Weill Cornell Medicine

Live Cell Imaging using RNA-Stabilized Fluorogenic Proteins

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Background & Unmet Need

- RNA imaging with fluorescent microscopy enables the study of RNA localization and spatiotemporal dynamics
- One technique involves the use of fluorogenic RNA aptamers, which induce fluorescence by binding not otherwise nonfluorescent molecules
- However, there are currently few fluorogenic dyes compatible with live cell imaging, as they must be added exogenously and often display nonspecific fluorescence activation by cellular lipids or DNA
- **Unmet Need:** Inducible RNA imaging system compatible with live cells

Technology Overview

- **The Technology:** A method for imaging mRNA using genetically encoded fluorogenic proteins that are specifically activated by an RNA aptamer named “Pepper”
- The inventors converted constitutively active fluorescent proteins, such EYFP and mNeonGreen, into conditionally fluorescent proteins through incorporation of a degradation tag (tDEG) that contains an RNA-binding site
- In the absence of Pepper RNA, tDeg-tagged proteins are rapidly degraded, enabling RNA-dependent imaging with fluorescent proteins
- **PoC Data:** EYFP-tDEG construct exhibits 38-fold increase in fluorescence in presence of Pepper RNA
- Doesn’t require addition of nuclear localization elements to the fluorescent protein
- Ideal tool for tracking and quantifying RNA expression in live cells

Inventors:
Samie R. Jaffrey
Jiahui Wu

Patents:
US Application Filed
EP Application Filed

Publications:
Wu et al. *Nature Methods.* 2019.

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Technology Applications

- Visualization and imaging of cellular mRNA using standard microscopy techniques
- Temporal measurement of RNA expression
- Screening for novel RNA-binding proteins in live cells
- Tunable regulation of protein expression for synthetic biology applications

Technology Advantages

- Minimal impact to mRNA turnover rates and translation efficiencies
- Compatible with numerous fluorogenic proteins, providing a wide range of spectral properties
- Regulated reporter degradation delivers low background fluorescence

Supporting Data / Figures

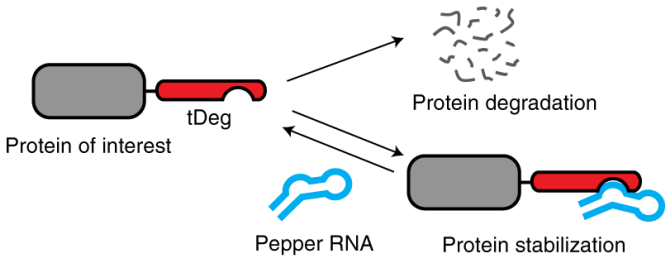

Figure 1: Addition of an RNA aptamer-specific degradation tag (tDEG) transforms fluorescent proteins into fluorogenic proteins for mRNA imaging in live cells.

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