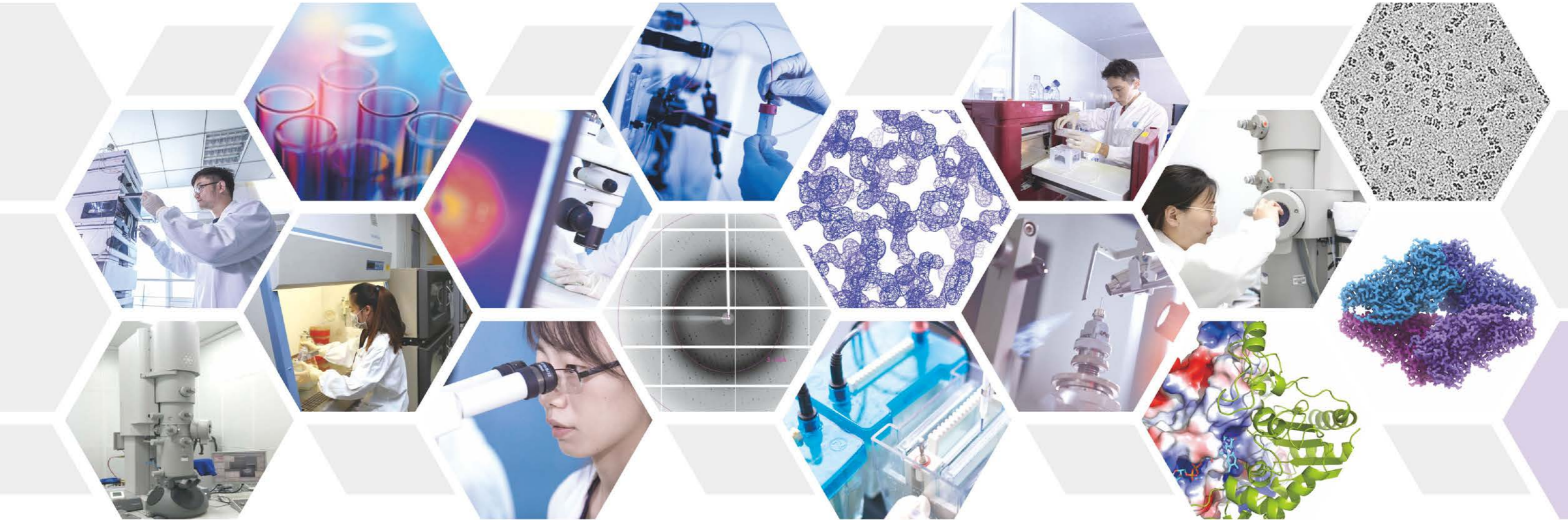


## Protein Focused Services for Drug Discovery From Gene to Structure



**WUXI BIORTUS BIOSCIENCES CO., LTD.**

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**BIORTUS**

## About Us

Founded in 2009, Wuxi Biortus ("ortus" meaning sunrise in Latin) Biosciences Co. Ltd. is located in Jiangyin city at the Yangtz Delta. We are an innovation-driven contract research organization (CRO) committed to high quality R&D services in support of drug discovery.

We have established four world-class research platforms:

- Recombinant Protein Production
- Structural Biology (X-ray Crystallography, Cryo-EM, and MicroED)
- *In Vitro* Assays and Screening
- Medicinal Chemistry and Process Development

With our wide-range research capabilities and strong relevant expertise, we have successfully delivered many projects to global clients including pharmaceuticals, biotechnology companies, and research institutions.

## Technical Platforms

### Protein Expression, Purification and Production

- ✓ Construct design, generation and mutagenesis
- ✓ Expression systems such as *E. coli*, insect cells, and mammalian cells
- ✓ Purification with affinity chromatography, IEX, and SEC
- ✓ Achieving purity > 95%

### Structural Biology

- ✓ X-ray Crystallography: in-house X-ray system and access to synchrotron
- ✓ Cryo-EM: in-house FEI TF20 and access to Krios
- ✓ MicroED: small molecule structure determination using in-house FEI TF20

### *In vitro* Assays and Screening

- ✓ Fragment libraries with 3522 unique fragments
- ✓ Screening with various biochemical and biophysical methods
- ✓ SPR / Caliper / CE / ThermoFluor / Radiometric Assay etc.

### Medicinal Chemistry and Process Development

- ✓ Asymmetric synthesis
- ✓ Transition metal catalyzed coupling reactions
- ✓ Heterocycle compounds



## Protein Expression

- ✧ Construct Design, Generation and Mutagenesis
- ✧ Small and Large Scale Protein Expression
  - Expression systems: *E. coli*, insect cells, mammalian cells
  - Expression screening with split gfp
- ✧ Capabilities
  - Over 500 proteins / complexes delivered
  - 400 L (flask) and 50 L (fermenter) *E. coli* culture per week
  - 200 L insect culture per week
  - 50 L mammalian culture per week



4x Fermenters



## Protein Purification

- ✧ General Procedure



- ✧ Standard QCs
  - Purity (SDS-PAGE)
  - Concentration (Nanodrop or Bradford Method)
  - MW and Protein Modification (LC-MS)
  - Oligomerization (Analytical SEC)
  - Stability (Thermal Shift Assay)

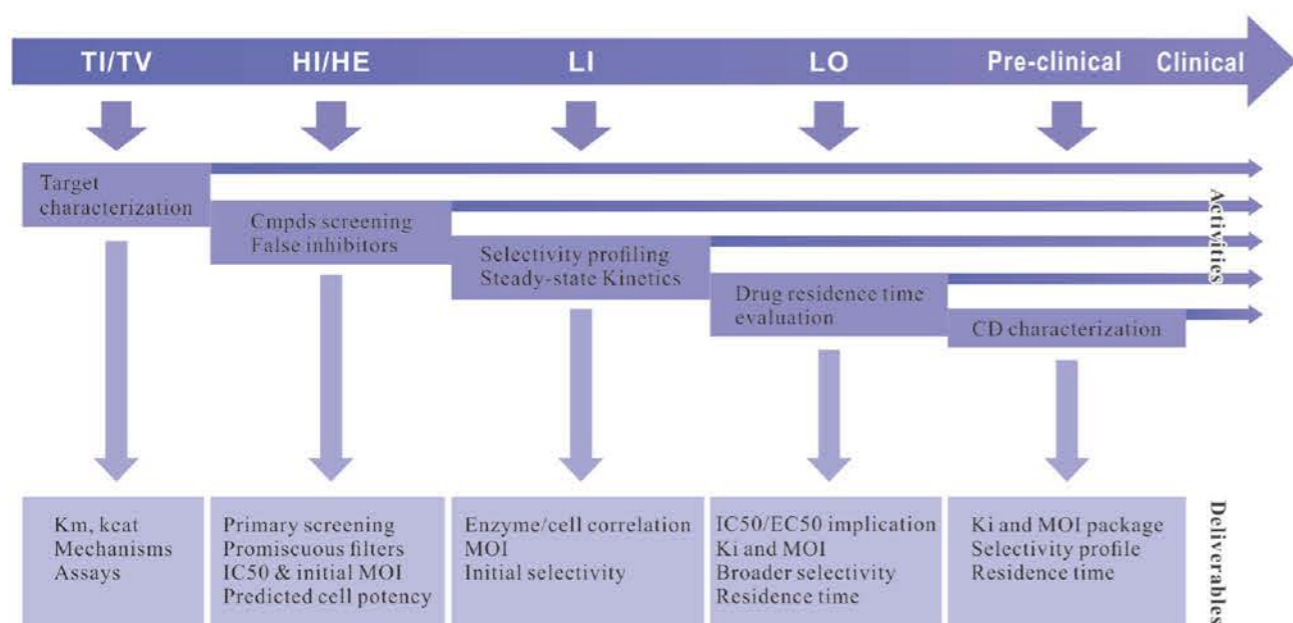


TOF-MS



15x GE AKTA

“Stage-Specific Target and Compound Characterization”



Biophysical Assay

- ✓ Surface plasmon resonance (SPR)
- ✓ Capillary electrophoresis (CE)

Biochemistry Assay

- ✓ LANCE assay (TR-FRET)
- ✓ Fluorescence polarization (FP)
- ✓ Caliper mobility shift assay
- ✓ Radiometric assay
- ✓ Thermo fluorescence assay
- ✓ Cell based assay (CTG, WB)

Broad Service Scope

- ✓ Selectivity panel screening
- ✓ High-throughput screening
- ✓ IC50 dose response
- ✓ Enzyme kinetics
- ✓ Compound mode of action



Caliper EZ Reader II



Biacore S200



Bravo



Top count



CE



M1000



Envison

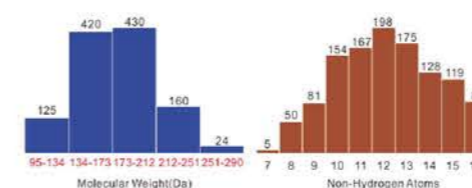


MD M5e

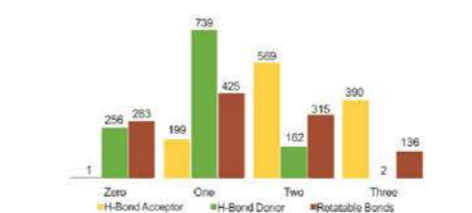
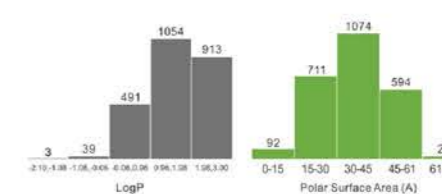
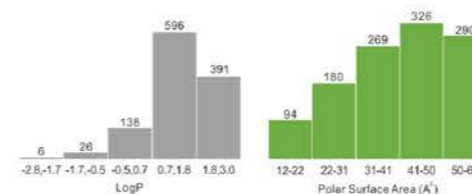
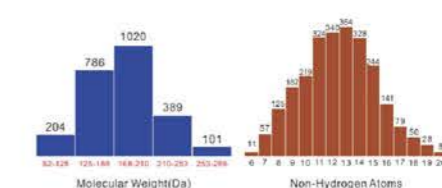
※ Biortus Fragment Libraries

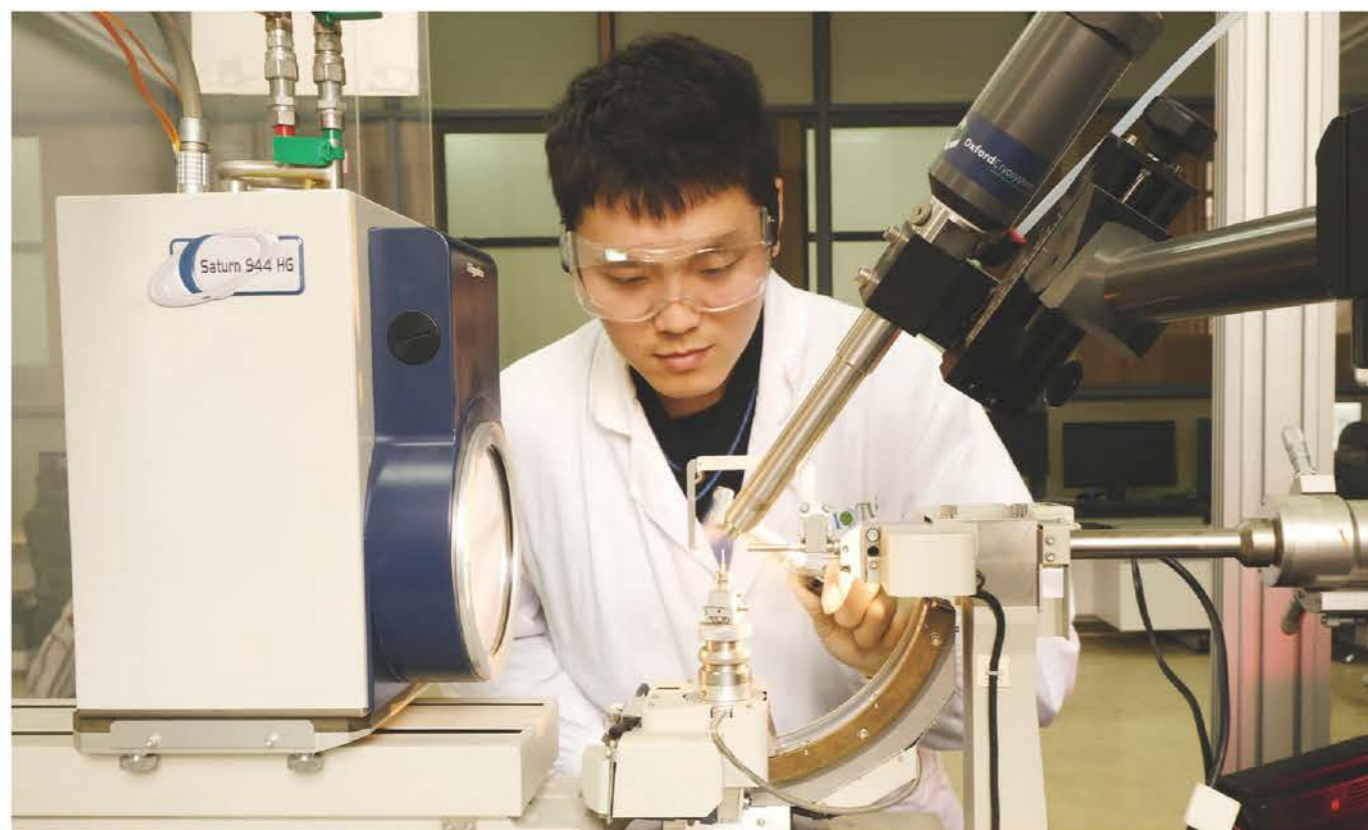
Biortus retains two Rule-of-3 compliant fragment libraries dissolved in DMSO at 100 M in 96- and 384-well format. Fragment Library 1 has a total of 1159 compounds of which 137 overlaps with Fragment Library 2 which has 2500 fragment in total. Depending on the expected hit rate of the target, clients may choose and screen the smaller or larger library, or the combined one with a total of 3522 unique fragments.

Biortus Fragment Library 1 (1159 Fragments)



Biortus Fragment Library 2 (2500 Fragments)





### ※ X-Ray Crystallography

Biortus constantly strives to provide timely, accurate and high-quality structural data, which made us one of the preferred partners of many global pharmaceutical companies for structure-based drug design (SBDD) services. The crystallography team at Biortus has hitherto delivered over 2000 crystal structures, many of which were in complex with ligands, The structural information helps our clients to speed up their drug discovery process.

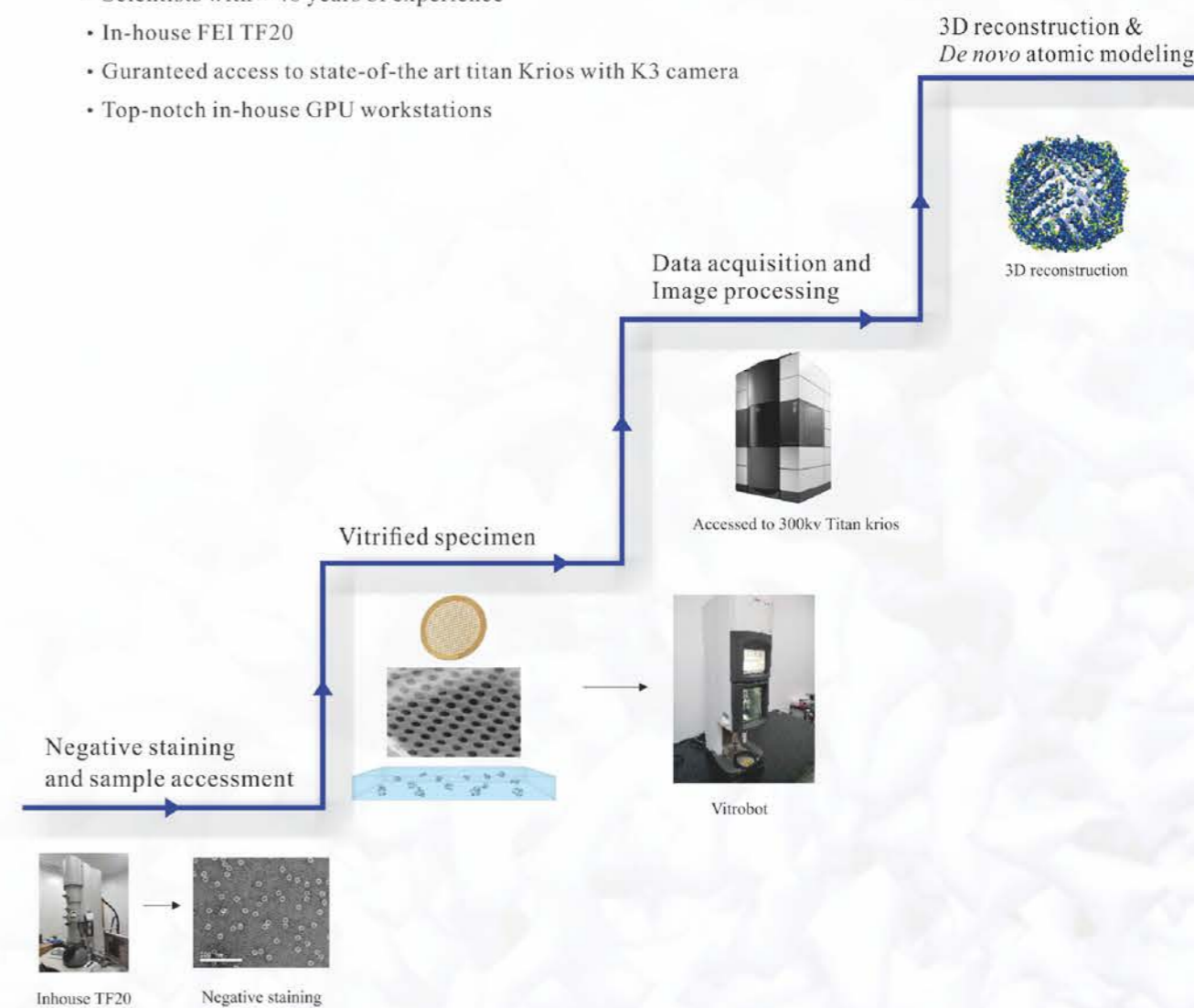
With our in-house Rigaku FR-E+ SuperBright rotating anode coupled with R-axis IV++ plate area diffractometer, we could readily collect high resolution data. To increase data collection throughput, Biortus has frequent access to the Shanghai Synchrotron Radiation Facility (SSRF), of which high resolution data sets are collected within minutes. Biortus also has access to multiple data collection facilities like APS in Chicago, ESRF in Grenoble, and CSRF in Canada.



### ※ Cryo-EM and Atomic Modeling

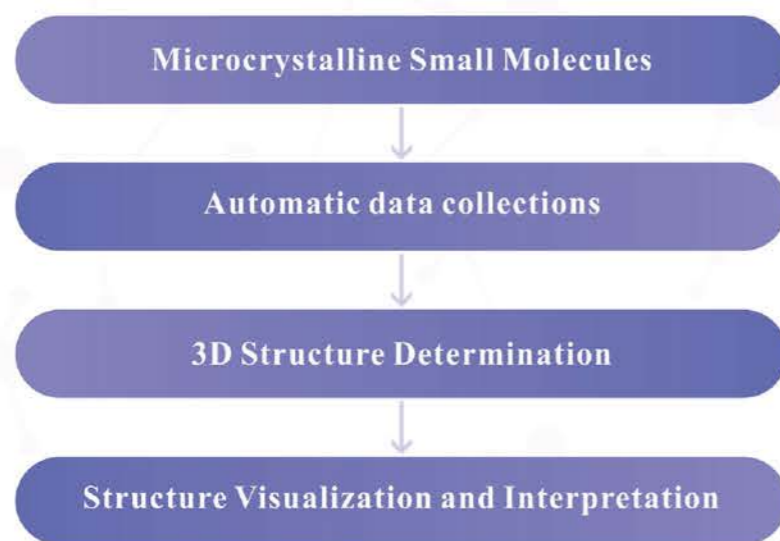
Complementary to X-ray crystallography, Biortus has a competent *cryo*-EM team ready to work with none crystalline large proteins such as membrane proteins and their complexes. Vitrified samples are pictured in the electron microscope for structure determination. Resolution around 3.5Å or better would allow us to identify side-chain of amino acids as well as bound ligands.

- Debut in 2018, multiple structures delivered
- Highest resolution = 2.7Å
- *De novo* atomic models delivered
- First & Only available commercial service in China from gene to cryo-EM structure
- Scientists with > 40 years of experience
- In-house FEI TF20
- Guaranteed access to state-of-the art titan Krios with K3 camera
- Top-notch in-house GPU workstations

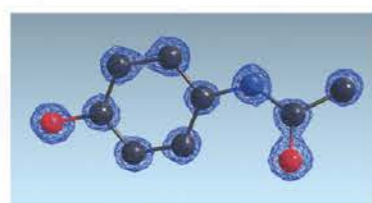
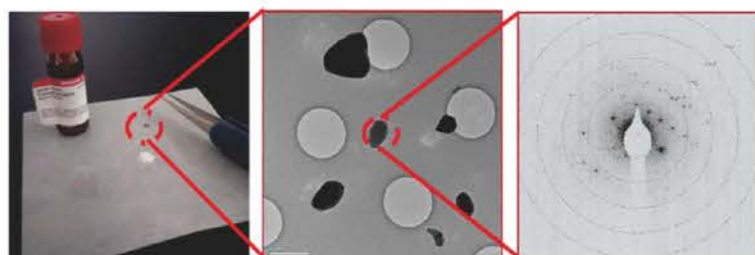


Milestone-based Cryo-EM Service at BIORTUS

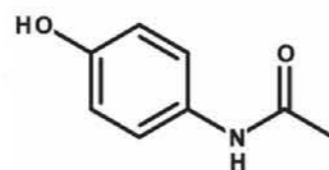
Work flow of **one-stop** MicroED service at BiorTus



Example case of Acetaminophen



0.75 Å



C<sub>8</sub>H<sub>9</sub>NO<sub>2</sub>



- Chemistry lab with 50 fume hoods in more than 1,100 square meter space
- Scale-up facility with 100L jacketed reactors and walk-in fume hoods
- State-of-the-art analytical equipment such as LC/MS, NMR, HPLC, X-ray analysis, and MicroED

Experience in specialty chemistry

Asymmetric synthesis such as Sharpless Epoxidation, Corey-Bakshi-Shibata (CBS) reduction, Olefin Metathesis using Grubbs catalyst II, and biocatalysis.

Transition Metal-catalyzed Coupling Reactions such as Suzuki coupling, Negishi reaction, Stille cross coupling, Heck reaction, Sonogashira coupling, Buchwald-Hartwig reaction, and Ullman reaction

Synthesis of heterocycle compounds, such as substituted thiophene, pyridine, pyrimidine, indole etc.