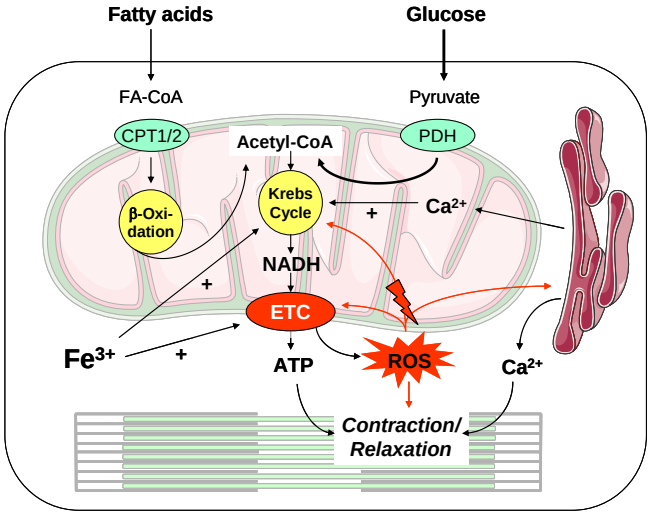
Heart Failure Association
of the European Society of Cardiology

Translational Research Workshop 2012

Mitochondria and Metabolism – Targets for the Treatment of Heart Failure

Palace of Academies, Brussels, BE
May 3-4, 2012

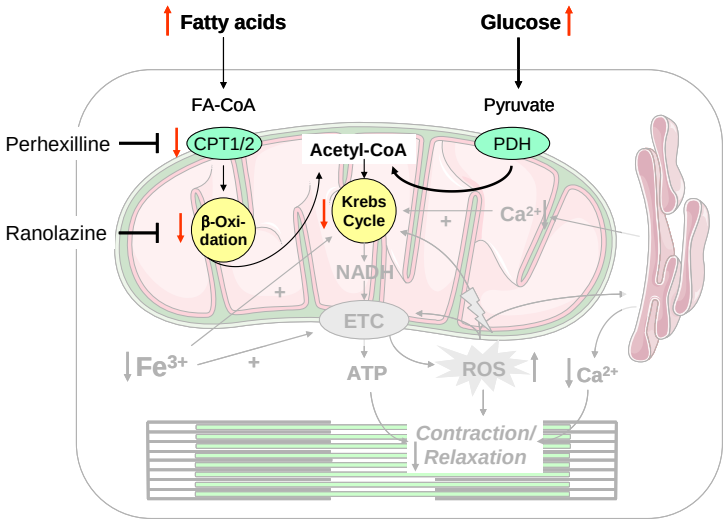


Thursday, May 3rd, 2012

12:00 – 13:15 Arrival and lunch at ***Royal Palace of Academies***, Brussels

13:15 – 13:30 **Welcome** (Stefan Janssens, Christoph Maack)

Session 1: Substrate utilization in heart failure: Compensation or maladaptation?



The normal heart utilizes ~70% fatty acids and ~30% glucose. In heart failure, various changes of substrate utilization occur, dependent on the severity of the syndrome, but also on the species investigated. It is currently controversial whether the changes in substrate metabolism are maladaptive or an adaptive compensation. This session is aimed at – if possible – reaching a consensus on the most important and consistent changes in substrate utilization of the failing heart, and whether they are adaptive or maladaptive. Furthermore, possible treatment options with a focus on clinical results will be discussed.

Discussants: **Gerd Hasenfuss** (Göttingen, DE)
Wolfram Doehner (Berlin, DE)

Talks: 10 min, ***Discussion***: 15 min

13:30 – 13:55 **Juhani Knuuti** (Turku, FI)
Substrate utilization and the metabolic switch in heart failure – adaptation or maladaptaion?

13:55 – 14:20 **Heiko Bugger** (Freiburg, DE)
Metabolic changes in diabetic cardiomyopathy – role of free fatty acids

14:20 – 14:45 **Renée Ventura-Clapier** (Châtenay-Malabry, FR)
Which drugs improve impaired mitochondrial biogenesis in heart failure, and why?

14:45 – 15:10 **William Stanley** (Baltimore, US)
Food supplementation with polyunsaturated fatty acids in CHF– animal models and clinical trials

15:10 – 15:35 **Michael Frenneaux** (Aberdeen, UK)
Inhibiting fatty acid oxidation in patients with chronic heart failure: Clinical results with perhexilline

15:35 – 16:00 Coffee break

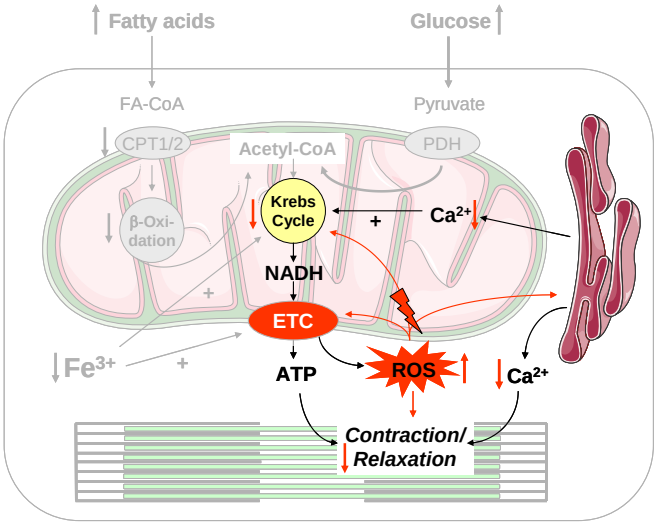
Session 2: Metabolic interventions in heart failure: Which treatment options do we have?

Discussants: **Burkert M. Pieske** (Graz, AT)
Thomas Eschenhagen (Hamburg, DE)

16:00 – 16:25	**Juhani Knuuti** (Turku, FI) Clinical results with trimetazidine
16:25 – 16:50	**Lars S. Maier** (Göttingen, DE) Ranolazine – metabolic intervention, ion channel blockade, or both?
16:50 – 17:15	**Ewa Jankowska** (Wroclaw, PL) Clinical results with iron supplementation in heart failure
17:15 – 17:40	**Hossein Ardehali** (Chicago, US) Role of iron for mitochondrial function in the heart
17:40 – 19:00	**General discussion**
20:00	Dinner

Friday, May 4th, 2012

Session 3: Mechanisms of oxidative stress in heart failure and treatment options



Oxidative stress plays a causal role in the progression of heart failure and yet, no antioxidant treatment was successful in patients with cardiovascular diseases. The sources of oxidative stress in the failing heart are manifold, but include mitochondria and NADPH oxidases. The regulation of the production of reactive oxygen species (ROS) in mitochondria is complex and involves dynamic variations in pro- and antioxidative processes. Recently, crosstalk between NADPH oxidases and mitochondria and the phenomenon of "ROS-induced ROS release" from mitochondria has been put forward. Controversial results have been obtained as to the role of the NADPH oxidase subtype Nox4, which is unequivocally upregulated in heart failure, but whose role (protective or maladaptive) and location (mitochondria, ER) is not fully resolved. This session aims at understanding the basic concepts of mitochondrial and NADPH-oxidase dependent ROS production, its dynamic fine-tuning in a working heart and pathophysiological changes in the failing heart. Furthermore, therapeutic concepts with special emphasis on clinical results will be discussed.

Discussants	**Rainer Schulz** (Giessen, DE) **Andrew Halestrap** (Bristol, UK)
08:00 – 08:25	**Brian O'Rourke** (Baltimore, US) Mechanisms of mitochondrial ROS production and the concept of "Redox-optimized ROS balance"
08:25 – 08:50	**Alexander Nickel** (Homburg, DE) How increased workload provokes mitochondrial ROS production
08:50 – 09:15	**Fabio Di Lisa** (Padova, IT) MAO and p66 as sources of mitochondrial ROS in heart failure
09:15 – 09:40	**Ajay Shah** (London, UK) ROS-mediated protective effects in heart failure
09:40 – 10:05	**Peter S. Rabinovitch** (St. Louis, US) The importance of targeting mitochondrial oxidative stress in heart failure
10:05 – 10:30	**General Discussion**
10:30 – 11:00	Coffee break

Session 4: Novel techniques for the analysis of cardiac metabolism: Interface to industry

This session is aimed at introducing state of the art in particular, novel techniques to monitor parameters of mitochondrial energetics and cardiac function and how to dissect signalling pathways involved in metabolic remodelling. The session also represents an interface between science and industry and may catalyze fruitful interaction between basic and clinical scientists and the industry.

Discussants:	**Ludwig Neyses** (Manchester, UK) **Zoltan Papp** (Debrecen, HU)
11:00 – 11:30	**Manuel Mayr** (London, UK) Combining transcriptomic, proteomic and metabolomic analyses to approach metabolic remodelling in heart failure
11:30 – 12:00	**Stuart Cook** (London, UK) Integrative genomics to identify mechanism of metabolic dysfunction in heart failure
12:00 – 12:30	**Kieran Clarke** (Oxford, UK) Clinical Cardiac Magnetic Resonance Spectroscopy
12:30 – 13:10	**General Discussion**
13:10	Closing remarks (Christoph Maack)
13:20	Lunch, departure