Project title: Unraveling the process of cellular energy production: identifying novel mitochondrial proteins

Project leader: Dr. M. Gerards

Function: Postdoctoral fellow

Collaborators: Prof. Dr. H.J.M. Smeets, Dr. G. Ertaylan, Dr. M. Adriaens

Proposal (250 words):

Introduction:
Mitochondria are dynamic organelles which play an essential role in cellular energy production. Their role is especially critical for energy demanding tissues such as the heart and the brain. Mitochondrial dysfunction has been associated with a spectrum of diseases including neurological disorders and aging.
Mitochondria engage in repeated cycles of *fission and fusion* which are processes that play a critical role in maintaining functional and healthy mitochondria. Despite the importance of these processes, not all proteins involved in these processes are known. It is crucial to understand the full mechanism of mitochondrial fusion and fission which is essential to develop therapeutic strategies for patients with defects in this system.
Hypothesis and Objectives:
We hypothesize that computational approaches combined with functional studies will result in the identification of novel mitochondrial fission and fusion proteins.
The objectives for this study are 1) identifying candidate proteins utilizing computational methods and 2) provide experimental evidence of the identified candidates for involvement in mitochondrial fission and fusion
Setting and Methods:
Novel mitochondrial fission and fusion genes will be identified using several computational approaches, including co-expression analysis and phylogenetic analysis. The subcellular localisation of relevant candidate proteins will be investigated. Subsequently, candidates localized in the mitochondria will be functionally investigated using subcellular localization studies, gene knock down (using CRISPR/Cas9) and overexpression studies, followed by assessment of, among others, mitochondrial morphology and cellular respiration.
Impact:
Identification and functional analysis of novel mitochondrial proteins, will improve the understanding of mitochondrial processes and their role in health and disease.

Requirements candidate: Highly motivated student with good English communication skills and proactive and resolute attitude.

Keywords: Computational Biology, Big data, Mitochondria, CRISPR/Cas9, Functional studies

Top 5 selected publications:

1. **Gerards M.**, S.C. Sallevelt and **H. Smeets** (2016) “Leigh syndrome: Resolving the clinical and genetic heterogeneity paves the way for treatment options”. Mol. Genet. Metab. Mar;117(3):300-12
2. Nguyen M, I. Boesten, D. Hellebrekers, N.M. Mulder-den Hartog, I. de Coo, **H. Smeets** and **M. Gerards** (2017) “Novel pathogenic SLC25A46 splice-site mutation causes an optic atrophy spectrum disorder”. Clinical genetics.
3. **Gerards, M.**, B. J. van den Bosch, K. Danhauser, V. Serre, M. van Weeghel, R. J. Wanders, G. A. Nicolaes, W. Sluiter, K. Schoonderwoerd, H. R. Scholte, H. Prokisch, A. Rotig, I. F. de Coo and **H. J. Smeets** (2011) "Riboflavin-responsive oxidative phosphorylation complex I deficiency caused by defective ACAD9: new function for an old gene." Brain 134(Pt 1): 210-219.
4. **Ertaylan, G**. K., et al. (2014). Gene regulatory network analysis reveals differences in site-specific cell fate determination in mammalian brain. *Frontiers in Cellular Neuroscience*, *8*. http://doi.org/10.3389/fncel.2014.00437
5. Küffner, R, Zach, N, Norel, R, Hawe, J, **Ertaylan, G,** Schoenfeld, D, Wang, L, Guang, Li, Fang,L et al. (2014) Crowdsourced analysis of clinical trial data to predict *amyotrophic lateral sclerosis* progression. *Nature Biotechnology* doi:10.1038/nbt.3051