Focus of research group (I)

Name PI: Coert Zuurbier; staff member Nina Hauck
Department, UMC: Anesthesiologie
Size of research group: 2 PhD, 1 technician, 2 senior researcher and 2-4 MSc/BSc students

Mission:
Understanding how Diabetes increases CardioVascular Disease

Vision:
Disturbances in cardiac ion homeostasis with Diabetes results in CVD through ↑oxidative stress and ↓mitochondrial function

Aims:
Unraveling the mechanism along which SGLT2 inhibitors work, the first effective diabetic drugs showing reduced CVD events.

Approach: studying drugs effects and mechanism at the level of:
  a) cardiomyocyte, b) endothelium cell, b) intact heart,
  c) intact animal, d) human tissue
Focus of research group (II)

Current expertise

- Empa/Dapa/Canagliflozin lowers Na$^+$/Ca$^{2+}$ in cardiomyocytes; increase mitochondrial Ca$^{2+}$; impair NHE.  
  *Baartscheer; Uthman Diabetolog. ‘17 (top cited paper); ‘18*

- *Empa delays ischemic contracture in isolated heart*  
  *Uthman et al Cardiovasc Res (in revision)*

- *Empa has minor effects on endothelial cells (HUVEC/CAEC)*

Current funding

- European Foundation Study Diabetes
- Chinese Scholarship Council
- Alliance Vumc-AMC (OOTB)
Future plans

**Short term (1-2 year) plan**
Plan:
SGLT2i effect on T2 isolated diabetic heart: function + metabolism
SGLT2i effect on heart failure in SGLT2 KO mice
SGLT2i effect on endothelial cells

Necessary infrastructure:
Isolated heart platforms, metabolomics $^{13}$C heart, in vivo mouse heart function/metabolism (small animal MRI/PET), animal facility

**Long term (>2 year) plan**
Plan: if proven correct, extend concepts, therapy and research to heart failure (HFpEF, HFrEF, HCM) and T2DM cardiac dysfunction
Necessary infrastructure:

**Collaboration in ACS:**
Clinical Anesthesiology, AMC (Hermanides)  Clinical application/evaluation SGLT2i
Exp. Cardiology, AMC (Baartscheer, Coronel)  Ions in cardiomyocytes
Lab Gen Metab Dis, AMC (Houtkooper)  $^{13}$C metabolism intact heart
Physiology, Vumc (van der Velden, Wijnker)  human engineered heart tissue Biomed
Eng Physics, AMC (Strijkers, Wust)  small animal MRI/PET function/energetics