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# **PopTag: A modular platform for engineering function of natural and synthetic biomolecular condensates**

Researchers at Stanford have developed a protein, PopTag, that drives phase separation when it is part of a chimeric fusion protein.

Biomolecular condensation is a powerful mechanism underlying cellular organization and regulation in cell physiology and disease. Biomolecular condensates can adopt a broad spectrum of material properties, from highly dynamic liquids to semi-fluid gels and solid amyloid aggregates. Perturbing protein condensation and other pathological phase transitions have been implicated in human disease, indicating that the material properties of a biomolecular condensate may be important for its function.

## **Stage of Research**

The inventors have created PopTag, a modular and functionalizable platform for designer condensates with tunable material properties. PopTag, a C-terminal protein tag of only 76 amino acids, is derived from the intrinsically disordered protein PopZ, which forms membraneless condensates in the bacterium *Caulobacter crescentus*. The inventors generated rationally designed PopZ mutants to codify a robust set of design principles used to repurpose PopZ as a modular platform for generating synthetic condensates of tunable function in prokaryotic and eukaryotic cells. Moreover, they developed EGFP-NanoPop, an N-terminal fusion with an EGFP-targeting nanobody to efficiently sequester EGFP-tagged proteins into cytoplasmic condensates. Together, PopTag provides a flexible platform for the design and manipulation of condensate properties and function.

## **Applications**

- Generation of synthetic phase separated protein droplets in prokaryotic and eukaryotic cells and organisms
- Recombinant protein purification as phase-separated bodies
- Selective protein sequestration for therapeutic benefit or to perturb cellular pathways
- Compartmentalization of biochemical reactions (e.g., TurboID fusions) to optimize yield, specificity, and off-target reactions

## Advantages

- Modular and versatile design of chimeric fusions to facilitate various cellular localizations, inducible expression and/or degradation, and biochemical functionalities
- NanoPop, nanobody PopTag fusions, efficiently sequester proteins into cytoplasmic condensates

## Publications

- Lasker K, Boeynaems S, Lam V, Stainton E, Jacquemyn M, Daelemans D, Villa E, Holehouse AS, Gilter AD, Shapiro L. [A modular platform for engineering function of natural and synthetic biomolecular condensates.](#) bioRxiv. 2021.

## Innovators

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