Project 1.8 The role of transcriptional condensates in regulating embryonic development and stress response

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Background:

During animal development, the initially undifferentiated cells divide and gradually specialize into tissues. This process is steered by specialized transcription factors that bind to regulatory regions in DNA and activate specific genes leading to cell fate determination. Gene activation occurs by recruiting enzymes and transcriptional cofactors that collectively catalyze mRNA production. How the interactions between transcription factors, cofactors and chromatin lead to precise control of an extremely complex genome are key questions in cell biology and development. Microscopic examination revealed that proteins needed to activate transcription, such as the Mediator and RNA Polymerase (RNA Pol-II) complexes, form dense condensates at the sites of gene activation during differentiation. Biomolecular condensates are membrane-free intracellular assemblies that are formed by phase separation and are capable of concentrating biopolymers. These transcriptional condensates organize transcription into nuclear domains during cell cycle, in development and in response to hormonal signaling. Another example of condensates are nuclear stress bodies that form in the cell nucleus of eukaryotes at high temperature or in an unfavorable chemical environment. Despite much research, how genetic and environmental factors regulate the formation and properties of nuclear condensates and their role in regulating embryonic development and stress response remains still poorly understood.

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, and ease of cultivation and microscopic imaging. We will study condensates formed by transcription factors and RNA Pol-II as well as nuclear stress bodies using confocal microscopy. We will identify the most important components of these condensates using transgenic tools such as CRISPR / Cas9 and characterize their dynamics during the cell cycle and throughout the entire embryonic development. The project includes functional studies such as cell reprogramming and thermotolerance tests, as well as molecular studies such as gene expression analysis and chromatin immunoprecipitation. We will perform RNA interference screens to identify genes that regulate the spatial organization of transcription. We will also use optogenetic tools to precisely control the formation and properties of condensates and examine how it affects the functions of the proteins studied. Experiments on nematodes will be complemented by biochemical and biophysical studies on recombinant purified proteins. The innovative and interdisciplinary scope of the project, which includes high-resolution imaging, optogenetics and in vitro condensate reconstruction in vitro, will provide a new insight into the basic mechanisms regulating gene expression during embryonic development and stress response. Project funded by NAWA Polish Returns (BPN/PPO/2021/1/00026/U/00001).

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