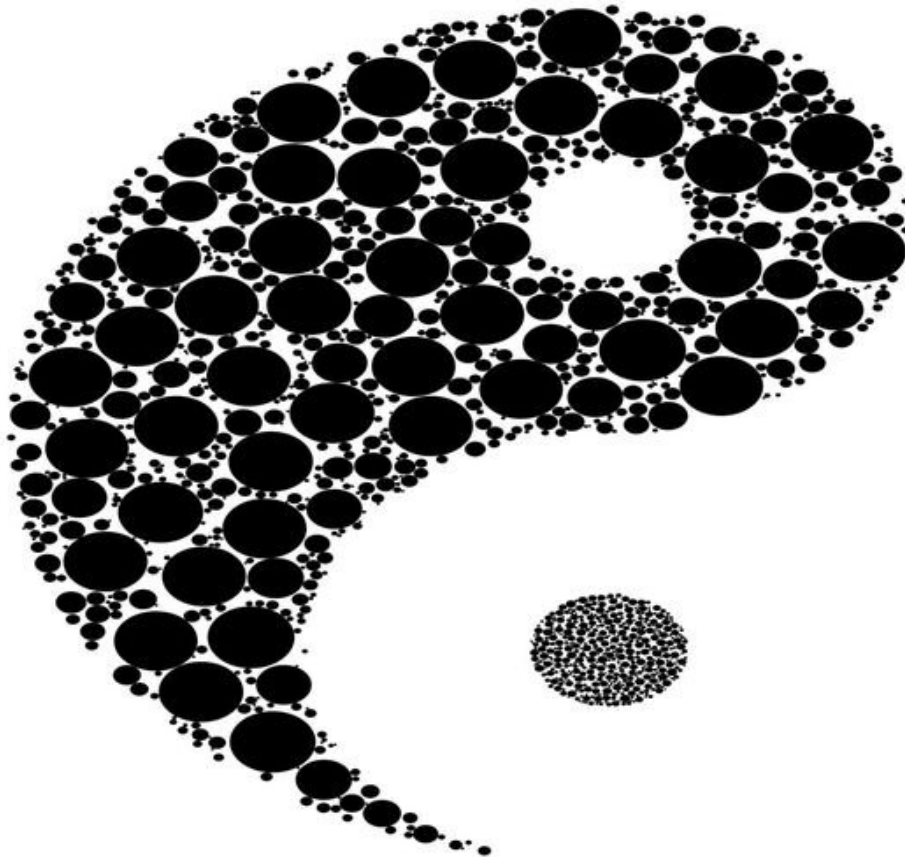


Researchers reveal 'Yin and Yang' mechanisms of stress granules by Caprin-1

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In a study published in *PNAS*, a research team led by Prof. Gong Weiming from the University of Science and Technology (USTC) of the

Chinese Academy of Sciences and his collaborators revealed the "Yin and Yang" regulation of stress granules (SGs) by Caprin-1.

SGs are a type of biomolecular condensation that forms when cells are faced with stress stimuli like heat shock and osmotic pressure. When ubiquitin-specific peptidase 10 (USP10) and Caprin-1 bind to the nuclear transport factor 2-like (NTF2L) domain of Ras GTPase-activating protein-binding protein 1 (G3BP1), Caprin-1 facilitates the formation of SGs while USP10 suppresses the process. However, the mechanisms of the two proteins regulating the processes remain unknown.

By utilizing NMR spectroscopy and isothermal titration calorimetry, the researchers bound the G3BP1 NTF2L to the G3BP1-interacting motif (GIM) of Caprin-1 and USP10, and analyzed their crystal structures, respectively. They discovered that both the Caprin-1 GIM and the USP10 GIM bind to the same hydrophobic pocket on G3BP1, which acts to inhibit the G3BP1 liquid–liquid phase separation (LLPS). The findings indicated that another domain of Caprin-1 may promote LLPS.

Then, the team dissected Caprin-1 into [different domains](#), and studied their functions in the LLPS of G3BP1 in vitro and SG formation in cells. They found that the C-terminal domain (CTD) of Caprin-1 could induce spontaneous LLPS in vitro, but the N-terminal domain (NTD) restrained LLPS.

The results demonstrated the "Yin and Yang" mechanisms of NTD and CTD of Caprin-1 when the disassembly and assembly of SGs were regulated.

As SGs are implicated in pathological processes like cancer pathogenesis and progression and [neurodegenerative diseases](#), the research lays a solid theoretical foundation for SGs control and provides a potential way to

treat related diseases.

More information: Dan Song et al, Yin and yang regulation of stress granules by Caprin-1, *Proceedings of the National Academy of Sciences* (2022). [DOI: 10.1073/pnas.2207975119](https://doi.org/10.1073/pnas.2207975119)

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