

Unraveling the Role of Calcium in Modulating the Structure and Phase Behavior of Annexin A11

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Abstract

Annexins are calcium-dependent proteins that bind to phospholipids and play key roles in maintaining organismal health and cellular homeostasis. They are implicated in diverse biological processes, including cell signaling, apoptosis, vesicle trafficking, and membrane repair. Annexin A11 (AnxA11), a unique member of this family, possesses an unusually long and intrinsically disordered N-terminal domain, which is essential for its ability to form biomolecular condensates, and has been linked to various pathological conditions. Notably, multiple ALS-associated mutations have been identified within this disordered region of the protein, highlighting its potential relevance in neurodegenerative disease. These mutations promote intracellular aggregates and may disrupt calcium homeostasis. Despite increasing interest, the functional implications of AnxA11's interaction with calcium ions, particularly in modulating its disordered domain and condensate behavior, remain poorly understood. This project aims to elucidate the biophysical and structural consequences of calcium binding to AnxA11. Circular dichroism analysis revealed that AnxA11 undergoes significant structural changes upon calcium binding, altering its spectral profile and thermal stability. Microscopy studies further demonstrated that calcium modulates AnxA11's propensity to undergo phase separation: at low concentrations, it enhances condensate formation, while at higher levels, it triggers a reversible transition from a liquid to a solid-like state. Ongoing investigations reveal that ALS-related mutations alter the dynamics of condensate formation and maturation. These findings offer new insights into the calcium-dependent regulation of AnxA11 and its potential role in ALS pathogenesis.

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Programme

16:00 to 16:45 on 11/05/2025

Tucuns/Tartaruga

Institutions

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Track

- Protein structure, function, conversion, and dysfunction

Keywords

Intrinsically Disordered Domain

Biomolecular condensates

AnnexinA11

Calcium

ALS