



Master project 2024-2025

Personal Information

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Project

Computational genomics

Project Title:

Role of somatic mutagenesis in human aging.

Keywords:

Genomics, mutagenesis, aging, cancer, tRNA

Summary:

Transfer RNAs (tRNAs) have occupied a central spot in cell biology and the biotechnology industry in recent years. In particular, the possibility of using these molecules to treat unapproachable diseases such as Huntington's has sparked the emergence of new biotech companies dedicated to the engineering of tRNAs. We have very recently discovered a potential link between the mutational dynamics of tRNA genes in the human genome and the process of aging. Our working hypothesis is that cellular and tissue degeneration during aging is promoted by the loss of functional tRNAs in cells, caused by the gradual accumulation of mutations in genes coding for tRNA. This hypothesis offers a mechanistic explanation for prominent characteristics of aging, such as loss of muscle mass and neurodegeneration. Moreover, it opens the door to potential anti-aging interventions directed towards the improvement of tRNA function. We will try to prove our hypothesis through the comparative analysis of short- versus long-lived reptiles and mammals, and through the implementation of experimental frameworks where the physiological impact of tRNA mutations can be directly assessed, and the potential benefits of reversing these mutations can be studied. This will be done in collaboration with IRB groups that are experts in the study of the mutational mechanisms affecting the human genome.

References:

1. Somatic mutation rates scale with lifespan across mammals - Nature (604)517-524 (2022) 2. tRNAsudio: facilitating the study of human mature tRNAs from deep sequencing datasets - Bioinformatics 38(10):2934-2936 (2022).

Expected skills:

R and Python

Possibility of funding:

Yes

Possible continuity with PhD:

Yes