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Platform for Quantification of Transmembrane Protein Binding Kinetics

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-Membrane proteins, notably G-protein-couple receptors (GPCRs), are responsible for many critical cellular functions and are an important family of drug targets. Because of this, it is important to measure their binding activities with molecular ligands and drug candidates. Studying membrane proteins is challenging for two reasons. The first is because transmembrane proteins are difficult to extract and purify, often losing their native conformations after isolation. The second is because even if a membrane protein is successfully isolated, measuring ligand binding isn't easy, particularly if the ligand is small (which encompasses about 90% of the current drugs).

Researchers at the Biodesign Institute of Arizona State University and a collaborator at the Johns Hopkins, have developed a novel virion oscillator microarray technology to measure molecular binding to GPCRs. Virions, with human GPCRs displayed on them, are tethered to a sensor chip via a flexible linker to form an oscillator. Oscillation amplitude can be tracked and amplitude changes from binding of ligands or drugs to the GPCRs can also be tracked. From these changes in oscillation, binding kinetics and affinity can be quantified. This technology can be used to study cellular functions of membrane proteins and quantify binding of large and small molecule drugs to said membrane proteins.

This technology finally provides a long-sought technique to determine disease-related cellular signaling processes, screen drugs targeting membrane proteins and validate new therapies for cancer and other diseases.

Potential Applications

- Tool to study membrane proteins
  - Screen drugs targeting membrane proteins
  - Study cellular functions and determine disease-related cellular signaling processes
  - Validate new therapies for cancer and other diseases

Benefits and Advantages

- Label-free, real-time detection with sub-nanometer precision
- Quantifies binding kinetics and affinity
- Sensitivity does not diminish with the molecular mass of the ligand
  - Suitable for both large and small ligands
- The microarray assembly is easy to fabricate
- Can provide a large collection of important GPCRs and other transmembrane proteins that are easily accessible and mass-producible

For more information about this opportunity, please see

Syu et al – Nat Commun – 2019

Ma et al – J Am Chem Soc - 2018

For more information about the inventor(s) and their research, please see

Dr. Wang's departmental webpage