Hector Fellow Academy

Single cell genomic approaches to study mitochondrial genetics and disorders

Project description

Mitochondria are central to numerous physiological processes and are unique organelles that carry their own genome, often in high copy number, encoding a subset of proteins, transfer RNAs, and ribosomal RNAs essential to their function. Germline inherited mitochondrial DNA (mtDNA) mutations are a major cause of human disease and hundreds of point mutations and deletions have been associated with a variety of overlapping phenotypes, estimated to affect ~1 in 4,300 individuals, placing them among the most common inherited metabolic disorders. Mitochondrial diseases are characterized by remarkable heterogeneity and while variable heteroplasmy (fraction of mitochondrial genomes carrying a variant) of associated pathogenic mutations/deletions may present a natural modulator of disease severity, many syndromes include cell-type specific phenotypes. Moreover, the accumulation of somatic mtDNA mutations has been associated with ageing phenotypes and malignancies. However, establishing genotype-phenotype correlations on a cellular and molecular level has been challenging due to the unique nature of mitochondrial genetics that include variant heteroplasmy as a dynamic variable, but also tissue-dependent differences in mtDNA copy number, its cell cycle-independent turnover and the uncertainty about rates and mechanisms underlying accumulation of somatic variants. To bridge this gap, we develop and apply single cell multi-omic technologies to enable the linkage of an individual cells' mtDNA genotype to its phenotype, such as its gene expression, protein expression and/or chromatin accessibility profile to enhance our understanding of mitochondrial genetics and underlying human disease. In particular, we are interested to understand adaptive genomic and cellular responses to high levels of pathogenic mtDNA or an increased mutational burden in cellular and animal models, including primary patient specimens.

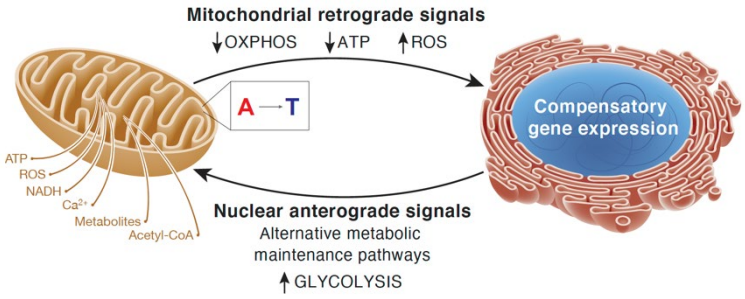

Figure adapted from Vendramin et al. *EMBO Journal*, 2017

Keywords

Single cell multi-omics, mitochondrial genetics, mitochondrial disease, hematology, immunology

Entry requirements

Strong interest in life sciences, computational biology, method development and/or translational research. Master's degree in computer science, bioinformatics, biotechnology, biochemistry, engineering, mathematics, physics, biology, (molecular) medicine or a related field. Expertise and interest to work computationally and/or experimentally, in particular with (single cell) sequencing data. Projects can be tailored accordingly. We in particular encourage applications from students with a computational background. Strong motivation to work independently as well as in an interdisciplinary research team. Very good language and communication skills in English.

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Interdisciplinary Network for Cutting-Edge Research

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Lab Location
Berlin Institute of Medical Systems Biology, Hannoversche Str. 28, 10115 Berlin

Starting date
Between August and December 2021

Funding
limited to 3 years

How to apply
Please apply via the HFA application portal. The Hector Research Career Development Awardees will arrange interviews (via skype or if feasible in-person) with the most promising applicants. The final candidates will be invited for a personal presentation on July 8, 2021 in Bremen (Germany). The final decisions will be announced by August 2021.

Application Deadline
March 31st, 2021

Enquiries
For further details about the research group, please contact the Hector Research Career Development Awardee at: leif.ludwig@bihealth.de. For questions related to making your application, please contact Hector Fellow Academy Office: application@hector-fellow-academy.de or www.hector-fellow-academy.de

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