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Dissecting the mechanisms of liquid to solid phase transition associated with neurodegenerative diseases

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FUS/TLS is a prion-like protein that contains intrinsically disordered domains and is associated with neurodegenerative disease. We recently showed that intracellular FUS/TLS compartments form under various cellular conditions and that these compartments exhibit liquid-like properties *in vivo* and *in vitro*. "Aging" experiments revealed that FUS/TLS liquid droplets undergo a phase transition to a solid-like state which is accelerated by disease mutations. We discovered that concentrating proteins by phase separation comes with the trade-off that can also promote protein aggregation. Solid-like aggregates of prion-like proteins are a hallmark of many aging-associated diseases. Aberrant phase transitions might be one trigger causing aging-associated diseases. However, the molecular mechanisms underlying this aberrant phase transition and the strategies cells have developed to sustain the function of these aggregation-prone proteins remain largely enigmatic. Here, we present recent advances we made in understanding the mechanisms cells might have developed to prevent the liquid-solid phase transitions by using a wide range of biochemical, biophysical and cell biology techniques. We find that electrolytes, small compounds and protein interactors affect the liquid-liquid, as well as liquid-solid transitions. Insights gained from studying liquid-solid phase transition might help us developing drugs targeted to treat age-associated diseases.

Biography

Avinash Patel has completed his PhD from the Manchester Cancer Research Institute, UK in 2012. He is currently pursuing Post doctoral research in the lab of Prof Tony Hyman, Max Planck Institute for Cell Biology and Genetics, Dresden, Germany. He has recently published a paper in the journal Cell, which showed general principles underlying Liquid-to-Solid phase transitions might be a key mechanism behind neurodegenerative diseases.

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