# Offre de stage (M2)

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# Titre du projet de recherche :

Epigenetic inheritance of small RNAs as a mechanistic basis for speciation in *Paramecium tetraurelia*?

### **Description du projet :**

Reproductive isolation constitutes an important evolutionary process, in that it promotes divergence between closely related populations, as opposed to homogenization, and thus underlies macrobiodiversity. Among the possible causes of reproductive isolation stand epistatic interactions among loci, that can generate so called "Dobzhansky-Muller" incompatibilities: through a diversity of molecular mechanisms, following the fixation of new alleles at two distinct loci in two distinct populations, hybrids may carry combinations that severely diminish fitness, which reduces gene flow among populations.

On the basis of genomic data, previously obtained following crosses between two strains of the unicellular eukaryote *Paramecium tetraurelia*, we initiated the investigation of the genetic basis of an observed 80% mortality in the progeny of hybrids. We incidentally found out that this pattern may stem in large part, not from genetic, but epigenetic changes, inherited through the cytoplasm. One peculiar feature of these organisms is that within a single cell compartment, they include both a micronucleus, containing the entire genome in a usual diploid state, and a macronucleus, made of only a fraction of the genome but present in many more copies, of the order of 800. Only the macronucleus, where the genes are effectively expressed, drives the phenotype; in that sense, it is analogous to the somatic tissue of multicellular organisms. The content of the macronucleus, that is, the delimitations of the genomic regions that are deleted or maintained during its development, is known to be maternally (cytoplasmically) inherited at conjugation because it depends on small RNAs that reflect the rearrangement patterns of the parental macronucleus in each conjugant. The cytoplasmic inheritance of alternative rearrangement patterns can thus be independent from the Mendelian inheritance of genetic alleles, and preliminary evidence suggests that this could potentially cause genetic/epigenetic incompatibilities, and hence mortality, in the progeny of hybrids. Furthermore, we found that rearrangement patterns may occasionally be transferred to the other conjugant (as determined by mitochondrial haplotypes), suggesting that the effects of parental small RNAs are not strictly confined to each cytoplasm.

The main objective of this internship would be to screen more exhaustively for variation in the composition of the macronucleus in hybrids that may be driven by cytoplasmic inheritance, and further investigate whether such variations could be responsible for Dobzhansky-Muller

incompatibilities. Such a result would be indicative that not only genetic but also epigenetic changes may contribute to reproductive isolation and speciation.

#### Methods

Reference genomes and F2 re-sequencing data are already available. The analysis of these empirical data will offer an opportunity to learn to master the computational methods and the software programs classically used in this scientific domain (read mapping, variant calling, ...), while learning to appreciate the limitations and biases inherent to high-throughput sequencing data. This project will give a thorough training in bioinformatics, scripting, high-performance computing and high-throughput data analysis.

# Expected profile and skills of the candidate

The candidate should have a particular interest in genetics, genomics and molecular evolution; should be willing to acquire an extensive training in bioinformatics and high-throughput data analysis, and should lean toward team and collaborative work.

# **Bibliography:**

- **Lynch M and Force AG** 2000 The Origin of Interspecific Genomic Incompatibility via Gene Duplication. *The American Naturalist 156*: 590–605. https://doi.org/10.1086/316992
- **Duharcourt S, Lepère G and Meyer E** 2009 Developmental genome rearrangements in ciliates: a natural genomic subtraction mediated by non-coding transcripts. *Trends in Genetics* 25: 344–350. <a href="https://doi.org/10.1016/j.tig.2009.05.007">https://doi.org/10.1016/j.tig.2009.05.007</a>
- **Betermier M and Duharcourt S** 2014 Programmed Rearrangement in Ciliates: Paramecium. *Microbiology Spectrum 2*. <a href="https://doi.org/10.1128/microbiolspec.MDNA3-0035-2014">https://doi.org/10.1128/microbiolspec.MDNA3-0035-2014</a>
- Singh DP, Saudemont B, Guglielmi G, Arnaiz O, Goût J-F, Prajer M, Potekhin A, Przybòs E, Aubusson-Fleury A, Bhullar S, Bouhouche K, Lhuillier-Akakpo M, Tanty V, Blugeon C, Alberti A, Labadie K, Aury J-M, Sperling L, Duharcourt S and Meyer E 2014 Genome-defence small RNAs exapted for epigenetic mating-type inheritance. *Nature 509*: 447–452. <a href="https://doi.org/10.1038/nature13318">https://doi.org/10.1038/nature13318</a>
- **Allen SE and Nowacki M** 2017 Necessity Is the Mother of Invention: Ciliates, Transposons, and Transgenerational Inheritance. *Trends in Genetics 33*: 197–207. <a href="https://doi.org/10.1016/j.tig.2017.01.005">https://doi.org/10.1016/j.tig.2017.01.005</a>
- **Rzeszutek I, Maurer-Alcalá XX and Nowacki M** 2020 Programmed genome rearrangements in ciliates. *Cellular and molecular life sciences: CMLS*. <a href="https://doi.org/10.1007/s00018-020-03555-2">https://doi.org/10.1007/s00018-020-03555-2</a>