Text or Talk?

A Liquid-to-Solid Phase Transition of the ALS Protein FUS Accelerated by Disease Mutation

Many proteins contain disordered regions of low-sequence complexity, which cause aging-associated diseases because they are prone to aggregate. Here, we study FUS, a prion-like protein containing intrinsically disordered domains associated with the neurodegenerative disease ALS. We show that, in cells, FUS forms liquid compartments at sites of DNA damage and in the cytoplasm upon stress. We confirm this by reconstituting liquid FUS compartments in vitro. Using an in vitro "aging" experiment, we demonstrate that liquid droplets of FUS protein convert with time from a liquid to an aggregated state, and this conversion is accelerated by patient-derived mutations. We conclude that the physiological role of FUS requires forming dynamic liquid-like compartments. We propose that liquid-like compartments carry the trade-off between functionality and risk of aggregation and that aberrant phase transitions within liquid-like compartments lie at the heart of ALS and, presumably, other age-related diseases.

	text	talk
Personal introductions		
Humour		
Rapport-building		
Basic examples		
Basic definitions		
Complex definitions		
Techniques / equipment		
Research rationale		
Results		
Reactions to results		
Reported dialogues		
Wider implications		

Excerpt 1 **00:47**

in our biology textbooks we learn about organelles that are surrounded by membranes but there are many compartments in the cell without membranes these compartments are a way for cells to concentrate components for a wide variety of biochemical reactions, and it turns out they form through a process of liquid-liquid de-mixing or phase separation we can think of this much like how oil and vinegar separate from each other in a vinaigrette to keep this liquid state the proteins inside compartments have to be able to slither around over each other easily but a crucial question is what kinds of proteins have this behaviour

Excerpt 2 **02:02**

to test whether FUS forms liquid compartments we use the following criteria: first a steady state without any external deforming force liquid droplets assume spherical shape second molecules within liquid droplets move around freely and rearrange third liquid droplets that come close to each other fuse and become one larger droplet to look at this we used a new microscope built for us by Jean Myers and his lab we found that both FUS compartments in the cell and those in a test-tube do meet these criteria FUS droplets are spherical and molecules move around within these droplets we also see FUS droplets fuse so it was clear to us that FUS normally behaves like a liquid.