



ERA-CVD NEWSLETTER 1

January 2017

ERA-NET on Cardio Vascular Diseases (ERA-CVD)

Cardiovascular diseases (CVD) are the major cause of death in Europe. CVD research is a crucial area in health research, hence an effective coordination of research at national and EU level, increased cross-disciplinary interaction and research advancements are needed. By gathering their forces and funding capacities so far **18 countries** joined to set up a new **ERA-Net Cofund** action (European Research Area Network co-funded by the European Commission, EC) dedicated to cardiovascular diseases (ERA-CVD) .

More details at: <http://www.era-cvd.eu>

In the ERA-CVD first and co-funded call with the EC, **14 transnational projects were chosen to be funded for three years**

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Giulio Pompilio



ACM-HF

Non myocyte interplay as a novel platform for mechanistic insights and therapeutic approaches in ACM heart failure

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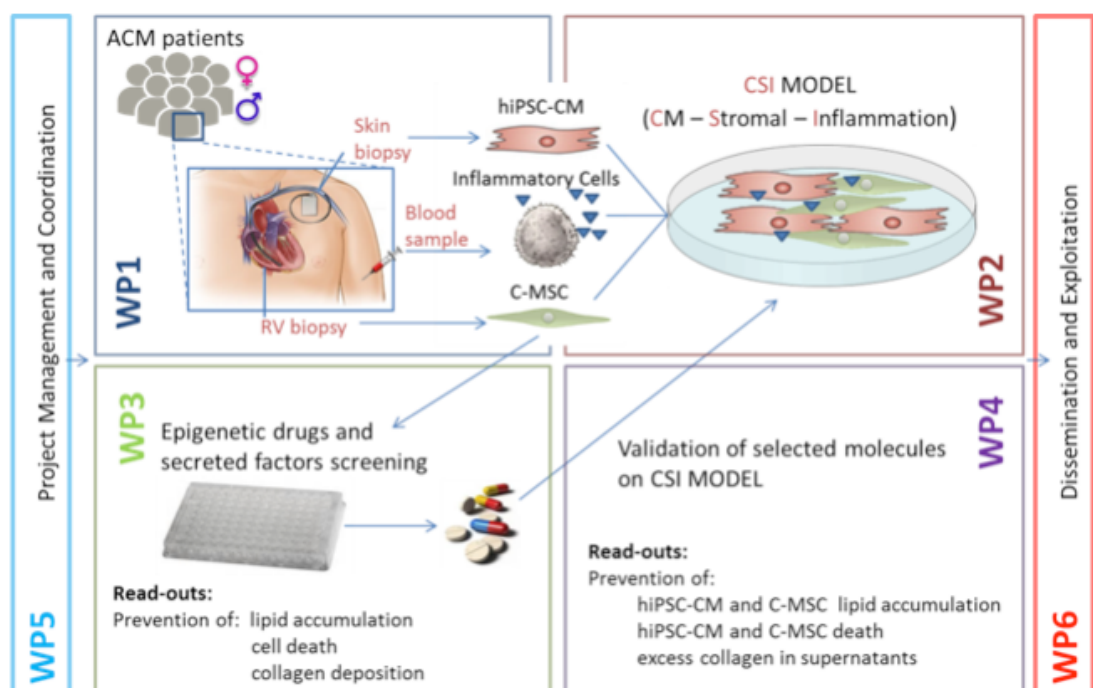
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Arrhythmogenic Cardiomyopathy (ACM) is a genetic cardiac disease, mainly affecting young people and athletes, characterized by heart failure and life-threatening arrhythmias. This project will study the cardiac cell interplay and develop a platform to test potential therapeutics, by exploiting an innovative patient-derived cell model combining CMs from induced pluripotent stem cells, Stromal cells and Inflammatory mediators (CSI model). This project is expected to elucidate mechanisms underlying ACM pathogenesis and to identify new disease targets and potential therapeutics. Engagement activities towards patient associations and advocacy groups will explain why the project questions and outcomes are relevant to patients and caregivers.





Canan Nebigil



Cardio-Oncology

Early detection and prevention of cardiac dysfunction and heart failure induced by cancer chemotherapeutics

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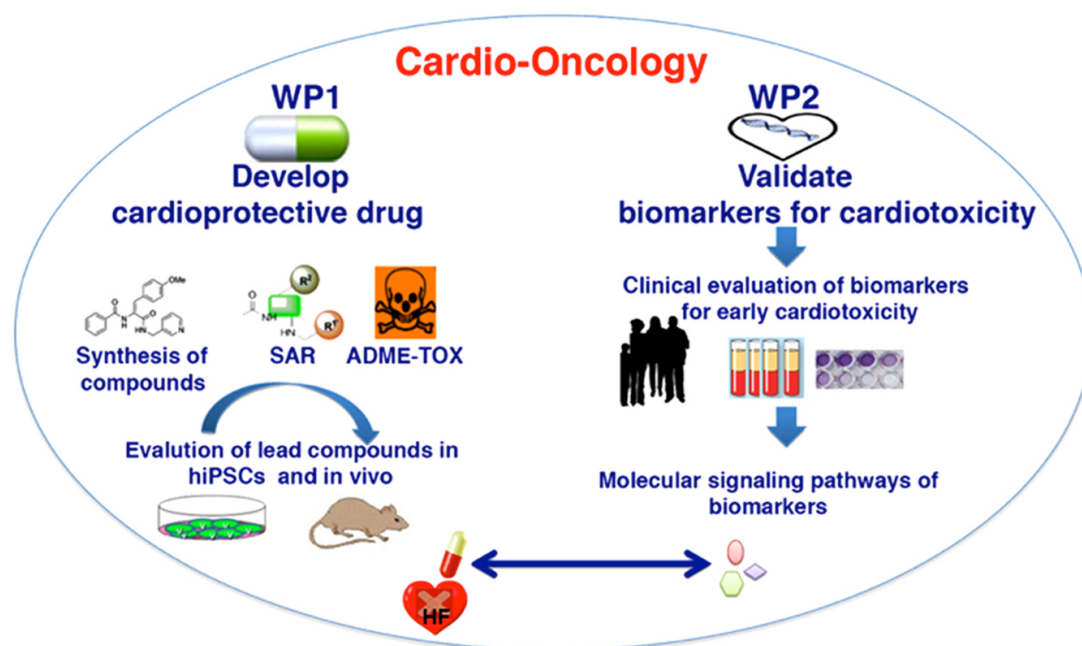
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Cardiac dysfunction leading to heart failure can result from anticancer treatments. The ultimate goal of the Cardio-Oncology project is to minimize adverse cardiotoxic effects of anticancer treatments, which will enable clinicians to fully exploit the benefits of modern cancer therapy. The development of novel and more effective and safe cardio-protective therapeutics will reduce the risk of mortality and improve quality of life of patients with anticancer drug-induced cardiotoxicity. In addition, by identifying novel and reliable biomarkers for early detection of cardiotoxicity, the consortium ensures that treatment with the novel cardio-protective therapeutic will be specifically used in high-risk patient subgroups.





Jeroen Bakkers

Cardiopro

Mechanisms of regenerative cardiomyocyte proliferation

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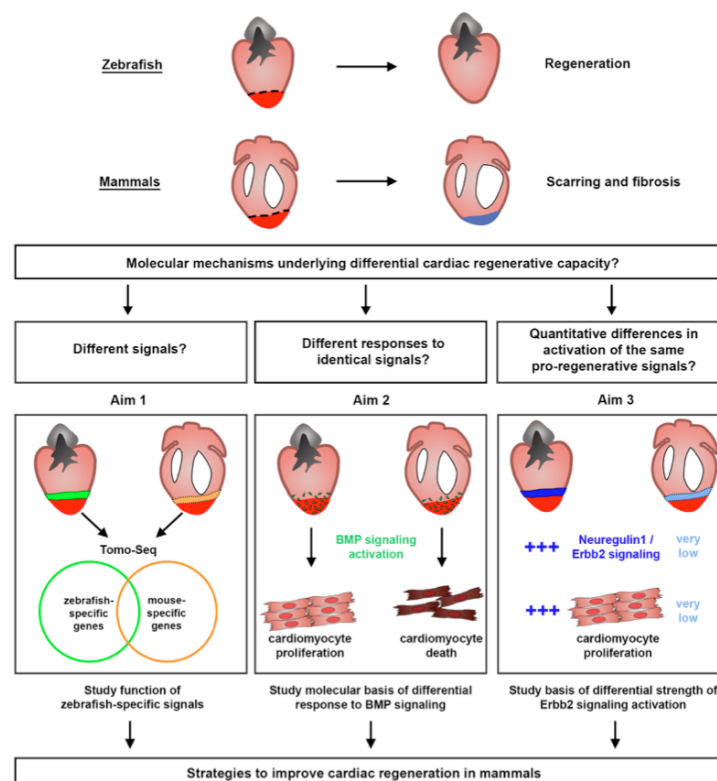
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Ischemic heart disease, such as myocardial infarction, causes a massive loss of cardiomyocytes and leads to the formation of fibrotic scar tissue, resulting in impaired cardiac function and ultimately, heart failure. Recently, it has been demonstrated that myocardium is naturally regenerated in the human heart. However, the rate of replacement is too low to repair large areas of damaged myocardium. Stimulating the very low intrinsic proliferation rate of cardiomyocytes is a promising strategy for cardiac repair in patients with heart failure. To identify such repair signals, this project will use zebrafish, where cardiomyocyte regeneration occurs naturally, and mice, where it does not. Different possible reasons for the difference in the regenerative capacity of lower vertebrate versus mammals will be explored. The goal is to develop regenerative medicine strategies based on endogenous cardiomyocyte capacities.





Eva van Rooij

CLARIFY

Communication between cardiomyocytes and innate immune cells in failing hearts

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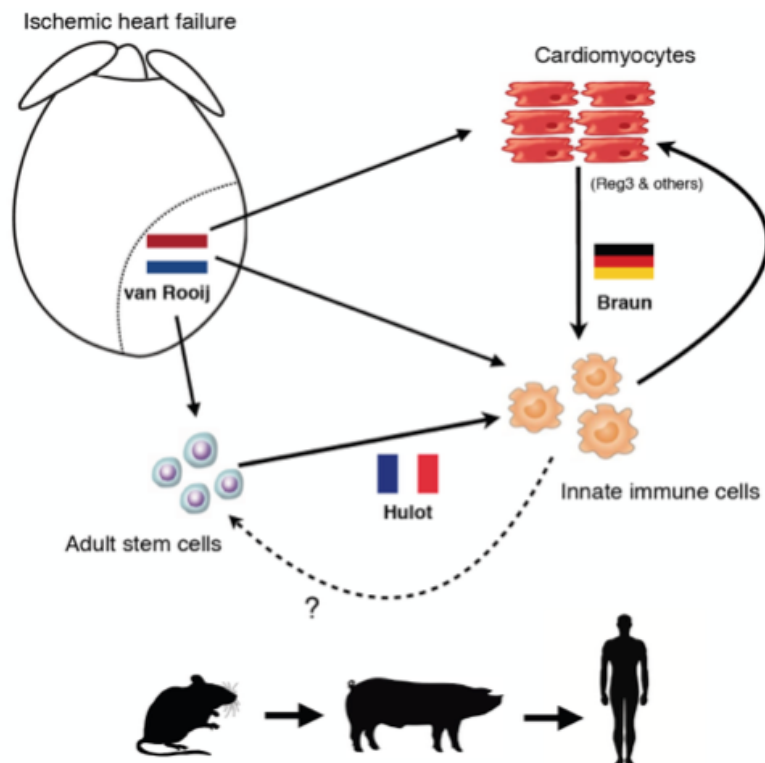
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Ischemic heart disease due to a shortage of oxygen delivery to the heart is a leading cause of hospitalization and mortality in Europe. This unmet challenge asks for a better understanding of the mechanisms causing this damage to the heart to support the development of new and improved therapies. The immune system plays a decisive role for initial inflammatory responses following cardiac damage and subsequent repair responses. This project will investigate how immune cells communicate with the rest of the heart to improve heart repair during injury.





Hugo A. Katus

DETECTIN-HF

Determining the role of clinical and epigenetic risk markers in dilated cardiomyopathies and heart failure

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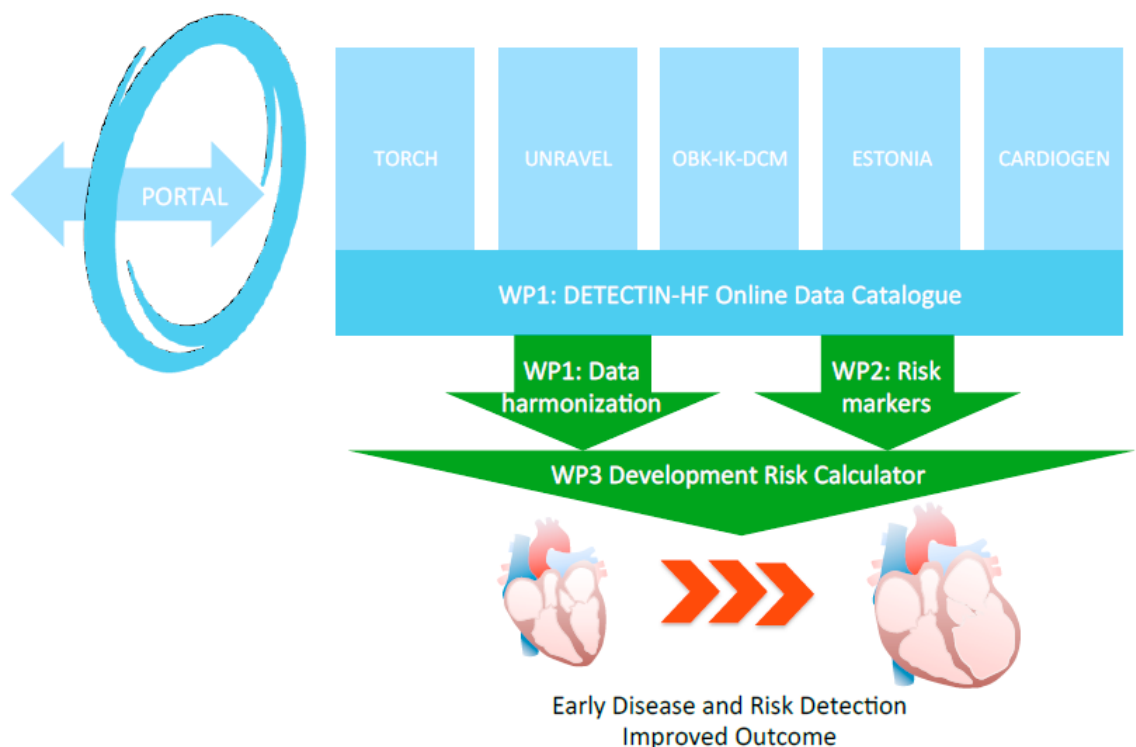
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Dilated cardiomyopathy is a major cause of heart failure and is the main indication of cardiac transplantation. About 30-50% of the cases can be explained by genetic predisposition. However, the precise mechanisms that lead to variations in disease susceptibility and phenotype presentation including risk for heart failure or sudden cardiac death are thus far unknown. The DETECTIN-HF project will work with selected clinical and molecular markers in a multi-center, multi-national cohort. The facility which arises by creating this single, harmonized portal is unique in setup and scale and is invaluable for research and improved clinical practice.





Thomas Thum

EXPERT

Exploring new pathways in age-related heart diseases

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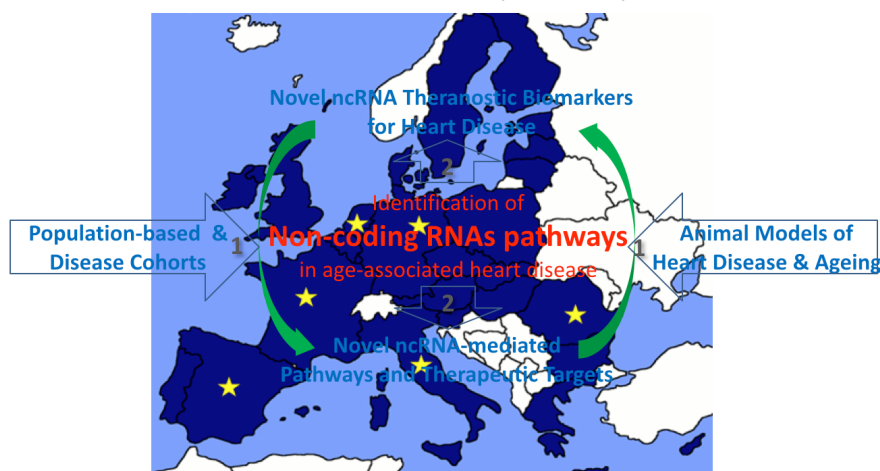
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EXPERT is aiming at the development of new strategies for the diagnostic and treatment of age-associated diseases such as heart failure, atherosclerosis and myocardial infarction by exploring non-coding RNA (ncRNA)-mediated regulatory pathways. For a long time regarded as evolutionary junk, ncRNAs are currently emerging as pivotal players in virtually all biological processes. As their levels fluctuate during ageing and disease, ncRNAs are believed to significantly contribute to biodiversity and disease susceptibility including cardiovascular disease. EXPERT will lay the foundation that will lead to novel diagnostic and therapeutic strategies for the treatment of heart failure and other cardiovascular alterations, such as atherosclerosis and myocardial infarction.

Exploring new pathways in age-related heart diseases – EXPERT

A European transnational project involving partners from Germany, The Netherlands, France, Romania, Spain and Italy.



1. EXPERT will perform population-based and disease cohort studies to identify theranostic biomarkers complemented by experimental studies in animal models of heart disease and accelerated ageing.
2. Identified novel ncRNA pathways will build the foundation for the development of innovative treatment strategies.



Borja Ibanez

FAT4HEART

Heart Failure Rescue by Nutritional Approaches: relevance of mitochondrial substrate utilization

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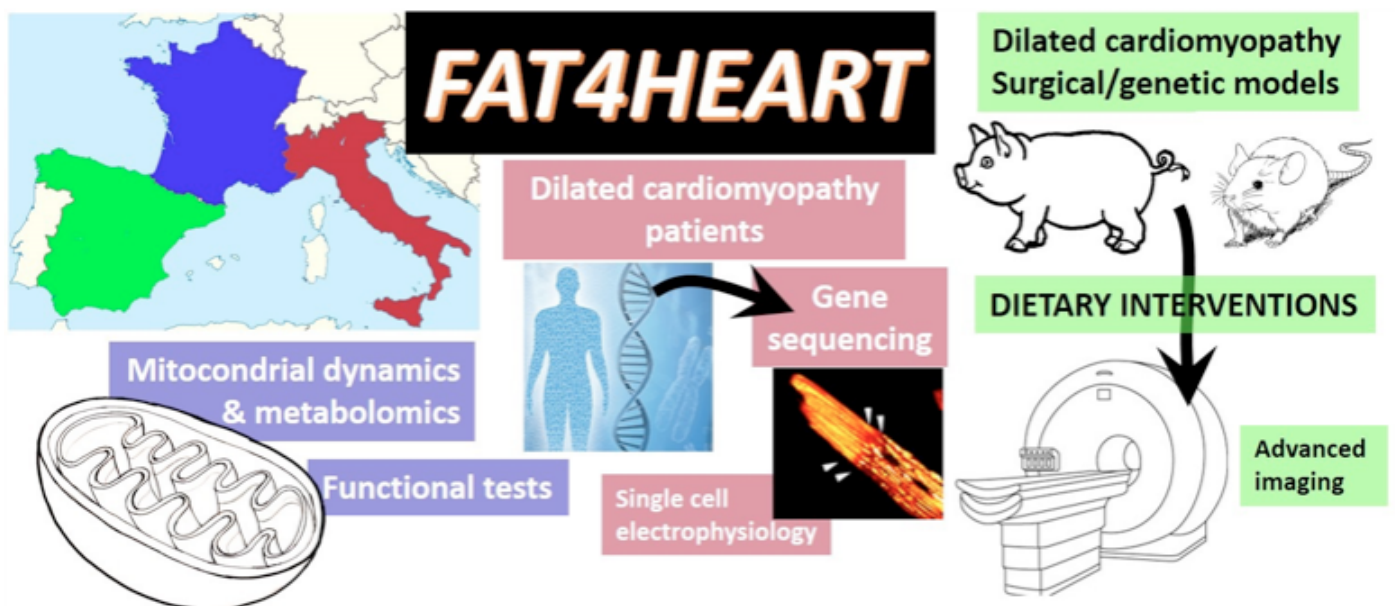
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Dilated cardiomyopathy is the most common cause of heart failure in the young/middle age population, with no specific treatments. The group of investigators of this project recently demonstrated that a genetic defect leading to mitochondrial dysfunction results in altered cardiac metabolic fuel utilization, dilated cardiomyopathy and heart failure. Interestingly, a diet with very high fat content was able to cure the disease in these mice. FAT4HEART will study the interplay between mitochondrial defects, dietary components and dilated cardiomyopathy as well as the role of specific diet fat contents as a potential therapy for dilated cardiomyopathy.





Heinz-Peter
Schultheiss



GENPROVIC

Gene Profiling Test for Identification of Treatable Patients with Acute and Chronic Heart Failure

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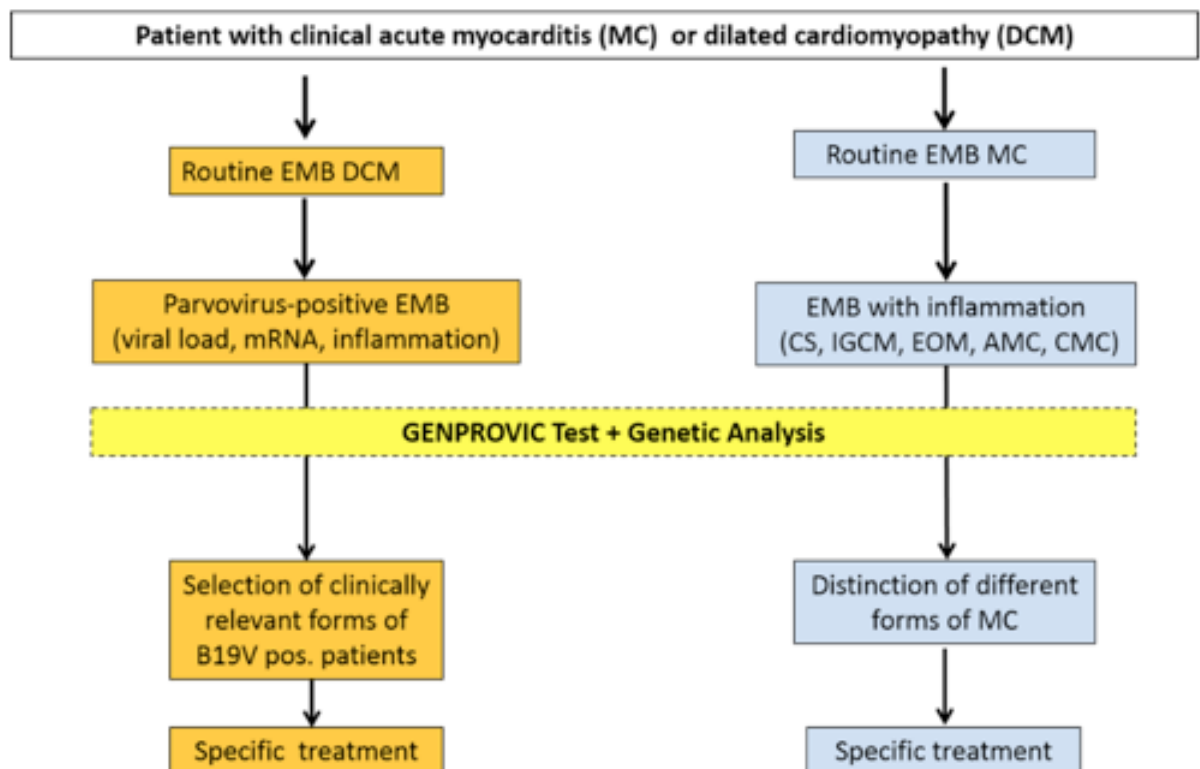
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Myocarditis (MC) and inflammatory cardiomyopathy (DCMi) are acute or chronic disorders of myocardium caused by myocardial virus infection and/or inflammation with poor prognosis without specific treatment. The GENPROVIC project will validate a gene profile biomarker diagnostic test, allowing the identification and differentiation of patients with fulminant forms or virus-induced heart muscle diseases. GENPROVIC will overcome endomyocardial biopsy associated sampling error in diagnosis of different forms of MC for initiation of tailored immunosuppressive therapy of affected patients. GENPROVIC test will help to detect the patients with active viral replication, which is the pathophysiological mechanism responsible for the disease progression.





Florence Pinet

LIPCAR-HF

A prognostic marker of heart failure with impaired ejection fraction (LIPCAR-HF)

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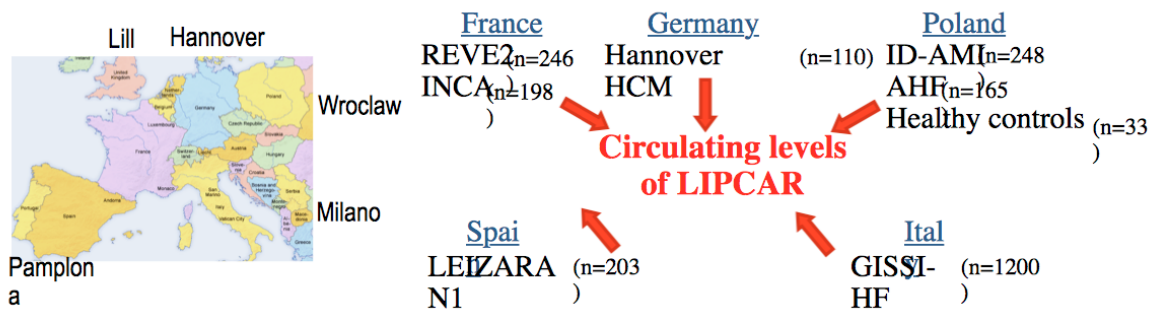
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The objective of this project is the development of the long noncoding RNA (lncRNA) LIPCAR as a new diagnostic and prognostic marker for heart failure patients. In this project, we will measure circulating levels of LIPCAR in blood samples of cohorts of patients with different ranges of heart failure such as MI, cardiomyocyte stress/injury, inflammation and myocardial fibrosis and healthy controls in order to develop a new cardiac biomarker.

LIPCAR, a prognostic marker of heart failure with impaired ejection fraction

Consortium of 5 countries: France (Lille), Germany (Hannover), Italy (Milano), Poland (Wroclaw), Spain (Pamplona)



➔ Evaluation of LIPCAR combined or against circulating biomarkers of myocardial fibrosis, cardiomyocyte stress/injury and inflammation in heart failure (HF) patients and controls

➔ New molecular phenotyping of patients who are at greater risk for adverse outcome in heart failure with reduced (HFrEF) and mid-range (HFmrEF) ejection fraction

European Research Area Network on Cardiovascular Diseases (ERA-CVD)



Ebba Brakenhielm

LYMIT-DIS

Targeted LYmphatic and Microvessel Treatments in metabolic-DISEase HFpEF

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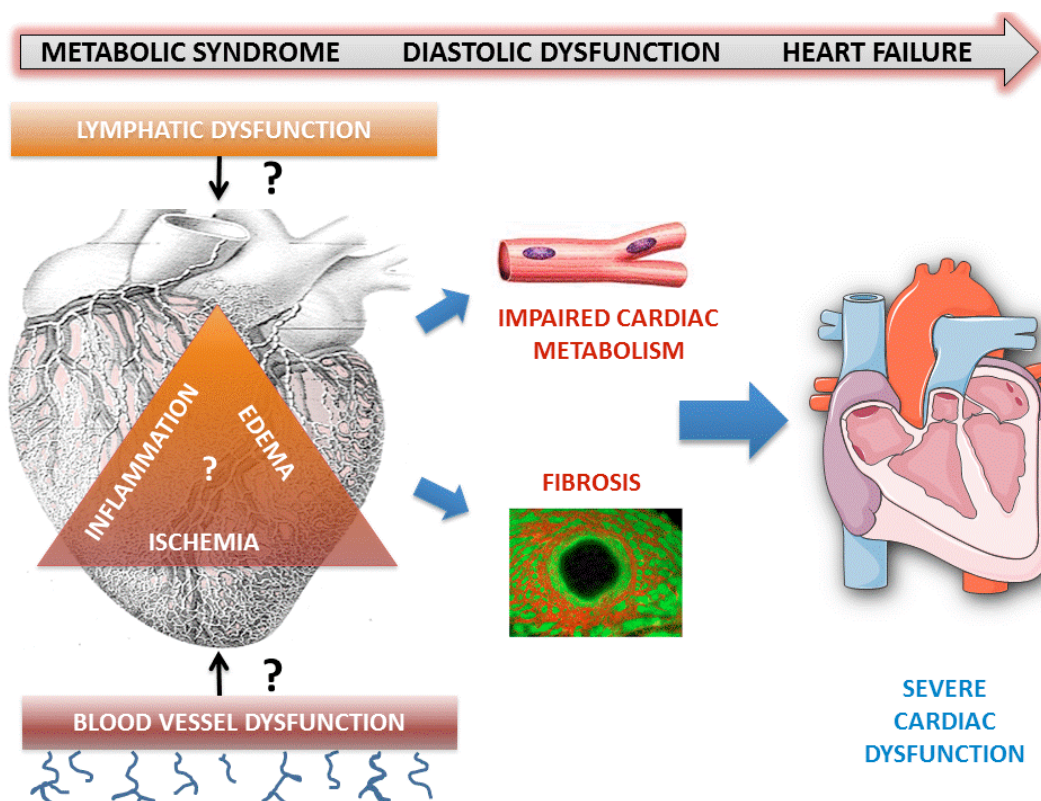
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Heart Failure (HF) represents a serious health challenge, with an estimated 6.5 million patients suffering from HF in the European Union. LYMIT-DIS is aimed at improved diagnosis, prognosis, and the development of new treatments for HF, focusing on HF with preserved Ejection Fraction (HFpEF). This type of HF with diastolic cardiac dysfunction, affects more than 50% of HF patients, notably women, and is linked to metabolic syndrome, an increasingly common condition characterized by insulin resistance, abdominal obesity, dyslipidemia, and hypertension. The overall objective of LYMIT-DIS is to forward our understanding of the mechanisms involved in the cardiac diastolic dysfunction in HFpEF, with the aim to identify and evaluate innovative treatments.





Stefan Engelhardt

MacroERA

Non-coding RNAs in cardiac macrophages and their role in heart failure

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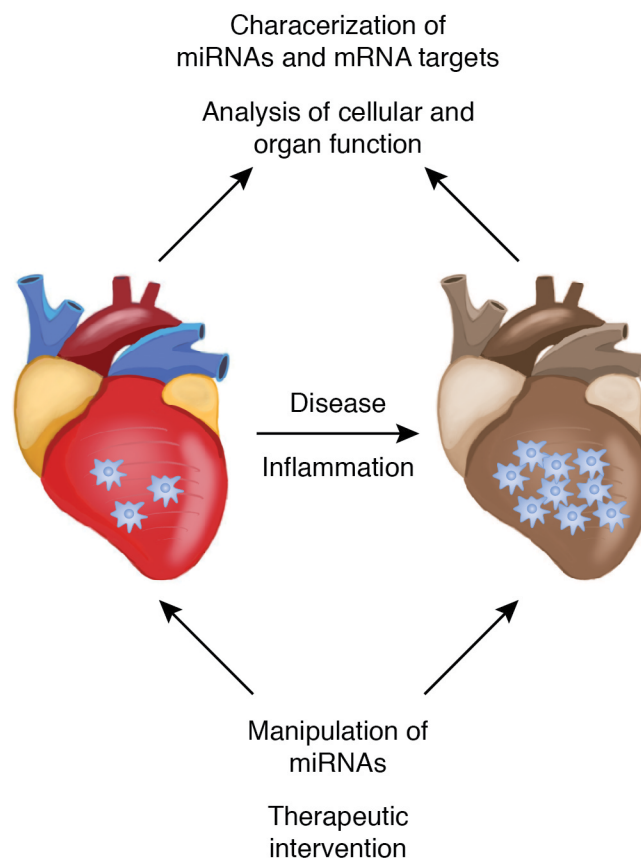
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Long-term prognosis for patients suffering from acute heart failure is still poor. Immune cells in the myocardium are key players in heart failure development. The idea is that endogenous, non-coding microRNAs regulate essential functions in cardiac immune cells. The aim of MacroERA is thus to screen the microRNA portfolio of immune cells in disease models (e.g. chronic pressure overload of the left ventricle) and to characterize the function of candidate microRNAs. Given this, MacroERA will exploit the potential of immune cell microRNAs for heart failure therapy.





Simon Sedej

MINOTAUR

Metabolic Therapy for Managing Diastolic Heart Failure

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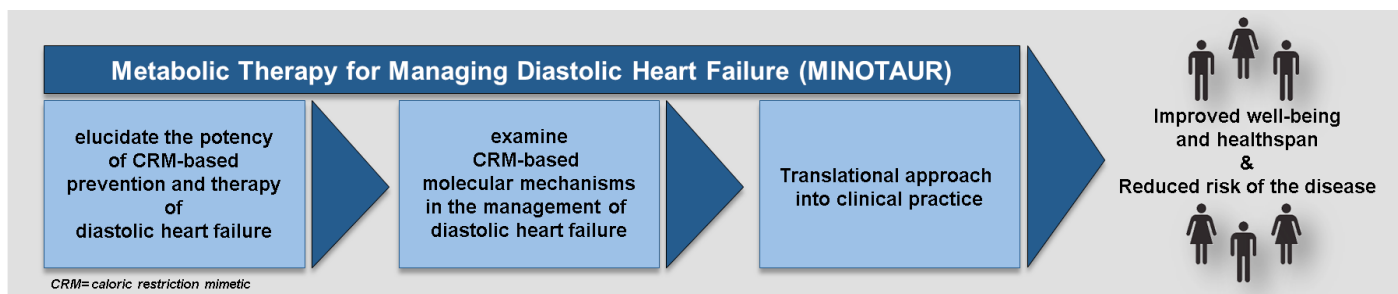
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Every fifth person aged >65 years is at increased risk to develop diastolic heart failure essentially due to metabolic disorders, such as obesity or Diabetes Mellitus Type 2. No treatment has yet been shown to convincingly target and prevent diastolic heart failure. The MINOTAUR consortium will test whether caloric restriction-like acting compounds (also known as caloric restriction mimetics) prevent the development of diastolic dysfunction and improve diastolic function in a clinically relevant experimental model of diastolic heart failure, and taking into consideration gender aspect. Unraveling the molecular details of the disease can lead to nutrition-based personalized therapy (i.e., functional food-based nutritional regimes) as a novel and innovative protective and/or therapeutic approach that will likely result in fewer hospitalizations and promote healthy (cardiac) aging in future.





Rodolphe
Fischmeister

PDE4Heart

Gene therapy with phosphodiesterases to treat heart failure

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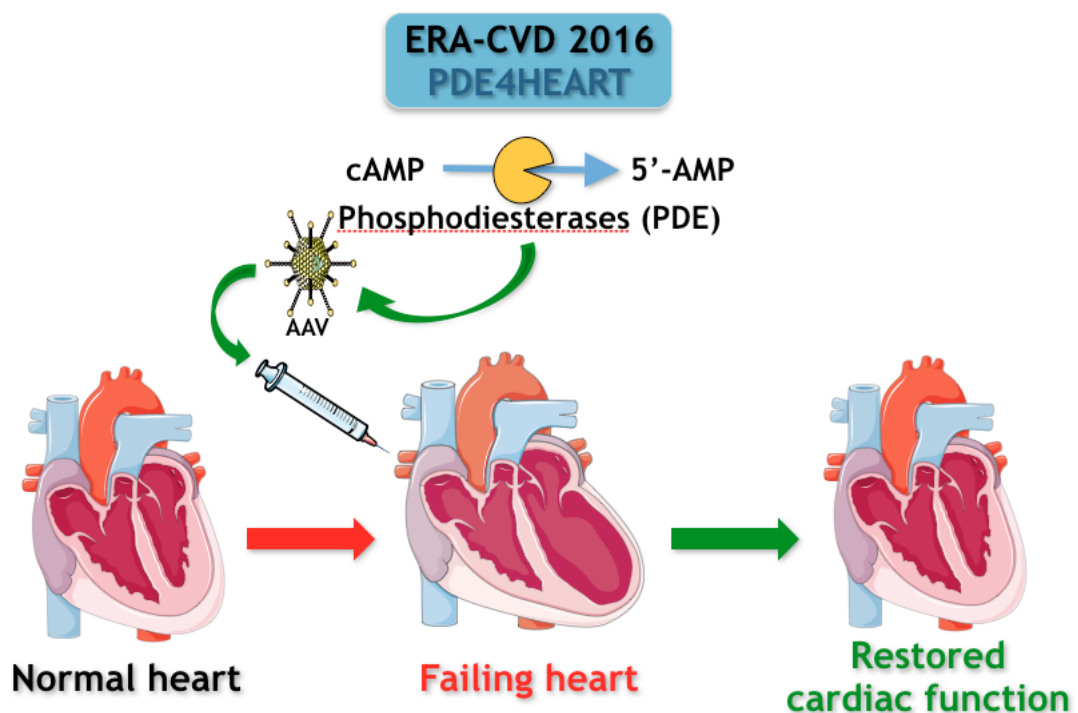
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In heart failure (HF) patients, the heart is unable to meet the hemodynamic needs, such as during a physical exercise or an emotional stress. The sympathetic nervous system, activated upon exercise or stress acts on the heart by the release of noradrenaline which activates beta-adrenergic receptors. Once activated, these receptors cause the production of cyclic AMP (cAMP). However, when the body demand stops, the heart returns to its normal activity by a family of enzymes called phosphodiesterases (PDEs). Thus, beta-adrenergic receptors serve as an accelerator and PDEs as a brake. In HF, the accelerator pedal is stuck to the floor and the brakes are ineffective. This project will use a new gene therapy approach to reintroduce different defective/missing types of PDEs into the heart, with the hope to prevent the associated heart rhythm disorders which are the main cause of death in HF.





Yigal Pinto

Variation

Novel RNA based therapies for treatment-resistant forms of severe cardiomyopathy caused by LMNA mutations

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Some forms of heart failure are often very difficult to treat. Patients who have a mutation in Lamin A/C can develop a form of heart disease that often does not respond well enough to existing therapies. VARIATION aims to develop a new technology to inhibit mutated Lamin A to halt the disease. The project will test this new RNA based technology in human cell that are derived from stem cells obtained from patients that actually carry the disease. VARIATION is expected to provide the first steps towards a treatment that is applicable to most patients that carry such a mutation and can halt progression of the associated heart failure.

