



Your Partner in Drug Discovery

Biortus Hit Identification to Lead Generation Service

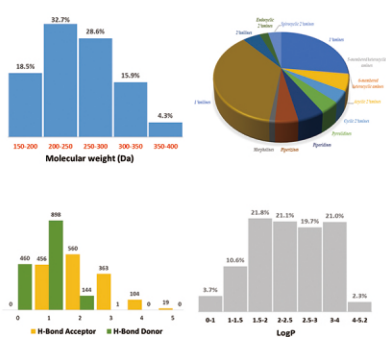


Libraries

Fragment Libraries at Biortus

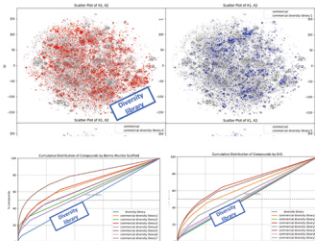
- 3 Commercially Available fragment libraries
- 1 Proprietary Covalent Library

Biortus Unique Covalent Library



Lead-Like Libraries at Biortus

- Diverse, 50K
- Sp³ enriched library, 1.3K



- Visualizing compound chemical space
- A smaller number of compounds spans a broader range of chemical space
- Library have more diversified scaffold and pharmacophore distribution than commercial diversity library and large service platform library

Molecular Glue Library

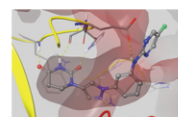
General information

- Commercial → 986 compounds
- Rational design → 1893 compounds
- 250<mw<550; Sp³ enriched

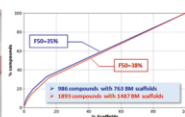
Structural analysis

- Fragments from reported compounds (clinical, patents and papers)
- Rational designed and selected from commercial library by experts
- Highly diverse: One BM scaffold covered 1-3 compounds

Molecular glues library



Library Scaffold analysis



Hit Finding with Fragment screening

Reagent production

- Protein generation
- Stable cell line generation
- Reagent labeling
- Primary screening
- Confirmation in CRC
- Orthogonal assays

- Co-Crystallization

Assay development & validation

~ 1 - 2 weeks

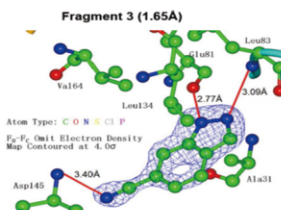
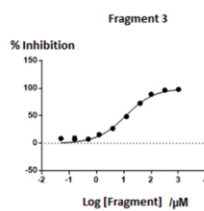
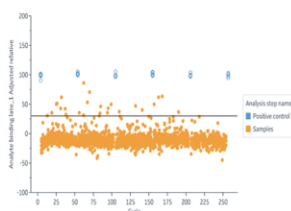
~ 4 - 8 weeks

Assay formats:

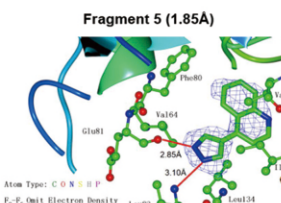
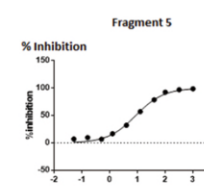
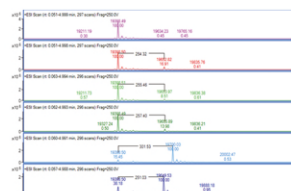
- SPR
- LC/MS
- TRIC
- TR-FRET
- FP, FI
- Caliper
- TSA/DSF
- NanoDSF

> 50 screens run

Fragment screen



Covalent library screen



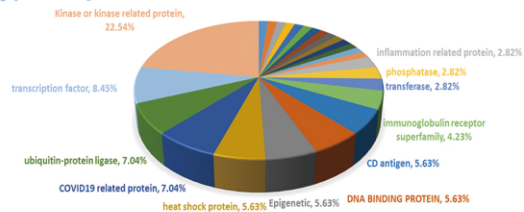
In vitro assays

Biophysical assays

Assay types

- NanoDSF/Thermal Shift Assay (TSA)
- Surface Plasmon Resonance (SPR)
- Octet Fortebio (BLI)
- Temperature Related Intensity Chang (TRIC)
- Mass Photometry

Types of proteins tested



Light Cycler® 480 II



Prometheus NT.Plex



Octet RED96



Biacore S200



Biacore 8K+



Refeyn Two^{MP}

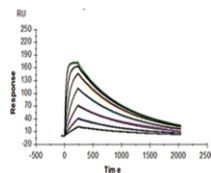


Dianthus NT.23 Pico Duo

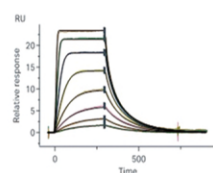
SPR

- Affinity and Kinetics determinations
- Competition Assays
- 2 – Biacore 8k+
- 1 – Biacore S200
- CM5, SA, CAP, Protein A/G, NTA chips

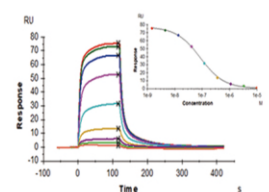
Protein - protein



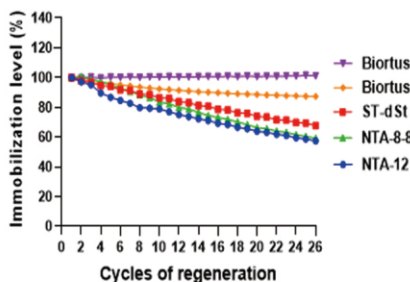
Protein - Small Molecule



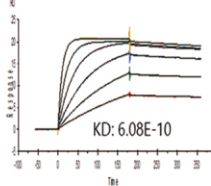
Blocking of PPI by SM



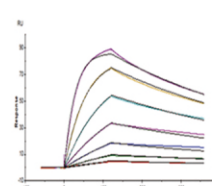
Regeneration stability of Biortus Chip



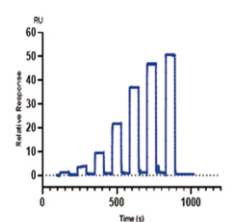
Antibody - Antigen



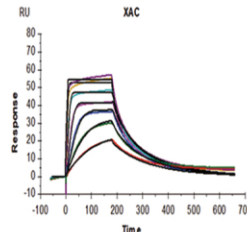
Protein - Nucleic Acid



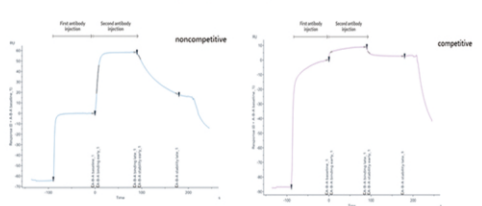
Nucleic Acid - Small Molecule



GPCR - Small Molecule



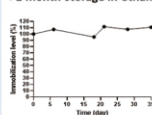
Epitope binning



Advantage of Biortus SPR Chip:

- Reusable for >25 cycles
- Stable for >1 month storage
- Cost effective
- Feasible for unstable target
- Patent covered

Biortus SPR chip is stable after >1 month storage in ethanol



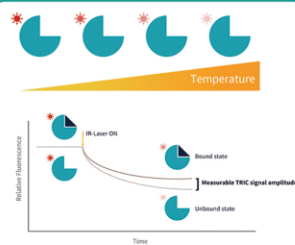
TRIC Technology for Membrane Proteins



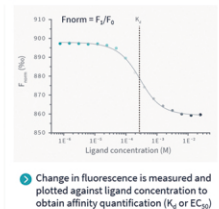
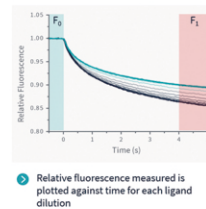
Dianthus NT.23PicoDuo

Top notch. Fastest time to result with highest picomolar sensitivity

Principle of TRIC



Determination of binding affinity



Benefits

- Do more with less protein.
- Measure broad range of interaction, including protein-ion/carbohydrate.
- Measure Kd independent of size and mass of binding partners.
- Measure in solution, in close to native conditions, no immobilization required.

Applications:

- Kd measurement in solution, include cell lysate
- Membrane Protein
- Fragment screening

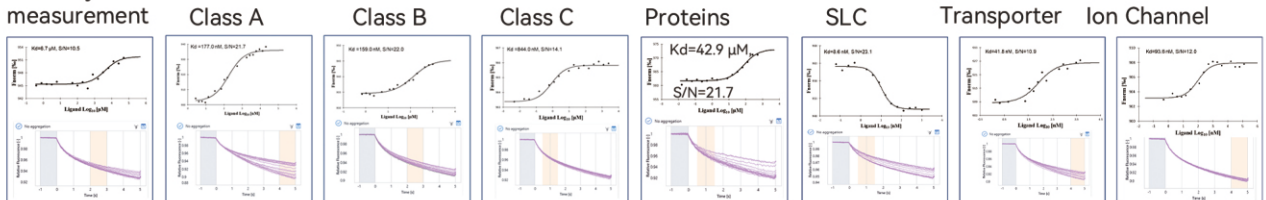
Cell lysate

Directly Kd measurement

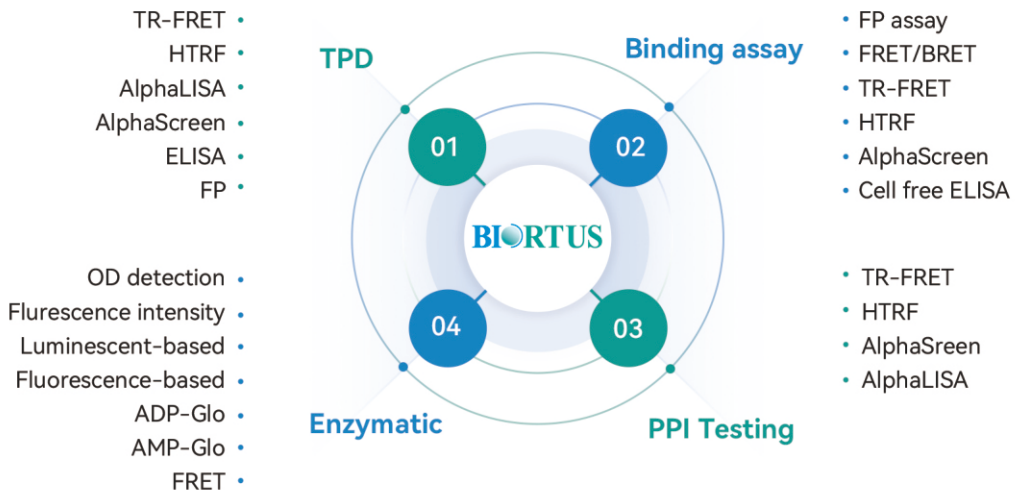
GPCRs

Cytosolic

Other membrane proteins



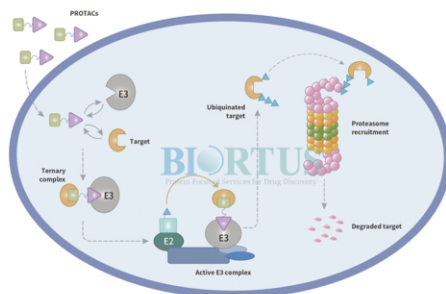
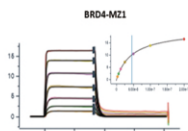
Biochemical Assays



Assays for PROTAC Drug Discovery

Binary binding assay:

- SPR
- TR-FRET
- ELISA
- FP
- DSF

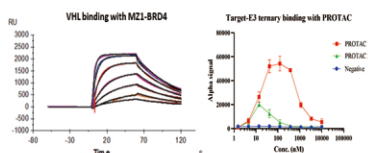


Cellular assays:

- HCS, WB for target degradation
- qPCR for mRNA level detection
- NanoBRET & NanoLuc for PPI and ubiquitination
- CETSA (split NanoLuc)

Ternary binding assays:

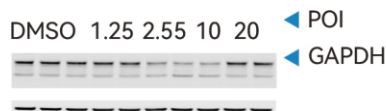
- AlphaLisa / AlphaScreen
- SPR
- TR-FRET



Target ubiquitination assays:

- WB
- TR-FRET
- AlphaLisa / AlphaScreen
- NanoBRET
- In vitro ubiquitination

Active Cmpd (uM)



- 8 E1 (ubiquitin-activating enzyme)
- 36 E2 (ubiquitin-conjugating enzyme)
- 178 E3 (ubiquitin-protein ligase)

Cell-based assays

01

Stable cell line generation

02

FACS

03

High content assays

04

Reporter assays

05

Cell viability/proliferation

06

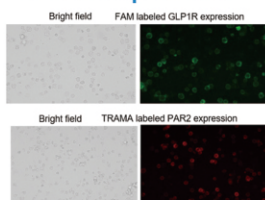
BRET

Cell-based assays for MOA & SAR

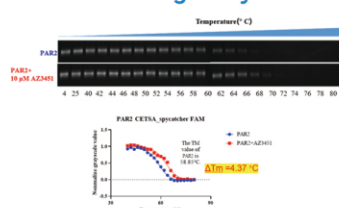
GPCR assay panel

- cAMP assay
- β arrestin recruitment assay
- Calcium flux assay/IP1
- GPCR internalization or trafficking
- G Protein recruitment assay
- Tag lite assay
- FP assay
- CETSA

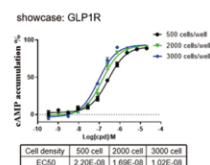
Surface expression:



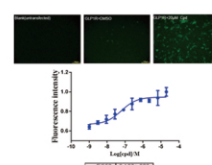
CETSA binding assay:



cAMP assay:



β arrestin recruitment assay:



For your pipeline

- GPCR surface expression validation
- GPCR signal transduction research
- GPCR biased signaling
- GPCR compound/ligand binding
- GPCR pharmacological study

over 10+ tested Targets, over 300+ ready-to-use Targets					
GLP1R	GCGR	OX2R	DRD2	HRH1	GPR75
GIPR	OX1R	A2AR	HRH3	M1R	A1AR
					PAR2



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