UNIVERSITY OF MINNESOTA
Driven to Discover℠

Assay to measure intrinsic efficiency of GPCR ligands

FRET-based GPCR biosensors to measure specific ligand activation in a cell independent manner.

Technology No. 20180126

Applications

- GPCR targeted drug development
- High-throughput drug screening
- Basic GPCR research

Key Benefits & Differentiators

- **Directly measures specific GPCR activation:** Activity is measured in giant plasma membrane vesicles (GPMVs), avoiding tissue and cell-type variations in GPCR signaling.
- **Amenable to high-throughput screening:** Highly stable GPCR sensors incorporated into GPMVs facilitates scaling for high-throughput drug screening and analysis.
- **Consistent, replicable results:** Unlike live cells, GPMV sensors provide consistency and reliability in FRET measurements regardless of expression levels, handling, and ligand stimulation time.

Targeting GPCRs

G-protein-coupled receptors (GPCRs) are a prominent pharmacological target for the treatment of a wide variety of diseases and disorders. Exemplifying the success of this approach, more than 30% of FDA approved drugs target at least one GPCR and worldwide more than 25% of drug sales come from GPCR modulating compounds. However, with more than 800 different types of human GPCRs (that function in a cell-type and tissue dependent manner), a straightforward method to measure the efficacy of ligands on specific GPCRs is not currently available. A new technology developed at the University of Minnesota introduces a precise method to measure the intrinsic efficacy of GPCR ligands. This approach employs systematic protein affinity strength modulation (SPASM), a modular assay to analyze the interaction between two peptides using fluorescence energy transfer (FRET).

Measuring ligand-induced activity directly and precisely

Current methods of measuring GPCR ligand efficacy using live cells or crude preparations are complicated by the heterogeneity inherent in different cell or membrane batches. In addition, assays that utilize purified GPCRs require time and resource intensive optimization for each GPCR. The new approach from the lab of Dr.Sivaraj Sivaramakrishnan uses a FRET-based biosensor that detects the ligand-induced interaction between a GPR and the Gα subunit of a G protein in live cells. This biosensor is paired with giant plasma membrane vesicles (GPMVs), which provides a stable, relevant environment for the GPCR studies without the complexity of the intracellular environment. Not only does this method allow for adaptability between different GPCRs, but is also scalable for high-throughput drug screening and analysis, making research on these drug targets easier to advance.

Phase of Development

TRL: 3-4
Using the biosensor, the direct correlation between ligand induced changes in FRET intensity and previously reported intrinsic efficacy has been demonstrated (R2=0.99). Biosensors tested with multiple class A GPCRs including adrenergic receptors, dopamine receptors, and cannabinoid receptors.

Researchers

Sivaraj (Shiv) Sivaramakrishnan, PhD
Professor, Dept. of Genetics, Cell Biology and Development
External Link (proteinacrobaticslab.umn.edu)

Publications

ER/K linked GPCR-G protein fusions systematically modulate second messenger response in cells
Nature Scientific Reports, 7, 7749 (2017)

Desired Partnerships

This technology is now available for:

- License
- Sponsored research
- Co-development

Please contact us to share your business' needs and learn more.