

WuXi AppTec HitS

- WuXi AppTec HitS is a unit under WuXi Biology;
- HitS offer a service covering the whole target to hit platform: protein production, DEL and Fragment Based screening (FBDD), and hit validation (biophysical & biochemical panel, structure-based drug discovery).
- HitS has four operational sites located in China, Germany and the USA and about 250 proficient scientists, assuring the high quality data delivery in a timely manner.

Protein Production

All Target Classes and Challenging Proteins

Cancer and Inflammation ATM, AMPK, NEK7, PI3K, ROR1, SRC, ULK1, WEE1, NLRP3
Membrane Proteins Glucose transporter, P2X3, GPR40, CNR1, β 2AR...
DNA Damage Response ATM, ATR/ATRIP, CHK1, CHK2, CDKs and cyclins ...
Neurodegeneration BACE1, PDE, NFE2L2, PTPN1, MAO-B, NTRK1, JNKs...
RNA/DNA Mod. Proteins Cas9, FEN1, EME1, RIG-I, SND1, WRN, SMARCA...
Epigenetic Targets BRD2, BAZ1A, CREBBP, SIRTuins, HDACs, EHMT1...
Immune System cGAS, STING, IL1, ILRL1, MMPs, antibodies...

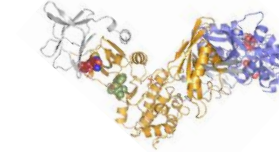
Over **1500** Proteins Produced

1200 Assay Grade Proteins (verified for biophysical methods)

>250 Crystallization Grade Proteins (verified crystallization protocols)

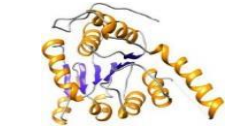
Protein Complexes

AMPK – AMP activated protein kinase



DNA Modifying Proteins

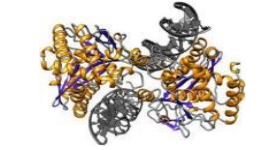
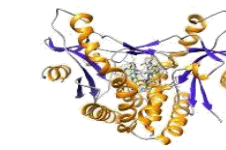
SMARCA2 – transcriptional regular / chromatin remodeling



Immune Therapy / Rare Diseases

STING-stimulator of interferon genes

cGAS-DNA sensor in the STING pathway



Membrane Proteins

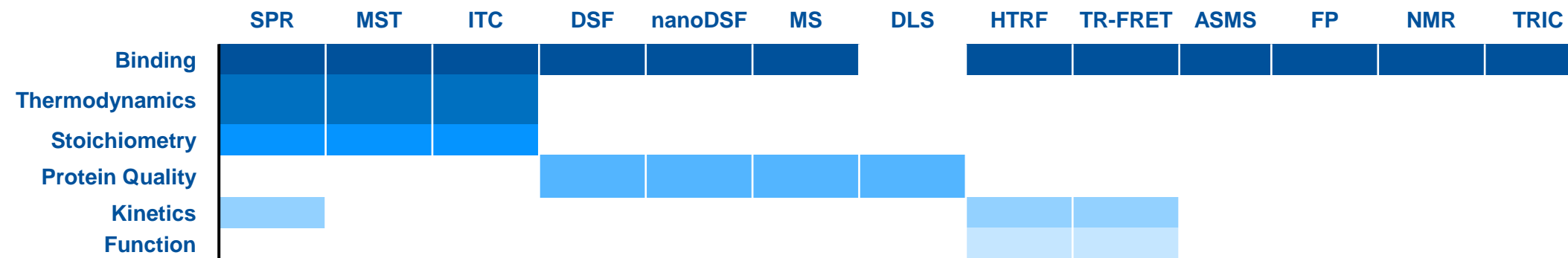
P2X3-ATP-gated ion channel, CNR1, GPR40, Glucose transporter...

RNA Modifying Proteins

DDX58 – ATP-dependent RNA helicase...

Biophysical & Biochemical Platforms

Broadest Technologies Suit for Hit-finding Globally



Ready-To-Go Assay for Broad Range of Drug Targets

nanoDSF • MST • SPR • ADP-Glo • Nucleotide-exchange



Established Assays

Optimized assay conditions



Flexible

Single/multiply assay in parallel



Cost-effective

Low budget, high quality data



Fast Turnaround Time

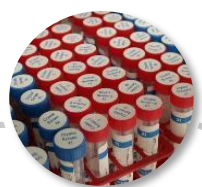
Up to 2 weeks

Structural Biology Platforms

X-Ray Crystallography



Crystal grade protein production



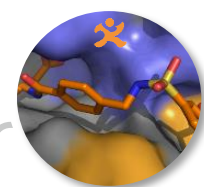
Screening of myriad crystallization conditions



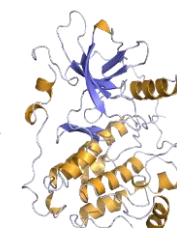
Fine-tuning of crystallization conditions to grow well diffracting crystals



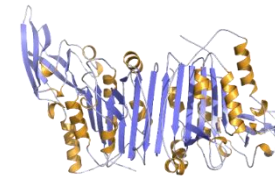
Preparation of crystals for collection of X-ray diffraction data



Data processing, structure solution and refinement



EGFR, 1.7 Å



MALT1, 2.0 Å

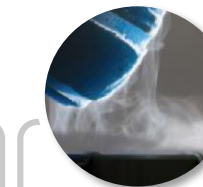
Cryo-EM



Cryo-EM grade protein production



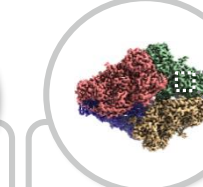
EM feasibility analysis (negative staining EM)



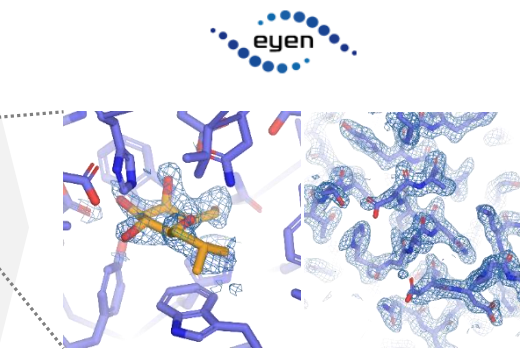
Cryo-EM conditions optimization



Cryo-EM imaging



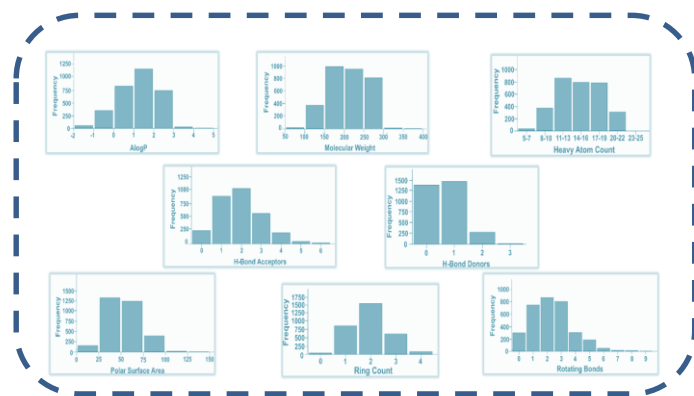
Data processing structure solution



β -Galactosidase, 2.1 Å

Fragment Library & Screening

~3100 "Rule of three" compliant fragments



High Throughput Biophysical Assays for Fragment Screening



SPR

Affinity range: pM – mM
 >1000 cmpds per day
 Kinetic characterization of 64 interactions in 4h
 8 channels HTS system
 Dissociation rates: 10⁻⁶ to 0.5 s⁻¹



Automated MST

K_D range: 10 nM – mM
 500-800 cmpds per day (Single Concentration)
 80 K_Ds per day
 Fully automated MST Screening Unit
 Labeled & labelFree MST



TRIC

K_D range: 10 pM – mM
 1500 cmpds per day (Single Concentration)
 > 150 Full K_Ds per day
 HTS Screening Unit
 384 Plate format

X-ray Crystallography-based Fragment Screening



Bruker MetalJet
 X-ray source in-house

Capabilities at HitS (Munich & Suzhou)

- >250 different protein crystalized
- >10 *de novo* structures / year
- Complete **XPRESS** Portfolio



HitS web



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Hits, Hit Success

One-Stop Target-to-Hit Solutions

Protein	Screening	Hit Confirmation
Protein Production <ul style="list-style-type: none"> All Target classes High level protein engineering Tailored tagging strategies Recombinant protein production <i>E.coli</i>, yeast, insect cells, mammalian cells Customized conjugation (e.g., biotinylation) Isotope labeling (15N, 13C) Antibody screening and Nanobody Comprehensive protein QC 	Fragment Based Screening (FBDD) <ul style="list-style-type: none"> WuXi fragment library (~3100) Automated screening (MST/Dianthus, SPR, DSF/nanoDSF) Fragment screening via X-ray or NMR DNA-Encoded Library (DEL) <ul style="list-style-type: none"> 80+ billion synthetic compounds Bioinformatics system to collect, process and analyze data, facilitate involvement of the client to make collective decisions DEL + AI 	Biophysical Panel <ul style="list-style-type: none"> Over 10 biophysical methods available Affinity, thermodynamics, stoichiometry, kinetics, thermal & chemical stability, aggregation Biochemical Panel <ul style="list-style-type: none"> Various technologies (incl. HTRF, AlphaScreen) Various luminescent, fluorescent, colorimetric assays Structure-based Drug Discovery <ul style="list-style-type: none"> X-Ray crystallography, Cryo-EM, NMR

