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« Phase separation of a virulence factor in Mycobacterium tuberculosis »

Protein phase separation or liquid-liquid demixing is an important mechanism of compartmentalization in eukaryotic cells, creating specialized reaction and signaling environments by assembly of separated protein-rich phases and clusters. It has been shown to be biologically relevant in eukaryotic cells in a wide variety of processes such as RNA processing and T-Cell receptor signalling. Despite the fact that liquid liquid demixing has so far only been reported in eukaryotes, certain prokaryotic systems also possesses the two main characteristics associated with protein phase separation, weak interactions and multivalency. Here, we show that the cytoplasmic part of a transmembrane virulence protein of *Mycobacterium tuberculosis*, which contains two phospho-interacting domains, undergoes phase separation into liquid droplets with commonly reported dynamic characteristics upon phosphorylation by several serine threonine kinases from *Mtb*. Phase separation is reversible by the *Mtb* serine threonine phosphatase PstP. Furthermore, we show that the linker connecting the phospho-interacting domains by itself possesses the ability to phase separate at higher concentrations, pointing to a synergy between classical modular interactions and weak self-association of a disordered region. Our results suggest that protein phase separation plays a role in phospho-dependent clustering of a transmembrane protein in *Mtb* that is important for its virulence. Furthermore, we show that phase separation is a mechanism also utilized in bacteria, posing exciting avenues of research and new challenges to microbiology.