"SPARK (Separation of Phases-based Activity Reporter of Kinase)"_A Genetically-encoded Fluorescent Reporter Platform for Studying Cell Signaling in Living Cells

Tech ID: 29105 / UC Case 2018-007-0

INVENTION NOVELTY

This novel class of genetically-encoded fluorescent reporters can be used as powerful tools to study protein-protein interactions (PPIs) in living cells. These bright, reversible reporters have a large dynamic range and fast kinetics, demonstrating significant advantages over traditional FRET-based fluorescent reporters.

VALUE PROPOSITION

Studying protein-protein interactions in living cells reveals critical information about cell signaling dynamics and cellular mechanisms in both normal and disease conditions. Genetically-encoded fluorescent reporters are ideal for these purposes because they allow non-invasive imaging. However, many PPI reporters, including Fluorescence Resonance Energy Transfer (FRET)-based reporters, have limited dynamic range because of their small fluorescence ratio change of acceptor over donor fluorophores. Transcription-based PPI reporters have poor temporal dynamics, at the timescale of hours, and are not reversible. Therefore, there is a great need for improved fluorescent reporters for imaging of dynamic cell signaling processes and PPIs.

ADVANTAGES OF THE TECHNOLOGY:

- **Modular platform** enables highly customizable reporter design
- **Fast kinetics, large dynamic range (fluorescence change), intense brightness, and simple signal pattern** enables quantitative and robust visualization of PPIs
- **Rapid and reversible** system allows investigation of protein-protein dissociation/inactivation kinetics
- **Applicable to live cells** so that PPIs are detected in the biological context

TECHNOLOGY DESCRIPTION

The Shu lab at UCSF has developed a novel class of genetically-encoded fluorescent reporters that phase separate upon protein interaction. Dubbed SPARK (Separation of Phases-based Activity Reporter of Kinase), the modular platform can be easily customized to test a large array of interacting proteins. Short peptide Homo-oligomeric Tags (HO-Tags) and a fluorescent protein (e.g. GFP), are genetically fused to proteins of interest, which introduces multivalency. Upon interaction of proteins, the multivalent PPI leads to GFP phase separation, resulting in highly concentrated droplets (reversible upon PPI inhibition), forming bright puncta within the cell.

CONTACT

Lei Wan

lei.wan@ucsf.edu

tel: .



INVENTORS

- Shu, Xiaokun
- Zhang, Qiang

OTHER INFORMATION

KEYWORDS

Genetically-encoded reporter, Protein-protein interaction, Cell signaling, Cell assay, Fluorescent reporter, GFP

CATEGORIZED AS

- **Research Tools**
  - Nucleic Acids/DNA/RNA
  - Screening Assays

RELATED CASES

2018-007-0

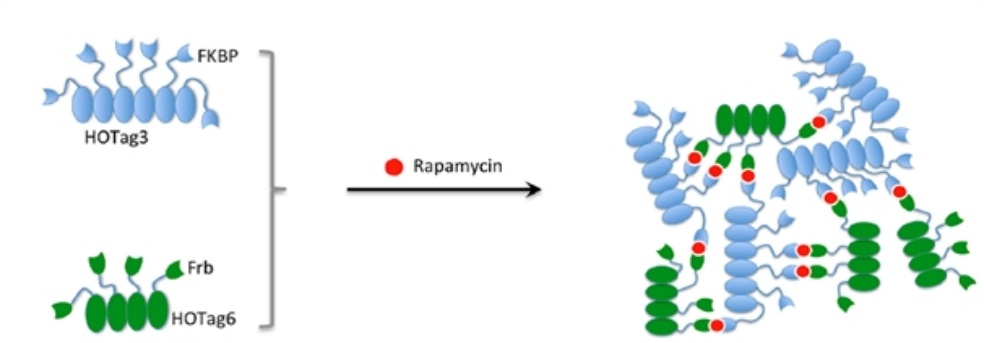
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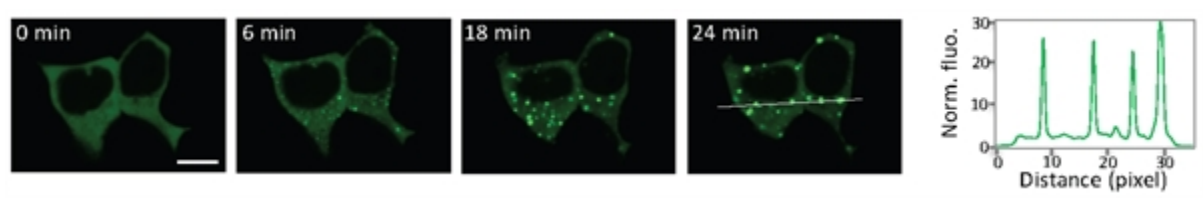
To develop & commercialize the technology as a tool for drug discovery and research.

STAGE OF DEVELOPMENT

Proof of Concept

DATA AVAILABILITY





RELATED MATERIALS

- Zhang, Q., Huang, H., Lu, Q., Wu, R., Chung, C. I., Zhang, S. Q., ... & Shu, X. (2018). Visualizing Dynamics of Cell Signaling In Vivo with a Phase Separation-Based Kinase Reporter. Molecular Cell.

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	11,448,654	09/20/2022	2018-007

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- A Novel Reversible Fluorescent Protein Complementation Assay for Imaging of Protein-protein Interactions

ADDRESS

UCSF

Innovation Ventures

600 16th St, Genentech Hall, S-272,

San Francisco,CA 94158

CONTACT

Tel:

innovation@ucsf.edu

https://innovation.ucsf.edu

Fax:

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