be compared and used for research. Their team includes four echocardiography technicians trained at the CHFC.

One concept penned by the CHFC, in which Stefan Störk played a major role, is the Heart Failure Units (HFUs). These are care units that are specially equipped for treating heart failure patients. Specialized practices, specialized hospitals and supraregional centers form a HFU network: They ensure needs-based care, including the transition from inpatient to outpatient care. The main pillar is the specialized heart failure staff, whose training is particularly important to Stefan Störk..

More than 100 clinical studies

Both the training courses and the multicenter studies, which the CHFC coordinates on a national level, contribute to the steady growth of the vital network. The Clinical Trial Office supervises all phases of large clinical trials, ranging from planning, execution, monitoring and analysis to publication. In addition to national and international studies, the Clinical Trial Office at the CHFC also conducts smaller studies. For example, the CHFC has cared for more than 10,000 patients in more than 100 clinical studies over the past ten years. In addition, 5,000 heart-healthy Würzburg residents have so far come to the CHFC for two comprehensive examinations, which were undertaken as part of the large STAAB cohort study. 3,000 of these test subjects also participated in the STAAB Covid study. This versatility and clout also reflect the excellent network at the research campus in Würzburg, not only with other hospitals, but also with theoretical departments such as Artificial Intelligence or Clinical Epidemiology and Biometry. The center's campaigns to raise awareness of heart failure as a social problem are also visible regionally and internationally. For example, more than 20,000 data sets on heart failure awareness have been collected and analyzed in more than 30 European countries..

Data on 5 million cases

In addition, routinely collected data and biomaterials are made available for patient-relevant research projects. More than five million cases are now filed in the data warehouse in a pseudonymized fashion. Anyone planning a study and looking for patients with a specific age, gender and heart failure stage will find what they are looking for in this intelligent combination of data warehouse and search engine. Biomaterials are stored in great varieties in the neighboring interdisciplinary biomaterial bank and database in Würzburg (Interdisziplinäre Biomaterial- und Datenbank Würzburg, ibdw) according to quality-controlled standards.

The fact that Stefan Störk can rely on his team was recently demonstrated during the Corona pandemic. He is supported by researching physicians and motivated doctoral candidates, study nurses and certified medical assistants, project managers, data analysts and computer scientists. Cooperation within and outside the campus is the be-all and end-all for Stefan Störk's mission. His credo: "Together for a strong heart!"

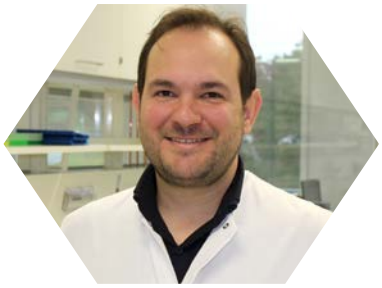
"The best-researched patient is the best-cared-for patient."

Stefan Störk

SPRINGBOARD for bright & creative minds

In addition to the departments, there are various junior working groups and other working groups, which are studying heart failure, its development, prevention and treatment.

How the heart heals after a heart attack



Gustavo Ramos's junior group

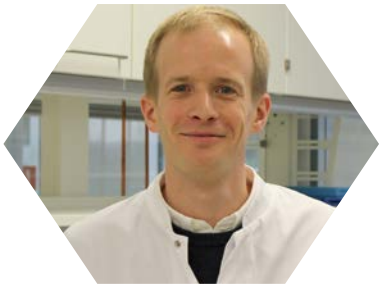
Biologist Gustavo Ramos has been looking for the part of the protein responsible for creating the immune cells that support early healing after a heart attack for a long time, and now he's found it. Ramos and his junior group, which is funded by the Interdisciplinary Center for Clinical Research (Interdisziplinäres Zentrum für Klinische Forschung, IZKF), have not only discovered the MYHCA614-629 molecule segment, but also the site where the immune cells are formed: The so-called CD4+ T cells are not formed in the heart tissue, but in the lymph nodes. Initially, inflammatory processes should not be blocked after the infarction so that the healing process is not disrupted. In some patients, however, the healing process is impaired because they produce fewer and possibly also bad T cells, which do more harm than good. Therefore, another goal is to find a biomarker for the quality of the healing process and a T-cell-based therapy to improve infarct healing. The collaborative project with the Medical University of Graz and the Sorbonne University of Paris is supported by the European Research Area Network ERA-CVD with a total of 810,000 euros and the Ramos working group is funded by the DFG with a further 438,600 euros..

Dysfunctions in the power plants of the heart

Jan Dudek's junior group

The heart is one of the most energy-intensive tissues, consuming six kilograms per day of ATP – a molecule that provides energy in the body's cells. Ninety-five percent of this energy demand is covered by mitochondria. "Mitochondria are the power plants of the heart. If the energy supply is disturbed, the heart becomes ill," states Jan Dudek. Together with his junior group, the biologist is researching the causes and mechanisms of mitochondrial dysfunctions. What mechanisms cause mitochondrial dysfunction to promote the development of heart disease? What is the role of the cardiolipin molecule, which is found in the mitochondria of heart cells? Cardiolipin changes are associated with a large number of heart diseases. In order to elucidate the role of cardiolipin in the pathogenesis of heart disease, Jan Dudek and his team are studying Barth syndrome – a rare, inherited disorder that causes immune deficiencies, muscle weakness and heart failure. It is caused by a mutation in an enzyme needed for the maturation of cardiolipin. The work of Jan Dudek is supported by the Barth Syndrome Foundation and the German Research Foundation.

The benefits and harms of macrophages



Clément Cochain's junior group

A heart attack often leaves scars and scars can lead to the development of heart failure. Clément Cochain and his junior group, funded by the IZKF, want to better understand the healing process by carefully examining macrophages. These immune cells can facilitate the survival and growth of cardiac muscle cells and the development of new blood vessels. However, they also have harmful properties. Cochain's goal is to understand the mechanisms that control the balance between beneficial and harmful functions of macrophages in the damaged heart. But even before macrophages come into play, neutrophil granulocytes rush from the bloodstream into the heart. These immune cells cause inflammation in the heart, triggering the healing process and breaking down dead tissue. But while some of these cells eat dead tissue, others cause oxidative stress. A study published in Circulation Research in August 2020 shows how difficult it is to investigate the mechanisms of these "scavenger cells." In collaboration with the Helmholtz Institute for RNA-based Infection Research (HIRI), Cochain found that neutrophils migrate to the heart at different times and change how they function there.

On the trail of new tracers

Takahiro Higuchi's working group

Takahiro Higuchi is not just looking inside the body but is seeing how it works. He is visualizing the molecules, glucose utilization, and the activity of the nerves. The specialist in nuclear medicine and head of Nuclear Cardiology at Andreas Buck's Clinic and Policlinic conducts research both in Würzburg and in his home country of Japan and has been working at the DZHI since 2011. His focus is on positron emission tomography (PET) – a technique that is used in nuclear medicine, which serves to diagnose heart disease at an early stage and thus provide optimal treatment. During a PET scan, the patient is injected with a tracer, which is a weak radioactive substance that acts as a marker as it accumulates in the heart muscle depending on the blood flow. Compared to scintigraphy, it provides higher resolution and sensitivity as well as more details about tracer accumulation. Tracers can be used to depict functional and molecular processes. Takahiro Higuchi and his international team are developing these types of tracers. Higuchi believes his field of research is endless: "When we develop new tracers, we also get new images." His dream is to one day combine PET scans with MRI scans in order to see form and function simultaneously..

EXCELLENT teams & technology

The new CHFC building offers the best conditions for cutting-edge research. Core facilities have been set up to provide working groups, hospitals and institutes with access to technologies and methods. They provide excellent technical infrastructures and offer internal and external research teams support, consulting and analyses.

Clinical Research Unit

The Outpatient Study Clinic and Clinical Research Unit offer researchers the opportunity to plan, conduct and evaluate clinical studies. One area of research being focused on is data collection while patients are hospitalized. At the same time, the "ibdw" provides a comprehensive biomaterial bank for blood, tissue and DNA samples. The Clinical Trial Office cooperates with national and international clinical research organizations and pharmaceutical companies. It acts as the national coordinating office for Germany and specializes in conducting multicenter, clinically controlled, randomized trials in cardiovascular medicine. The CHFC offers advanced training courses for heart failure medical personnel, including nurses and certified medical assistants who work in hospitals or cardiology practices.

Echocardiography Lab and Core Lab

In the field of ultrasound-based cardiac and vascular imaging, the Echocardiography Laboratory offers not only all types of cutting-edge examination methods, but also advanced training courses and qualification schemes, services, and expert opinion findings. The Academic Core Lab Ultrasound-based Cardiovascular Imaging, ACL-UCI for short, serves to enhance the quality of multicenter studies. To minimize measurement errors, all images are evaluated in a standardized manner.

Cardiovascular Imaging

The Core Facility provides access to state-of-the-art imaging with 7-Tesla MRI, 7-Tesla experimental MRI, fluoroscopy techniques and nuclear medicine

tomography such as PET and SPECT. A radiofrequency laboratory with mechanics workshop and a 3D printer for development of MRI coils and experimental setups are also available. In addition, mathematical simulation calculations are offered in the field of radiofrequency and coil technologies as well as in the simulation of fluid flow and transport processes in biological systems, especially for coronary arteries.

Cellular electrophysiology

The lab uses a wide range of electrophysiological and microscopic optical fluorescence methods, which allow a detailed analysis of the electromechanical coupling and of the associated regulation of mitochondrial energetics. In this context, sarcomere shortening, cytosolic and mitochondrial calcium, and sodium concentrations are particularly important as are mitochondrial redox state and oxygen radical production.

Cardiovascular genetics

The zebrafish model system is being used to model cardiac diseases. Zebrafish have been used to conduct extensive phenotypic studies of cardiac structure and function as well as arrhythmias. Another focus is the cultivation and differentiation of human induced pluripotent stem cells (iPSCs) in cardiomyocytes, and their genetic modification using CRISPR-Cas9 technology. The Core Facility also provides support for the implementation and evaluation of new DNA sequencing technologies such as Next Generation Sequencing (NGS).

Mitochondrial function

The Core Facility maintains a wide range of methods for analyzing mitochondrial function in various tissues – from respiratory function, redox state, reactive oxygen species production and mitochondrial function in intact cells to processes of glucose and fatty acid metabolism using the Seahorse technology. The assembly of respiratory chain complexes and their individual activities can also be analyzed.

Animal husbandry

Animal husbandry at the CHFC offers a flexible space concept with attached examination rooms, operating rooms and separate access points. Up to six different species can be housed simultaneously: pigs, rats, mice, guinea pigs and rabbits, as well as zebrafish. The center assists registered users with caring for the animals and supports them by offering advice on laboratory animals and veterinary services.

VALUABLE data treasures

From prevention to basic research: The example of the systemic disease heart failure illustrates how data can be of benefit to science and the population.

Peter Heuschmann (left) and Stefan Störk jointly launched the STAAB study.

How often do the precursors of heart failure occur in Würzburg residents aged 30 to 79? How are they related to various risk factors such as lifestyle and pre-existing conditions? And how often and how quickly do precursors progress to a higher stage of heart failure? These questions are being examined in the STAAB study. Study participants were randomly selected and contacted by the City of Würzburg. Those who had no known heart failure at the start of the study have already been examined twice within about four years. Stefan Störk, Head of Clinical Research at the CHFC, and Peter U. Heuschmann, Director of the Department for Clinical Epidemiology and Biometry (IKE-B), had initiated the STAAB study in 2013 as a joint, long-term project.

The first major analysis of the data has already provided some surprises. Forty-two percent of the study participants are in heart failure precursor stage A. This means they have at least one risk factor for developing heart failure. The most common risk factor, at 45 percent, is high blood pressure. In second place is obesity, at 20 percent. What is more, a strikingly large number of young people between the ages of 30 and 39 are already in stage A.

Are there unknown risk factors?

17 percent of the study participants exhibit a structural change in the heart, corresponding to precursor stage B. Examples of these structural abnormalities include thickened heart walls, dilated heart chambers or restrictions in the pumping or filling function. These changes were detected by cardiac ultrasound, but did not yet cause any symptoms. The study team was puzzled by the fact that one in three of this group had no risk factor for heart failure. This seems to call into question the previously held belief that heart failure develops gradually over time, beginning with having a risk factor (stage A), developing changes in the heart structure (stage B) and ultimately progressing to heart failure with recognizable symptoms (stage C). It is also remarkable that the study subjects are rather young, with an average age of 47, and that they are predominantly female (78%).

The study team has not yet found a clear cause for this phenomenon. However, it seems likely that there are unknown risk factors or genetic changes that have not been looked for yet in screening. Thus, the current prevention measures are unlikely to be effective in this particular group.

Ready on call for future projects

The data from the STAAB study are a treasure that will benefit many scientists and ultimately the entire population. The extensive data collected on risk factors, pre-existing conditions and quality of life, as well as the biomaterials that have been collected are suitable for use in numerous other studies besides heart failure. For example, a number of highly relevant questions about Covid-19 can be answered particularly well in the short and long term. The study participants have already been tested for SARS-CoV-2 antibodies and have provided a nasal swab.

The valuable biomaterials are stored under quality controlled conditions in the Interdisciplinary Biomaterial Bank and Database Würzburg (ibdw). They can be retrieved at any time if required. They can also be used to support sequencing projects with DNA isolations in high-throughput procedures.

The data sets are stored in a so-called data warehouse, which also accommodates other valuable data. In the Acute Heart Failure (AHF) Registry the progression of the disease in 1,000 patients with acute heart failure is documented in detail; it contains information obtained during their hospitalization in the University Hospital of Würzburg. In addition, data from an additional 1,000 heart failure patients were allowed to be anonymously and scientifically evaluated from their inpatient stay. These are predominantly patients with a special disease profile and higher mortality rate. Thus, a complete picture of all patients with acute heart failure is available for the first time, including the most severely ill.

The AHF Registry's clinical trial database facilitates the analysis of numerous scientific issues. In the collection phase, twelve doctoral candidates began examining the quality of the data and its significance for the short-term prognosis of patients, and gained valuable insights from their analysis. Among other things, they examined what can be deduced from ECG, X-ray images, a wide variety of laboratory tests and echocardiographies.

PREVENTION instead of treatment

There is no glory in prevention" is a saying widely used in medicine and much quoted especially in the CHFC anniversary year 2020 – the Corona Year. There is no glory in prevention – because, when prevention is successful, you see virtually nothing. But prevention is also highly important for the same reason: namely, to prevent worse things from happening.

Prevention of heart failure is therefore an important goal of the CHFC, in addition to research and treatment. In many cases, the development or progression of heart failure is avoidable.

Prevention includes implementing new procedures in diagnostics, disease management and therapy in order to detect risk factors at an ever earlier stage and to counteract them.

In the STAAB observational study, for example, the influencing factors and progression of the disease in the early stages of heart failure are being determined on the basis of 5,000 randomly selected people from Würzburg. As shown in the STAAB and in other studies, hypertension is still inadequately treated, and the impact of being overweight and having diabetes is increasing. This makes raising public awareness even more important. Surveys have shown that there is insufficient awareness of heart failure in the general population and there are basic misconceptions about the disease. The CHFC therefore intends to conduct a multifaceted public relations campaign to educate people and motivate them to take preventive measures.

Right from the cradle

Because obesity and diabetes are on the rise, especially among children and young adults, and public relations work needs to start with the very young, which is why the center organizes activities like art competitions for different age groups. School children paint, design, compose and write texts on various topics related to the heart, such as what it does and what is good for a healthy heart. Numerous artworks by the young artists adorn the rooms of the DZHI. The students are allowed to visit the premises in advance and look over the shoulders of the scientists and doctors.

Another important tool is Heart Failure Awareness Day. Around 30 European countries participate in the event every year in May. It serves to draw attention to the widespread disease and inform people about how to prevent it and how to recognize the first signs of the disease. This special day of action was initiated by the Heart Failure Association (HFA) of the European Society of Cardiology. The impetus came from the CHFC, which has been actively involved since the first European Heart Failure Day was held in 2010.

The CHFC has since developed a vital network with partners from the region and all over Germany so that the awareness campaign with the slogan "active against heart failure" can be

held nationwide. The campaign includes several information events, hands-on activities and special bicycle tours highlighting cardiac health. The DZHI has received several awards for its campaigns and organizations. For example, Stefan Störk took part in the third World Congress on Acute Heart Failure in Florence in May 2016, where he accepted a gold-plated heart as a special award on behalf of all German participants.

If one considers these awards and also the commitment of all those involved, the interest of the population, the eagerness of the students and the decreasing mortality rate thanks to better therapies, it follows that there is indeed "glory in prevention". Although demographic trends mean that more and more people are suffering from heart failure, the number of deaths caused by this condition is now falling.

With numerous campaigns for young and old, the CHFC draws attention to the widespread disease of heart failure.

The core idea behind the founding of CHFC was to no longer view heart failure as an isolated disease of the heart, but as a systemic disease. After all, heart failure patients are often older and therefore suffer from multiple diseases. Other diseases can have an unfavorable effect on the progression of heart failure, and conversely, heart failure often has a negative impact on other organ systems. More than half of heart failure patients have seven or more comorbidities.

THE HEART-KIDNEY-DIABETES dilemma

The heart's three levels of communication

The heart communicates with other organs primarily in three "languages": through hormones, inflammatory processes and metabolism. The CHFC conducts research on the interfaces between the heart and other organs, in particular on these three levels of communication as well as their interfaces with each other and with the respective organs. This approach formed the basis for the development of the concept of „heart failure interfaces".

Diabetes mellitus is one of the most important risk factors for heart failure because it damages blood vessels and the cardiac muscle itself. Diabetes also attacks the kidneys. Heart failure affects the function of the kidneys through changes in blood pressure, and renal insufficiency makes it more difficult to treat heart failure with drugs that target the kidney's hormone systems, among other things. New data suggest that heart failure patients are also more likely to develop cancer. It has also been known for some time that cancer therapies in particular may damage the heart.

An "unhappy triad" is the combination of diabetes, chronic kidney disease and heart failure. Every second to third heart failure patient has chronic kidney disease, which increases mortality by a factor of 2 to 3. Patients with diabetes suffer from heart failure 15 years earlier on average, which significantly worsens their prognosis. Christoph Wanner, Head of Nephrology at the University Hospital of Würzburg and President of the European Renal Association ERA-EDTA, has been researching these interacting diseases for many years.

The treatment of patients with diabetes and heart failure has long been a clinical dilemma. Although many drugs lower the glucose levels, they have very different effects on the progression of cardiac and vascular diseases. This suggests that other effects are responsible for the effectiveness of some drugs and not just lowering the glucose level.

The most common comorbidities in heart failure

- High blood pressure (66%)
- Chronic renal insufficiency (50%)
- Diabetes (32%)
- Overweight (26%)
- Lung diseases (26%)
- Cancer (17%)
- Neurodegenerative disorders, such as Alzheimer's or Parkinson's disease, stroke, depression (17%)

Christoph Wanner

New drugs offer hope

Christoph Wanner was one of the first to recognize the potential of SGLT2 inhibitors. These drugs not only help with diabetes, they also slow the progression of heart failure and renal insufficiency. They have meanwhile become a critical cornerstone in the treatment of patients with diabetes, but also heart failure and chronic kidney disease, with or without diabetes.

In the EMPA-REG OUTCOME study, Wanner and his team were able to show

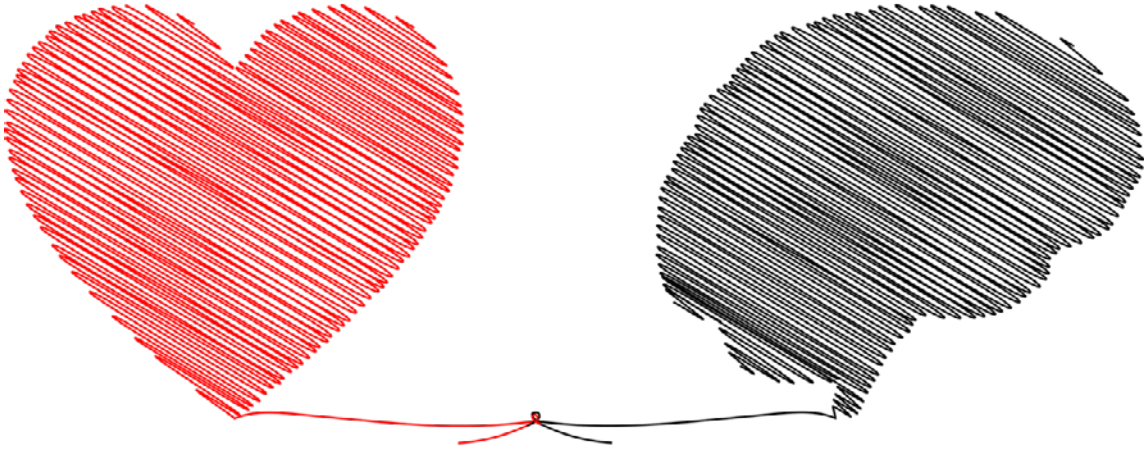
SGLT2 inhibitors are successfully used in heart and kidney patients – with and without diabetes!

that the SGLT2-inhibitor empagliflozin-not only has a blood sugar-lowering effect in patients with heart disease and type 2 diabetes and reduces the risk of death from heart disease, it can also halt the progression of renal insufficiency. The effects on the heart and kidneys were so clear that they inspired a whole series of follow-up studies. SGLT2 inhibitors are now used worldwide in patients with diabetes and an increased risk of heart disease or with pre-existing heart disease.

Whether empagliflozin also benefits kidney patients without diabetes is currently being investigated in the EMPA Kidney study. This international study is being coordinated by the University of Oxford in cooperation with the University of Würzburg. A total of 5000 patients in the U.S., Canada, China, Japan, Malaysia, the UK and Germany are being examined. The study center is located at the Medical Clinic and Polyclinic I of the University Hospital of Würzburg..

How SGLT2 inhibitors work

Our lifestyle is characterized by consuming too many carbohydrates and too much sugar and insufficient exercise, which is why widespread diseases such as diabetes and high blood pressure are on the rise, which in turn lead to heart and kidney diseases. SGLT2 inhibitors appear to break this spiral. This can be attributed to the fact that they ensure that more sugar – about 10 teaspoons per day – is excreted through the urine. This lowers blood glucose levels and can lead to a slight decrease in weight and blood pressure. At the same time, the kidneys and circulation are decisively relieved.



Stress and stroke can lead to heart failure – and this in turn to memory impairment and depression. The close interaction between heart and brain has encouraged the CHFC to dedicate a separate research project to focus on this topic while collaborating closely with experts from neurology, psychiatry and epidemiology.

HEART & brain

Antidepressants do not help heart failure patients

In general, depression is already detrimental to a person's quality of life. If it is coupled with heart failure, the risk of premature death increases two- to three-fold. Given the close correlation between heart failure and depression, cardiologists Christiane Angermann and Georg Ertl as well as psychiatrist Jürgen Deckert and their teams tested whether treatment with antidepressants could improve outcomes in heart failure patients. However, treatment with an effective antidepressant failed to prevent the frequency of hospitalizations or deaths in a randomized trial, as has been shown by the findings published in 2016 in the Journal of the American Medical Association (JAMA).

"Without a healthy brain, the heart cannot do its job and vice versa."

Jürgen Deckert, of the Clinic for Psychatry, Psychosomaticy and Psychotherapy at the University Hospital of Würzburg

Decreased brain power with a weak heart

Würzburg researchers have shown how brain weakness and anatomical brain changes are related to one another in heart failure patients.

The fact that many patients are unable to comply with the comprehensive therapy recommendations, such as taking medication regularly or weighing themselves daily, is often not due to their willpower or carelessness – but rather to a disorder of memory and attention, so-called cognition, which is induced by the cardiac insufficiency. This is because a weak heart also affects brain function. Anna Frey and Guido Stoll confirmed in the "Cognition.Matters-HF" study that 41 percent of the patients examined showed deficits in reaction time, 46 percent had deficits in verbal memory and 25 percent in working memory. A head MRI showed greater tissue loss in the temporal lobe, which plays an important role in memory, compared to subjects with a healthy heart. The shrinkage in this region of the brain was related to the study participants' cognitive impairments. The findings were published in the Journal of the American College of Cardiology: Heart Failure. No further accelerated tissue loss or decline in cognition occurred over the three-year period. This underscores the importance of optimal heart failure therapy. The results appeared in the European Heart Journal in 2021.

Less anxiety thanks to nternet based training for ICD patients

Many patients with an implanted cardioverter defibrillator (ICD for short) are afraid of the shock – on the one hand, because the violent electric shock in the chest can be painful, and on the other hand, because they would possibly die without it. Psychologist Paul Pauli and his team have already scientifically proven that a defibrillator can increase anxiety in patients. They have also shown that telephone support can alleviate this anxiety. Finally, psychologists from the University of Würzburg, together with cardiologists from the DZHI, have found a modern, easy and, above all, sustainable solution for improving the lives of heart patients in the long term who suffer from significant psychological problems as a result of the defibrillator. A six-week, moderated Internet training program with guidance for self-help verifiably reduces anxiety and the depression that often accompanies it. The study's findings were published in the European Heart Journal in 2019.

The researchers primarily responsible for the "Cognition.Matters-HF" study: Mirko Pham, Stefan Störk, Anna Frey, and Guido Stoll.

All heart failure patients are now also screened for depression, and the recommendation has been incorporated into the guidelines.

WEAK HEARTS increase cancer risk

Another widespread disease associated with the heart is cancer. It has been known for some time that chemotherapies in particular can damage the heart. Only in recent years has it become clear that heart failure patients are more likely to develop cancer. The reasons for this correlation have not yet been clarified. But here, too, systems that are typically activated in heart failure might play an important role, such as the sympathetic nervous system or inflammatory processes. This field of research is still a young and developing area of the CHFC. Edoardo Bertero and Christoph Maack from the Department of Translational Research, in collaboration with the San Martino Policlinic in Genoa, Italy, analyzed a large number of clinical trials on heart failure. They found that tumor disease was a relatively common cause of death in these trials. However, it was often not explicitly analyzed. With the decline in cardiovascular-related deaths in recent decades, due in part to improved drug treatment of heart failure, cancer-related deaths are becoming statistically more important. They should therefore be considered more systematically in future studies. In collaboration with the Norwegian Institute of Public Health in Oslo, Norway, the significance of inflammatory processes for the occurrence of tumors and heart failure in the general population is currently being analyzed in ongoing studies.

In close collaboration with Matthias Kroiss and Martin Fassnacht from the Department of Endocrinology and Diabetology, the department is studying a drug used in adrenal carcinoma. The chemotherapeutic agent has a specific effect on rapidly dividing cells of the adrenal gland, but not on heart cells. Since the substance exerts its effects particularly in the power plants of the cell, the mitochondria, researchers are comparing the mitochondria of different tissues to figure out its mode of action.

LOSE WEIGHT & breathe more easily

Being overweight and obesity in particular – i.e. very overweight with a BMI of 30 or more – have profound consequences for those affected. The heart suffers in two respects: Excessive weight weakens the heart and mind. It is also associated with diseases such as diabetes, high blood pressure and joint problems.

Basically, most obese patients know the importance of eating a healthy diet, sports and exercise. Nevertheless, they do not manage to transfer this knowledge to their everyday lives to a sufficient extent. They often have had many attempts at dieting, but these have not led to long-term success. Weight reduction surgery could help some patients. So far, the costs of bariatric surgery have only been covered by health insurance companies upon application and only after a case-by-case review. Martin Fassnacht and his team want to use a new treatment concept to increase the chances that the operation will be approved. As part of the Würzburg Obesity Study (Würzburger Adipositas-Studie, WAS), they investigated the effect of weight loss on the function of the heart.

One cohort of the patients received gastric bypass surgery for weight reduction, while the other cohort received support in the form of psychotherapy to change their lifestyle. Among others, two factors were examined: the performance capacity of the heart and the patients‘ quality of life. A total of 93 patients were recruited and followed up for a total of 36 months. The final evaluation was still ongoing when this brochure was being produced. Thematically related to the clinical WAS study is the concept behind the experimental WARS study. The aim of the WARS study is to present biochemical, molecular and blood flow parameters that are not accessible in this depth and to this extent in humans. Researchers want to take a closer look at the functional relationships between overnutrition and the development of cardiac and vascular diseases, including chronic heart failure. A special focus is also on tissue hormones and how they are released after bariatric surgery compared to how they are released when only calories are reduced. The project will thus contribute to a better interpretation of the data from the WAS study.

A Bavaria-wide study under the name ACHT (Adiposity Care & Health Therapy) is also underway under the direction of Martin Fassnacht. It involves a new aftercare concept for patients who have undergone gastric reduction surgery. A nutritionist at the clinic acts as a pilot and checks the patients‘ levels via app. If there are any abnormalities, she contacts the patients so that problems can be identified at an early stage and hospital stays can be prevented.be prevented.

Specialized nurses and certified medical assistants – THE KEY TO SUCCESS

Together with the German Society of Cardiology (Deutsche Gesellschaft für Kardiologie, DGK), the University Hospital of Würzburg has long been committed to improving healthcare structures for heart failure patients. In 2019, for example, current research results from the CHFC have once again been incorporated into the new edition of the National Care Guidelines for Chronic Heart Failure. In these guidelines non-drug therapy plays a role that is just as important as guideline-compliant drug therapy. In particular, the guidelines recommend close cooperation between hospital physicians, specialists and general practitioners as well as the use of specialized heart failure assistance staff.

The Patients benefit from telephone support

The Interdisciplinary Heart Failure Network (INH) was founded in Würzburg in 2001 as a research and medical care network. Within this framework, the HeartNetCare-HF™ program was developed for high-risk patients. It encompassed:

- Contact between a heart failure nurse, hospitalized patient and family members
- Materials for information on the disease and self-monitoring
- Phone-based monitoring and patient education
- Interface role of specialized nursing staff in interdisciplinary patient care
- Supervision of caregivers and quality management

The efficiency of the program was proven in a randomized, controlled trial. After just 180 days, mortality was reduced by 33 percent in the group participating in the HeartNetCare-HF™ program. Older and more severely ill patients in particular benefited from telephone support, but depressed patients profited the greatest in terms of survival. Quality of life and physical performance also improved significantly. Patients took their medication more regularly and carried out more effective self-monitoring. Current long-term evaluations show that the effects of this type of care are highly sustainable and remain effective for more than ten years.

In addition, medical care can be supplemented by device-based telemonitoring, e.g., by measuring pulmonary artery pressure in patients with severe heart failure. On behalf of the Federal Joint Committee (G-BA), the CHFC has been examining whether the CardioMEMS™ HF telemonitoring system should be integrated into standard care in the PASSPORT-HF study, which it has been conducting since the end of 2020.

"The Würzburg Way"

Effective discharge management and standardized, individualized follow-up care help in the transition from hospital to everyday life. Numerous studies show that this can significantly improve the long-term prognosis of heart failure patients in terms of mortality, hospitali-

Specialized nursing and medical assistants in medical practices are trained at the CHFC. Their work is demanding and important.

zation and quality of life in heart failure patients. The CHFC is currently demonstrating this with the "Würzburg Way" network and the pilot project "Discharge Heart Failure Nurse." The "Würzburg Way" is a network including of all established cardiologists in the city, some local general practitioners, the hospital Klinikum Würzburg Mitte and the University Hospital. Specialized nurses and certified medical assistants play a key role in the complex communication between doctors, patients and relatives because they are the medical personnel which ensures a smooth transition between inpatient and outpatient care.

Advanced training for nurses and certified medical assistants

For this demanding task, the DZHI, in cooperation with the DGK, has developed a training course for assistant staff in cardiology practices, which is now a model for the whole of Germany. The four-day advanced training course to become a Specialized Heart Failure Assistant enables healthcare workers to care for heart failure patients in a structured and individualized manner according to the latest level of knowledge in the field. While advanced training for certified medical assistants is still relatively new, the CHFC has already been training nursing staff as heart failure nurses for past ten years.

The CHFC has been an advocate of health insurance companies covering the costs for telemedicine services for many years. At last, funding for the "phone nurses" is on the horizon. For the first time, the GKV-Spitzenverband (National Association of Statutory Health Insurance Funds) and the Kassenärztliche Bundesvereinigung (National Association of Statutory Health Insurance Physicians) have included telemedicine services in their Uniform Standard of Evaluation (Einheitlicher Bewertungsmaßstab, EBM). Within the framework of the PASSPORT study, flat rates may be charged for the telemedicine follow-up care that heart failure patients receive.

I HAVE SOMETHING no one knows about

A disease is considered rare if it affects no more than 5 in 10,000 people. But in the end, rare diseases are not that rare – there are more than 8,000 of them. In Germany, about four million people live with a rare disease. In most cases, the diseases are complex and multi-faceted. Three centers of the CHFC and the Medical Clinic I are part of the Center for Rare Diseases (Zentrum für Seltene Erkrankungen, ZESE): the Interdisciplinary Amyloidosis Center of Northern Bavaria, the Fabry Center for Interdisciplinary Therapy (Fabry-Zentrum für Interdisziplinäre Therapie, FAZiT) and the Center for Genetic Cardiac and Vascular Diseases. These centers are a contact point for people affected by the diseases and their relatives.

Fabry Center for Interdisciplinary Therapy (FAZiT)

Fabry's disease is a rare hereditary disease that, among other things, thickens the heart muscle. The mutation on the X chromosome impairs heart function in more than half of the cases. The organism does not produce the enzyme alpha-galactosidase A or produces it only sparsely, with the result that fat molecules are not broken down and are deposited in tissues and organs. CHFC researchers led by the directors of the Fabry Center for Interdisciplinary Therapy (FAZiT), Christoph Wanner and Peter Nordbeck, have found that in advanced Fabry disease, the heart tissue is severely scarred. The disease shows typical changes in the heart rhythm which indicate that the autonomic nervous system – the control center that keeps vital functions such as heartbeat or digestion in balance – is impaired. In these cases, physicians consider implanting a defibrillator. FAZiT is the largest Fabry center in Germany. In the special outpatient clinic, experts from 16 disciplines have been providing medical care to more than 300 adults and children suffering from this rare metabolic disease since 2001.

At the CHFC, a team from various departments is also working on the mechanisms of heart damage caused by the genetic defect. Model systems are being used to investigate how the described deposits in cardiac muscle cells affect the heart rhythm, structure, inflammatory processes and metabolism of the cells.

Help for families with genetic heart disease

A mother cares for her critically ill son who is waiting for a new heart. The mother will one day also be in need of a donor heart. Another mother can't rest until she knows what caused her four-year-old daughter to die suddenly in the middle of the night. Is her family genetically predisposed? If so, does her son also carry the mutation? These are just two cases out of hundreds that Brenda Gerull encounters in the special consultation for genetic heart diseases at the CHFC. The disease patterns are complex and their research and treatment are thus multifaceted. Under Brenda Gerull's leadership, the Center for Genetic Cardiac and Vascular Diseases (Zentrum für Genetische Herz- und Gefäßerkrankungen, ZGH) combines the expertise of several departments at the University Hospital and the Department of Human Genetics at the University of Würzburg. Here, Adult Cardiology cooperates very closely with Pediatric Cardiology and Cardiac Surgery. Outpatient clinics for arrhythmias and devices as well as imaging are also involved in addition to the outpatient clinic at the DZHI. Psychological support can also be arranged if needed.

Early detection and treatment of amyloidosis

In amyloidosis, misfolded proteins are deposited in the body. They often weaken the heart, but also kidneys, nerves or the gastrointestinal tract. Because early signs are absent and the symptoms are unspecific, amyloidosis is often only detected at a later stage. However, rapid and targeted diagnosis is crucial for treatment and sometimes for survival. For this reason, specialists from more than ten disciplines have founded the first Interdisciplinary Amyloidosis Center in Bavaria and the second in Germany at the University Hospital of Würzburg. The center is managed in equally by hematologist Stefan Knop and cardiologist Stefan Störk. The outpatient clinic at the CHFC is the main pillar of the center. In the Interdisciplinary Outpatient Clinic, the medical coordinators Sandra Ihne and Caroline Morbach and their team have already treated more than 200 patients in the last three years. Another focus of the center is on research into the clinical picture of amyloidosis. A self-help group rounds out the center's program.

HELP FOR thickened hearts

The most common genetic heart disease is hypertrophic cardiomyopathy (HCM). In this disease, genes are altered that encode the "motor," i.e. the contractile proteins of the heart muscle. As a result of the changes, the heart beats permanently too strongly and it relaxes too slowly. In this process, the muscle has to expend too much energy, which generates oxidative stress and, in the long term, causes a pathological thickening of the heart chambers. If this thickening progresses far, it hinders the outflow of blood from the heart, which is then referred to as obstruction (HOCM). This type of obstruction occurs to varying degrees in about 70 percent of cases and means the heart has to work even harder, causing patients discomfort in the form of shortness of breath, chest pain or arrhythmias.

At least 150,000 Germans are affected by H(O)CM, many without knowing it. Since April 2020, Hubert Seggewiss and Angelika Batzner as experienced HOCM specialists have joined the team of the CHFC. Together with other specialists, they have since established an interdisciplinary team for diagnostics and therapy of H(O)CM at the CHFC and the Medical Clinic and Polyclinic I. If drug therapy fails to be successful, surgical options or cardiac catheter-guided ablation can be considered. By injecting alcohol into the coronary artery branch that supplies the thickened muscle, a small artificial heart attack is induced so that the heart muscle becomes thinner and no longer obstructs the outflow of blood from the heart during the heartbeat. The treatment leads to a significant improvement in symptoms and is associated with a favorable long-term outcome, as Seggewiss and Batzner were able to demonstrate in nearly 1,000 patients over the past 20 years. Seggewiss has pioneered the procedure of alcoholic septal ablation (or PTSMA) and is an internationally recognized interventional specialist for HOCM. Recently, there have also been specific drugs that act directly on the heart muscle and slightly reduce its pumping force, which improves the outflow of blood and thus the symptoms.

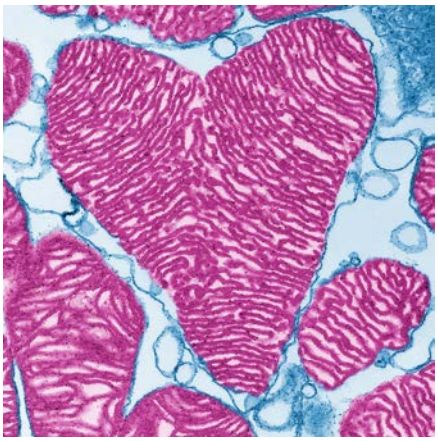
The Translational Research team of Christoph Maack has been working for years on the interplay between gene mutations, muscle function and energy supply. They discovered that arrhythmias in HCM are caused by an overload of the cells' power plants, the mitochondria. The HCM team includes Hubert Seggewiss, Angelika Batzner, Brenda Gerull, Stefan Störk, Caroline Morbach and Christoph Maack as well as colleagues from Imaging and Cardiac Surgery. The HCM team is establishing a new focus in research and in medical care at CHFC: tailoring diagnostics and therapy to the individual needs of patients and studying the mechanisms and long-term progression of the disease further.

UNDERSTANDING THE language of the heart

Heart failure is accompanied by many concomitant diseases. The focus of cardiac research is therefore not solely on the heart. Understanding the language of the heart and the interfaces between the heart and other organs is the major goal of researchers conducting basic research at the CHFC. They give priority to the interplay of inflammation, metabolism and stress hormones. .

Neuroendocrine activation

Kristina Lorenz (Chair of Pharmacology and Toxicology) and her team are investigating the causative mechanisms of hypertrophy. In hypertrophy, the heart becomes excessively large, cardiac muscle cells die, and scars and cardiac insufficiency develop. Lorenz has found that the ERK1/2 enzymes in the cardiac muscle cells are particularly decisive for the development of hypertrophy. She has also discovered a new control mechanism for this form of hypertrophy. Her aim is to specifically stop this mechanism without affecting the vital functions of the enzymes and thus to find new prevention and therapy approaches. The role of ERK1/2 enzymes in other diseases, such as cancer and atherosclerosis, is also the subject of Kristina Lorenz's research.



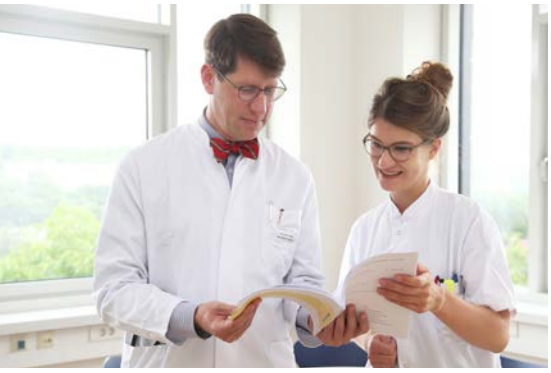
A mitochondrion under the electron microscope, which was isolated from a mouse heart by Kristina Lorenz and Nilgün Gedik. The fact that it has the shape of a heart is pure coincidence.

Michaela Kuhn (Department of Physiology) is a world-renowned expert on the effect of natriuretic peptides in the cardiovascular system. Hormones play a special role in heart failure. One of them, BNP, is used for making a diagnosis and prognosis assessment and for monitoring therapy in heart failure. So-called neprilysin inhibitors increase the concentration of natriuretic peptides in the blood. In heart failure, this therapy has been shown to prolong life. In a recent paper, Michaela Kuhn and her team found that C-type natriuretic peptide (CNP) regulates blood flow in the smallest vessels. This could explain the good efficacy of neprilysin inhibitors.

Inflammation

For many years, an important research focus in Würzburg has been on inflammation, i.e., the inflammatory response to harmful stimuli. Stefan Frantz and Ulrich Hofmann (Director and Senior Physician of Medical Clinic I) as well as Gustavo Ramos (IZKF Junior Group) are concentrating on the role of the immune system and how it can protect our heart. However, immune cells do not only have positive effects, they can also damage the heart. The researchers are convinced that if they understand the mechanisms that regulate inflammation, new therapeutic options will emerge. One approach is T cells. Hofmann and Frantz had already discovered in 2012 that T cells play an important role in wound healing after a heart attack. Biologist Gustavo Ramos followed up on this discovery.

The IZKF junior group led by Clément Cochain is dedicated to macrophages, which are important for the regeneration of the heart after an infarction but are also potentially harmful (p. 21). Together with Alma Zernecke-Madsen (Ex-



Stefan Frantz, Director of the Medical Clinic and Policlinic I, has submitted a funding application for a new collaborative research center on inflammation and immunity in cardiovascular disease..

Ulrich Hofmann, Senior Physician at the Medical Clinic & Policlinic I, is researching the significance and function of immune cells after a heart attack and is testing new immunotherapeutic treatment approaches.

perimental Biomedicine II), Cochain has, for example, identified different macrophage populations that might influence the development of atherosclerosis in different ways, including macrophage populations that have not been described thus far.

In light of this extensive knowledge on inflammation and immunity in cardiac and vascular diseases, Stefan Frantz, as spokesperson of an interdisciplinary team, has received funding for a Collaborative Research Center (Sonderforschungsbereich, SFB 1525) from the German Research Foundation (DFG). The team includes many DZHI members, Bernhard Nieswandt (Experimental Biomedicine I), Georg Gasteiger and Wolfgang Kastenmüller (both from the Department of Systems Immunology), as well as many other partners from Würzburg.

Mitochondria and metabolism

The heart requires enormous amounts of energy, which is produced in the form of ATP in the cell‘s power plants, the so-called mitochondria. Since the heart must constantly adapt its pumping capacity to changing requirements, it needs mechanisms that coordinate energy demand and supply. Calcium is an important messenger substance in this respect, as it is responsible for increasing both pumping power and energy production. In heart failure, the calcium balance is disturbed, which is one of the main reasons for the heart‘s limited beating power. But the mitochondria are also affected. This contributes to energy depletion and increased production of oxygen radicals and oxidative stress. The consequences are cell death, remodeling processes and further loss of cardiac output.

Important risk factors for the development of heart failure are being overweight and having diabetes. The body is virtually overloaded with sugar, salt and fats. The heart is normally a flexible “omnivore” that can feed on sugar, fat and other energy sources depending on their availability. In diabetes and heart failure, it loses this flexibility and cells are damaged by too much fat and sugar.

At the CHFC, several groups are investigating the role of metabolic processes in heart failure. The Department of Translational Research and its DZHI junior group led by Jan Dudek have been investigating the close interplay between the mechanics of the heart and metabolic processes for many years. It collaborates with Cardiovascular Genetics, Imaging and Nuclear Cardiology to visualize metabolic processes in the heart and other organs using MRI and PET. A special focus with a lot of future potential is the interface between metabolism and inflammation, which will also be further investigated in the SFB Collaborative Research Center 1525 funded by the DFG.

A multi-directional NETWORK

Interdisciplinary cooperation is a characteristic of the CHFC. And it is also extended to the outside world. Thus, interdisciplinary collaboration takes place not only within the University Hospital and the campus, but also within all Federal States, throughout Germany and worldwide.

Patient networks

Sharing experiences and coping strategies as well as information on self-selected topics during discussions with other affected patients and experts – these are the most important goals of self-help groups. The CHFC is a direct home for three such groups: for patients with heart failure in general, for patients with implanted cardioverter defibrillators (ICD), and for patients with amyloidosis, for whom the Interdisciplinary Amyloidosis Center of Northern Bavaria was founded at the CHFC.

In addition, there are close contacts to nationwide self-help groups, e.g., for arrhythmogenic cardiomyopathy (AC) or hypertrophic obstructive cardiomyopathy (HOCM). Cardiac sports groups encourage people to remain physically active in the company of others and under medical supervision.

They cooperate closely with the German Heart Foundation, which sees itself as an information portal and advocacy group for cardiac patients. Among other things, it supports the campaign "Active against Heart Failure", which is coordinated nationwide by the CHFC. Conversely, the CHFC participates in the Heart Awareness Weeks campaign, which the Heart Foundation organizes every year in November.

Clinical networks

Patients with heart failure are always optimally cared for when hospitals, cardiology practices and general practitioners work together with specially trained staff. Several such networks were initiated by the CHFC and are now established as exemplary care concepts.

Heart Failure Bavaria was initiated as a quality assurance project by the CHFC in cooperation with the Professional Organization of Medical Specialists for Cardiology in Free Practice (Berufsverband der Fachärzte für Kardiologie in freier Praxis e.V., BFK). Among other achievements, the project developed into the Heart Care Bavaria care model, which bundles cardiological and general practices in clusters.

"Together we are unbeatable."

Christoph Maack, Spokesman of the CHFC

The Interdisciplinary Heart Failure Network (INH) has evolved from the largest German study conducted on health services research related to heart failure thus far. It includes ten hospitals and more than 400 practices. The impact of the HeartNetCare-HF™ care program was studied and followed up in nine internal medicine hospitals in the region. One focus of the CHFC is the co-development of guidelines and medical care programs. Researchers cooperate with representatives of health care policy and health insurance companies to develop new strategies and structures for the German health care system.

Scientific networks

Collaborative Research Centers (SFB), which are funded by the German Research Foundation (DFG), are an ideal platform for scientific cooperation. The CHFC is already involved in two SFBs and is contributing to a new initiative for a Würzburg SFB for cardiac and vascular diseases, which involves many departments and working groups. In the Clinician Scientist Program UNION CVD, several institutions at the University Hospital of Würzburg, including the DZHI, build on young medical talent (p. 44). The CHFC is involved in various studies of the German Center for Cardiovascular Research (DZHK). The study group German Ultra-high Field Imaging (GUFI) networks all research centers with ultra-high-field magnetic resonance imaging (UHF-MRI) systems in Germany. Its aim is to establish uniform standards for their use and for the interpretation of examination findings. The CHFC is part of this network. What is more, the Department of Cardiovascular Imaging is investigating heart-brain interactions in the European Network for Ultra-high Field Imaging in Neurodegenerative Diseases (EUFIND).

Professional societies

Members of the CHFC are involved in numerous professional societies for cardiac and vascular diseases. The aim is to represent professional political interests, to act as an expert contact and to establish general guidelines and standards. Among other institutions, they are active in the German Cardiac Society (DGK), the Heart Failure Association (HFA) of the European Society of Cardiology (ESC), the German Society of Internal Medicine (DGIM), the International Society for Heart Research (ISHR), the German Society for Medical Physics (DGMP), the German Radiological Society (DRG), the International Society for Magnetic Resonance in Medicine (ISMRM), and the European Alliance of Medical and Biological Engineering and Science (EAMBES).

ROOM and PROTECTED TIME for research

The CHFC supports young physicians who want to achieve excellence in clinical or preclinical research in addition to achieving in patient care. They have access to various programs which exempt them from clinical care so that they can devote their time they thus gain to research.

One of these programs is UNION CVD – Understanding InterOrgan Networks in Cardiac and Vascular Diseases. In this program, which is funded by the German Research Foundation (DFG), physicians in training who are enthusiastic about research have the opportunity to combine specialist training with research activities. This concept is intended to strengthen translational research by allowing the clinician scientist to implement research results directly at patients' bedsides and to integrate clinical experience directly into research. The program is organized by the Interdisciplinary Center for Clinical Research (IZKF). Start-up projects also support outstanding projects by young scientists in clinical or translational research. These can be converted into full-fledged projects or receive third-party funding.

Award winning scientists

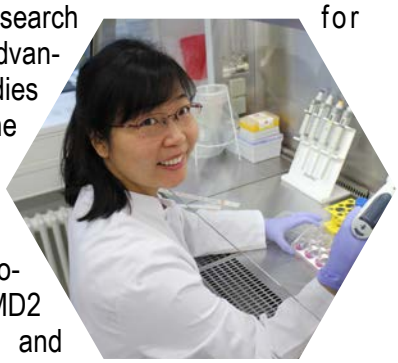
Edoardo Bertero was awarded the Young Investigator Award at the winter meeting of the Heart Failure Association of the ESC (European Society of Cardiology) in Switzerland in February 2018. Together with Christoph Maack's team, he found that regulating calcium uptake in cardiac muscle cells could be a promising therapy for treating Barth syndrome, a hereditary disease that affects only boys and develops in early childhood. Edoardo was also awarded the 2nd prize of the Rudi Busse Young Investigator Award of the German Society of Cardiology in the same year.

Rudolf Werner from Takahiro Higuchi's team has already been recognized in Europe and the U.S.A. for his several achievements in preclinical research with radioactive substances that make the innervation of the heart visible by means of PET. The greatest success to date was the prestigious Marc Tetalman, MD Memorial Award, which was presented to him in June 2018 at the annual meeting of the American Society of Nuclear Medicine and Molecular Imaging (SNMMI).

Resident physician **Theresa Reiter** from the Wolfgang Bauer working group was awarded the Orlovic Young Investigator Prize at the 2018 Congress of the German Society of Cardiology for her imaging of activated macrophages, which are the cells that heal damage to the heart muscle.

Cardiologist **Martin Christa** used MRI technology to determine the sodium content in heart muscle tissue. His evaluations of the heart as a salt reservoir were awarded the Orlovic Young Investigator Prize at the DGK Congress in Mannheim in April 2019.

In Brenda Gerull's department, biomedical scientist **Ruping Chen** discovered a new gene mutation that causes heart muscle disease. She was honored with the Hans Blömer Young Investigator Award for Clinical Cardiovascular Research for her advanced studies of the mutant nuclear membrane protein LEMD2 in mice and was able to secure a grant from the German Society of Cardiology (DGK) and a research grant from the German Foundation for Heart Research (Deutsche Stiftung für Herzforschung, DSHF). She also won the Young Investigator Award at the Heart Failure Winter Research Meeting in 2021.



Alexander Dietl from Christoph Maack's team investigated the significance of heart rate and ejection time on heart failure and was honored for his work on the topic of heart failure at the Young Investigator Awards.

"Successful research is achieved solely by coordinating efforts and sharing ideas as a group. Scientific thinking is not an immanent attitude, but an acquired skill that requires continuous diligence and education."

Edoardo Bertero

November 2010
The CHFC begins work with funding from the BMBF. Applicants: Georg Ertl (in charge), Christiane E. Angermann, Stefan Störk, Stefan Frantz, and Martin Lohse.

September 2012
The HeartNetCare-HF™ medical care program developed at the CHFC is published. It is the first quality-assured care program for heart failure patients developed in the German health care system.

November 2014
Laura Schreiber becomes head and professor at the Department of Cellular and Molecular Imaging.

April 2015
The Heinrich and Ingeborg Müssig Foundation supports research at the CHFC with 500,000 euros.

May 2016
At the 3rd World Congress on Acute Heart Failure in Florence, Stefan Störk receives a gold-plated heart on behalf of all German participants as an award for Germany's commitment to the Heart Failure Awareness Day.

January 2017
After only three years of construction, the new CHFC building is inaugurated with a ceremonial act.

June 2017
Launch of the "Würzburg Way": The CHFC, all Würzburg hospitals and all established cardiologists in the city, as well as numerous general practitioners, have agreed to improve the inpatient and outpatient care of heart failure patients by ensuring that all of the professional groups involved continue to share information with each other. This also involves certified medical assistants who have a special role to play.

August 2017
Ethics committee approval for the first test subject in the 7-tesla MRI scanner.

May 2011
Opening ceremony. The CHFC initially moves into building A9 on the grounds of the University Hospital of Würzburg.

January 2014
Ground-breaking ceremony for the new research building A15.

January 2015
An international review panel certifies the CHFC's excellent performance in research and patient care during an inspection. The BMBF will fund research and treatment for another five years.

February 2016
Brenda Gerull becomes the new Research Professorship for Cardiovascular Genetics.

June 2016
The 17-ton, 7-tesla magnetic resonance imaging scanner arrives by heavy-duty transport, it is lifted over the building by a large crane and lowered onto the courtyard. The introduction of a completely newly developed magnet into the new research and treatment building of the CHFC marks the start of a new era in imaging in Würzburg.

April 2017
Stefan Frantz returns from Halle to become spokesperson of the CHFC and director of the Medical Clinic and Polyclinic I.

August 2017
Christoph Maack becomes Head of Translational Research and later spokesperson of the CHFC.

September 2017
The first subject is examined in the 7-tesla MRI scanner. The extremely strong magnetic field is generally harmless, but for safety reasons, exclusion criteria is used to determine the suitability of the test subjects. The exclusion criteria includes pregnancy, claustrophobia, permanent make-up, metallic foreign bodies or implants.

October 2017
Interim goal achieved! After almost four years, the STAAB study has examined its five thousandth test subject.

November 2017
The first Interdisciplinary Amyloidosis Center in Bavaria and thus the second in Germany is founded at the University Hospital of Würzburg.

October 2018
Starting signal for the Clinician Scientist Program: Together with numerous other colleagues at the University Hospital of Würzburg, a qualification concept was developed that gives young scientists the room to conduct research and provides researching physicians with special qualifications for their future careers. The DFG funds the program with 1.7 million euros. The first nuclear medicine imaging device moves into the CHFC, a small animal SPECT/CT. The first experimental trials begin after radiation protection instructions are issued in November.

November 2018
In order to provide even better care for patients with inherited cardiac and vascular diseases and their families in the future, the Center for Genetic Cardiac and Vascular Diseases (ZGH) is founded as part of the Center for Rare Diseases (ZESE). It is headed by Brenda Gerull.

February 2020
At the University Hospital, the thousandth patient is enrolled in the Acute Heart Failure (AHF) registry – researchers expect the data to provide new insights into heart failure. The AHF registry started in August 2014.

June 2020
Start of the STAAB-COVID study: Participants in the STAAB cohort study are tested for COVID infection and SARS-CoV-2 antibodies at the CHFC. The Bavarian State Ministry of Science and the Arts is supporting the program with 1.5 million euros.

October 2017
The Collaborative Research Center SFB 688 looks back on twelve successful years of research in the field of cardiac and vascular diseases. Top researchers present new findings and therapeutic developments related to cardiac and vascular diseases at the three-day symposium in Würzburg.

January 2018
The permit to operate the animal husbandry and experimental facilities has finally arrived. Initially, 40 teeny zebrafish move in to the fish facility. They are the first animals to inhabit building A15. A few days later, the first mice move in, followed by four more animal species.

November 2018
Green light is given for Bavaria's first heart failure sports group. The DFG is funding the program for three years.

July 2019
200 leading scientists from Germany and around the world exchange ideas on the language of organs and discuss heart failure and its concomitant diseases at the 3-day Joint Symposium "Heart Failure Interfaces" in Würzburg. The collaborative event between CHFC and DZHK (German Center for Cardiovascular Research) aims to promote dialogue between basic researchers, clinicians and imaging experts (www.heartfailureinterfaces.de).

April 2020
New consultation hour for thick hearts: Angelika Batzner and Hubert Seggewiss research and treat hypertrophic cardiomyopathy (HCM), which is associated with thickening of the heart muscle, at the CHFC.

June 2020
The first patient is examined in the 7-Tesla MRI scanner.