Measuring Protein-Protein Interactions (PPI)

A snapshot of TruBind Assay work completed by researchers in MSI Drug Discovery Services laboratories worldwide

SUMMARY

The Importance of PPI

Protein-protein interactions play an important role in cell cycle function and homeostasis, but have proven to be challenging targets to address with small molecule inhibitors.

Challenges of Measuring PPI Inhibition

One of the key challenges with PPI systems is the development of robust and relevant assays.

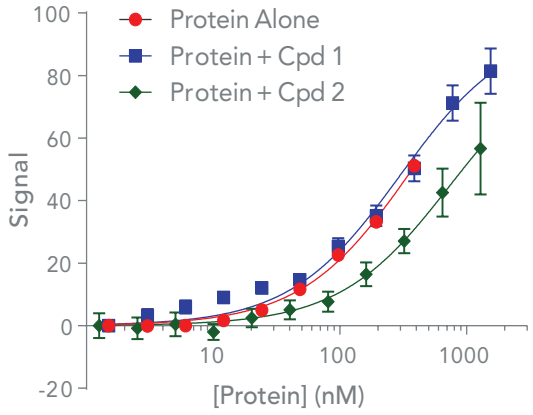
Current methods for measuring small molecule effects on PPI inhibition such as FP, FRET, ELISA, AlphaScreen, NMR, SPR, or ITC require labeling and/or tethering of the target, or are size limited, all of which directly impact the system being monitored.

In contrast, BSI isn't limited by label, tethering or size restrictions, thereby enabling true binding and inhibition to be directly monitored.

SUPPORTING DATA

PPI Small Molecule Binding

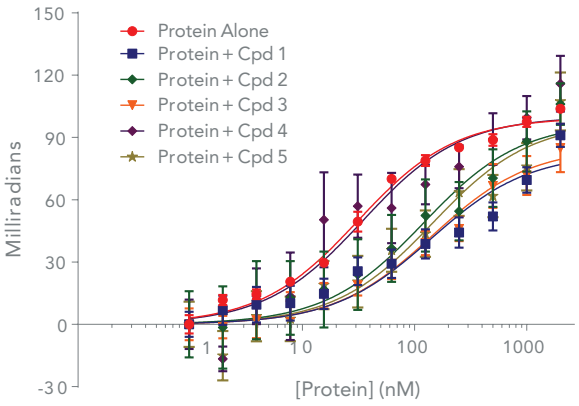
BSI succeeds in determining the effects of small molecule ligands on protein-protein interactions. In the example below, two small molecules were investigated for their direct binding to a protein-protein interaction related to cholesterol metabolism and homeostasis. Compound 2 can be shown to lower the affinity of the interaction 2x below the native state.



Comparison of the effect of two small molecules on protien receptor binding to a protien target.

Small Molecule Protein Fibril Aggregation

BSI succeeds in accurately determining the effect of small molecules on protein fibril aggregation. Here, five small molecules were investigated for their effect on fibril formation for a single aggregating protein involved in the progression of Alzheimer's disease. Compounds can now be ranked on their ability to prevent aggregation in pre-clinical SAR's.



Small molecule effects on protein fibril aggregation.

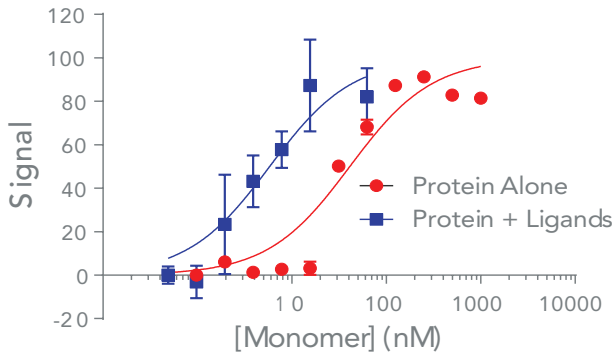
MOLECULAR SENSING

TruBind™ Assay Services

Back-Scattering Interferometry at Work

Small Molecule Effects on Protein Dimerization

BSI succeeds in measuring the effects on endogenous ligands on protein dimerization. Here, a protein involved in nucleotide biosynthesis is demonstrated to dimerize more effectively when both its native substrate and another substrate analog are present.



Effect of native ligands and substrate analogs on protien dimer formation.

KEY BENEFITS

TruBind BSI Technology delivers key benefits in the investigation of protein-protein inhibitors, with no tags, no surface attachments for true binding characterization.

- Uniquely informs medicinal chemistry for complex and difficult to address targets
- Maintains target integrity: label- and tether-free, free-in-solution; target in native, or native-like, environment
- Target conformation sensitive detection
- Sensitivity to directly detect small molecule binding to large, complex targets
- Determination of mode of allosteric modulation
- Rapid assay development
- Discovery of high-value 'next-generation' therapeutic candidates

Company

Molecular Sensing, Inc. (MSI), is a commercial stage drug discovery tools and contract research services company with headquarters and drug discovery services laboratories in Nashville, Tennessee and an R&D center in Los Gatos, California, along with a European operations center near Frankfurt, Germany.

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