

Unleashing the Power of Spectral Shift Technology for Ultra-High-Throughput Binding Assays

WuXi Biology

Moran Jerabek-Willemsen¹, Julia Flesch¹, Annika-Niedner-Boblentz¹, Enrico Perini¹, David Dai², Weihui Guo³, Andreas Schoop¹

1. Crelux GmbH – A WuXi AppTec Company, Am Haag 16, 82166 Gräfelfing, Germany

2. Encoded Library Chemistry Team, WuXi Biology, WuXi AppTec, 288 Fute Zhong Road Waigaoqiao Free Trade Zone, Pudong District, Shanghai, 200131, China

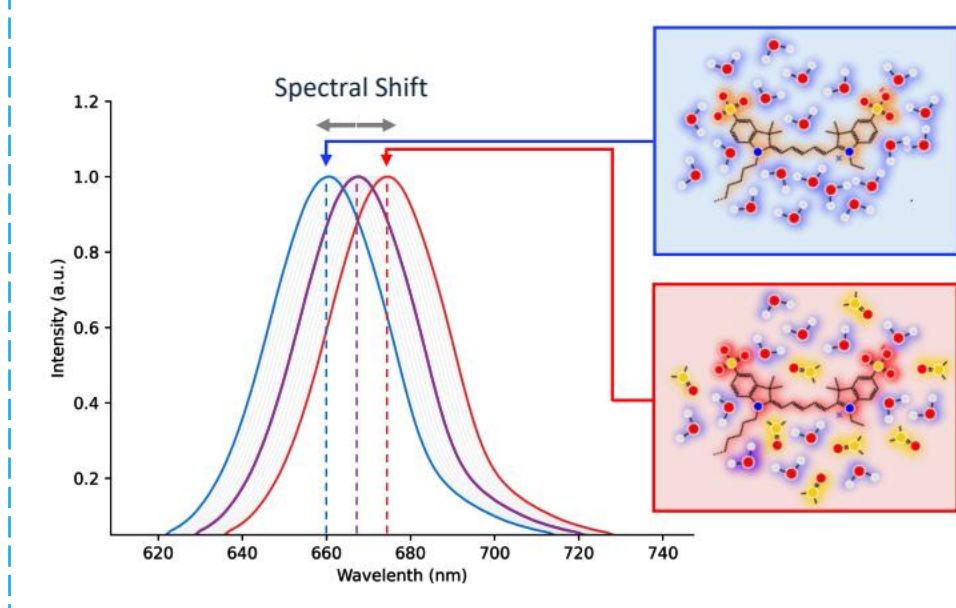
3. HTS Platform, WuXi Biology, WuXi AppTec, 288 Fute Zhong Road Waigaoqiao Free Trade Zone, Pudong District, Shanghai, 200131, China

CRELU
a WuXi AppTec company

Abstract

High-throughput screening (HTS) is vital in drug discovery, yet traditional methods like biochemical assays and ASMS face potential limitations. We introduced a spectral shift-based direct binding assay that enhances precision, sensitivity, and efficiency while reducing sample consumption and turnaround time. In this poster, we present the underlying technology, detail our in-house implementations and optimized screening workflows, and highlight a successful case study targeting PIK3CA H1047R. The results demonstrate the assay's robust performance and broad applicability in accelerating early-stage drug discovery.

Spectral Shift Technology:



Technology Background:

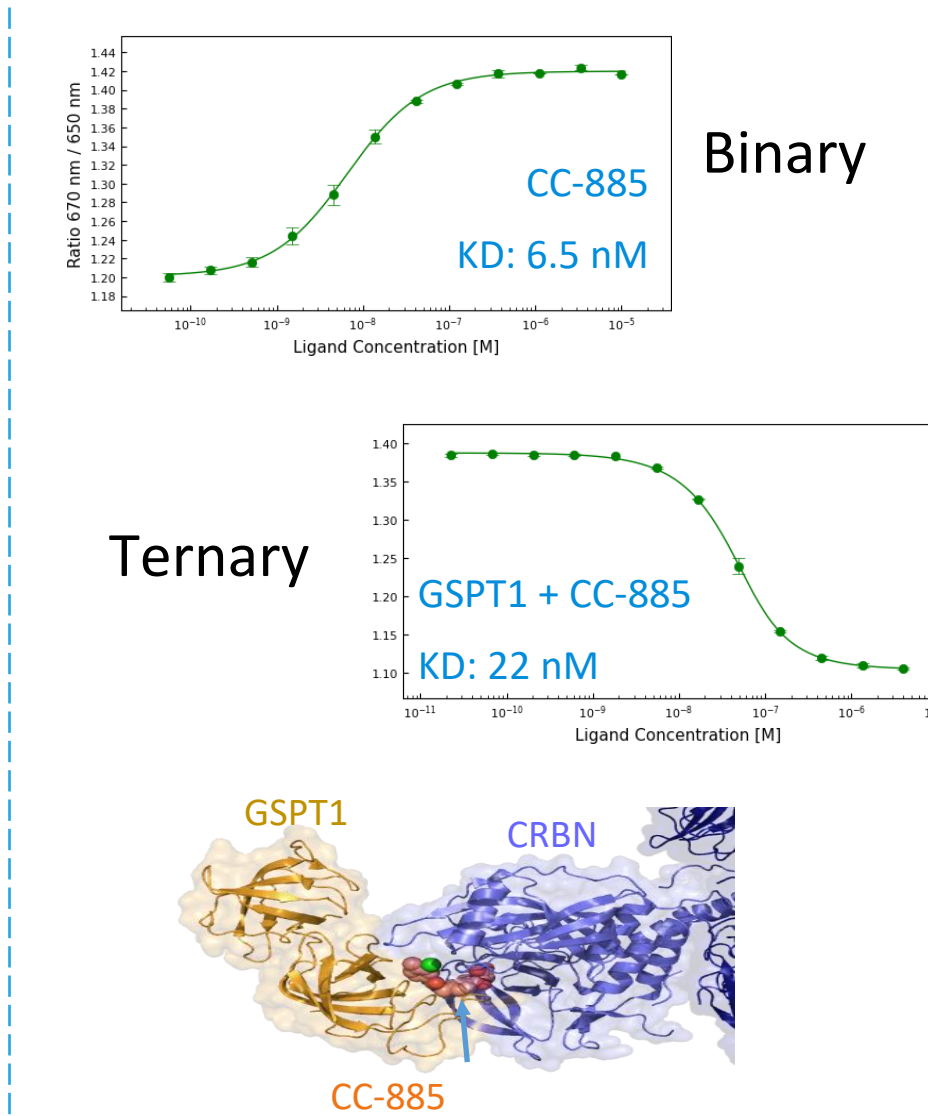
Ligand binding to a labeled target changes the surrounding properties & induces a shift in the emission of the fluorescent probe

uHTS Dianthus - Spectral Shift Technology:

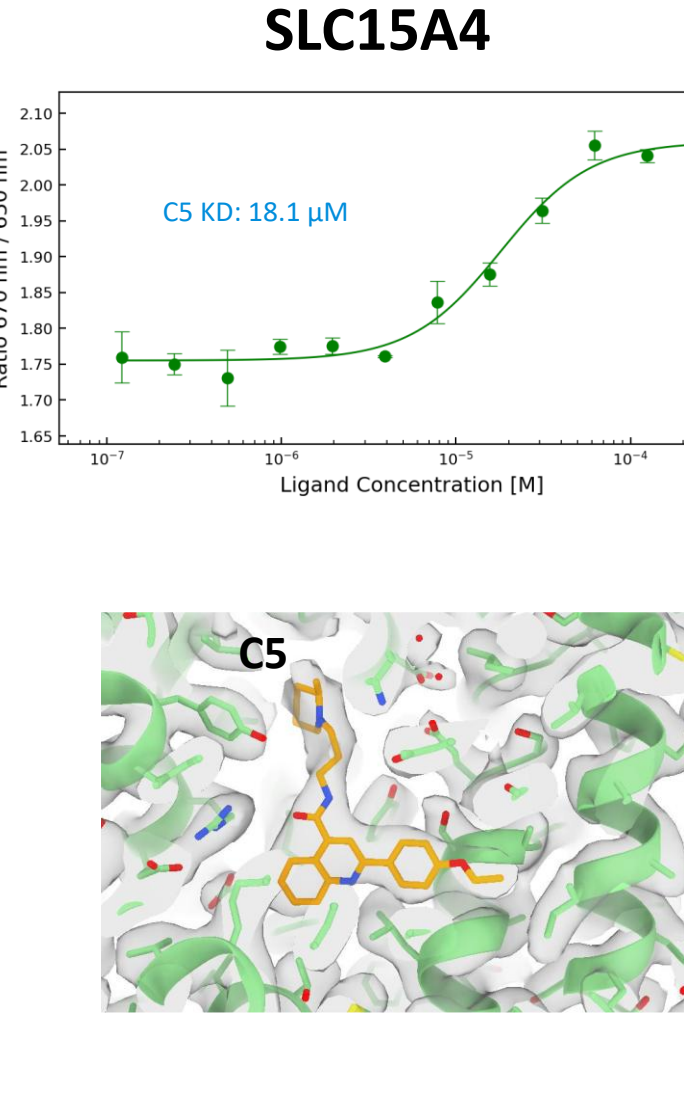
- Affinity Measurements in free solution at isothermal conditions
- High Sensitivity enables studying all target and ligand classes
- Very Fast: One 1536 well plate in 5 min - 370k small molecules in 2 weeks



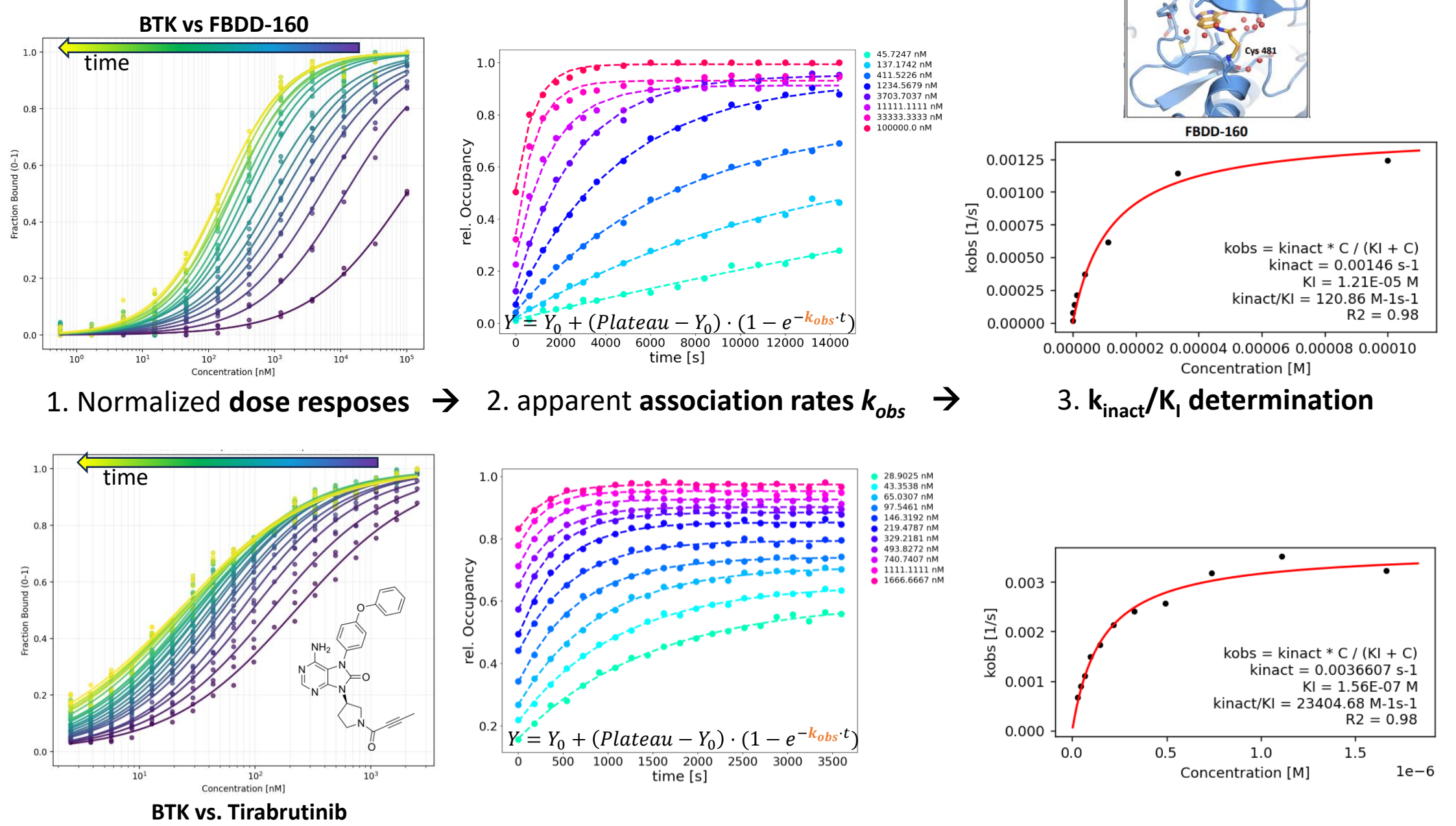
Targeted Protein Degradation



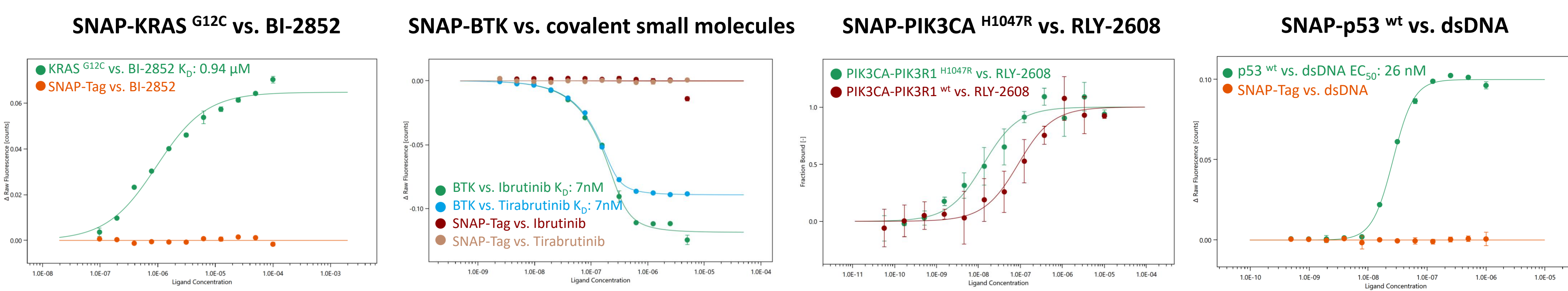
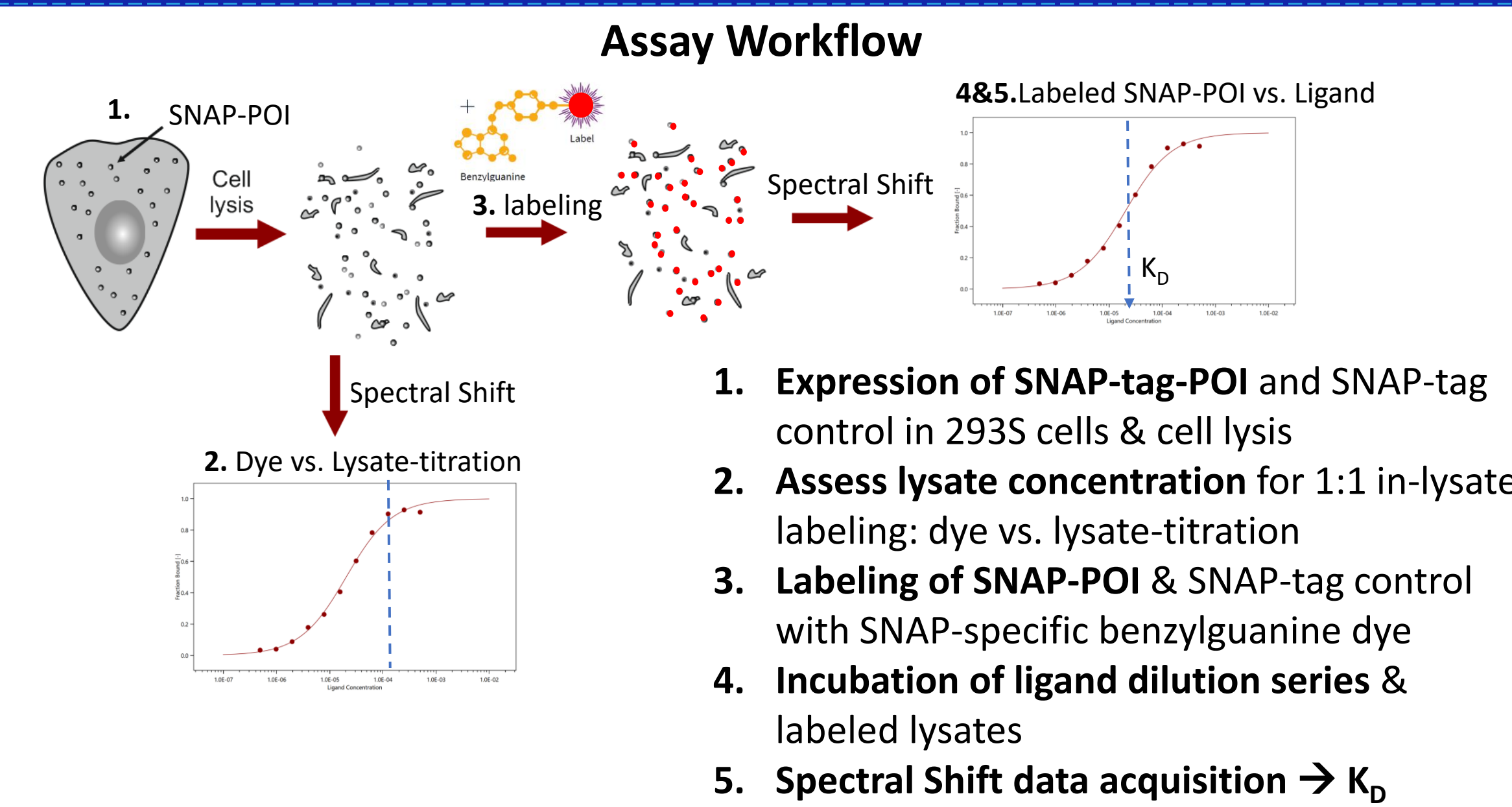
Membrane Proteins



Covalent Molecules: k_{inact}/K_i

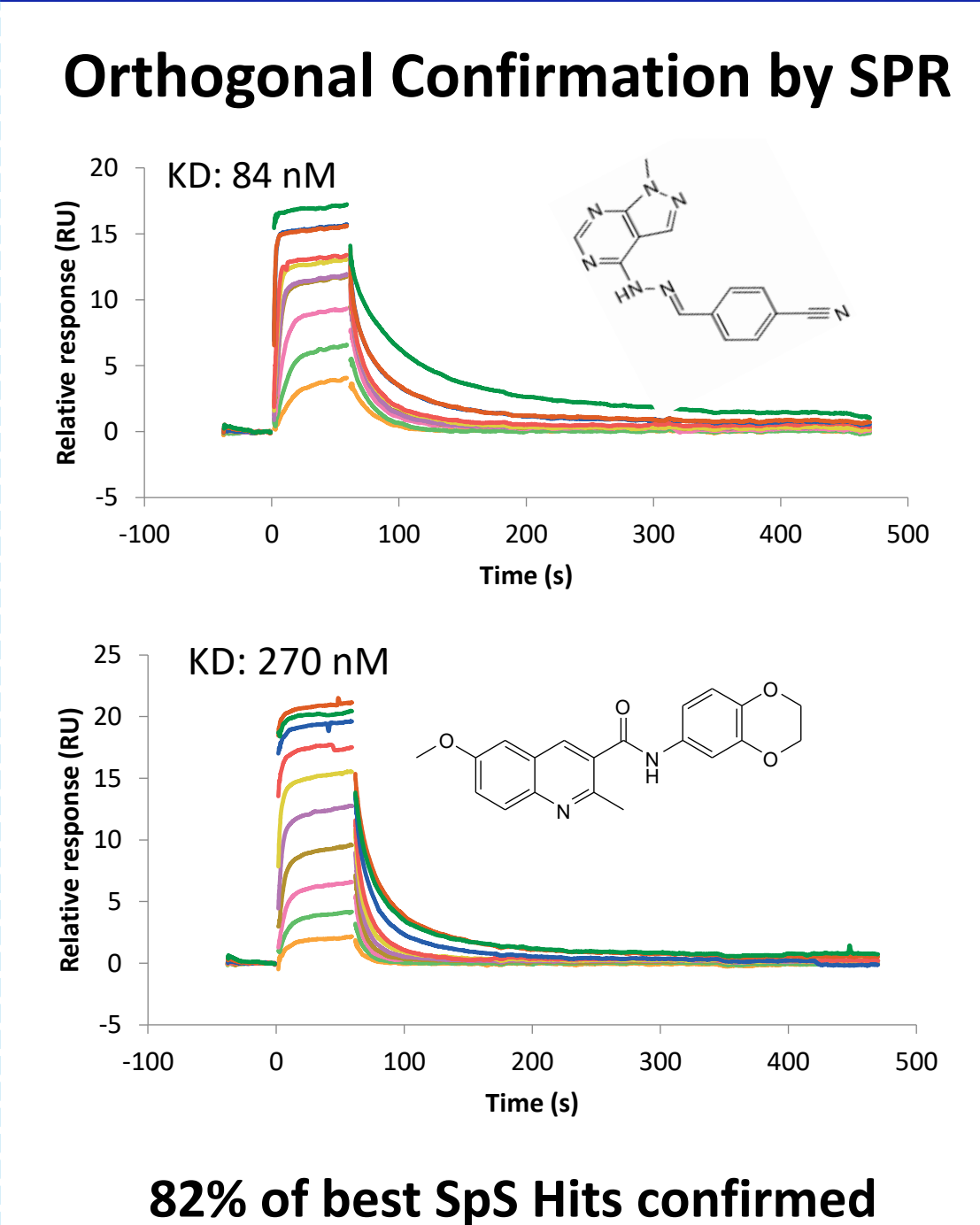
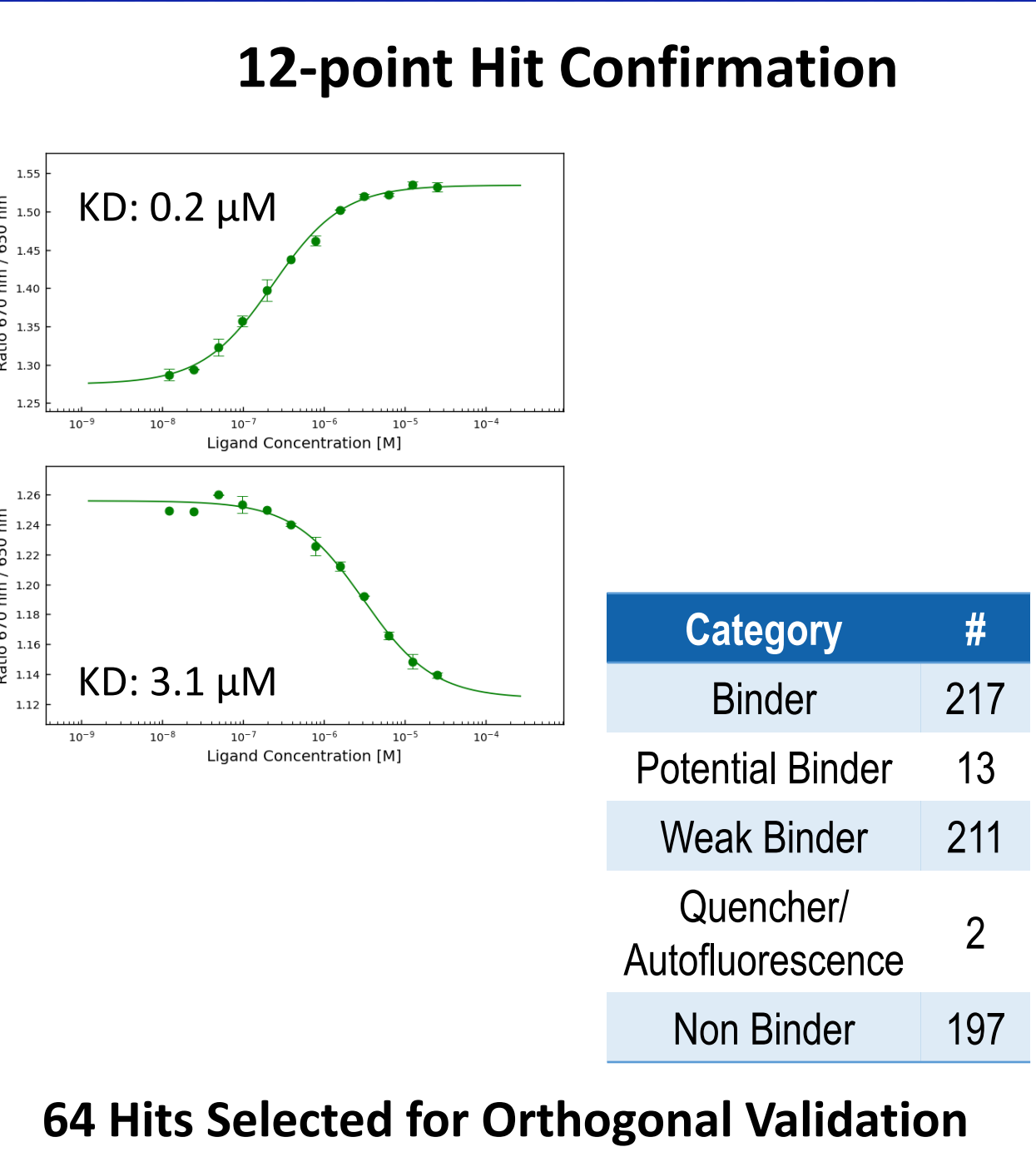
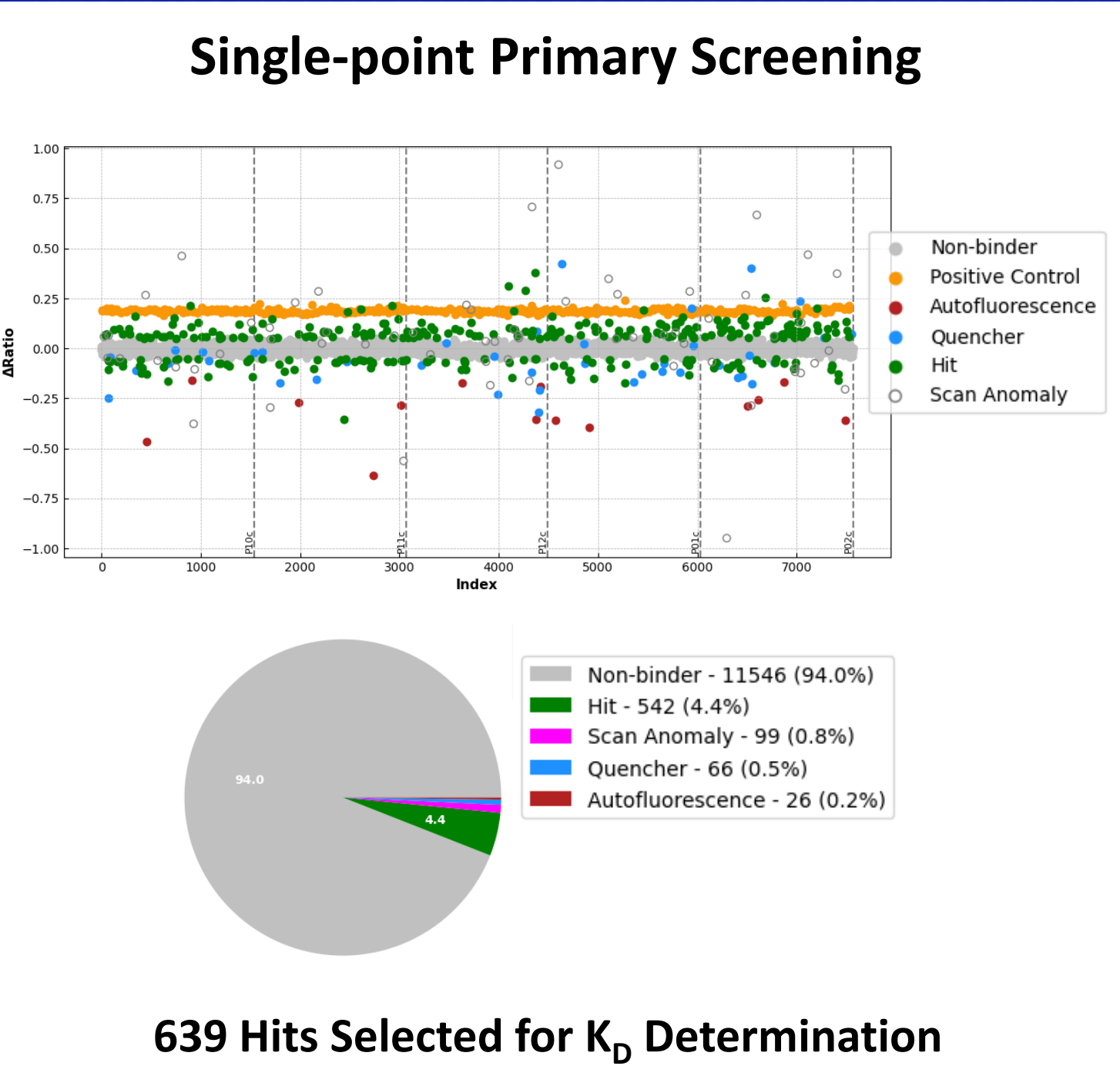
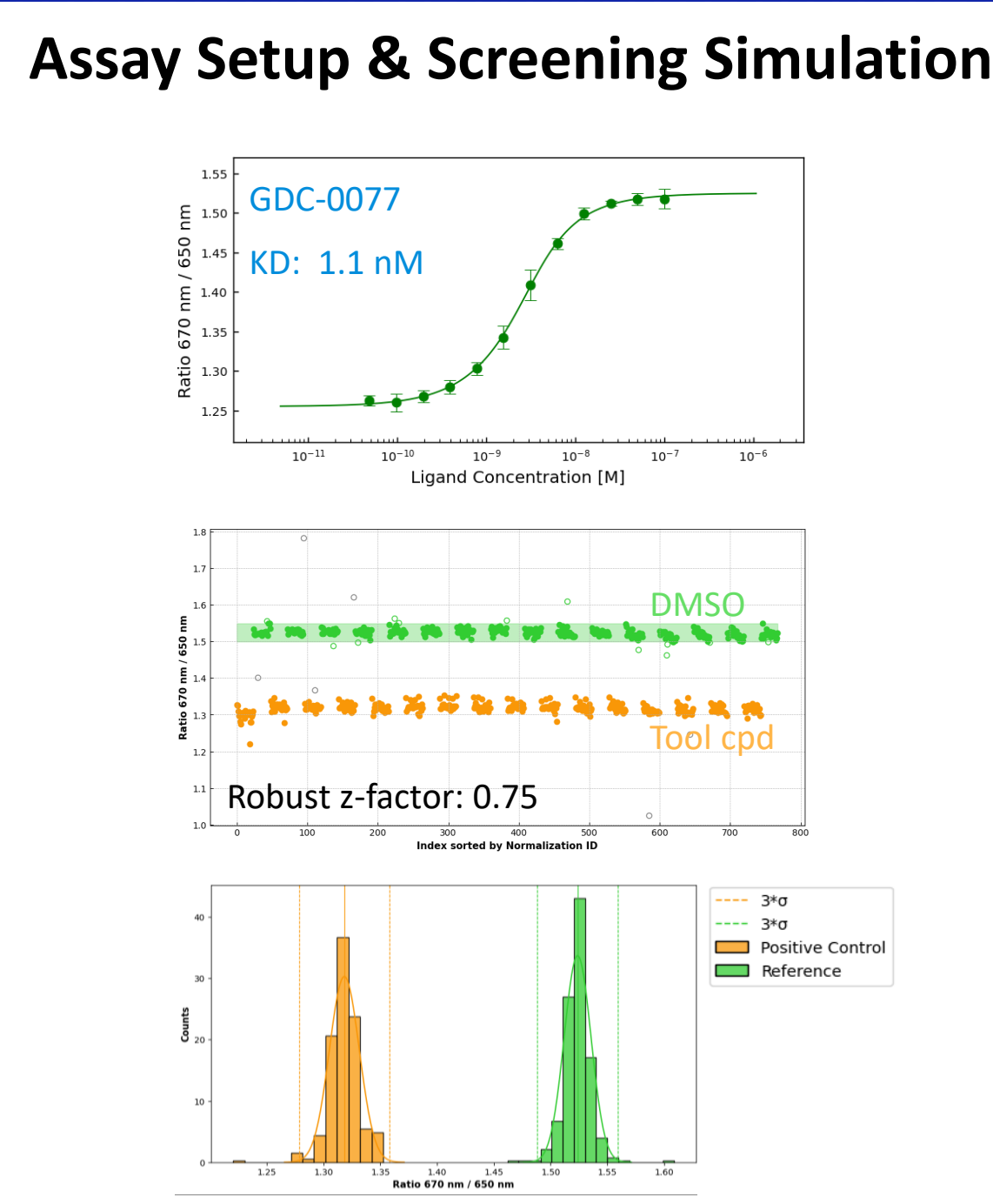
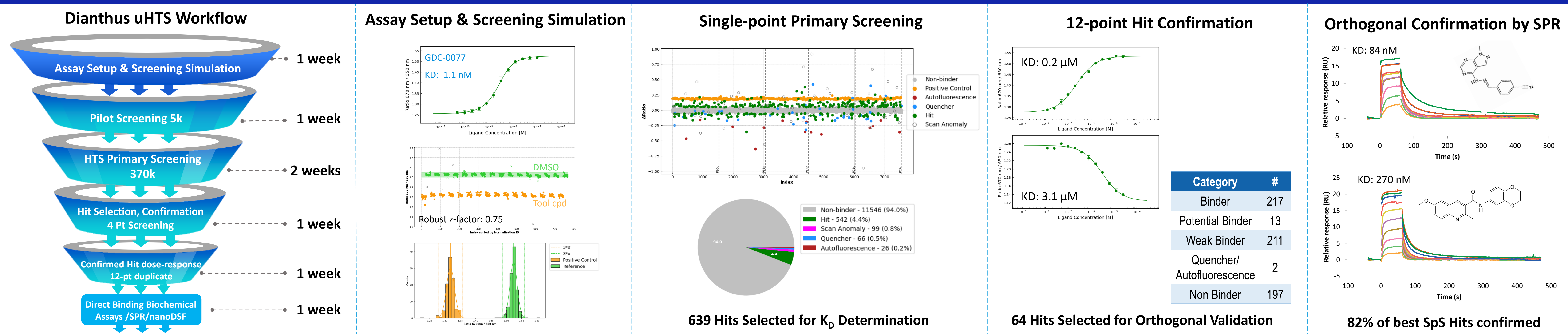


Cellular Biophysics: Purification-free Spectral Shift Assays in 293S Cell-Lysate



- Biophysical Binding Assays in Near-Native Conditions: purification free sample preparation meets isothermal data acquisition in solution
- Potential Applications: HTS screenings, efficiency of covalent binders: k_{inact}/K_i , Mode-of-action studies, Functional Assays, Membrane proteins

Dianthus uHTS – Screening Workflow Showcase using PIK3CA H1047R vs. WuXi AppTec Kinase Focused Library (16.5 k)



Summary

- Spectral Shift uHTS Dianthus platform is fully integrated into the Biophysics Hit ID and Characterization Workflow in WuXi Biology. This versatile system supports a broad range of targets and assay conditions, offering a powerful alternative to classical HTS—especially for challenging proteins, including detergent-solubilized membrane proteins. It excels in detecting ternary complex formation and enables screening for molecular glues and bifunctional molecules.
- In-lysate screening using uHTS Dianthus offers near-native conditions for various applications such as HTS screening, covalent ligand profiling, and mode-of-action studies.
- To exploit the method's full potential, robust assay design—particularly protein labeling—is critical and must be tailored to each target.
- In future, machine learning tools will accelerate analysis of the large datasets generated and improve both speed and user experience

References

Spectral Shift: A New Spectral Shift-Based Method to Characterize Molecular Interactions: Andreas Langer, Annemarie Lüdecke, Tanja Bartoschik, Ondrej Cehlar, Stefan Duhr, Philipp Baaske, and Werner Streicher; ASSAY and Drug Development Technologies 2022 20:2, 83-94; DOI: 10.1089/adt.2021.133
Covalent compound analysis (k_{inact}/K_i): Strelow JM. A Perspective on the Kinetics of Covalent and Irreversible Inhibition.; SLAS DISCOVERY: Advancing the Science of Drug Discovery. 2016;22(1):3-20. doi:10.1177/1087057116671509



Business contact: mahnaz_arjomand@wuxiapptec.com (US)

Business contact: dave_madge@wuxiapptec.com (EU and Israel)

Business contact: xu_longji@wuxiapptec.com (China and Singapore and Australia)

Business contact: sycho@wuxiapptec.com (Korea)

Business contact: fumio_ito@wuxiapptec.com (Japan)