"Mitochondria, Peroxisomes and Lysosomes - the "menage a trois" of cellular metabolism"

From 2014-02-01 to 2019-01-31, ongoing project

Project details

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<th>Total cost:</th>
<th>Topic(s):</th>
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<td>EUR 1 345 200</td>
<td>ERC-SG-LS4 - ERC Starting Grant - Physiology, Pathophysiology and Endocrinology</td>
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Objective

The metabolic roles of mitochondria, peroxisomes and lysosomes are well established. Numerous genetic defects affecting the function of these organelles result in a wide spectrum of metabolic diseases. The involvement of these organelles in signalling pathways is receiving increasing attention. Furthermore, interactions between them and other cellular components have been elucidated. Evidence is now emerging that dysfunction in mitochondria, peroxisomes or lysosomes causes secondary perturbations in the other two organelles. The fundamental hypothesis presiding to this proposal is that mitochondria, peroxisomes and lysosomes form an interdependent network (MytoPexLyso), which is likely to have fundamental roles in cell biology, metabolism and metabolic diseases.

To test this hypothesis and elucidate the role of the MitoPexLyso network in physiology and disease, we will employ state-of-the-art imaging and systems biology approaches. First, we will uncover how dysfunction of each MitoPexLyso organelle affects the network. We will test if mitochondrial dysfunction can trigger lysosome biogenesis, and also systematically address how perturbations in one organelle affect the other two. Second, we will identify signalling pathways sensing perturbations on the MytoPexLyso network, and elucidate their pathologic significance, both in cell lines and in animal models of metabolic diseases. Third, we will test a novel strategy to cure mitochondrial diseases: enhanced removal of damaged mitochondria through increased lysosomal autophagic capacity. We will generate a novel mouse model with higher lysosomal capacity in the skeletal muscle, and use a mouse model of mitochondrial myopathy, to test this premise in vivo.

This proposal addresses key questions in cell biology and metabolism, and will lay the foundation for a new field of “organelle networks” which will profoundly impact our understanding of metabolism and metabolic diseases and drive future research endeavours.

Related information

Report Summaries

- Mid-Term Report Summary - MITOPEXLYSONETWORK (Mitochondria, Peroxisomes and Lysosomes - the "menage a trois" of cellular metabolism)
**Principal Investigator**

Nuno Filipe Viegas Das Neves Raimundo
Tel.: +495513912809
Fax: +49551395979

**Host Institution**

UNIVERSITAETSMEDEZIN GOETTINGEN - GEORG-AUGUST-UNIVERSITAET GOETTINGEN - STIFTUNG ÖFFENTLICHEN RECHTS
Robert-Koch-Strasse 40
37075 GOETTINGEN
Germany

**Activity type:** Higher or Secondary Education Establishments

**Administrative contact:** Christiane Hennecke
Tel.: +49551398770
Fax: +495513922593

**Beneficiaries**

UNIVERSITAETSMEDEZIN GOETTINGEN - GEORG-AUGUST-UNIVERSITAET GOETTINGEN - STIFTUNG ÖFFENTLICHEN RECHTS
Robert-Koch-Strasse 40
37075 GOETTINGEN
Germany

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Tel.: +49551398770
Fax: +495513922593

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**Subjects**

Biotechnology - Life Sciences - Medicine and Health

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