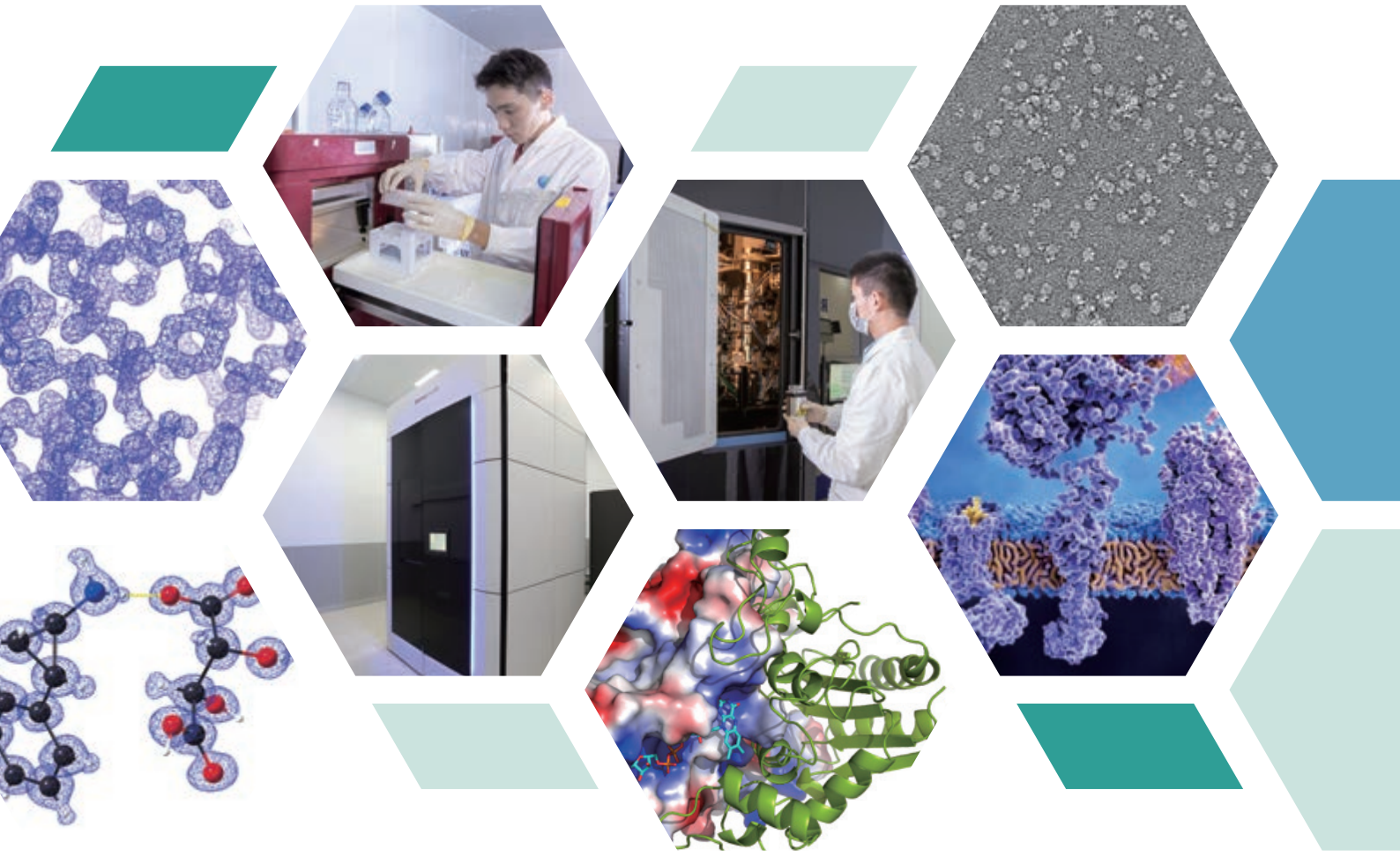
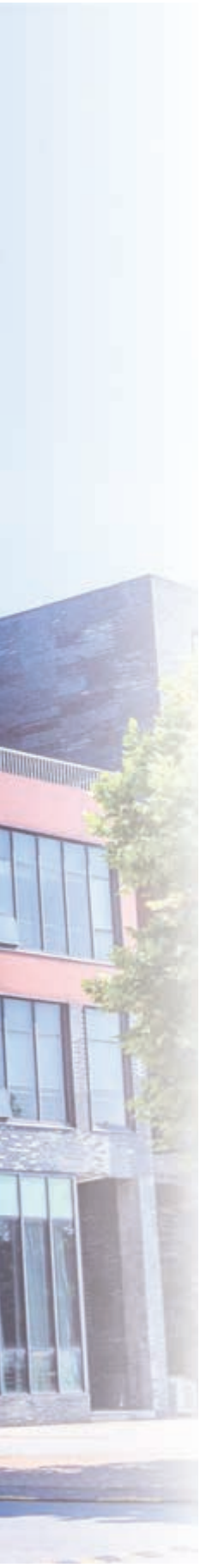
BIORTUS
A Pharmaron Company



Your Protein-Focused Partner for Drug Discovery

From Gene to Structure

Your Partner in Drug Discovery



About Us

Biortus, a wholly owned subsidiary of Pharmaron, is a protein-focused CRO serving global drug discovery community in protein production, assay and screening, and structural biology including protein NMR, X-ray crystallography, and cryo-EM. Since 2009, Biortus's fully integrated pipeline has contributed to SBDD programs to large body of clients including top 20 pharmaceutical and bio-pharma multi-national corporations (MNCs). Biortus's top notch protein production team has delivered more than 4000 target proteins and protein complexes including degradation complexes, GPCR, transporters, ion channels, and many others. Biortus owns several unique compound libraries and has delivered many novel hits to clients for FBDD and non-classical modalities including covalent targeting cystine and lysine residues. Biortus's NMR structural biology capability is well poised to drive hit finding and hit confirmation for discovery programs targeting intrinsically disordered proteins (IDPs). Biortus' crystallography platform has delivered over tens of thousands of co-xtal structures to support clients' SBDD programs. Biortus owns one of the top cryo-EM service platforms in the industry, with a line of state-of-the-art microscopes and computation clusters, a team of cryo-EM specialists, and more importantly, rich experiences in the application of SPA, MicroED, and cryo-ET, to variety of drug targets and novel modalities.

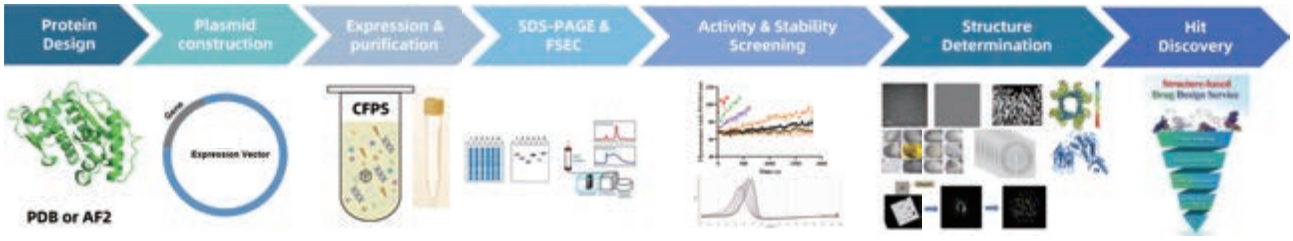
To help clients expedite discovery process, Biortus launched non-competing internal lead generation campaign and the goal is to build lead generation packages (LGSuite) for a series of drug targets. Each LGSuite contains essential drug discovery tools and materials including ready-to-use proteins, crystal and/or cryo-EM structures, and assays and hits. So far Biortus has assemble a protein catalog with over 3,000 novel targets, a structural database of more than 1,000 protein structures, and a compound library with over 10,000 novel ligands. The company is committed to providing strong support for pioneering innovation through "novel targets, novel mechanisms, and novel molecules." Within Pharmaron family, Biortus joins force with other teams to accelerate and empower the advancement of global biopharmaceuticals.

Quality · Speed · Cooperation · Innovation

Structure- and AI/ML-Based Protein Design & Hit Discovery Platform

This platform integrates high-resolution protein structural data with advanced Al/ML algorithms to deliver a complete workflow from protein design to hit discovery. Leveraging cell-free protein synthesis (CFPS), it enables rapid protein expression and shortens the design-evaluation cycle.

Through modular steps—plasmid construction, expression and purification, structural characterization, and high-throughput screening—combined with structure- and Al/ML-based virtual screening, the platform supports hit-to-lead optimization and provides an integrated framework for drug discovery. Applications include enzyme engineering, antibody design, and early-stage therapeutic development.



BiortusAI Computing Center

High-Performance Computing Cluster

Tens of thousands of CPU cores and hundreds of GPUs providing robust computational capacity for Al/ML-driven protein design and structural biology.

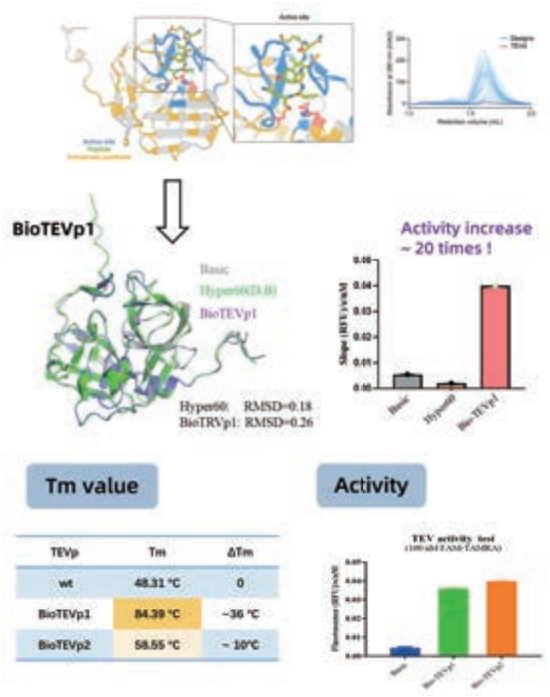
AI Design Suite

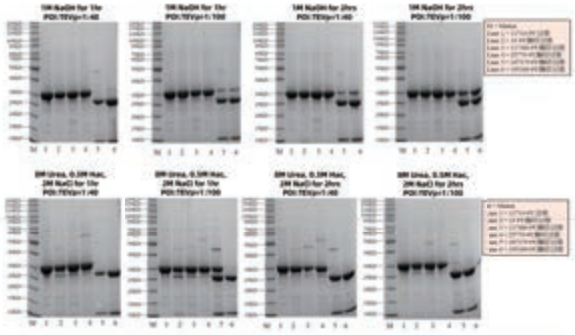
End-to-end protein design capabilities, integrating engines such as ProteinMPNN, RFdiffusion, AlphaFold2, Boltz-2, molecular dynamics (MD), among others.

Large-Scale Data Platform

Billion-compound-scale virtual screening supported by in-house curated fragment, covalent, and targeted compound libraries.

AI/ML-based design and engineering of proteases (e.g., TEV protease)





- **BioTEVp1 (lane 5)** is still active after incubation with 1M NaOH or 8M Urea, 0.5M HAC buffer for 2hrs.
- BioTEVp1 can be stored at RM for 2 weeks.

Tm value

TEVp	Tm	ΔTm
wt	48.31 °C	0
BioTEVp1	84.39 °C	~36 °C
BioTEVp2	58.55 °C	~ 10°C

Activity

HRV 3C	Tm	ΔTm	Activity
wild type	49.25	0	1
BioHRV3C	69.68	20.43	2.4

- CN202411805464.X

SUMO	Tm	ΔTm	Activity
wild type	40.85	0	1
BioSENP1	70.98	30.13	4.4

- CN202411966744.9
- CN202510744711.8

Structure- and AI/ML-based hit discovery for the Adenosine A2A Receptor (A2AR)

Virtual Screening (2 days)

1. Docking of Biortus Fragment Library, 3,659 fragments.
2. 60 top ranking fragments were selected for TRIC assay.

Assay development (1-2 weeks)

1. Affinity test: Test the affinity of positive control towards labeled target.
2. Buffer optimization: Select suitable buffer for fragment screening as needed.

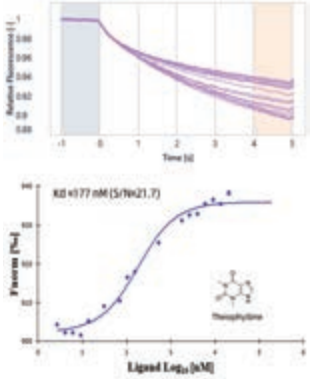
Preliminary Screen (1-2 weeks)

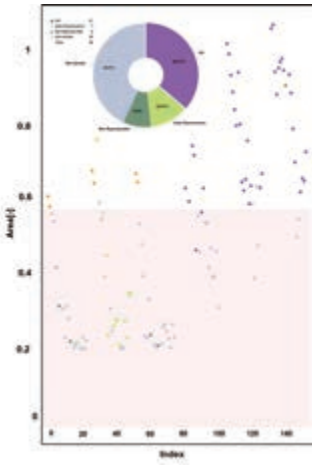
1. 60 top ranking fragments were used for TRIC assay.
2. Binding level screen: The fragments with significant response will be screened out for further dose affinity screen. (27 shows binding)

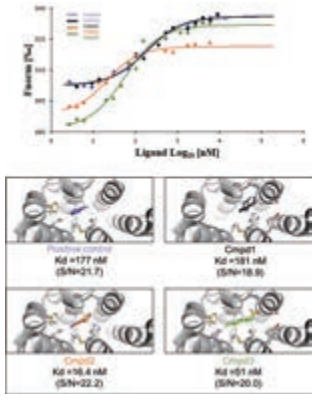
Dose affinity screen (1-2 weeks)

1. The fragments with Kd ≤ 1000 μM and good behavior (TRIC trace, S/N) will be screened out as potential hits.
2. Confirmation of Docked pose with structure

A2AR
(PDB: 5MZJ)







Protein Production

Constructed over 60,000 plasmids and expressed over 8,000 recombinant proteins and protein complexes.

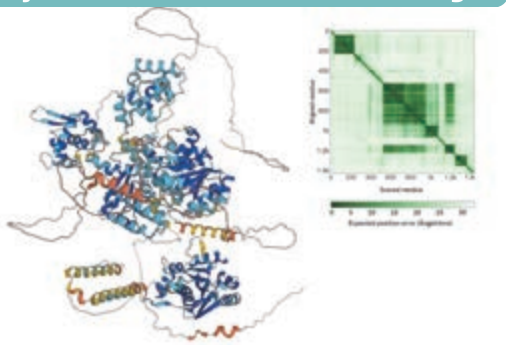
Proteins include: GPCRs, SLCs, ABC transporters, E3 Ligases, CDKs, Kinases, DUBs, TFs, enzymes, virus proteins.

Expression systems: Mammalian cells, insect cells, *E.coli*, yeast and cell-free expression systems.

Diverse Purification Strategies: Affinity Chromatography (AC), Ion Exchange Chromatography (IEX), Hydrophobic Interaction Chromatography (HIC) and Size Exclusion Chromatography (SEC).

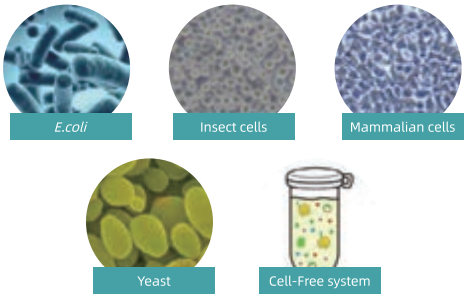
***In vitro* modifications:** Biotinylation, phosphorylation, dephosphorylation, deglycosylation, ubiquitination, methylation, palmitoylation, depalmitoylation, iodination, deiodination, other modifications.

Project Evaluation & Plasmid Design



- AI-powered Project Evaluation
- Reference to Published Literature and Structures
- Unique Plasmid Design:
  His-Strep II-TEV-GG-POI
- Plasmid Design Assisted by AlphaFold2 Prediction

Protein Expression

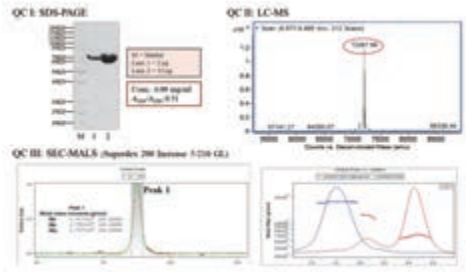


- FSEC High-throughput Screening
- Shake Flask, Fermenter and WAVE
- 1,000 liters of *E. coli* culture per week
- 400 liters of insect cell culture per week
- 200 liters of mammalian cell culture per week

Protein Purification

- Expert Protein Purification Team
- Over 60 AKTA purification systems
- Comprehensive Separation Techniques
- Endotoxin Removal Service

Quality Control



- Quality Control 1: SDS PAGE, LC-MS, Analytical SEC, SEC-MALS
- Quality Control 2: protein specific biochemical and biophysical assays, Mass photometry, nano-DSF, etc.


ÄKTA avant


Flow-cytometry Sony SH800S


LC-MS


Mass Photometer

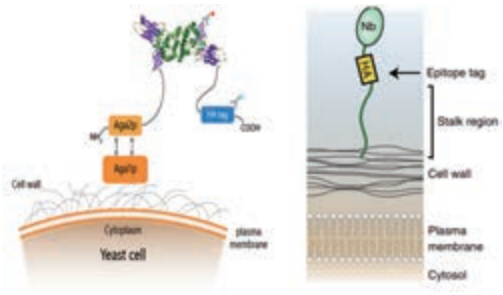

SEC-MALS


WAVE


Simple Western™ (Jess™)

Nanobody Selection Based on Yeast Surface Display

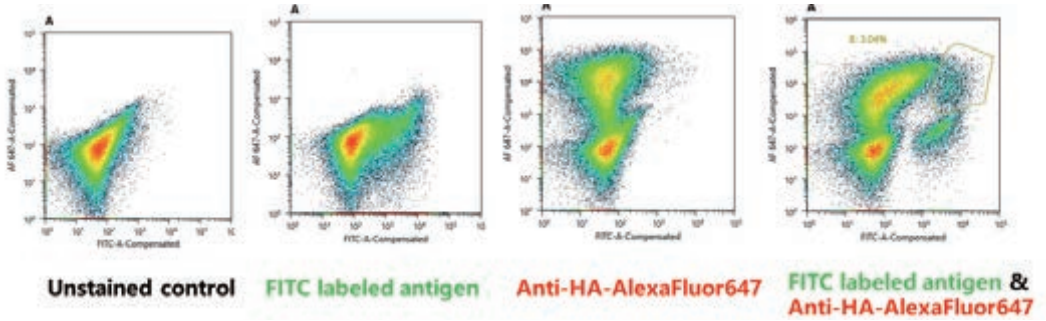
Yeast Surface Display



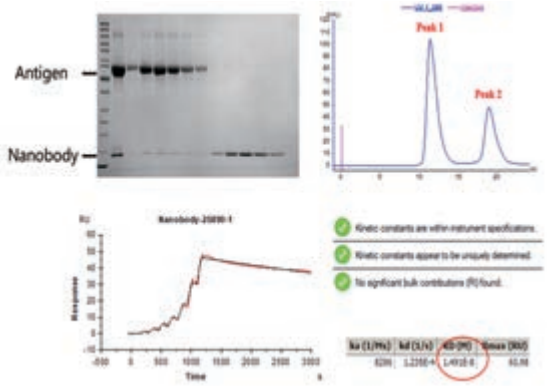
MACS

FACS

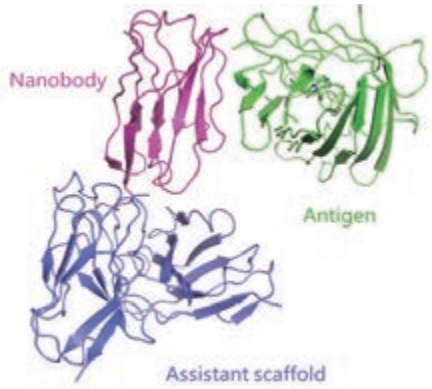
- **Synthetic nanobody library size:** 5.6×10^{8}
- **Screening strategies:** MACS + FACS
- **Expression and purification of nanobodies:** *E. coli* or mammalian cell
- **SPR confirmation:** Kd in range of ~nM
- **Antigen:** ~1 mg (50 kD) of soluble protein or membrane protein
- **Screening cycle:** ~2.5 to 3 months



Binding Validation by SEC and SPR



Assist Cryo-EM structure



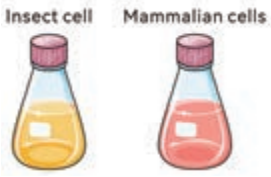
Workflow for eGFP-tagged membrane protein purification

eGFP tag: rapid screenings of expression systems, constructs, and detergents for solubilization, affinity purification

Construct design

- Homolog screening;
- Protein engineering;
- Affinity tags & vectors;
- N/C terminal truncation;
- Loop deletion;
- Mutagenesis;
- Fusion partners (T4L, BRIL...);
- ...

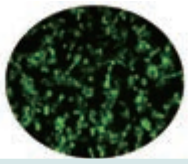
Expression system



- Insect cell expression:
  System: Bac-to-Bac
  Cell: Sf9, Sf21 & Hi5
- Mammalian cell expression:
  System: Transient Transfection; BacMam
  Cell: 293F; Expi293F; GnTI-

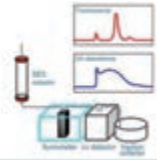
Small scale expression test

Fluorescence microscope



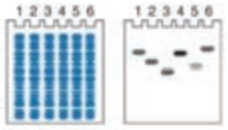
- Rapid expression screening
- Sub-cellular localization in host cell

Fluorescence size exclusion chromatography (FSEC)



- High-throughput screening monodisperisty for constructs and solubilization conditions
- Estimation of MPs overexpression level
- No need for purification
- Less than 5 ml expression media

Western Blot



- Confirm the expression of intact MPs

Large scale expression and purification

Anti-eGFP nanobody-based affinity purification

- Catch the eGFP-tagged protein with high specificity
- Higher purity than the TALON/ Streptactin resin
- Need to cleave the eGFP tag

Purified membrane protein

- Downstream application:
  Nanodisc reconstitution;
  SPR assay;
  TRIC assay;
  Activity determination;
  Thermal shift assay;
  Structure determination;

Membrane protein

Membrane proteins remain highly challenging in structural biology, demanding significant time and resources.Rapidly identifying optimal expression and purification systems using minimal materials can greatly reduce costs and accelerate early-stage projects.

At Biortus, we have developed small-scale screening workflows for membrane protein expression and purification. We enable fast cloning and parallel screening (3–5 mL culture per condition) in *E. coli*, yeast, insect, and mammalian cells. Using common tags (His, FLAG, Twin-Strep, GST) and reporters (eGFP, RFP, YFP, mStayGold), we efficiently optimize conditions including temperature, detergents, pH, and buffers.

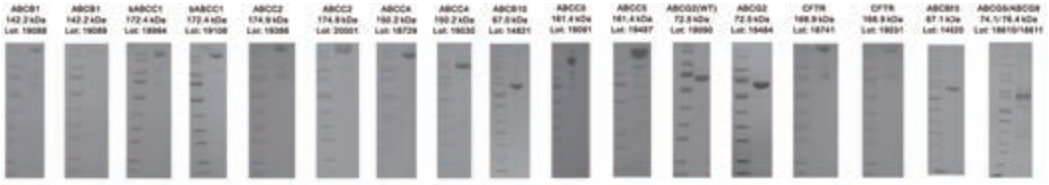
Screening results are evaluated by FSEC, SDS-PAGE, and Western Blot. To address low expression levels, we use high-affinity anti-eGFP nanobody resin (Kd ≈ 6 pM). With this approach, we have successfully purified over 300 membrane proteins, including GPCRs, ion channels, and transporters.

Various membrane proteins are available online. For more information, please contact us.

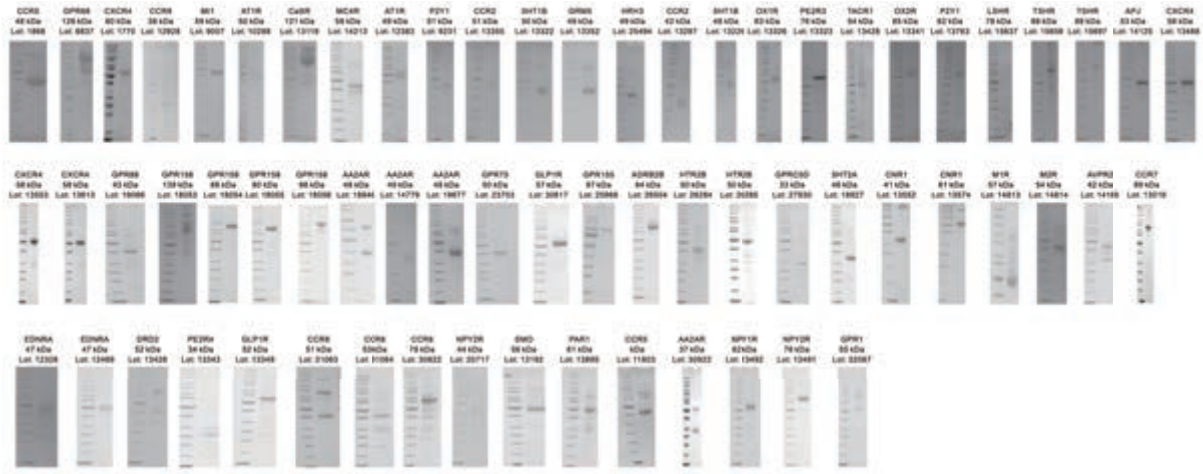
GPCR			G protein	SLC				ABC Transporter	Ion channel		other
5HT1B	FFAR1	M1R	Gs	SERT (SLC6A4)	CNT3(SLC28A3)	VGLUT2(SLC17A6)	SLC37A4 (G6PT)	ABCA1	CLC1	TRPC1	EGFR
5HT2A	GIPR	M2R	Gi	SGLT2(SLC5A2)	KCC1(SLC12A4)	NaPi-IIc(SLC34A3)	SPNS2	ABCA2	GABRA1/GABRB2/ GABRG2	TRPC1	ATP8A1
A2AR	GLP1R	MC4R	Gq	GLUT1(SLC2A1)	NCC(SLC12A3)	NTCP(SLC10A1)	SLCO1B3	ABCB1	GABRA1/GABRB3/ GABRG2	TRPC5	CD20
ADRB2B	GLR	MRGPRX2		tURAT1(SLC22A12)	SLC7A2/RBAT	GlyT1(SLC6A9)	SLC42A1(RhAG)	ABCB10	GABRA5/GABRB3	TRPC6	CD81
APJ	GP183	NPY1R		FPN1(SLC40A1)	SLC6A11	PDS(SLC26A4)	SLC9A9(NHE9)	ABCB11	GABRB3	TRPC6	CD9
AVPR2	GPR1	NPY2R		EAAT2(SLC1A2)	SLC6A6	UT1(SLC14A1)	SLC6A5(GlyT2)	ABCC2	GABRR1	TRPM4	DHHC20
C5AR1	GPR155	OX1R		EAAT1(SLC1A3)	ZnT8(SLC30A8)	NKCC1(SLC12A2)	SLC18A2(VMAT2)	ABCC4	GlyRα3	TRPM7	DPAGT1
CaSR	GPR158	OX2R		EAAT3(SLC1A1)	LAT1(SLC7A5)	NBCe1(SLC4A4)	SLC13A3	ABCC5	hERG	TRPML1	FLAP
CCR2	GPR17	OXYR		ACATN(SLC33A1)	GLUT2(SLC2A2)	SMCT(SLC5A8)	SLC26A3	ABCD3	KCNJ2	TRPV1	GGCX
CCR5	GPR52	P2Y1		GLUT3(SLC2A3)	PCFT(SLC46A1)	SLC7A3(CAT3)	SLC35A1	ABCG2	Kv1.3	TRPV3	HER2
CCR7	GPR75	P2Y12		PEPT1(SLC15A1)	ENT1(SLC29A1)	SLC29A3	SLC10A2	ABCG5/ ABCG8	Kv1.3/Kvβ2.1	VSD4-NaV1.7-NaVPas	HER3
CCR8	GPR88	PAC1R		LST1(SLCO1B1)	FLOT1(SLC19A1)	VACTH(SLC18A3)	SLC6A12	bABCC1	Kv3.1		hSTEAP1
CCR9	GPRC5D	PAR1		OCT2(SLC22A2)	DCT1(SLC11A2)	GLUT4(SLC2A4)	SLC24A3 (NCKX3)	CFTR	Kv7.4		Insulin receptor
CLTR2	GRM1	PAR2		MCT1(SLC16A1)-BSG2 complex	FATP4(SLC27A4)	ASCT1(SLC1A4)	SLC6A14		P2X3		JAGN10.25ptr
CNR1	GRM2	PE2R3		NPT1 (SLC17A1)	OAT1(SLC22A6)	GLUT5(SLC2A5)	SLC8A3(NCX3)		P2X7		SCD1
CXCR2	GRM2+ GRM3	SMO		ATA2(SLC38A2)	NRAM1(SLC11A1)	GLUT9(SLC2A9)	SLC22A4		PANX1		Sigma 2 receptor (TMEM97)
CXCR4	GRM2+ GRM4	SSTR2		NaPi-IIa(SLC34A1)	XCT(SLC7A11)	ENT2(SLC29A2)			RyR1		Sigma-1 receptor
DOR(OPRD)	GRM5	TACR1		GAT1(SLC6A1)	MCT4(SLC16A3)-BSG2 complex	SLC7A7			RyR2		TCR-CD3
DRD2	HRH3	TSHR		CHT(SLC5A7)	ASCT2(SLC1A5)	SLC10A4			TASK-1		VKOR1
DRD3	HTR2B			CTL1(SLC44A1)	MCT11 (SLC16A11)	SLC15A4 (Pht1)			TMEM175		
EDNRA	LT4R1			AE1(SLC4A1)	OCT1(SLC22A1)	SLC35A2 (UGALT)			TRPA1		

Note: Biortus supports custom protein services.

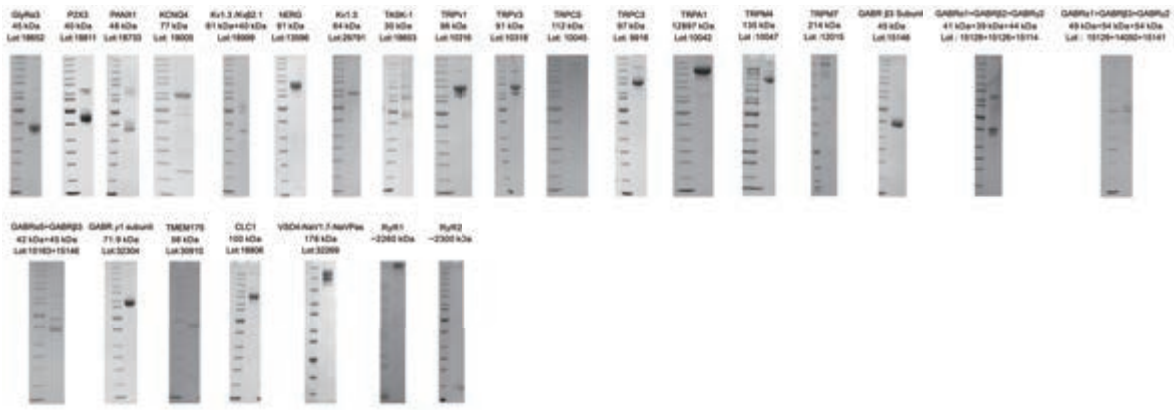
ABC Transporter



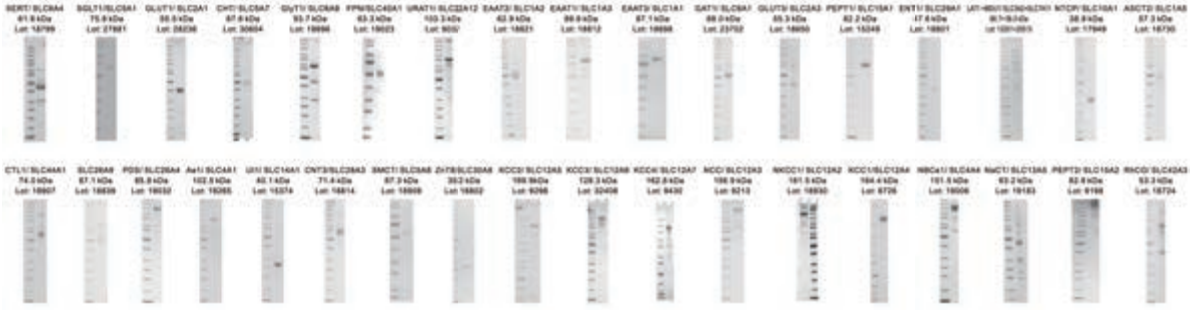
GPCRs



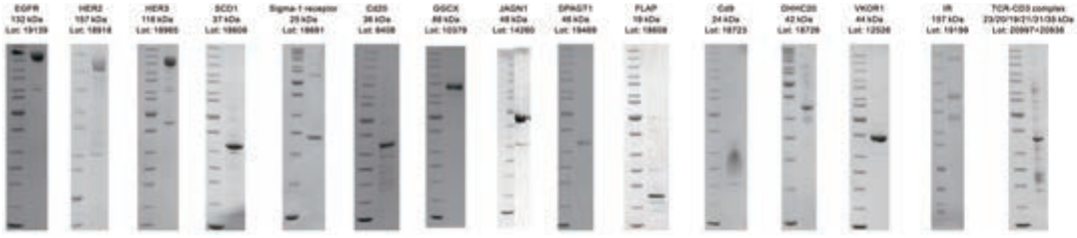
Ion channels



SLC

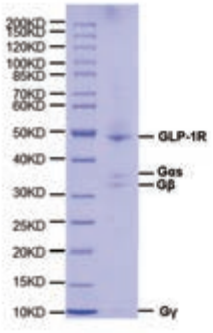


Other MPs



From Protein Preparation to Structural Determination

GPCR-Gs complex: Multiple complex structures to 2.7 Å

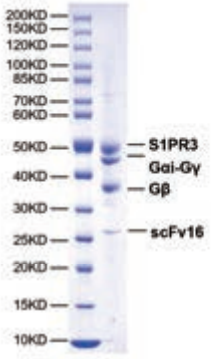


SDS-PAGE

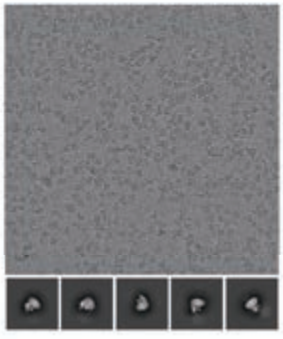
CryoEM micrograph and 2D classes

CryoEM map

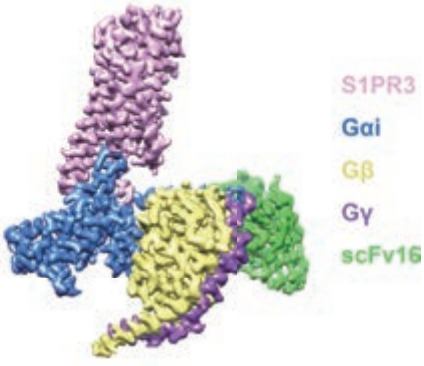
GPCR-Gi complex: Multiple complex structures to 2.8 Å



SDS-PAGE

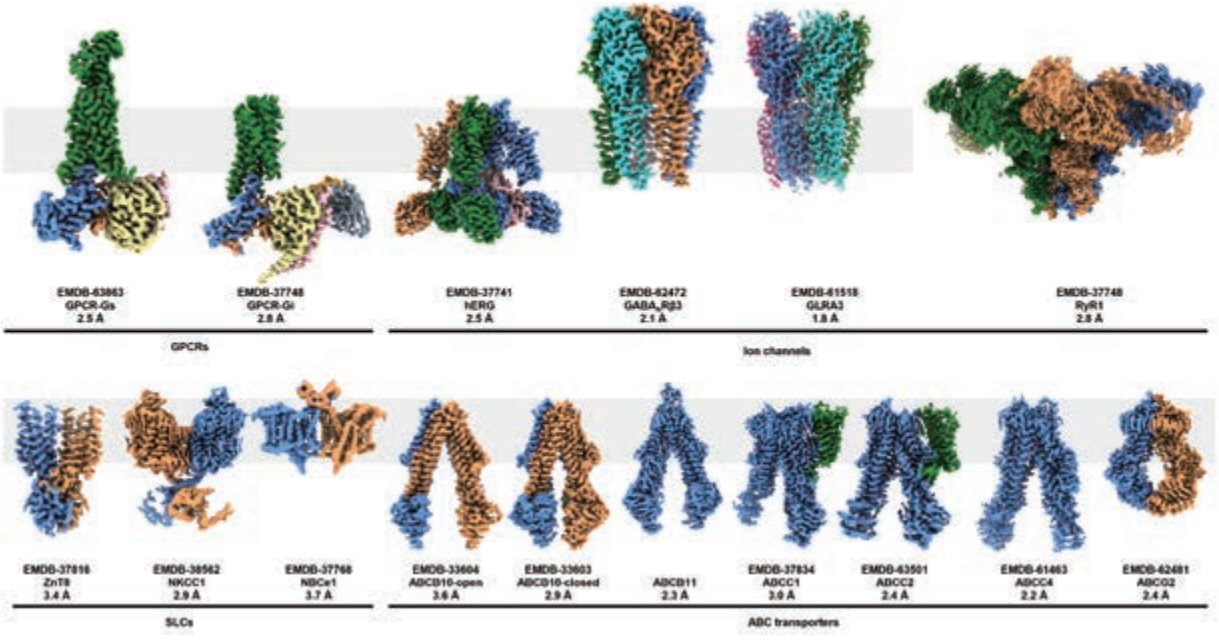


CryoEM micrograph and 2D classes



CryoEM map

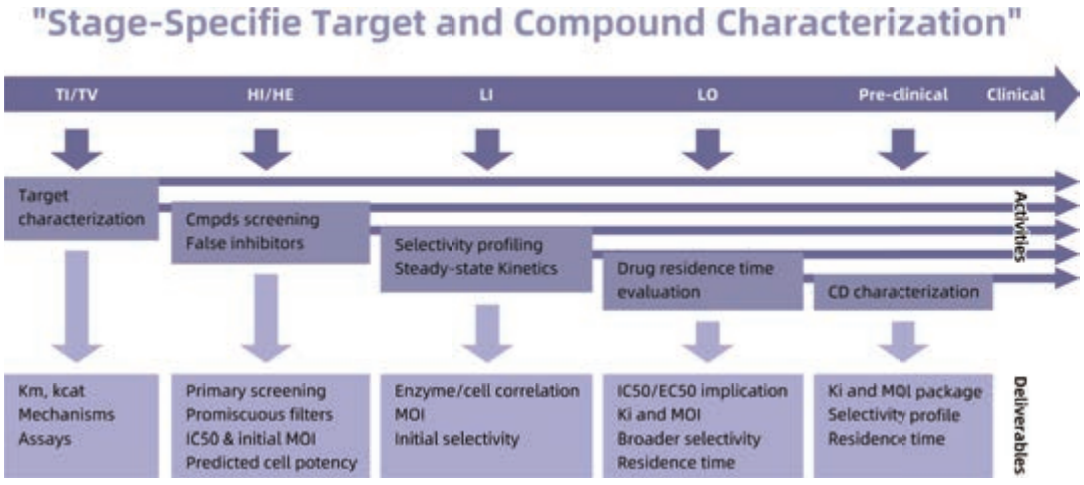
Membrane Protein Structures Solved by Biortus



In vitro Assays & Screening

Biortus presents itself as a comprehensive early-stage preclinical drug discovery CRO that can significantly shorten the time it takes to bring a new drug candidate to clinical trials by managing your entire project from initial "hit identification" to "lead optimization".

Biortus experienced drug discovery team provides a variety of screening options, including target engagement and phenotypic screening. Identifying hit molecules is a primary objective of your project. Biortus has an extensive range of testing equipment and skilled personnel dedicated to assay development, covering biochemical, biophysical, and cell-based assays for hit identification and validation. You will gain early insights into structure-activity relationships (SAR) and mechanisms of action (MOA), empowering you to make informed go/no-go decisions. As your one-stop provider for high-throughput screening, we are committed to advancing your novel therapeutic discovery.



Libraries

Multiple libraries to chose:

- Lead-like
- Covalent
- Fragment
- Molecular glue
- DEL through collaboration

Assay Platforms

Multiple formats:

- Biophysical assays
- Biochemical assays
- Cell-based assays
- Label free
- High Content Analysis

HTS Services

Comprehensive HTS triage strategy for your target:

- Design, development, validation of primary screening assay
- Design and develop secondary/counter/ orthogonal assays
- Screening condition and triage path recommendations

Target Specific Platforms

Mature experiences on target analysis:

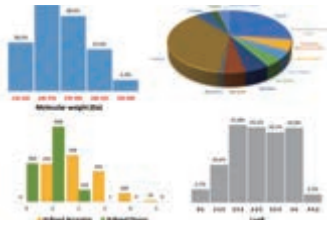
- Target degradation assays
- Kinase panel assays
- DUBs panel assays
- GPCR panel assays

Libraries

Fragment Libraries at Biortus

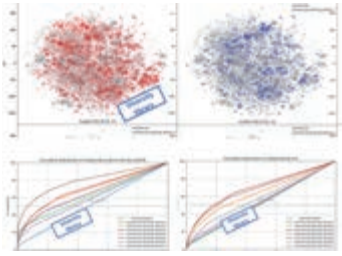
- 3 Commercially Available fragment libraries
- 1 Proprietary Covalent Library

Biortus Unique Covalent Library



Lead-Like Libraries at Biortus

- Diverse, 50K
- Sp^3 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

Hit Finding with Fragment screening

Reagent production

- Protein generation
- Stable cell line generation
- Reagent labeling

- Primary screening
- Confirmation in CRC
- Orthogonal assays

- Co-Crystallization

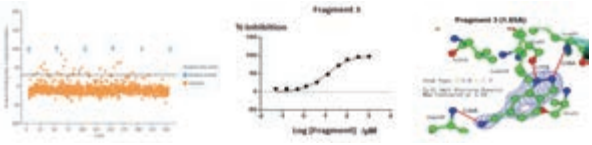
Assay development & validation ~1 - 2 weeks ~ 4 - 8 weeks

Assay formats

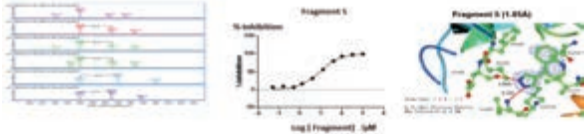
- SPR
- LC/MS
- TRIC
- TR-FRET
- FP, FI
- Caliper
- TSA/DSF
- NanoDSF

> 50 screens run

Fragment screen



Covalent library screen

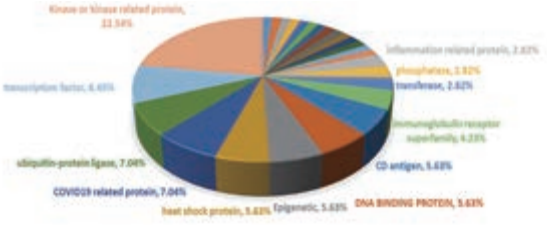


Biophysical assays

Assay types

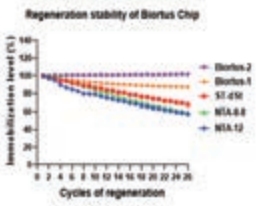
- Thermal Shift Assay (TSA)
- Surface Plasmon Resonance (SPR)
- Isothermal Titration Calorimetry (ITC)
- Temperature-Related Intensity Change (TRIC)
- Spectral Shift Method (SPS)

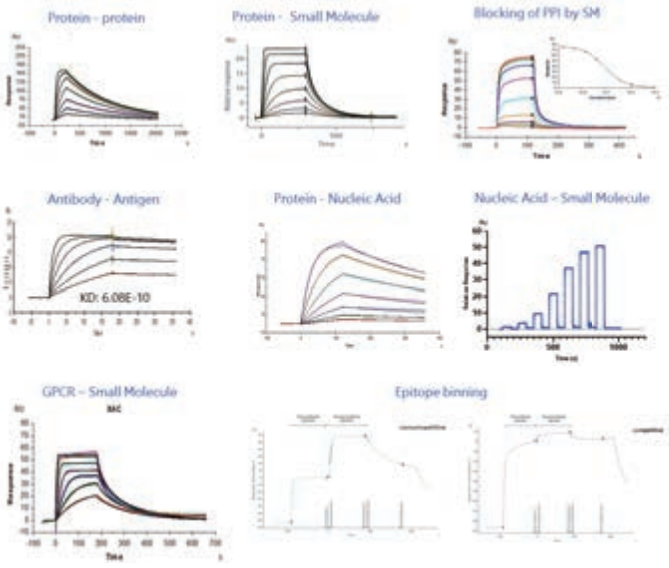
Types of proteins tested



SPR

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





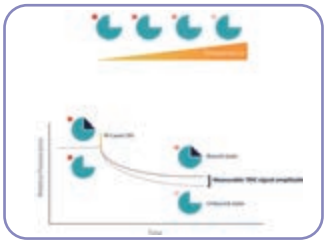
Advantage of Biortus SPR chip:

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

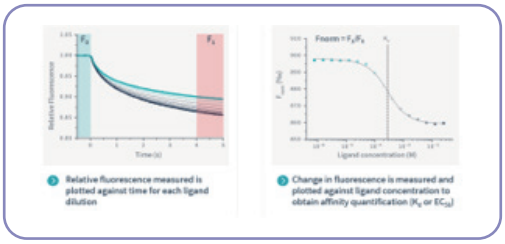
Dianthus Membrane Protein Technology

Dianthus NT.23 Pico Duo

Principle of Dianthus



Determination of binding affinity

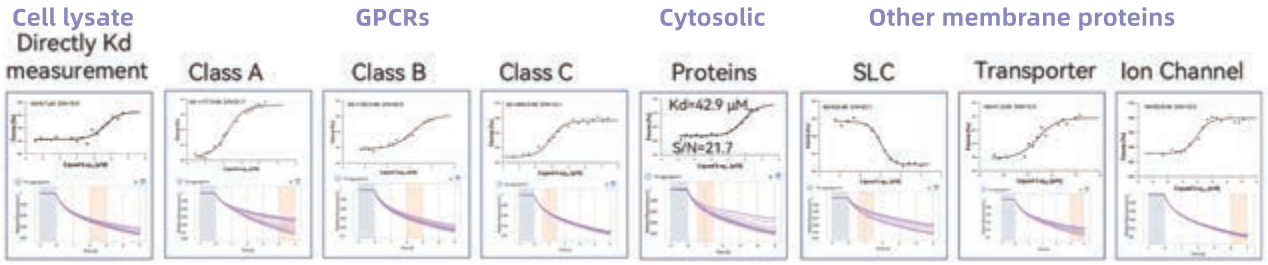


Benefits

- 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.

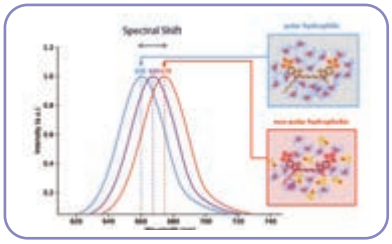
Applications

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

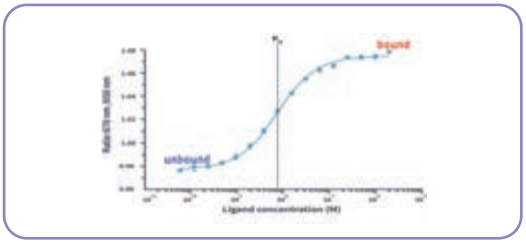


Spectral Shift Technology

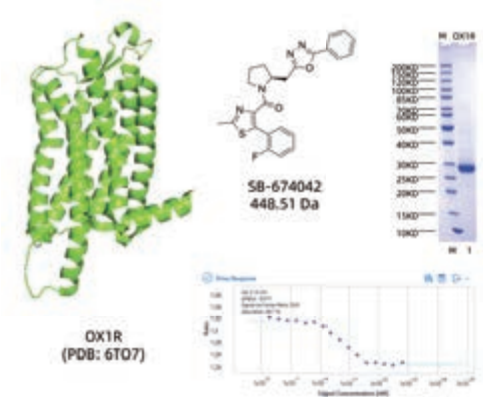
Principle of Spectral Shift



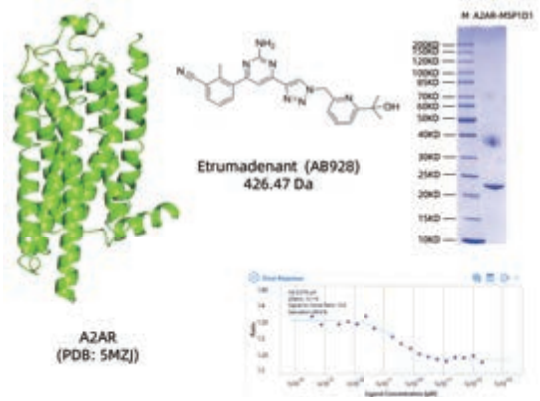
Determination of binding affinity



Under isothermal conditions, the microenvironmental changes induced by ligand binding are detected via picometer-scale fluorescence emission spectral shifts.



SB-674042 binds to OX1R with the Kd value of 2.13 nM (S/N=23.6).

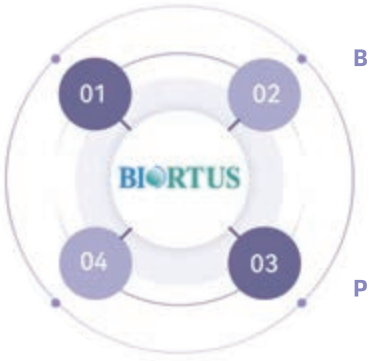


AB928 binds to A2AR-MSP1D1 with the Kd value of 0.279 μM (S/N=12.9).

Biochemical Assays

- TR-FRET
- HTRF
- AlphaLISA
- AlphaScreen
- ELISA
- FP

- OD detection
- Flurescence intensity
- Luminescent-based
- Fluorescence-based
- ADP-Glo
- AMP-Glo
- FRET



- FP assay
- FRET/BRET
- TR-FRET
- HTRF
- AlphaScreen
- Cell free ELISA

- TR-FRET
- HTRF
- AlphaSreen
- AlphaLISA

Cell-based assays

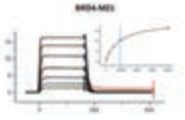
01	02	03	04	05	06
Stable cell line generation	FACS	High content assays	Report Gene assays	Cell viablity/ proliferation	FRET

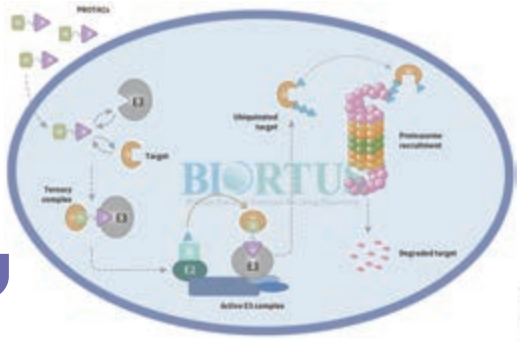
Cell-based assays for MOA & SAR

Assays for PROTAC Drug Discovery

Binary binding assay

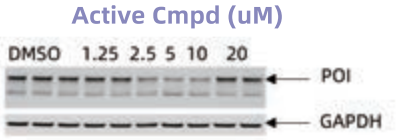
- SPR
- TR-FRET
- ELISA
- FP
- DSF
- TRIC
- Spcetral Shift





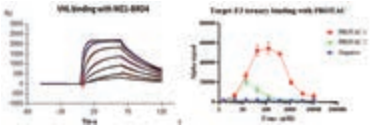
Cellular assays

- 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
- TRIC
- Spcetral Shift



Target ubiquitination assays

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

- 8 E1 (ubiquitin-activating enzyme)
- 37 E2 (ubiquitin-conjugating enzyme)
- 105 E3 (ubiquitin-protein ligase)

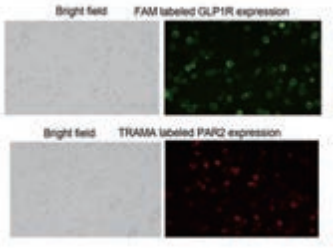
GPCR assay panel

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

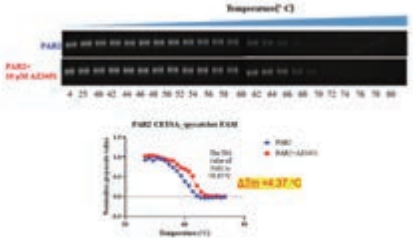
For your pipeline

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

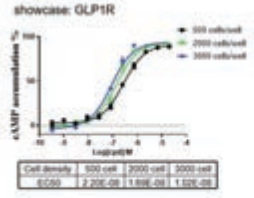
Surface expression:



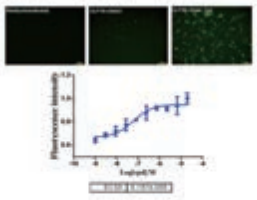
CETSA binding assay:



cAMP assay:



β arrestin recuitment assay:



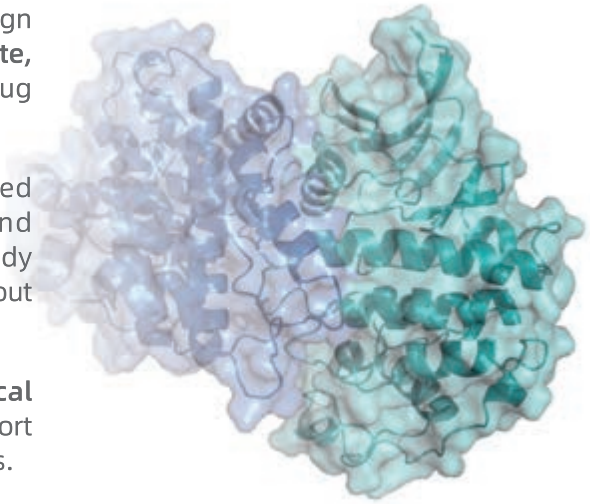
over 10+ tested Targets, over 300+ ready-to-use Targets						
GLP1R	GCGR	OX2R	DRD2	HRH1	GPR75	A1AR
GIPR	OX1R	A2AR	HRH3	M1R	β2AR	PAR2

X-ray Crystallography

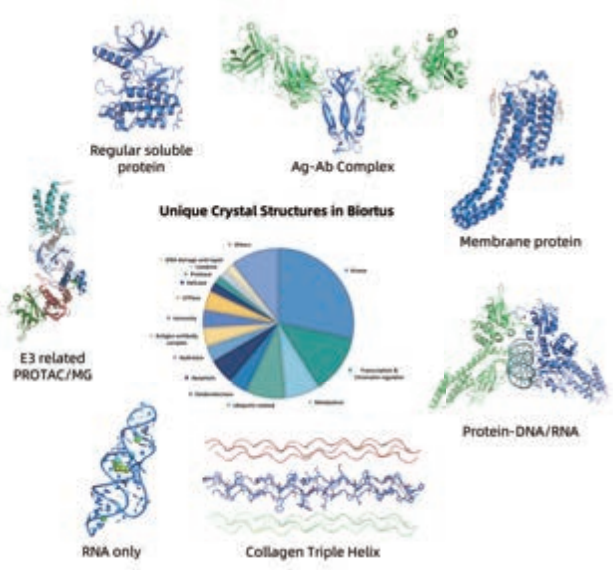
Biortus is a trusted partner for structure-based drug design (SBDD) services, committed to delivering **timely, accurate, and high-quality structural data** to accelerate your drug discovery programs.

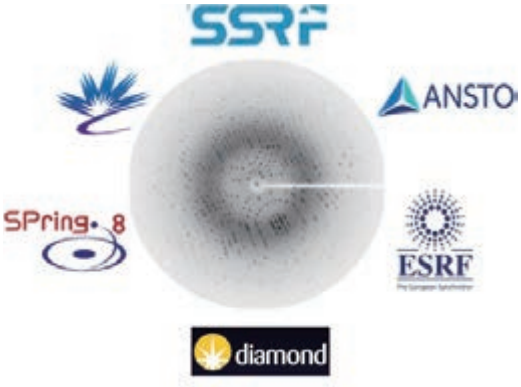
Our crystallography team has successfully determined **16,000+ crystal structures**, spanning protein-ligand complexes, protein-protein complexes, antigen-antibody complexes, and PROTAC complexes—both with and without prior literature precedent.

Backed by **state-of-the-art facilities and deep technical expertise**, we provide reliable structural solutions to support and advance every stage of your drug discovery process.



2.3 Å resolution structure of CDK3/Cyclin E1 complex
Protein produced in-house and determined using Biortus Crystallography

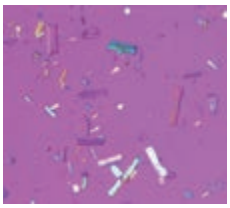




Weekly Access to Synchrotrons

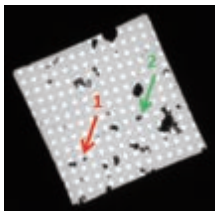
Microcrystal Electron Diffraction (MicroED)

Powder/final product

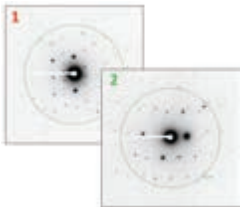


Microcrystal inspection (PLM/XRPD) and sample preparation

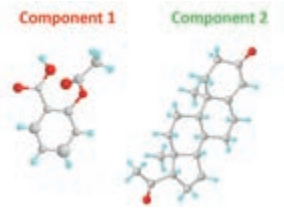
Talos F200C CryoEM



Location of suitable Micro-crystal in imaging mode



MicroED data collection



2D structure, crystal form and absolute configuration

MicroED is a diffraction based technique conducted in a Cryo-EM. This technique can be applled to both small molecule crystals and protein nanocrystals. Structures can be determined in as little as a day.

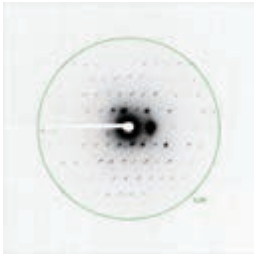
Sample requirements

- 1-2 mgs of sample, 5-10 mgs ideal
- Sample must have crystal forms or we can crystallize in-house

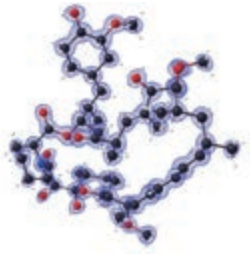
Applications

- Structure and chirality determination
- Characterization of active pharmaceutical ingredient (API) impurities, metabolites or crystal forms for formulation
- Reverse engineering

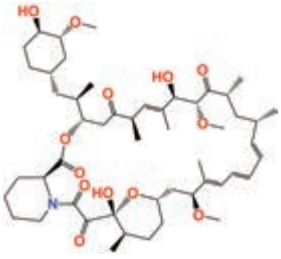
MicroED application: Absolute configuration determination of natural products



MicroED date



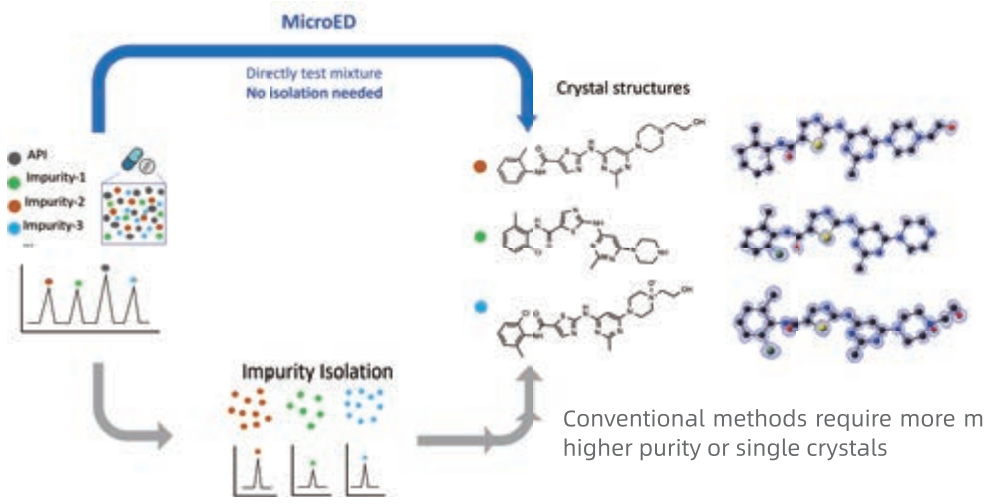
Structure model overlaid with electron potential map



Rapamycin, 914.19 Da
15 chiral centers

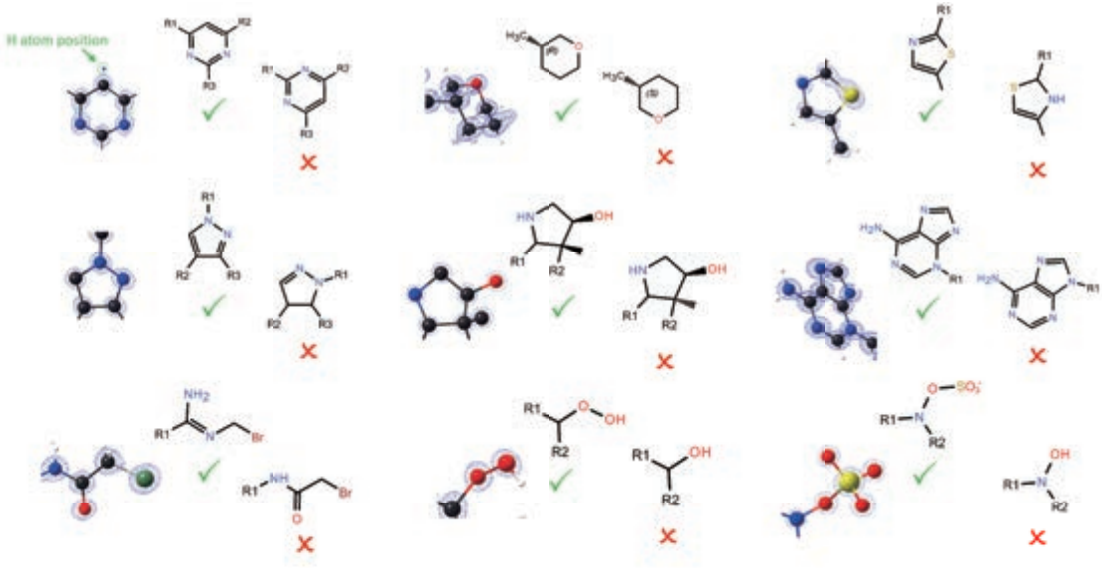
Absolute configuration determined within 10 hours

MicroED application: API impurities identification

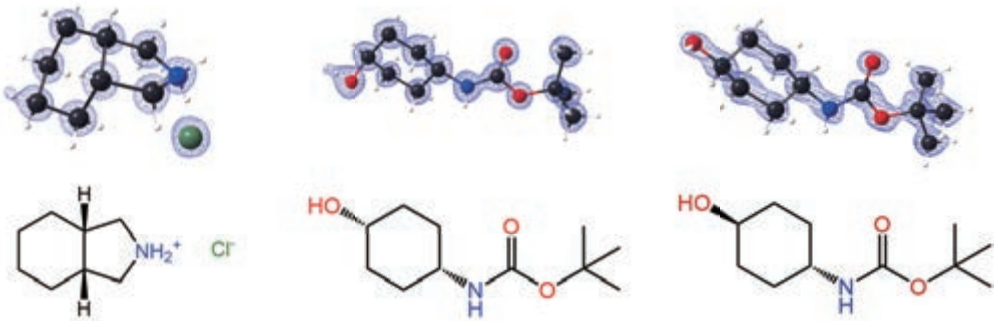


Conventional methods require more material, higher purity or single crystals

MicroED application: 2D structure confirmation from ambiguous NMR/MS results



MicroED application: Cis-trans isomerism determination

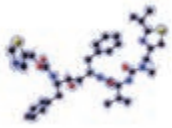


Cis-configured

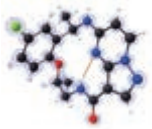
Cis-configured

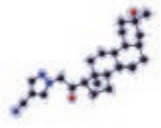
Trans-configured

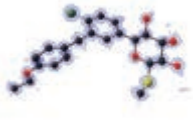
MicroED application: absolute configuration determination

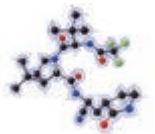

Ritonavir


Vamorolone


Repotrectinib


Zuranolone


Sotagliflozin


Nirmatrelvir


Mannitol


Cinchonine

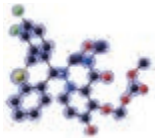

Biotin

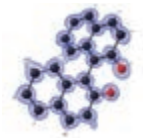

Levetiracetam

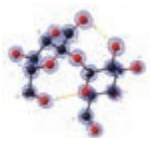

Abiraterone acetate

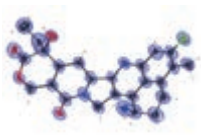

Progesterone

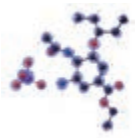

Cas3401-36-3


baloxavir marboxil

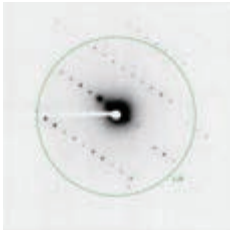

(S)-(-)-1,1'-Bi-2-naphthol


Sucrose

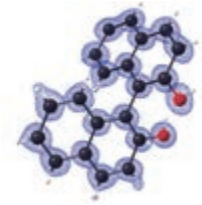

Exatecan

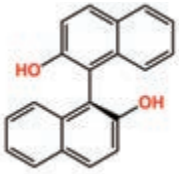

Oseltamivir phosphate

Chiral molecules without a chiral center


MicroED data

(S)-(-)-1,1'-Bi-2-naphthol


Structure model overlaid with electron potential map

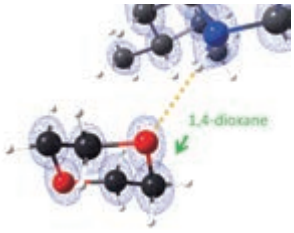


Chemical Formula: $C_{20}H_{14}O_2$
Molecular Weight: 286.33

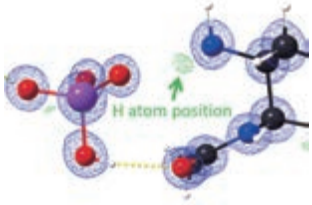
Absolute configuration determined by MicroED

MicroED application: Crystal form identification

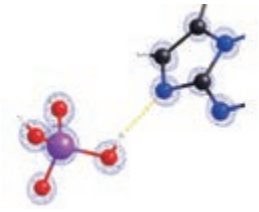
Hydrate



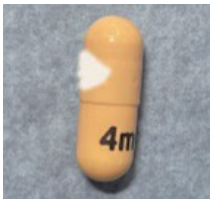
Solvate



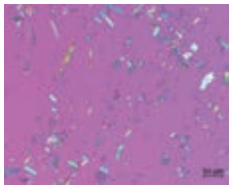
Salt

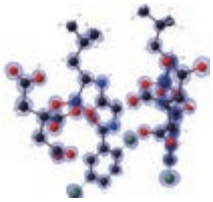

Co-crystal

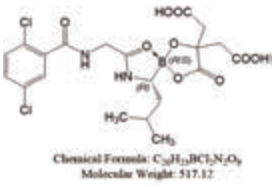
MicroED application: Crystal structure determination of the final product



Ixazomib citrate capsule


PLM image


Structure model overlaid with electron potential map



Absolute configuration determined by MicroED

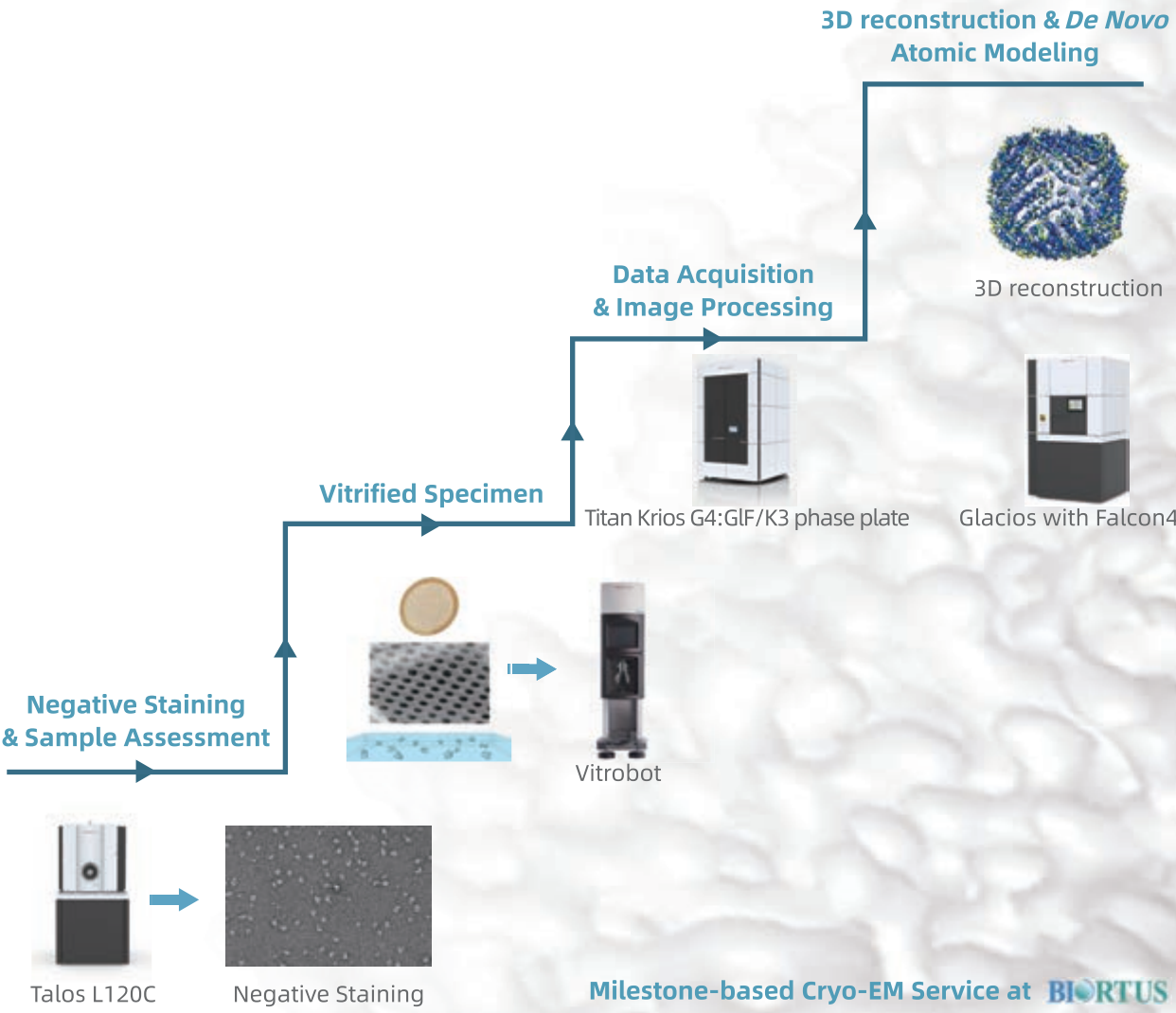
Cryo-EM and Atomic Modeling

Benefits of Cryo-EM

- In single particle analysis (SPA) studies, biological aqueous samples are applied to a grid mesh and flash frozen, preserving the native structure of the protein or protein complex in vitreous ice.
- Phase information is preserved as data is collected on Direct Detector Devices (DDD).
- Requires no special treatment as long as the sample is stable.
- Able to capture different orientations and conformations.

Biortus has an experienced team of scientists with a track record of resolving atomic resolution Cryo-EM structures for large proteins, protein complexes, ligand bound proteins, and membrane proteins.

- **Highest in-house resolution achieved 1.5 Å.**
- Multiple *de novo* atomic models delivered.
- Smallest protein resolved ~65 kDa.
- One-stop membrane protein cryo-EM service.

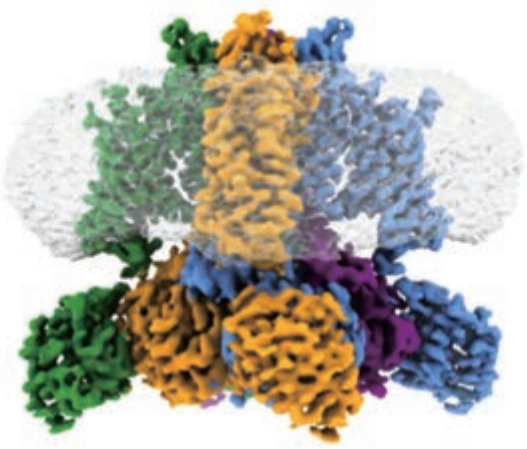


Largest Commercial Cryo-EM Facility

- » **Titan Krios G4/GIF/Phase plate/K3 300 kV**
- » **Glacios with Falcon4 200 kV**
- » **TF20 with CCD 200 kV**
- » **Talos F200C with Ceta-D 200 kV**

Classes of proteins resolved at Biortus

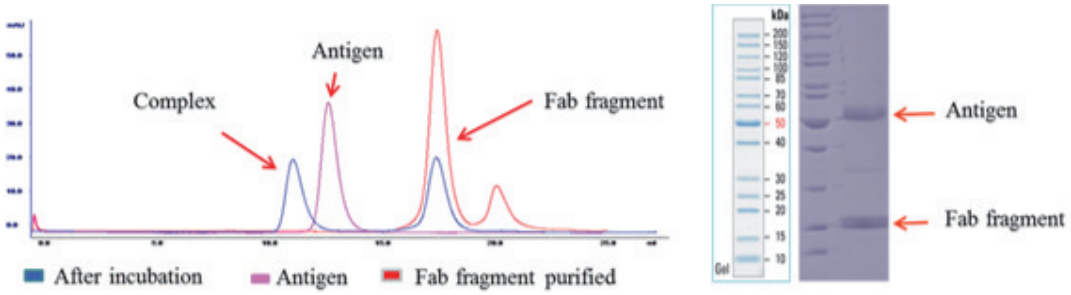
- Membrane proteins +/- ligands (GPCRs, Ion Channels, Transmembrane proteins, etc.)
- PROTAC-related ligase system +/- substrate
- AAA+ proteases +/- substrate
- Large enzyme complex assembly (>0.5 MDa)
- Antibody-antigen complexes (epitope mapping)
- Immune system related signaling pathway proteins
- Nucleic acid binding proteins (RNA polymerases, transcription factors, etc.)
- Epigenetic related proteins
- Deubiquitinases
- Viruses



2.56 Å resolution apo-hERG structure
Protein produced in-house and deterined using Biortus Cryo-EM

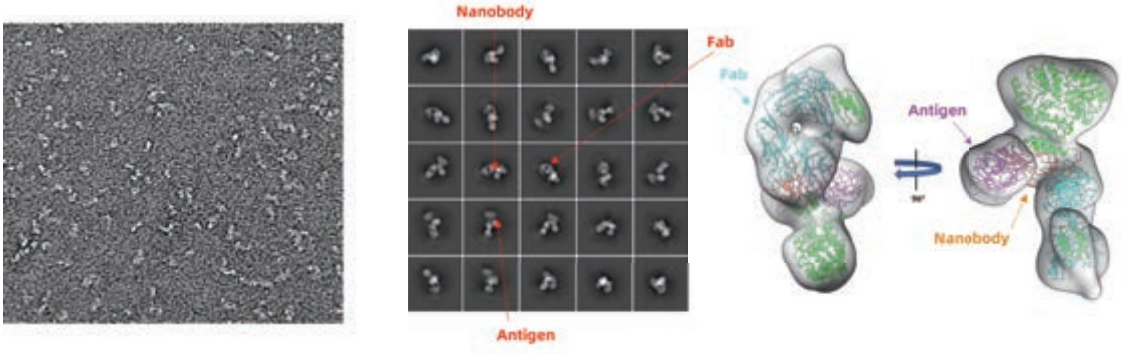
Antibody Analysis by Cryo-EM

Antigen/Fab complex preparation



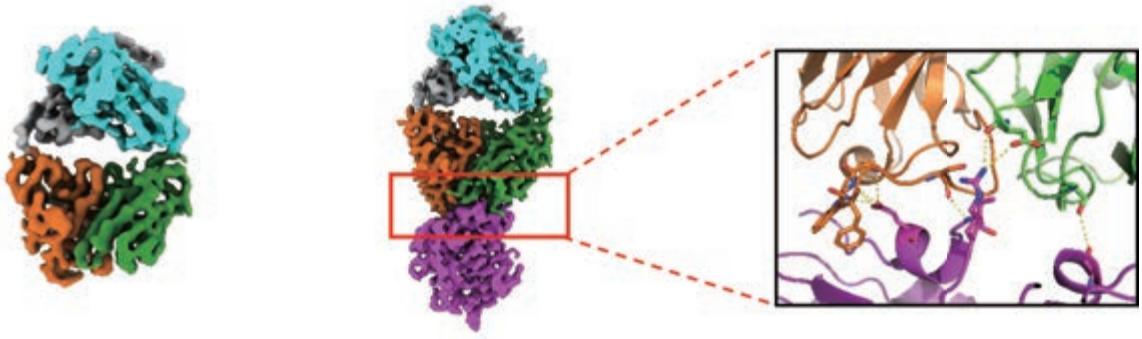
SEC SDS-PAGE

Quick antibody/fab analysis by negative stain



Negative staining 2D classification 3D density map

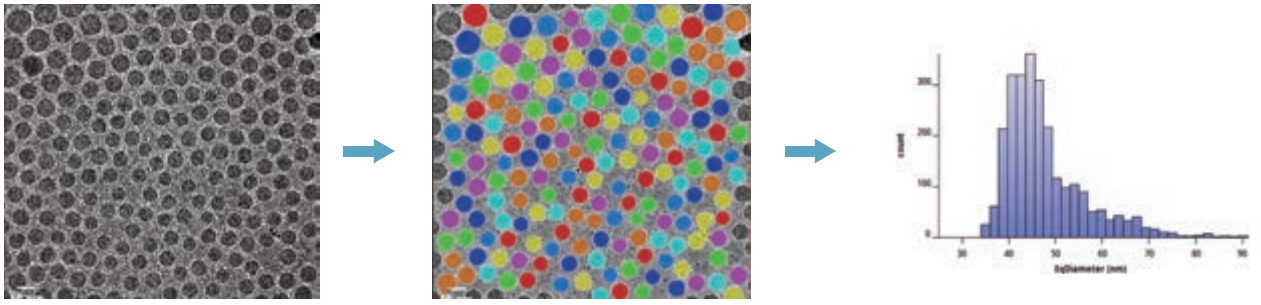
High resolution epitope mapping with cryo-EM



Fab (50 kDa) Fab + Antigen (~3.0 Å) Binding epitope

LNP analysis with Cryo-EM

LNP Analysis with Cryo-EM

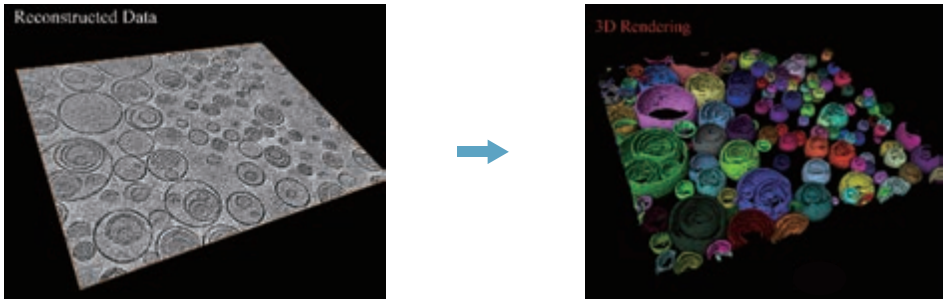


Cryo-EM Image

Analysis

Parameters
(Diameter, Area, Morphology, etc.)

LNP Tomography



Data Collection

3D Reconstruction

AAV Particle Analysis

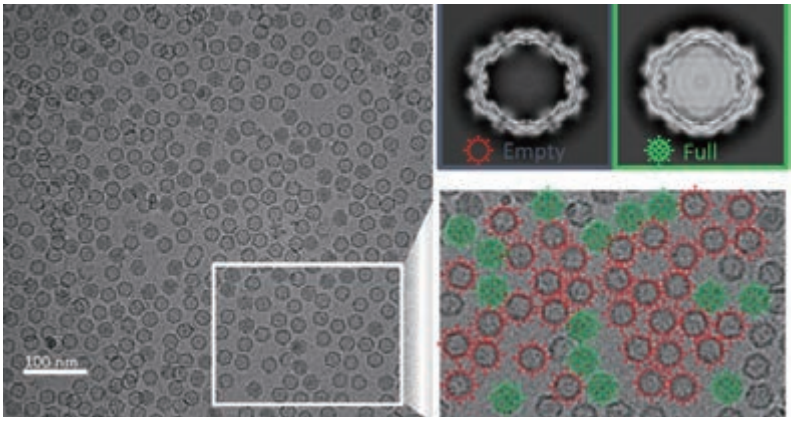
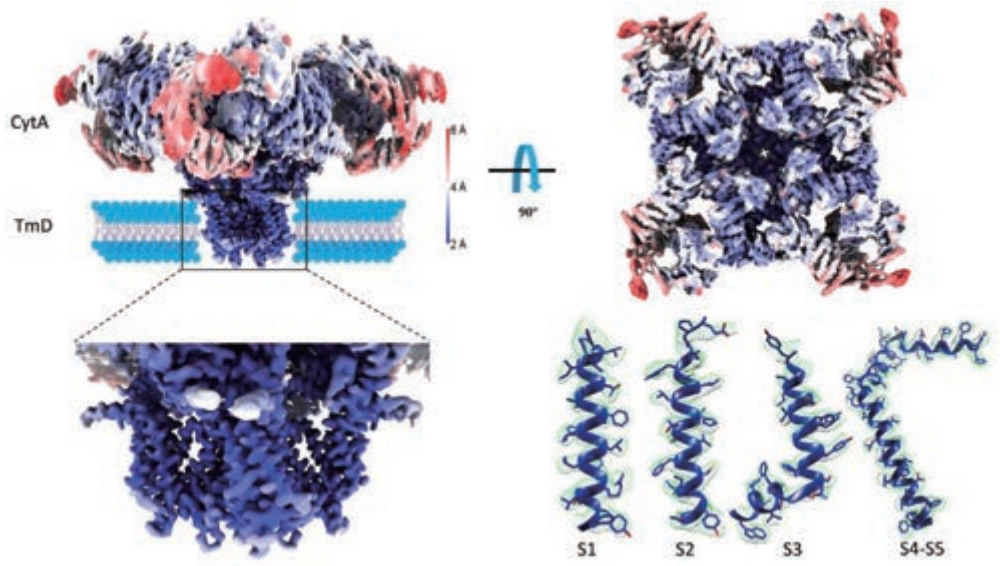


Image courtesy of Dimple Karia, ThermoFisher Scientific

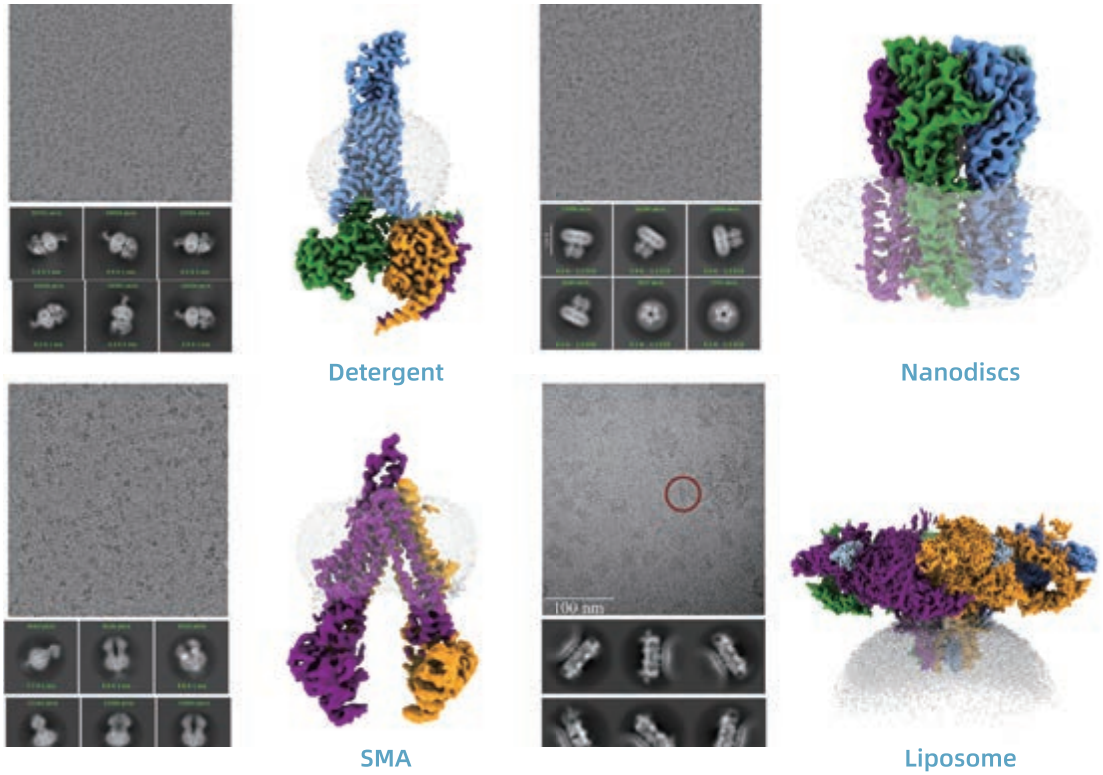
Cryo-EM Showcases

The Largest Known Ion Channel, RyR1

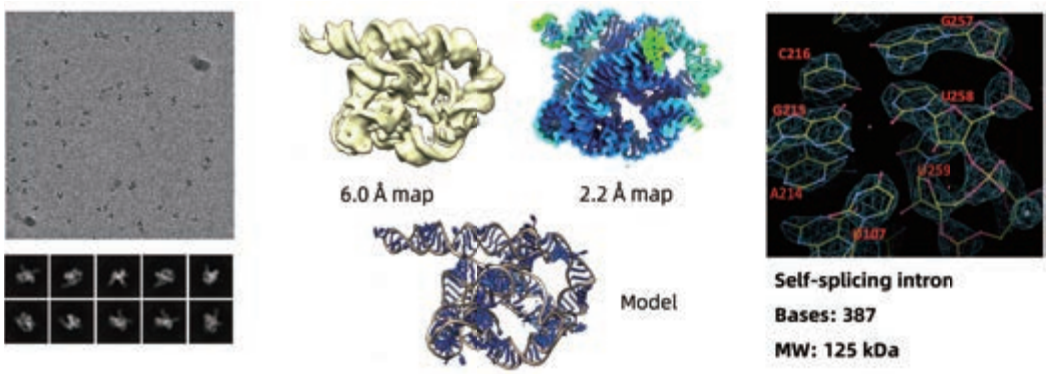


Our experienced team purified and solved a 2.8 Å Cryo-EM structure of RyR1 (2.3 MDa) from rabbit skeletal muscles within two weeks.

Multiple Solubilization Strategies for Membrane Proteins

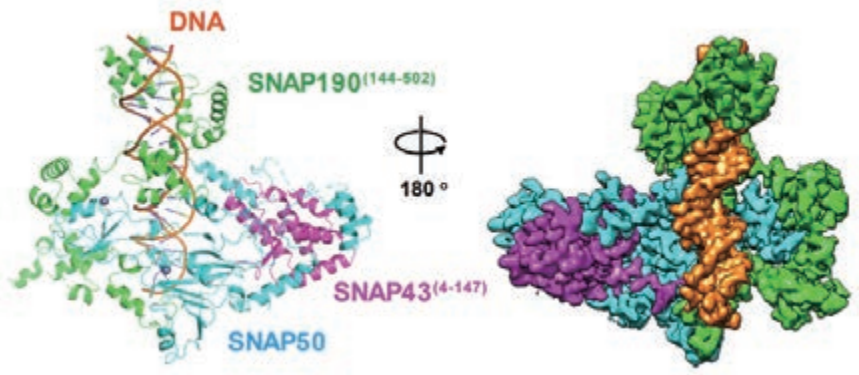


Cryo-EM Structure of RNA



Cryo-EM Structure of Human SNAPc with Shandong University

In collaboration with Professor Wei Wang of Shandong University, we resolved the structure of human snRNA activating protein complex SNAPc to 3.4 Å using CryoEM, furthering the understanding of PoI III dependent snRNA transcription.



Sun, J., et. al, Structural basis of human SNAPc recognizing proximal sequence elements of snRNA promoter. *Nature Communications,* 2022

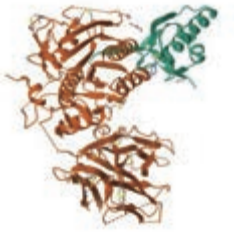
Structure Gallery

In order to expedite the SBDD process, Biortus has compiled a growing list of internal projects generated completely in-house from gene to structure to serve as examples of the quality of work that we can provide and as a launchpad for your project.

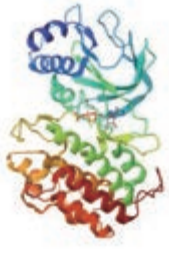
Please contact us at info@biortus.bio to receive the comprehensive list of structures in our gallery.

PPARg
X-ray, 8WFE, 2.2 Å

PCSK9
X-ray, 8WFR, 1.95 Å



NIK
X-ray, 8YHW, 2.9 Å



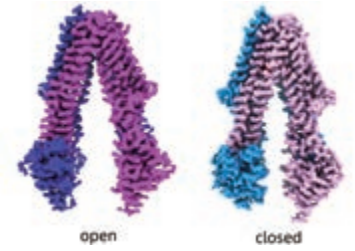
MAPK13
X-ray, 8X23, 1.5 Å

GLRA3

First-ever-seen high-resolution structure
Cryo-EM, 1.82 Å

ABCB10

2 conformations from 1 dataset
Cryo-EM, 2.8 Å

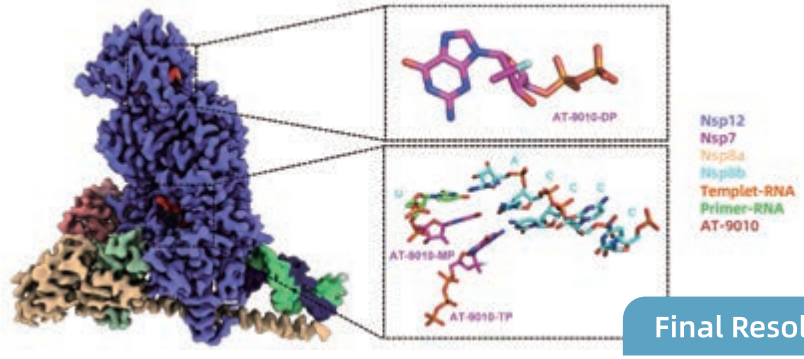


CD73 bound with Fab

Cryo-EM, 2.92 Å

Publication-Quality Work Is Our Standard

Co-complex structure of RNA and AT-9010 compound with RdRp for Atea Pharmaceuticals

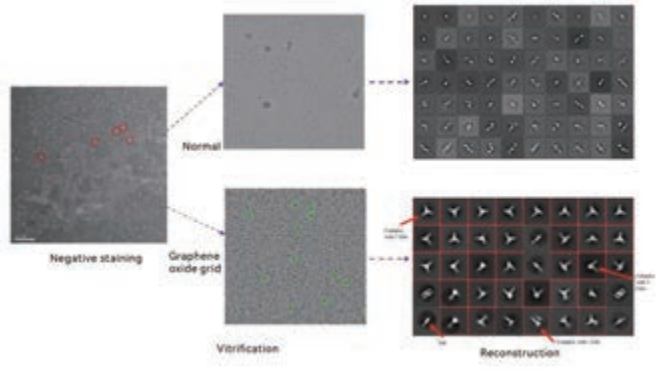


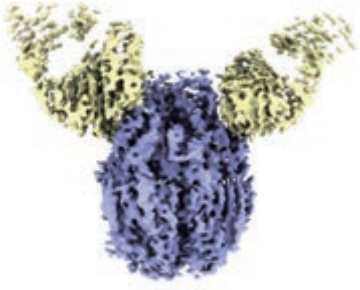
Final Resolution 2.98 Å

From gene to structure: ~2 months

Shannon A., et. al, A Dual Mechanism of Action of AT-527 against SARS-CoV-22 polymerase, *Nature Communications*, 2022

Cryo-EM structure of Fabs in complex with hMPV for Merck





Final Resolution 3.70 Å

Xiao, X., et. al, Profiling of hMPV F-specific antibodies isolated from human memory B cells, *Nature Communications*, 2022

For the complete list of publications, please visit our website at www.biortus.bio

2026.03

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