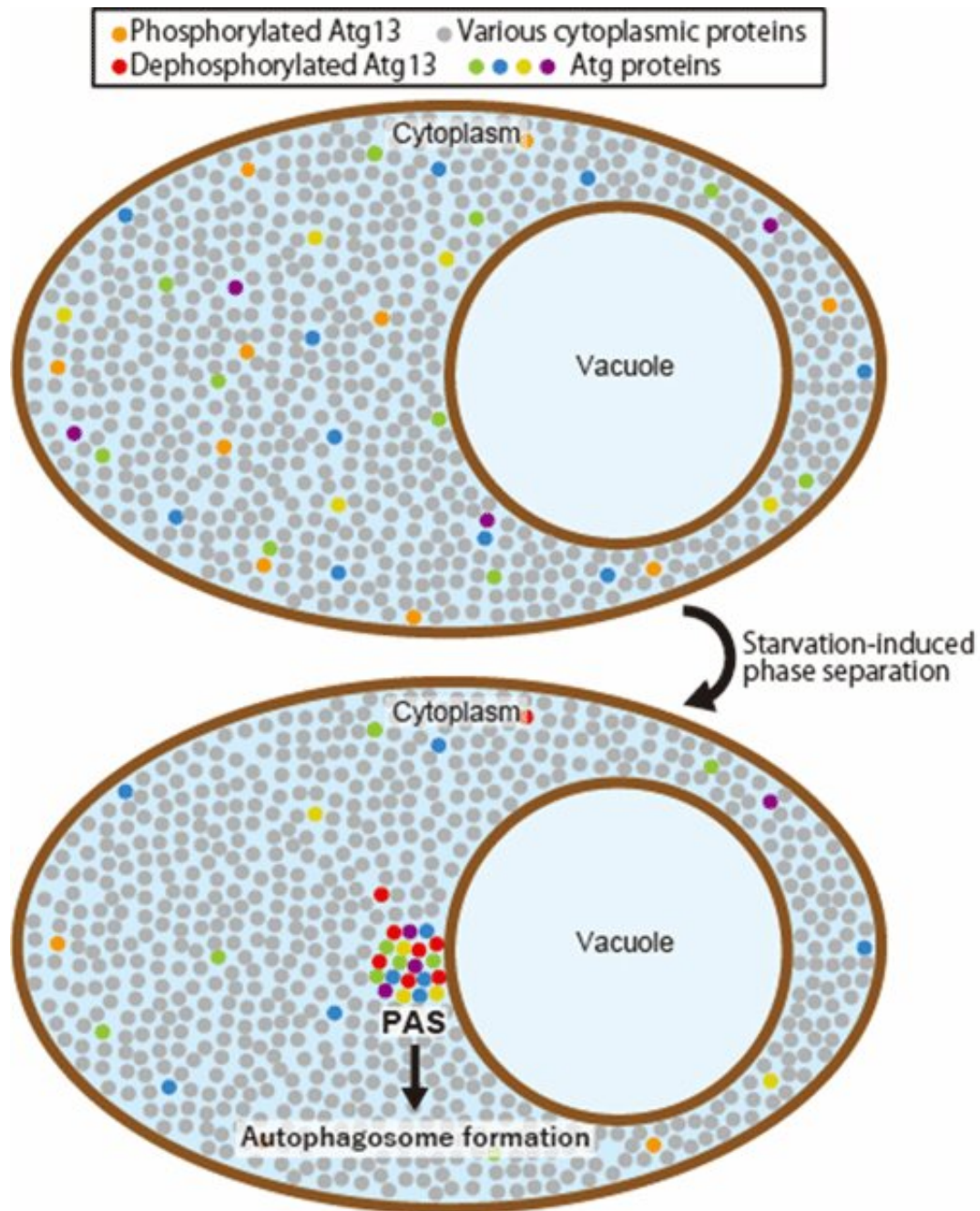


Mechanism of controlling autophagy by liquid-liquid phase separation revealed

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Model of PAS organization via liquid-liquid phase separation. Under nutrient-rich conditions, Atg proteins are dispersed and mixed with various proteins in the cytoplasm. Upon starvation, Atg13 is dephosphorylated, which triggers the phase separation of Atg13 with other Atg proteins to form a liquid droplet on the vacuolar membrane, where autophagosome formation proceeds. Credit: Japan Science and Technology Agency

Under JST's Strategic Basic Research Programs, Noda Nobuo (Laboratory Head) and Fujioka Yuko (Senior Researcher) of the Institute of Microbial Chemistry, in collaboration with other researchers, discovered that a liquid-like condensate (liquid droplets) in which the Atg protein is clustered through the liquid-liquid phase separation is the structure responsible for the progression of autophagy.

Autophagy is one of the mechanisms through which cellular protein is degraded. Previously, it was known that Atg proteins assemble to form a structure called PAS . However, the [mechanism](#) through which Atg proteins assemble and the physicochemical property of the formed structures had been unclear.

The research team elucidated characteristics of PAS through observing the Atg protein using a [fluorescence microscope](#) and successfully reconstituted PAS in vitro. The team revealed, for the first time, that PAS is in the state of [liquid droplets](#) formed by [liquid-liquid phase separation](#) of Atg13 together with other Atg proteins and that this liquid droplet is responsible for autophagy.

The finding that liquid-liquid phase separation directly controls autophagy suggests its involvement in a wide range of intracellular life phenomena. Reconsideration of molecular mechanisms underlying

various intracellular phenomena is expected to proceed. Moreover, development of autophagy-specific control agents that focus on the regulation of liquid-liquid phase separation in autophagy-related diseases is anticipated.

More information: Yuko Fujioka et al, Phase separation organizes the site of autophagosome formation, *Nature* (2020). [DOI: 10.1038/s41586-020-1977-6](https://doi.org/10.1038/s41586-020-1977-6)

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