Engineered MAPK Signaling Pathway with Scaffold-Mediated Feedback Loops

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BRIEF DESCRIPTION

UCSF scientists have developed a method to engineer a synthetic, feedback-regulated MAPK signaling pathway using scaffold-mediated feedback loops. This method can be used to systematically re-program MAPK signaling responses, allowing one to engineer and modify the MAPK signaling pathway to optimally control dynamic and complex behaviors in living cells. Many potential applications exist, including engineering of metabolic processes for optimal biofuel production.

FULL DESCRIPTION

Background

The mitogen-activated protein kinase (MAPK) pathway is a common molecular signal transduction system used to mediate eukaryotic cell responses to their environment. In different types of cells, this core pathway is adapted to perform the specific function of those cells. For each function, the pathway is specifically programmed to yield a tailored response. Therefore, the MAPK signaling cascade is an ideal candidate for use in cellular engineering. Using synthetic biology, one can re-design these signaling circuits for specific applications such as optimization of cell growth and increased production of recombinant chemicals, biofuels or proteins. While the importance of signaling pathways in disease states is well recognized, current therapies only involve binary responses. Common examples are small molecule protein kinase inhibitors that turn off certain pathways. However, as our fundamental understanding of disease mechanisms increases, the need for tunable therapies that provide customized cellular behaviors is becoming increasingly apparent.

Invention

Using a synthetic biology approach, UCSF scientists have developed a method to engineer MAPK signaling responses using synthetic scaffold interactions and scaffold-mediated feedback loops. This method can be used to build a synthetic genetic circuit that provides variable control of the MAP kinase pathway in yeast.

FEATURES/BENEFITS

Simple and effective method for achieving tunable control over a protein signaling pathway

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OTHER INFORMATION

KEYWORDS

engineered cell signaling

pathway

CATEGORIZED AS

- **Biotechnology**
  - Industrial/ Energy
  - Other
- **Energy**
  - Bioenergy
- **Research Tools**
  - Expression System
  - Other
  - Protein Synthesis

RELATED CASES

2008-119-0

APPLICATIONS

- Engineer yeast cells for optimized production of biofuels
- Engineer cell lines for drug screening
- Engineer immune cells that can respond in a tunable manner to different levels of antigen
- Engineer plant cells to detect and variably respond to environmental stimuli, such as pathogens or noxious chemicals
- Engineer mammalian cells capable of modulating differentiation, growth or apoptotic behavior in response to stimuli

OTHER INFORMATION

REFERENCE: Bashor, C.J. et al. Using Engineered Scaffold Interactions to Reshape MAP Kinase Pathway Signaling Dynamics. 2008. Science 319:1539-1543.

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	7,879,590	02/01/2011	2008-119

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