

# Multi-Purpose Hyper-Stable Fluorescent Proteins

## Lead Inventors:

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## Background & Unmet Need

- Fluorescent proteins (FPs) are used for a broad range of biology research applications, including as reporters of gene activity and to visualize proteins in live cells
- Most FPs lack the ability to withstand the adverse conditions in the cell that rapidly denature biological structures, including superfolder GFP
- Modern microscopy techniques such as CLEM and ExM, place even greater demands on FPs due to secondary fixation and staining chemicals such as osmium tetroxide that degrade protein functionality
- Most widely used FPs are susceptible to misfolding due to exposure to higher temperatures for a greater lengths of time and photo bleach quickly
- **Unmet Need:** There is a need for stable FPs that can withstand chaotropic conditions and may be used for various biochemical applications

## Technology Overview

- **The Technology:** Development of extremely stable FPs that withstand chaotropic conditions
- The engineered FPs Hyperfolder YFP (hfYFP) and LSSmGFP successfully survive CLEM sample preparation and ExM techniques
- hfYFP contains no cysteines, is chloride insensitive, and tolerates aldehyde and osmium tetroxide fixation better than common FPs
- The robust nature of hfYFP and LSSmGFP make them ideal FPs for the development of biosensors
- **PoC Data:** The chemical stability of hfYFP was employed to devise a fluorescence-assisted protein purification strategy, enabling all steps of denaturing affinity chromatography to be visualized using UV or blue light

## Inventors:

Benjamin Campbell  
Gregory Petsko

## Patents:

Provisional Filed

## Publications:

[Campbell et al. \*Nature Methods\*. 2022.](#)

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## Cornell Reference:

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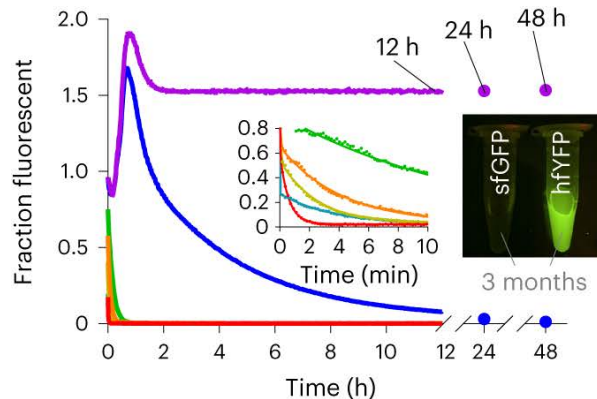
## Technology Applications

- Fluorescence-assisted protein purification
- Live cell imaging and the development of improved biosensors
- Stable FPs for use with CLEM and ExM techniques

## Technology Advantages

- Compatible with osmium tetroxide and aldehyde fixation protocols
- Chloride insensitive
- Improved acid resistance
- Greater thermodynamic stability and faster refolding than existing FPs

## Supporting Data / Figures



**Figure 1:** Hyperfolder YFP (hfYFP) is a highly stable fluorescent protein that retains fluorescence for up to three months and is stable in chaotropic conditions.

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