

## ***In silico* screen for proteins involved in programmed DNA elimination in nematodes**

Host Laboratory / Laboratoire d'accueil

Team: **BPGE (LBBE)**, in close collaboration with team **WORM at LBMC**.

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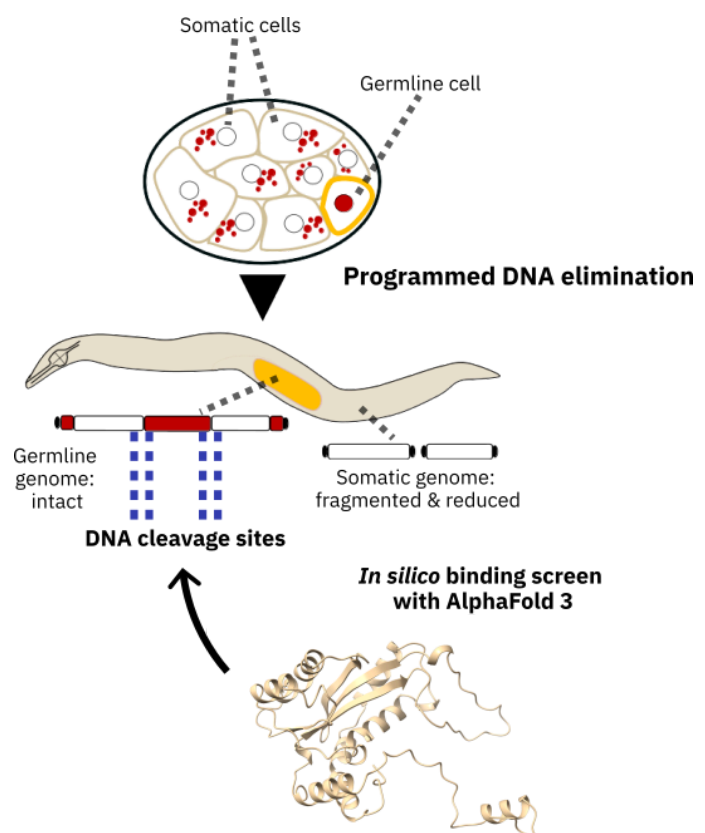
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### **Project Description**

We study the process of programmed DNA elimination (PDE) in nematodes, in which parts of chromosomes are systematically destroyed in the somatic cells of early embryos. This leads to a fragmented and reduced somatic genome; the genome of germline cells, by contrast, remains intact. PDE is surprisingly widespread in animals, but its function, evolution, and molecular mechanisms remain largely unknown.

We are characterising PDE in the genus *Mesorhabditis* of free-living nematodes (1), where we are looking for the molecular effectors of PDE, and in particular, the nuclease responsible for cleaving the DNA during chromosome fragmentation.

In this project, **you will screen a list of candidate effector proteins that we have established**, using prior bioinformatic data (comparative genomics, RNA-Seq). You will test whether these proteins could be involved in PDE **using state-of-the-art large language models such as AlphaFold 3** (2). In particular, you will screen these proteins for possible binding to known sites of DNA cleavage.



## Objectives

- Perform protein-DNA interaction predictions using AlphaFold3, in a high-throughput manner: several hundreds of candidate proteins screened against a number of different DNA motifs. You will develop a bioinformatic workflow to implement this.
- Parse the AlphaFold3 outputs to identify any candidate strong interactions. You will develop Python scripts to analyse the different confidence scores (PAE, pTM, ipTM, ranking score) of the models.
- Visualisation of structural interactions for the best candidates, using ChimeraX or similar software. Annotation of the best candidate proteins (domains, homologs) and characterisation of the interactions surfaces.

## Skills you will develop

- Testing biological hypotheses using structural bioinformatics
- Scripting in python; visualisation in R; workflow development using Nextflow
- In-depth analysis of protein structure and function
- Critical scientific reasoning, in particular, developing appropriate controls to ensure robustness of results.

We are looking for candidates with good experience in bioinformatics: masters-level bioinformatics students or equivalent. **A keen interest in biology, and of the PDE process in particular, is also a must!**

**Keywords:** Structural bioinformatics; programmed DNA elimination; AlphaFold3; *in silico* screens

## References

1. Rey C, Launay C, Wenger E, Delattre M. Programmed DNA elimination in *Mesorhabditis* nematodes. *Current Biology*. 2023 Sep;33(17):3711-3721.e5. <https://doi.org/10.1016/j.cub.2023.07.058>
2. Abramson J, Adler J, Dunger J, Evans R, Green T, Pritzel A, et al. Accurate structure prediction of biomolecular interactions with AlphaFold 3. *Nature*. 2024 Jun;630(8016):493–500. <https://doi.org/10.1038/s41586-024-07487-w>