Project 1.10 The role of transcriptional condensates in regulating embryonic development and stress response

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Background:

Master transcription factors cooperate with chromatin in regulating genomic activity that shapes animal development and regulates responses to stress. Local clustering of transcription factors into dense, sub-micrometer-sized condensates is emerging as a key feature of transcriptional regulation. This includes intranuclear condensates formed by pioneer factors and RNA Polymerase II during development. Despite the ubiquity of these assemblies, we know little about the biophysical mechanism of their formation or physiological function. In the last years, the field of cell biology has been revolutionized by the development of new frameworks to study such transient assemblies, including various types of phase transitions and tools to probe and modulate them. However, most research in this area has been limited to cell culture and in vitro experiments that suffer from many artifacts. Studying transcriptional condensates in a context of a whole organism would let us probe their importance for physiological functions and for organism fitness.

Aim:

The aim of the project is to investigate the processes governing the spatial organization of transcription during embryonic development and during stress response in Caenorhabditis elegans embryos. This small, transparent model organism is ideal for studying fundamental cellular processes due to the many transgenic techniques available (including CRISPR), as well as ease of cultivation and microscopic imaging. We will analyze the dynamics of condensates formed by fluorescently labeled transcription factors and cofactors during embryonic development using a dedicated state-of-the-art super-resolution live imaging system. The project also includes phase separation assays on purified proteins that will uncover the sequence determinants of the phase behavior and allow linking it to the function of the protein in a whole organism. We will apply high-throughput methods such as mass spectrometry and RNA sequencing to determine the molecular composition of condensates and their role in regulating gene expression. The obtained results will provide an unprecedented insight into the composition, assembly mechanism, and physiological relevance of biomolecular condensates formed by the transcriptional apparatus during differentiation and stress response.

Requirements:

- A master's degree (or an equivalent) in molecular biology, molecular biomedicine, biochemistry, medicine, genetics, bioinformatics, or biotechnology
- excellent written and spoken English,
- excellent scientific track record in relation to career stage,
- good organizational skills,
- strong motivation and ability to drive the project independently,
- well-developed collaborative skills,
- knowledge of the standard molecular biology and biochemistry techniques,
- curiosity for the discovery of biological processes