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Investigating actin nucleation through active phase separation

In the cytoplasm, proteins observed in liquid-like phases are thought to contribute to compartmentalization of the cytoplasm. However, it is unclear whether demixing of cytoskeletal components could also play a role in partitioning actin nucleators to the membrane during the formation of an actomyosin cortex. Members of the N-Wasp Cdc-42 Arp2/3 nucleation pathway contain intrinsically disordered domains, and have been shown to undergo liquid-liquid phase separation in vitro. However, it is unclear whether the F-actin nucleation module can undergo phase separation in vivo to promote local enrichment of nucleators. During actomyosin cortex formation in the C. elegans oocyte to zygote transition, I observed biphasic cortical F-actin network condensation during Meiosis. In addition to regulated clustering of the N-Wasp pathway components N-wasp and Arp2/3. To investigate the role of F-actin phase separation in vivo, I aim to first characterize and confirm liquid-like behaviour of the actin nucleators in C. elegans embryos. Then I will identify the molecular interactions necessary for cortical clustering of nucleators. Lastly, I will identify the biological role of the nucleation clustering by decoupling localization of function of the nucleators. These findings suggest that cortical dynamics during morphogenesis may be controlled through regulated phase separation of actin nucleators.

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