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An approach to identify allosteric modulators of kinases

Protein-based sensor for detecting kinase-substrate interactions suitable for screening therapeutically-relevant inhibitors.

Technology No. 20170278

IP Status: Pending US Patent; **Application #:** 16/619,798

Applications

- AGC kinase basic research
- Screening for kinase inhibitors (including allosteric)
- Drug identification for AGC-kinase relevant diseases
- Kit-based assay development

Key Benefits & Differentiators

- **Highly specific screening capabilities:** Capable of identifying compounds that display selective action on individual kinase isoforms.
- **Minimal reagent requirements:** Requires only small amounts of protein reagent for screening.
- **Flexible application to existing workflows:** Protein sensor can be used in a number of common assay formats (plate-readers, fluorimetry, time resolved-instrumentation, etc.)

AGC Kinases as therapeutic targets

The AGC kinase superfamily contains 60 family members that are involved in a variety of biological functions. Some well-known family members are cAMP-dependent protein kinase 1 (PKA) and cGMP-dependent protein kinase (PKC). Many AGC kinases are involved in diseases such as cancer and diabetes, making these proteins a tempting target for therapeutics. However, due to the large structural conservation between AGC kinases, it is difficult to design inhibitors that are specific to one kinase without affecting multiple family members. In an effort to overcome this challenge, researchers at the University of Minnesota developed a novel platform for the identification of allosteric small-molecule substrate-kinase inhibitors.

A sensitive assay to detect allosteric changes

This technology utilizes a small, protein-based sensor that detects specific interactions between AGC kinases and specific substrates. A kinase and a substrate of interest are connected through a protein linker flanked by a FRET donor and a FRET acceptor. Through the fluorophores, the sensor reports interaction strength between the AGC kinase and the substrate of interest. Requiring very little protein reagent, this technology is the first assay with the ability to detect allosteric changes in substrate-kinase interaction. With a convertible format, a small amount of reagents, and the ability to detect small changes in kinases and substrate interactions, this technology will provide a useful platform in the development of kinase-based therapeutics.

Phase of Development

In vitro assays carried out with a number of disease-relevant AGC kinases validating the use of this technology to identify substrate-selective small molecule allosteric modulators.

Ready for Licensing

This technology is now available for license! The University is excited to partner with industry to see this innovation reach its potential. Please contact us to share your business' needs and your licensing interests in this technology. The license is for the sale, manufacture or use of products claimed by the patents.

Researchers

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Publications

Substrate Affinity Differentially Influences Protein Kinase C Regulation and Inhibitor Potency
Journal of Biological Chemistry, 2016
The Role of Regulatory Domains in Maintaining Autoinhibition in the Multidomain Kinase PKCα
Journal of Biological Chemistry, 2017
Distinct structural mechanisms determine substrate affinity and kinase activity of protein kinase Cα
Journal of Biological Chemistry, 2017
Bitopic Inhibition of ATP and Substrate Binding in Ser/Thr Kinases through a Conserved Allosteric Mechanism
Biochemistry, 2018