Research Project

The role of DEAD-box ATPases in the regulation of membraneless RNA organelles and spatio-temporal control of gene expression.

Third-party funded project

Project title The role of DEAD-box ATPases in the regulation of membraneless RNA organelles and spatio-temporal control of gene expression.
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Background: Gene expression is central to any process in life, and every (m)RNA processing step is tightly regulated by specific macromolecular complexes. However, we still know little how processing is orchestrated in a temporal and spatial manner, and how this affects gene expression. In recent years, the concept of liquid-liquid phase separation (LLPS) has revolutionized our understanding of molecular processes in cell biology: rapid and regulated formation of membraneless organelles reversibly compartmentalizes cellular components and creates highly dynamic biochemical reaction environments. During my postdoc, I discovered that bacterial, yeast and human RNA-dependent DEAD box ATPases (DDXs), abundant enzymes that chaperone every aspect of RNA life, undergo RNA-dependent LLPS in vitro and are critical regulators of membraneless organelle formation in vivo. These compartments control the accumulation of RNA molecules and selectively enrich for RNA processing factors.

Rationale: I postulate that recruitment of RNA into DDX-compartments is a general, novel and conserved mechanism that controls the spatio-temporal flux of mRNA molecules between different steps of maturation and function.

Objectives: Chaperoning mRNAs into phase-separated compartments opens up a novel layer of gene expression regulation, and in my future research, I want to study the molecular mechanisms, cellular function and universality of this phenomenon.

Specific Aims: I will investigate how formation of two cytoplasmic DDX granules, P-bodies and stress granules, affects mRNA translation and turnover in vivo, and how DDX compartments influence remodelling of RNA-protein complexes in vitro. Moreover, I will probe the generality of my hypothesis and dissect which of the 65 human DDXs control formation of membraneless RNA compartments, how these enzymes are regulated by MIF4G domains, and quantify the influence of novel DDX compartments on gene expression.

Keywords RNA, phase separation, DEAD-box ATPases

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