



## Master project 2024-2025

### Personal Information

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### Project

## Computational genomics

#### Project Title:

Beyond the genetic code: elucidating gene regulation by stop codon readthrough

#### Keywords:

Gene expression, Comparative genomics, Ribosome profiling, Translation, Recoding

#### Summary:

Our lab employs comparative genomics to study the mechanisms of gene expression and protein synthesis. We focus in particular on “recoding” events, programmed exceptions to the genetic code [1]. A remarkable example of recoding is stop codon readthrough (SCR): a stop codon is recoded to insert an amino acid instead of causing termination of translation. There are ~40 known cases of SCR in human. In contrast, recent research is revealing that insects have thousands of readthrough genes [2]: it seems that SCR was widely adopted in this clade for gene expression regulation, akin to splicing. Yet, much is unknown about the mechanism, regulation, and function of SCR. In the last two years, we defined the landscape of SCR activation across tissues and developmental stages of *Drosophila*, revealing a regulated process (unpublished). To do so, we used protein sequence conservation across multiple species, and experimental data, in particular ribosome profiling (a popular high-throughput technique, consisting in a variant of RNAseq, wherein only the mRNA fragments under active translation are sequenced [3]). We have now a large collection of genes with SCR, which are we are testing experimentally. Our large repertoire of SCR provides many opportunities for studies focused in specific genes. The student may investigate genes of interest by a combination of database searches, analysis of high throughput data, in silico analysis of RNA structures and protein structures, and phylogenetic analysis. We expect the project to generate hypotheses that will be directly tested in our lab, leading to research publications.

#### References:

[1] M. V Rodnina, N. Korniy, M. Klimova, P. Karki, B.-Z. Peng, T. Senyushkina, R. Belardinelli, C. Maracci, I. Wohlgemuth, E. Samatova, F. Peske, Translational recoding: canonical translation mechanisms reinterpreted, *Nucleic Acids Res* (2019). <https://doi.org/10.1093/nar/gkz783>. [2] I. Jungreis, C.S. Chan, R.M. Waterhouse, G. Fields, M.F. Lin, M. Kellis, Evolutionary dynamics of abundant stop codon readthrough, *Mol Biol Evol* 33 (2016) 3108-3132. <https://doi.org/10.1093/molbev/msw189>. [3] N.T. Ingolia, J.A. Hussmann, J.S. Weissman, Ribosome profiling: Global views of translation, *Cold Spring Harb Perspect Biol* 11 (2019). <https://doi.org/10.1101/cshperspect.a032698>.

#### Expected skills:

Python and/or R; High throughput data analysis; basics of evolutionary biology

#### Possibility of funding:

To be discussed

**Possible continuity with PhD:**

To be discussed