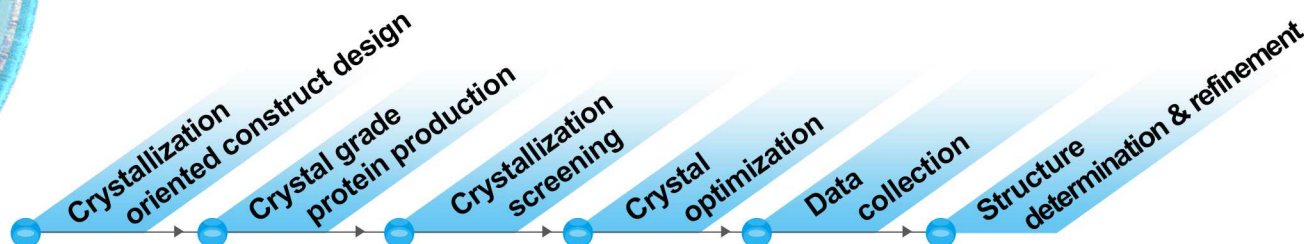


A Clearer Look For Hit Discovery

Comprehensive **structure** generation solutions for today's challenging targets provide insights and data to support hit finding through to lead optimization.



Cutting-edge Crystallization Facilities

STP Labtech Mosquito LCP crystallization robots

- ▶ 48 and 96 well trays
- ▶ Sitting-drop, hanging-drop & microbatch formats
- ▶ Setup for LCP membrane protein crystallization

Apricot Pipettor

ARI Scorpion

High-throughput creation of custom screens



Liquid Handling

Over 20 commercial sparse matrix screens 'in stock' at any time for extensive crystallization screening

Bruker D8 Venture World's most intense home-lab X-ray source

- ▶ Photon III detector
- ▶ Scout automatic sample changer for high-throughput testing of crystals and 24/7 data collection
- ▶ ISX stage for in situ diffraction



METALJET

X-ray Diffraction



Incubation & Observation

Standard protein QC

- ▶ SDS-PAGE
- ▶ HPLC
- ▶ MS (intact & fingerprinting)

Extended QC

- ▶ DLS
- ▶ nanoDSF
- ▶ MST
- ▶ SPR
- ▶ SEC-MALS



Sample Characterization

Formulatrix ROCK IMAGER plate hotels with UV imaging

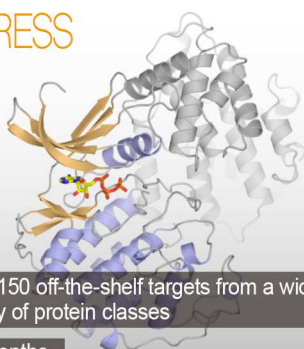
- ▶ 4, 12 and 20°C
- ▶ 1000 plates per temperature

Zeiss SteREO Discovery.V20 Microscopes

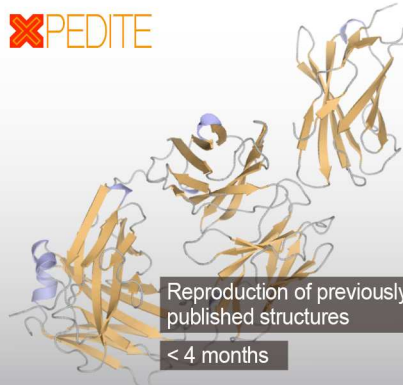
Crystallography Projects at HitS

Comprehensive solutions to support hit finding and hit expansion

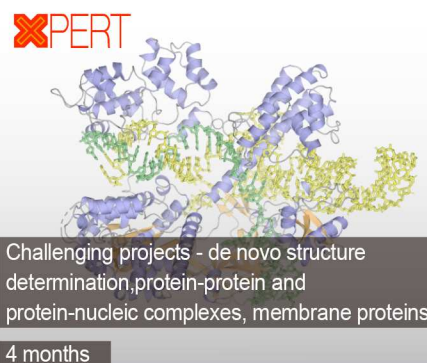
XPRESS



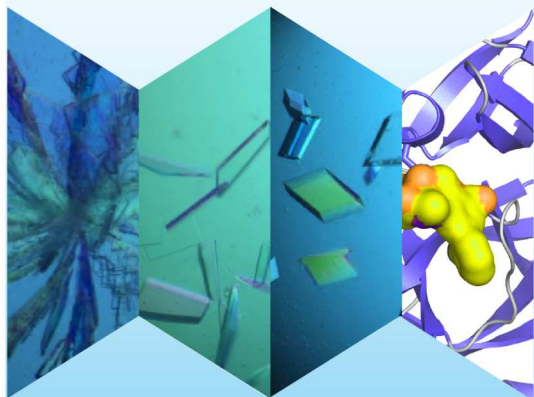
XPEDITE



XPERT



Case study 1: Structural validation of a DNA encoded library screening hits of SARS-CoV-2 main protease



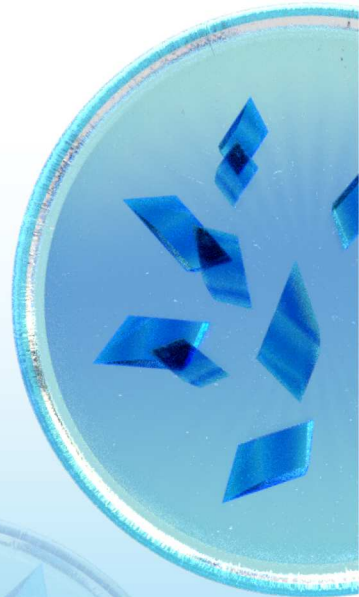
Timeline
2-3weeks

Initial screening

- 1200 crystallization conditions were tested using commercially available
- Crystals were obtained in over 20 conditions

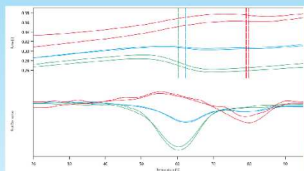
Crystal optimization & diffraction

- Diffraction grade crystals could be quickly obtained through optimization of pH and precipitant concentration
- Best crystals are obtained after streak-seeding and diffracted to 1.6 Å



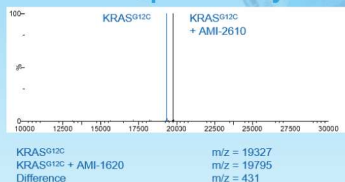
Case study 2: Crystal structure of KRAS in complex with a covalent inhibitor

Biophysics



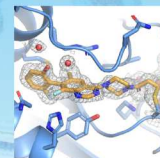
- Binding of AMI-1620 to KRAS (GDP-bound state) significantly increases the T_m
- MST, nanoDSF and SPR allow high-throughput screening of compounds and conditions

Intact Mass Spectrometry

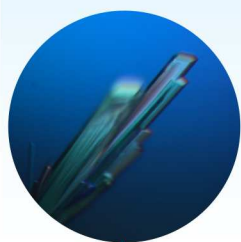


- Reaction of KRAS with AMI-1620 increases the m/z by 431 as expected
- Confirmation of covalent bond formation
- Optimization of covalent complex formation for crystallization screening

Crystallography



- Crystal structure of KRAS (GDP-bound state) in complex with AMI-1620
- Identification of the reactive amino acid and functional group
- Confirmation of the reaction mechanism



High Resolution

High Throughput

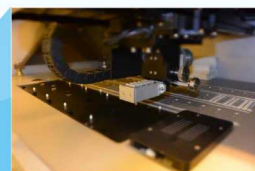
11Å resolution structure

1.45 Å resolution complex structure

Max capacity:

50+ projects in parallel

2000+ co-crystallization/year



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