Master internship
2023-2024
Team Delattre

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Why (and how) do some animal species systematically eliminate portions of their genome in their soma?

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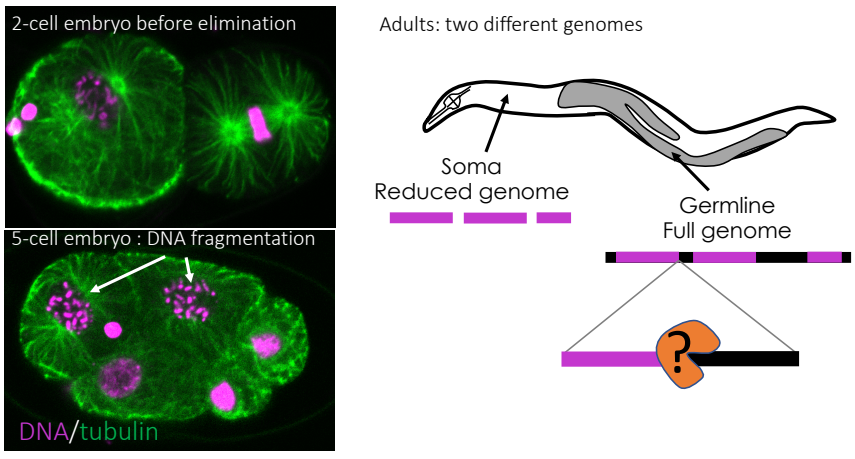
Laboratoire de Biologie et Modélisation de la Cellule
https://www.ens-lyon.fr/LBMC/equipes/NematodeCell

Some species systematically undergo excision and elimination of portions of their genome in somatic cells, in a process called programmed-DNA elimination (PDE) (while the germline cells maintain an intact genome). PDE has emerged multiple times throughout evolution. It has been extensively studied in unicellular Ciliates, which led to breakthrough discoveries on the role of smallRNAs in genome stability (1). In animals, although spotted for the first time in 1887, we still don't know how the genome is scanned and excised at specific locations and what is the ultimate function and PDE (2).

We fortuitously discovered PDE in the free-living nematodes *Mesorhabitis* (3, 4). In contrast to the other animal species so far described, *Mesorhabditis* are genetically tractable. This offers a unique opportunity to, at last, understand the mechanism, the role and the evolution of PDE.



Mesorhabditis nematodes eliminate portions of their genome during development in somatic cells only (in 5-cell stage embryos). The germline-restricted (*i.e.* eliminated) genome (shown in black) contains mainly repeated elements and few genes. The molecular machinery responsible for chromosome breakage is still unknown but the breakpoints are very precise, suggesting a specific nuclease (shown in orange) is involved.

We use a combination of comparative genomics, comparative cell biology and CRISPR/Cas9-based genetics to investigate:

1) the molecular machinery responsible for chromosome breakage and fragmentation: we recently identified a specific motif near breakpoints in one species and are now looking

for the protein(s) that are recruited at this motif to generate double-strand breaks. For this, we generate CRISPR-Cas9 mutants for in vivo analysis and also use in vitro assays with extracts to purify the enzyme(s).

2) the evolution of PDE: we have now a large collection of nematode species with or without PDE. We perform comparative genomics (based on Hi-C and long read Pacbio sequencing) to identify for instance if all species rely on the same motif for elimination and if the same kinds of sequences are eliminated

Techniques used:

The project can be oriented towards bench work, bioinformatics, or a combination of the two, depending on the profile and interest of the applicant.

-Dry lab: Handling 3rd generation (PacBio, Nanopore) and Hi-C sequencing data; genome assembly & annotation; comparative transcriptomics; bioinformatic scripting.
-Wet lab: CRISPR-Cas9 genetics, cytology and high resolution microscopy (single molecule FISH, DNA-FISH, expansion microscopy), biochemistry (DNA pull-down, Co-IP, chromatin-IP)

Contact: send a CV and a cover letter to Marie Delattre marie.delattre@ens-lyon.fr

References (*from the lab)

1. I. Rzeszutek, X. X. Maurer-Alcalá, M. Nowacki, Programmed genome rearrangements in ciliates. Cell. Mol. Life Sci. CMLS. 77, 4615–4629 (2020).
2. J. Wang, R. E. Davis, Programmed DNA elimination in multicellular organisms. Curr. Opin. Genet. Dev. 27, 26–34 (2014).
3. *C. Rey, C. Launay, E. Wenger, M. Delattre, bioRxiv, doi:10.1101/2022.03.19.484980. under revision @ Current Biology
4. *M. Grosmaire, C. Launay, M. Siegwald, T. Brugière, L. Estrada-Virrueta, D. Berger, C. Burny, L. Modolo, M. Blaxter, P. Meister, M.-A. Félix, P.-H. Gouyon, M. Delattre, Males as somatic investment in a parthenogenetic nematode. Science. 363, 1210–1213 (2019).