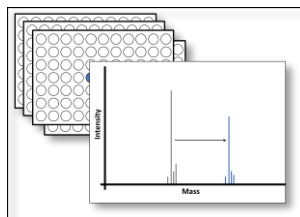


Drug Discovery Solutions – Screening for Covalent and Reversible Binders

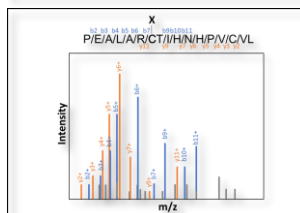
High throughput intact protein MS

Screening of covalent binders
Wuxi covalent fragment library with
2612 fragments ready to use



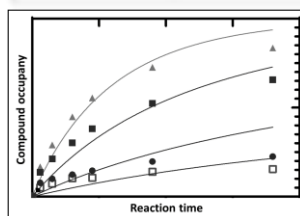
Binding site analysis

Peptide mass fingerprinting
Location of the compound conjugation site



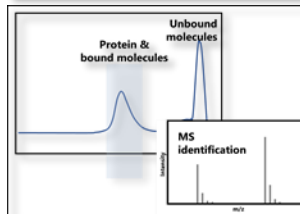
k_{intact}/K_i determination

Kinetics of covalent binding
Guide hit ranking and selection



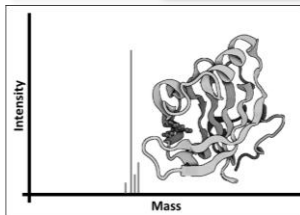
AS-MS

2D-LC Automated Ligand
Identification System setup
On-line affinity selection



Protein characterization

Intact mass and peptide mapping
Confirm protein integrity and identity
Characterization of PTMs



2 weeks

1 to 2 weeks

3 to 4 weeks

2 to 4 weeks

1 to 2 weeks

Identification and characterization of
covalent binders

Reversible
binders

Target QC

Cutting-Edge Facilities

Agilent 6456 Q-ToF
High resolution MS system



High-Throughput MS System

RapidFire 400
High throughput MS autosampler
with chilled sample storage

- Combination of protein and mass spectrometry expertise drive target specific experiment design
- Close integration with protein production, biochemistry and biophysics enables rapid orthogonal validation and characterization
- External as well as in-house fragment/compound libraries can be screened

Contact us

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Website: wuxibiology.com



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Covalent FBBD workflow demonstrated on Bruton's tyrosine kinase

Primary screening

1 week

Validation

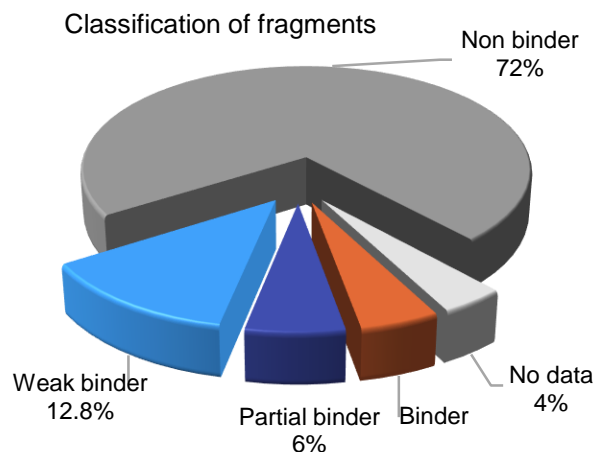
1 week

Characterization

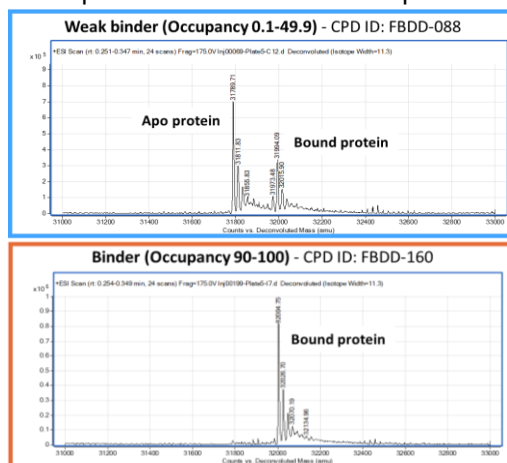
3 weeks

Primary screening by RapidFire intact protein MS

Classification of fragments

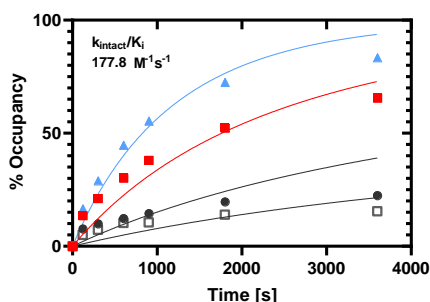


Example of deconvoluted mass spectra

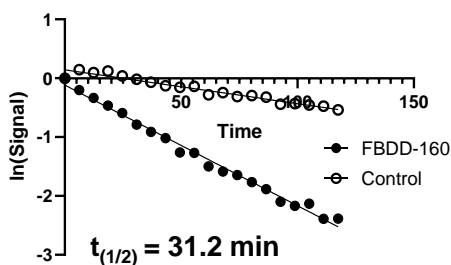


- Measurement time of only ~20 seconds per sample allows screening of the entire WuXi AppTec fragment library in less than 24 hours
- Automated in-house data analysis workflow allows rapid classification of fragments into different binder classes and assignment of binding stoichiometries to guide hit ranking

k_{intact}/K_i

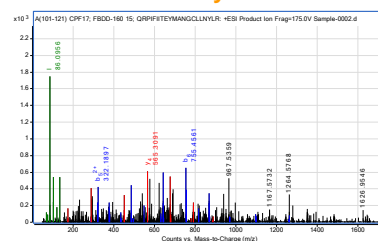


GSH reactivity assay



Peptide mapping

Fragmentation spectrum
QRPIFIITEYMANGC*LLNYLR
Cys481



- Characterization of covalent binding kinetics and reactivity
- Binding site identification by peptide mass fingerprinting
- In depth hit characterization enables hit selection for crystallography and optimization

Contact us

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