**TITLE PROJECT:** Defining targets to protect the non-diabetic and diabetic heart from transition to failure; a longitudinal *in vivo, ex vivo* and *in vitro* approach

**HOST LABORATORY:**

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**Overall aim**

Heart failure is one of the leading causes of death (WHO-Jan 2015). The aim of this proposal is to map myocardial structural, functional, and metabolic changes during the development of hypertrophy and subsequent failure, to define targets for prevention and treatment of heart failure in the non-diabetic and diabetic heart.

**Background**

Cardiac metabolic adaptations contribute to increased heart failure (HF) risk in diabetes patients. Yet, data largely originates from *ex vivo* rodent or cross-sectional human studies, which preclude studying the time course of cardiac changes in relation to declined function. In a longitudinal study in non-diabetic and diabetic rodents, we will examine to what extent *in vivo* changes in cardiac substrate uptake (Positron Emission Tomography), function (Magnetic Resonance (MR) Imaging), lipids and energetics (MR Spectroscopy) predict the development of HF. *In vitro* cell studies will be used for studying the underlying molecular mechanisms involved in the transition to heart failure.

**Hypothesis**

We hypothesize that maintenance of FAO, while preventing excess cardiac lipid deposition, protects against heart failure.

**Objectives/methods**

1. to develop a non-invasive *in vivo* myocardial imaging toolkit to map the structural, functional and metabolic changes during the development of cardiac hypertrophy and subsequent failure in the rodent heart  
2. to investigate to what extent excess lipid deposition is indicative of the development of cardiac hypertrophy and subsequently failure in the diabetic rodent heart  
3. to test, whether maintenance of fatty acid oxidation, without enhanced cardiac lipid accumulation, can delay or even prevent the transition to heart failure

**Skills/Techniques**

PET imaging, MRI imaging, Rodent handling, Cardiomyocyte isolation, Cell culturing & transfection, Metabolic labeling, Western blotting, RT-PCR, Enzyme assays, High-resolution respirometry