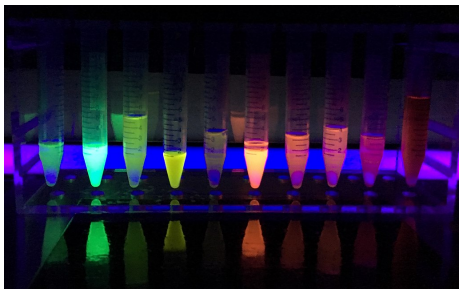
System for detecting three protein-protein interactions in living cells

Unmet Need

Recognizing Protein-Protein Interactions (PPIs) is central to many molecular biology studies aiming to identify important targets for the development of therapeutic drugs. There are thousands of PPIs that are essential to understand the biological functionalities of cells. With the knowledge of where and when PPIs occur, the mechanisms of normal biological activity can be compared to those of diseased cells. However, identifying and monitoring PPIs can be challenging and is currently limited to detecting and observing two proteins interacting when many signaling cascades include multiple interactions. Furthermore, the available technology is mostly limited to studying PPIs in fixed, dead cells. There is a need for methods to study PPIs in living cells for real-time observation and to study more than two proteins interacting.

Technology

Duke inventors have developed a method that allows for the detection of three protein interactions in living cells with the use of bioluminescent resonant energy transfer. The technology expands upon Promega Corporation’s NanoBiT ®, which detects two proteins. This method is intended to be used by biotechnology companies and academic laboratories studying protein interactions. Specifically, this technology adds to the NanoBiT ® system, which tags two proteins of interest with a split luminescent protein that creates a luminescent signal when in close proximity. The luminescent signal from the two proteins acts as an energy donor for the additional component created by the Duke inventors. The additional component is a red-shifted acceptor protein that can be tagged to a third protein of interest. This has been demonstrated in living



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Cell Biology

Publication(s)

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External Link(s)

• From the lab of Sudarshan Rajagopal, MD, PhD
• From the lab of Marc G. Caron, PhD

cells through a study looking at the interactions among the G protein, Gα, beta-arrestin, and a third agonist component, vasopressin type 2 receptor (V_2R). With their technology, the inventors were able to observe that the V_2R catalyzed the formation of Gαi:beta-arrestin scaffolds.

Advantages

- Invention allows for the observation of 3 protein interactions
- PPIs can be monitored *in vivo*
- Proof of concept study highlights the potential of this technology to understand key biological processes
- Integrates seamlessly into the industry standard Promega NanoBiT® system