Optogenetic Control of the Integrated Stress Response

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BACKGROUND

The Integrated Stress Response (ISR) is a conserved signaling network that allows cells to detect and react to cell-intrinsic and environmental stresses including nutritional deficits, mitochondrial dysfunction, redox imbalances, viral infections, harmful RNA conformers, and protein-folding perturbations in the endoplasmic reticulum. Dysregulation of the ISR has been implicated in the pathogenesis of our most widespread diseases, including diabetes, cancer, and neurodegeneration. Understanding the mechanisms that underly ISR computations has been difficult because natural stress inputs activate multiple parallel signaling pathways and classical ISR inducers have pleiotropic effects. The molecular structure and circuitry of the ISR in health and disease have been studied; however, questions remain about how the ISR encodes information at the systems level.

DESCRIPTION

Researchers at the University of California, Santa Barbara introduces an innovative optically sensitive protein that selectively activates the Integrated Stress Response (ISR) via the stress sensor kinase PKR using light. Unlike traditional stress inducers that cause molecular damage, this optogenetic tool offers precise, reversible control of stress signaling dynamics without collateral cellular damage. It allows researchers to probe how stress intensity, duration, and history influence cellular fate and resilience by controlling and mapping ISR dynamics at high resolution. This approach unravels complex signaling pathways involved in major diseases such as cancer, diabetes, and neurodegeneration and enables the development of more effective treatments by dissecting ISR function in a controlled, systematic manner.

ADVANTAGES

- Non-invasive, reversible control of the ISR without causing molecular or cellular damage
- High-resolution, precise modulation of stress sensor kinase activity
- Isolates single pathway activation to avoid pleiotropic effects seen with chemical stressors
- Enables study of stress input dynamics including timing, intensity, and duration
- Facilitates development of targeted therapies for diseases linked to ISR dysregulation
- Provides a novel platform to model stress memory and cellular resilience

APPLICATIONS

- Biomedical research in cellular stress and disease mechanisms

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OTHER INFORMATION

KEYWORDS

ISR, integrated stress response, stress, stresses, disease, health, protein, cell, cellular, biomedical, medical, drug, drug discovery

CATEGORIZED AS

- **Biotechnology**
- Health

RELATED CASES

2023-845-0

- Drug discovery and development targeting ISR-related disorders such as cancer, diabetes, and neurodegeneration
- Optogenetics toolkits for precision control of cellular signaling pathways
- Development of therapies that modulate stress responses without cellular damage
- Academic and pharmaceutical labs studying cellular resilience and stress memory
- High-throughput screening platforms for novel ISR modulators

PATENT STATUS

Country	Type	Number	Dated	Case
Patent Cooperation Treaty	Reference for National Filings	2024/238927	11/21/2024	2023-845

Patent Pending

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- Acquiring Cellular Spatial Information Using Unique Light-Sensitive DNA Barcodes

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