

5<sup>th</sup> World Congress on  
**Targeting Mitochondria**

**Strategies, Innovations & Clinical Applications**

**October 29-31, 2014 - Hotel Ritz Carlton, Berlin – Germany**

**Scientific Program**

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*Day 1 - October 29, 2014*

**How to Evaluate Mitochondria Function / Dysfunction?  
Mitochondria for Clinicians: How to Evaluate Mitochondria Function in Patient?  
Practical & Strategic Information**

**Pre-Conference Workshop**

09h00 – 18h00

Chaired by Mik Egbert & Joao Ramalho-Santos

**08h15 Opening of Registrations for Workshop**

**09h15 Welcome Note by Targeting Mitochondria Chairmen**

*Marvin Edeas – Volkmar Weissig*

**09h30 Monitoring Mitochondrial activity in challenging cells: Sperm and pluripotent stem cells**

*We will discuss some aspects of what exactly can be monitored in terms of mitochondrial activity, what information can be provided, and what controls may be needed.*

*We will also discuss some of the different probes and systems that can be used to study mitochondrial activity, and how they rarely work the same way in different cell types, with sperm and stem cells as specific examples. Finally, advantages and disadvantages of different monitoring systems (fluorescence microscopy, confocal microscopy, oxygen electrodes, TPP electrodes, Seahorse, flow cytometry, etc.) will also be included.*

*The goal is to provide an overview of these topics, showing examples of how things can go right or wrong.*

*Joao Ramalho-Santos, University of Coimbra, Portugal*

**10h45 Coffee Break**

**11h15 Measuring cellular oxygen metabolism in vivo: towards clinical monitoring of mitochondrial function**

- *Introduction/ why measure mitochondrial oxygenation and function at the bed site?*
- *History / previous attempts to monitor mitochondrial function*
- *Measuring mitochondrial oxygen tension / protoporphyrin IX technique*
- *Measuring mitochondrial oxygen consumption in vivo*
- *Preclinical data from animal studies and human volunteers*
- *The development and launch of COMET: the first commercial device based on PpIX technology.*  
*Will become available early 2015.*
- *Future perspectives*

*Mik Egbert, Erasmus MC, The Netherlands*

**12h15 Discussion: Mitochondria for Clinicians: How to evaluate mitochondria function in patients in the fields of cardiology, nephrology, cancerology, neurology and others...  
Invasive and non-invasive methods: Critics & Limitations**

**12h45 Lunch Break**

#### 14h00 Analysis of mitochondrial metabolism using live cell imaging technique

*The most prominent and disabling features in patients with mitochondrial disease are often due to neuronal dysfunction and neurodegeneration. Mitochondrial dysfunction shown to be associated with most common age related neurodegenerative diseases, such as Alzheimer's and Parkinson's Diseases. To address the mitochondrial health and function there are several bioenergetic parameters reflecting either whole mitochondrial functionality or individual mitochondrial complexes. Particularly, metabolism of nutrients in the tricarboxylic acid cycle provides substrates used to generate electron carriers (nicotinamide adenine dinucleotide [NADH] and flavin adenine dinucleotide [FADH<sub>2</sub>]) which ultimately donate electrons to the mitochondrial electron transport chain. The levels of NADH and FADH<sub>2</sub> can be estimated through imaging of NADH/NAD(P)H or FAD autofluorescence. Combination of the measurements of autofluorescence and mitochondrial membrane potential in single cells help to identify the mechanism of the mitochondrial dysfunction.*

**Andrey Y. Abramov, UCL Institute of Neurology, United Kingdom**

#### 15h00 New insights into mitochondrial diversity by a semi-automated mitochondrial isolation approach

*This presentation will focus on methodological approaches to investigate direct toxic effects on mitochondria. A new approach to obtain homogeneous mitochondrial isolates from cell culture and small tissue samples will be presented. Further, methods to quantify mitochondria, and to analyze mitochondriotoxic impairments and the consequences thereof will be discussed.*

**Hans Zischka, German Research Center for Environmental Health, Germany**

#### 15h45 Discussion

### 16h00 Coffee Break

#### 16h30 Real-time monitoring of Mitochondrial NADH redox state In Vivo: Current status of technology and Future clinical Perspectives

- Historical Overview – From Otto Warburg to Britton Chance.
- Principals of Mitochondrial Function and Tissue Energy Metabolism.
- Why to Monitor Mitochondrial NADH Oxidation Reduction State.
- How to Monitor NADH Redox state in real-time under in vivo conditions.
- Responses of Mitochondrial NADH to various perturbations in Animal Models.
- Monitoring of Mitochondrial NADH and microcirculatory blood flow and oxygenation in patients.
- Future Clinical perspectives in patient monitoring.

**Avraham Mayevsky, Bar-Ilan University, Ramat-Gan, Israel**

#### 17h15 Short Oral Presentations & Demonstrations

##### Using Seahorse XF Technology to measure mitochondrial function and more.

XF Extracellular Flux technology is now commonly used to measure cellular bioenergetics in cells and has been cited in over 1,500 peer reviewed publications since the introduction of the XF Extracellular Flux Analyzer in 2006. XF analysis has evolved from measuring basic mitochondrial function to include assays for the measurement of glycolysis, substrate selectivity, and metabolic switching/reprogramming. XF Analyzers are also used to measure the function of isolated mitochondria, enabling the examination of mitochondria from multiple samples simultaneously, saving valuable time and resources. This workshop will include:

- an overview of the gold standard XF Stress Tests for measuring mitochondrial function and glycolysis
- examples of the XF Stress Test in recent publications, including the recently proposed "Bioenergetic Health Index" [BHI] - an experimental blood test that can determine a patients' baseline bioenergetic status by indexing the performance of mitochondria
- a demonstration of the XF Mito Stress Test assay with the new XFp Analyzer

**Dennis Buurman, Seahorse Biosciences, Denmark**

#### 18h00 Discussion & Concluding Remarks by Mik Egbert & Joao Ramalho-Santos

From 14h30 to 18h30

Registrations for Targeting Mitochondria Conference  
Posters Installation

## Day 2 - October 30, 2014

07h30 Opening of Registrations

09h00 Opening of Targeting Mitochondria 2014 by Chairmen: *Pr Marvin Edeas & Pr Volkmar Weissig*

### Session 1: Recent Advances on Mitochondrial Dysfunctions in Chronic Diseases: The Mechanistic

#### Mitochondria & Microbiota: The Intriguing Relationship

09h05 **Mitochondria-Microbiota: The intriguing relationship**  
*Marvin Edeas, Chairman of Targeting Mitochondria Task Force Group, France*

09h25 **Upends current theories of how mitochondria began**  
*Martin Wu, University of Virginia, USA*

09h50 **Mislocalization of mitochondrial DNA regulatory proteins upon bacteria Helicobacter pylori infection**  
*Laurent Chatre, Institut Pasteur, France*

#### Mitochondria & Redox Regulation

09h55 **Mitochondria hyperactivity and nitroso-redox imbalance in a human disease**  
*Miria Ricchetti, Institut Pasteur, France*

#### Mitochondria & Viral Interaction

10h20 **Viral hepatitis and mitochondrial dynamics: lessons & perspectives**  
*Aleem Siddiqui, University of California, San Diego, USA*

#### 10h55 Coffee Break & Posters Session

#### Mitochondria & Metabolic Syndrome: Targeting Diabetes & Obesity

11h25 **Do mitochondria care about insulin resistance?**  
*Chrysi Koliaki, Institute for Clinical Diabetology, German Diabetes Center, Germany*

11h50 **Mitochondrial function as a target for therapy in type 2 diabetes**  
*Jeanine J. Prompers, Eindhoven University of Technology, The Netherlands*

12h15 **Nicotinamide N-methyltransferase knockdown protects against diet-induced obesity**  
*Daniel Kraus, University of Würzburg, Germany*

#### 12h40 Lunch Break & Posters Session

14h00 **Metformin, biguanides and mitochondrial OxPhos: where are the targets?**  
*Hannah Bridges, Medical Research Council Mitochondrial Biology Unit, United Kingdom*

#### Mitochondria & Neurodegenerative Diseases

14h25 **Merging the concepts of mPTP and BH3-only protein-mediated mitochondrial demise in neurons**  
*Carsten Culmsee, Marburg University, Germany*

#### Mitochondria & Cancer: Towards a Predictive & Therapeutic Approach

14h50 **Targeting mitochondria and metastasis: recent advances and perspectives**  
*Novel way blocks tumour growth into cancer*  
*Paolo E. Porporato, Université Catholique de Louvain, Belgium*

**15h15 Acquisition of mtDNA restores mitochondrial function and tumour-initiating efficacy**  
*Jiri Neuzil, Griffith University, Australia*

**15h40 Coffee Break & Posters Session**

**16h10 Short Oral Presentations**

**Targeting the mitochondrial unfolded protein response in cancer**  
*Doris Germain, Tisch Cancer Institute, Mount Sinai School of Medicine, United States of America*

**Mitochondrial substrates in cancer**  
*Vladimir Gogvadze, Karolinska Institutet, Sweden*

**The novel proapoptotic agent  $\omega$ -3-epoxyeicosanoic acid targets the mitochondrion in human breast cancer cells by death receptor signalling**  
*Michael Murray, University of Sydney, Australia*

**Targeting mitochondria to block the cell cycle in cancer: focus on the mitochondrial kinase PINK1**  
*Cora O'Neill, University College Cork, Ireland*

**Differences in mitochondria between normal and cancer cells as molecular cancer target**  
*Alexander Gossrau, BMCC-City University of New York, United States of America*

**Tissue variation of mitochondrial DNA maintenance in *Mus musculus***  
*Nina Johanna Kekäläinen, University of Eastern Finland, Finland*

**Pioglitazone mimics transcriptional and functional changes in mitochondria induced by a calorie restricted diet**  
*Jamie Louis Barger, LifeGen Technologies, United States of America*

**The cardiolipin-targeting peptide MTP-131 (Bendavia) restores mitochondrial bioenergetics in two different models of cardiomyopathy**  
*David A Brown, East Carolina University, United States of America*

**Association of Mitochondrial Mutations with Subclinical Carotid Atherosclerosis**  
*Alexander N. Orekhov, Institute for Atherosclerosis Research, Russian Federation*

**Targeting the Warburg Effect in Neuroblastoma Therapy by Ketogenic Diet**  
*Barbara Köfler, Paracelsus Medical University, Austria*

**Statin Treatment Induces Apoptosis by Increasing Mitochondrial Reactive Oxygen Species in Skeletal Muscles**  
*Jamal Bouitbir, University Hospital Basel, Switzerland*

**Mitochondrial SILAC reveals a role for CLIC4 in perinatal hypoxic-ischaemic brain injury**  
*Claire Thornton, King's College London, United Kingdom*

**Hypoxia-induced mitochondrial dynamics in neurons: identification of new molecular targets**  
*Antonella Scorziello, Federico II University of Naples, Italy*

**Monomeric alpha-synuclein plays a key role in ATP production**  
*Marthe Helene Regina Ludtmann, UCL, United Kingdom*

**Hepatitis C virus core protein suppresses mitophagy by interacting with Parkin in the context of mitochondrial depolarization**  
*Hino Keisuke, Kawasaki Medical school, Japan*

**Antiretroviral drug exposure induces immediate mitochondrial dysfunction that can be rescued by antioxidants**  
*Reuben Luke Smith, UvA, The Netherlands*

**The mitochondrial gas pedal: cytosolic calcium regulates pyruvate dependent energization of mitochondria - New evidences from synaptosomes, fibroblasts, white and red muscle**  
*Frank-Norbert Gellerich, Neurologische Universitätsklinik, Germany*

**The oncoprotein URI1 suppresses PGAM5-mediated mitochondrial stress-induced apoptosis**  
*Helene Jonasch, ETH Zurich, Switzerland*

**Targeting the mutational landscape of the human mitoribosome**  
*Antón Vila-Sanjurjo, Universidade da Coruña, Spain*

**Mitochondrial DNA physically contacts nuclear genes in mouse astrocytes**  
*Malina Dimchova Doynova, University of Auckland, New Zealand*

**The mitochondrial protein TCAIM regulates activation of T Cells and thereby promotes tolerance induction of allogeneic transplants**

*Julia Schumann, Charité - University Medicine, Germany*

**Effectiveness of creatine monohydrate in mitochondrial oxidatively injured myoblasts**

*Elena Barbieri, University of Urbino Carlo Bo, Italy*

**Processing of stalled replication forks in mammalian mitochondria**

*Ruben Torregrosa, University of Eastern Finland, Finland*

**Mutations of CLPP, encoding a mitochondrial ATP-dependent chambered Protease, cause deafness and ovarian failure**

*Meghan C. Drummond, National Institutes of Health, USA*

**Energy decompensation due to acute complex I dysfunction - an in vivo pig model**

*Michael Karlsson, Neurovive Pharmaceuticals, Sweden*

**Feed forward iNOS-mitochondrial ROS cycle in inflammation**

*Adelheid Weidinger, L. Boltzmann Institute Exper. Clin.Traumatology, Austria*

**Inhibition of mitochondrial genome expression triggers the activation of CHOP-10 by a cell signalling dependent on the integrated stress response but not the mitochondrial unfolded protein response.**

*Patricia Renard, University of Namur, Belgium*

18h30 End of the First Day of Conference

19h30 Dinner between Speakers & Attendees – at Hotel Ritz Carlton

*Day 3 - October 31, 2014*

**Session 2: Devices, Methods & Biomarkers:  
Innovations & New Opportunities**

09h00 Introduction: Why measure mitochondrial oxygenation and function at the bed site?

*What are the best methods to evaluate mitochondria in patients?*

*Mik Egbert, Erasmus MC, The Netherlands*

09h10 Microscopy enables Detailed Insights into Mitochondria

*Martin Kerschensteiner, Medical Center of the University of Munich, Germany*

09h35 Quantitation of the mitochondrial electron transport chain in living cells

*Roger Springett, Medical Research Council Mitochondrial Biology Unit, United Kingdom*

10h00 Non-standard methods to evaluate mitochondrial dysfunction caused by toxic bile salts

*Hans Zischka, German Research Center for Environmental Health, Germany*

10h25 Short Oral Presentations

**Mitochondrial function and metabolic states: on the differences between in vitro and in vivo evaluation approaches**

*Avraham Mayevsky, Bar-Ilan University, Ramat-Gan, Israel*

**Mitochondrial DAMPs: Novel Markers for Hepatic Ischemia Reperfusion Injury**

*Ian Alwayn, Dalhousie University, Canada*

**A novel in situ assay utilizing expression of mitochondrial cytochrome c oxidase subunit 4 isoform 2 for the early detection of lung cancer**

*Maik Huttemann, Wayne State University, United States of America*

10h50 Coffee Break & Posters Session

## Session 3: Strategies to Target Mitochondria: Recent Clinical Data and Potential Therapeutic Studies

### Strategies to Target Stem Cells

- 11h15 **Reprogramming-derived patient neural cells as a novel model system for mitochondrial DNA disorders**  
*Alessandro Prigione, Max Delbrueck Center for Molecular Medicine, Germany*
- 11h40 **Putting the wheels on mitochondrial donation by stem cells**  
*Anurag Agrawal, Delhi University, India*

### Mitochondria Replacement Strategy

- 12h05 **An evolutionary biology view on mitochondrial replacement**  
*Klaus Reinhardt, University of Tuebingen, Tuebingen, Germany*

### 12h30 Lunch Break & Posters Session

### Clinical & Therapeutic Directions

- 13h45 **Clinical studies of mitochondria-targeted plastoquinone derivatives as medicines to treat cataract, glaucoma and related diseases**  
*Vladimir Skulachev, University of Moscow, Russia*
- 14h10 **Mitochondria-targeted H<sub>2</sub>S donors: A novel twist to an old "tail"?**  
*Rotten egg gas holds key to healthcare therapies*  
*Matt Whiteman, University of Exeter Medical School, United Kingdom*
- 14h35 **Effective treatment of mitochondrial myopathy by nicotinamide riboside, a vitamin B<sub>3</sub>**  
*Nahid Akhtar Khan, University of Helsinki, Finland*
- 15h00 **Short Oral Presentations**

**Cell-permeable complex II substrates – a new compound class for treatment of mitochondrial complex I dysfunction**

*Johannes Ehinger, Lund University, Sweden*

**Design of therapeutic anti-replicative RNA imported into mitochondria of human cells**

*Nina Entelis, UMR 7156 Strasbourg University/CNRS, France*

**Rice bran extract improves mitochondrial dysfunction in brains of aged NMRI mice**

*Gunter Peter Eckert, Goethe-University of Frankfurt, Germany*

**Kolliphor® EL of branded intravenous ciclosporin, but not the novel ciclosporin lipid emulsion CicloMulsion®, induces mitochondrial inhibition in human platelets**

*Sarah Piel, NeuroVive Pharmaceutical, Sweden*

**Placental mitochondria as a target of in utero particulate air pollution and the modulating role thyroid hormones**

*Bram Janssen, Hasselt University, Belgium*

### 15h35 Coffee Break & Posters Session

- 16h00 **Effect of exposure to welding fumes on copy number of mitochondrial DNA – relevance for blood pressure?**  
*Yiyi Xu, Lund University, Sweden*
- Mitochondrial ROS-mediated damage can be prevented by interfering with cytoplasmic/mitochondrial crosstalk**  
*Sana Khalid, Innsbruck Medical University, Austria*

**Hepatotoxicity of tyrosine kinase inhibitors**  
*Franziska Paech, University Basel, Switzerland*

**Administration of CoQ10 analogue ameliorates dysfunction of the mitochondrial respiratory chain in a mouse model Angelman syndrome**  
*Virginia Kimonis, University of California, USA*

**CHCHD2, a new regulator of mitochondrial metabolism and stress response**  
*Lawrence Grossman, Wayne State University, USA*

**In vivo time-lapse imaging of mitochondria in the myelin sheath**  
*Nicolas Tricaud, Institute for Neurosciences of Montpellier, France*

**The circadian gene Rev-erba improves cellular bioenergetics and provides preconditioning for protection against oxidative stress**  
*Dennery Phyllis, University of Pennsylvania/Children's Hospital of Philadelphia, United States of America*

**17h00 Discussion & Conclusion of Targeting Mitochondria 2014**  
**In the presence of Organizers & Speakers from scientific committee**

**Targeting Mitochondria 2014 Awards:**

- ✓ **Scientific Contribution Award 2014**
- ✓ **Young Scientific Contribution for Oral and Poster Contribution**

**Concluding Remarks by Marvin Edeas & Volkmar Weissig**

**17h30 End of Targeting Mitochondria 2014**

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