Protein aggregation is a multiple step process that involves misfolded soluble and insoluble aggregates. These molecular events have been associated with a variety of diseases that are termed as protein misfolding diseases. To meet this need, I will present a novel AggTag (Aggregation Tag) imaging method and two types of fluorogenic AggTag small molecule probes, with a goal to directly monitor the entire protein aggregation process in live cells, in particular the intermediate misfolded oligomers. The AggTag method and probes have been applied to reveal folding states of RNA-binding proteins in membraneless granules during their formation and maturation, providing new mechanisms underlying how cells use these granules to manage proteins in stressed conditions. This work potentiates future studies on chemical biology of protein aggregation in various types of membraneless organelles and stressed proteome.