

INFRARED FLUORESCENT PROTEASE REPORTERS FOR DEEP TISSUE IMAGING

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INVENTION NOVELTY

This invention includes the design and use of protease imaging reporters which can be detected in deep tissue. These can be used to monitor the effects of protease inhibitors, proteases and protease mediated processes including apoptosis related to the treatment of disease states such as cancer.

VALUE PROPOSITION

Proteases play key roles in many diseases, such as cancer, HIV, HCV, Parkinson’s disease, and Huntington’s disease. The ability to better monitor protease activity *in vivo* would lead to improved treatments and treatment outcomes. Current commercially available protease assays rely on systems whereby protease cleavage causes a loss of quenching signal and result in high background. However, iProtease, a genetically encoded system which uses infrared fluorescent proteins, results in a gain of signal upon proteolysis. Additional advantages of this invention are:

- ▶ No exogenous molecules such as chemical dyes
- ▶ Protease **specificity**
- ▶ Safe for **biological** assays
- ▶ **Improved** contrast over fluorescent dye-based labeling systems
- ▶ **Visualize** protease activity in the **deep tissue** of live animals
- ▶ Facilitate **drug discovery screenings** of protease inhibitors in animal models
- ▶ Tissue-specific and whole-animal **imaging optimization**

TECHNOLOGY DESCRIPTION

Scientists at UCSF have developed an infrared fluorescent imaging reporter, iProtease, for the detection of protease activity in cells and animals. The reporter becomes fluorescent only when activated by a protease, creating better contrast than GFP-based fluorescence resonance energy transfer-based systems, as well as fluorescent dye-based

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OTHER INFORMATION

KEYWORDS

Infrared, Protease, Sensor, Apoptosis, Imaging

CATEGORIZED AS

- ▶ **Biotechnology**
 - ▶ Genomics
 - ▶ Other
- ▶ **Medical**
 - ▶ Delivery Systems
- ▶ **Research Tools**
 - ▶ Screening Assays

RELATED CASES

2014-059-0

labeling systems. The iProtease system is versatile and can be easily used to design specific protease reporters by genetically designing their cleavage sequence into the iProtease construct. It has been successfully used in designing the executioner caspases (caspase 3 and 7), TEV protease and hepatitis C virus (HCV) NS3/4A protease. These fluorogenic protease reporters have successfully and specifically detected caspase 3/7, TEV protease, and NS3/4A protease activity in live cell systems as well as in small animals.

APPLICATION

- ▶ Protease inhibitor drug screening
- ▶ Research tool for monitoring protease activity in live cell and animal systems
- ▶ Cell lines and transgenic animals can be created expressing the imaging reporter

LOOKING FOR PARTNERS

To develop and commercialize this technology as a research tool for proteases and protease inhibitors for therapeutic or industrial applications

STAGE OF DEVELOPMENT

Preclinical

RELATED MATERIALS

- ▶ [To, T.-L., Piggott, B. J., Makhijani, K., Yu, D., Jan, Y.-N., & Shu, X. \(2015\). Rationally designed fluorogenic protease reporter visualizes spatiotemporal dynamics of apoptosis in vivo. PNAS, 112\(11\), 3338–3343.](#)

DATA AVAILABILITY

Under NDA/CDA

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	10,201,282	02/12/2019	2014-059

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- ▶ [A Novel Reversible Fluorescent Protein Complementation Assay for Imaging of Protein-protein Interactions](#)
- ▶ [“SPARK \(Separation of Phases-based Activity Reporter of Kinase\)”_A Genetically-encoded Fluorescent Reporter Platform for Studying Cell Signaling in Living Cells](#)

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