Designer biomolecular condensates formed by peptide liquid-liquid phase separation.

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Most biocatalytic processes in eukaryotic cells are regulated by subcellular microenvironments such as membrane-bound or membranelles organelles. These natural compartmentalization systems inspired the design of synthetic compartments composed of a variety of building blocks. Recently, the emerging field of liquid-liquid phase separation facilitated the design of biomolecular condensates that are formed by proteins and nucleic acids, with most efforts been made towards controlling the properties of designer biomolecular condensates including polarity, diffusivity, surface tension and encapsulation efficiency. However, utilizing phase separated condensates as optical sensors has not been explored to date. Here, we have designed a library of LLPS-promoting peptide building blocks composed of various assembly domains. We show that the LLPS propensity, dynamics, and encapsulation efficiency of compartments can be tuned by changes to the peptide composition. Inspired by the biosynthesis of melanin pigments, a key biocatalytic process that is regulated by compartmentalization in organelles, we utilized the minimalistic biomolecular condensates as both microreactors and precursors of tyrosinase. Thus, upon partitioning of tyrosinase into the condensates and their subsequent oxidation-polymerization, the condensates gain unique optical properties including far-red fluorescence. We show that individual condensates can serve as sensors to detect tyrosinase activity. This approach opens opportunities to utilize designer biomolecular condensates as a diagnostic tool for various disorders involving abnormal enzymatic activity.