

PIK3C α and PIK3C α -PIK3R1 Structural Biology

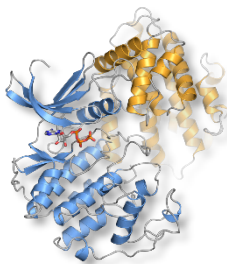
Structural Biology
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Structural Biology Services

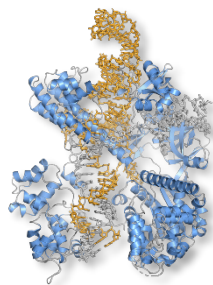
Comprehensive Range of X-Ray Crystallography and Cryo-EM Services

Off-the-Shelf Targets



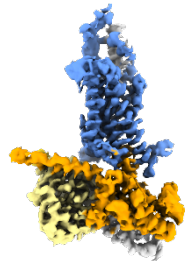
- Over 150 targets from broad range of classes
- Rapid turnaround time

Gene-to-Structure Targets



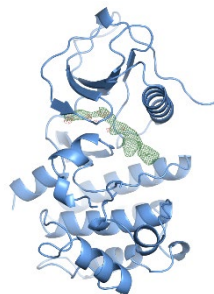
- Full gene-to-structure service
- Previously characterized and new targets

Membrane Proteins



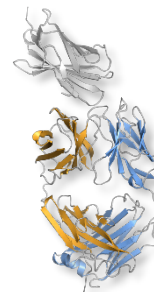
- Structure determination by cryo-EM and crystallography

Fragment Screening



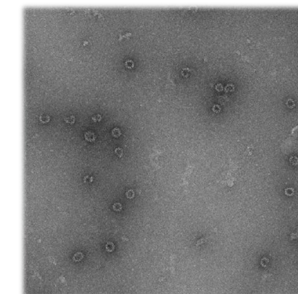
- High-throughput screening as primary or secondary screen

Biologicals



- Fab fragments, VHs, IgGs and their complexes

Particle Characterization



- Lipid- and virus-like particle characterization

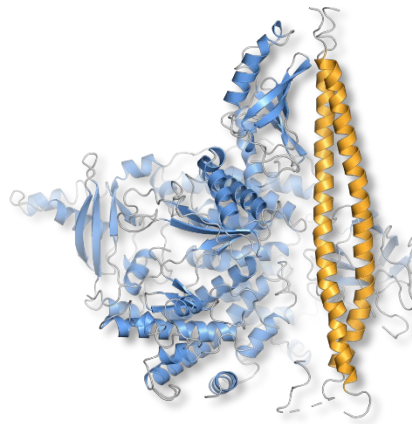
Custom Services

- Construct design
- Crystallization screening and optimization
- Crystal soaking
- Data collection
- Model building and refinement

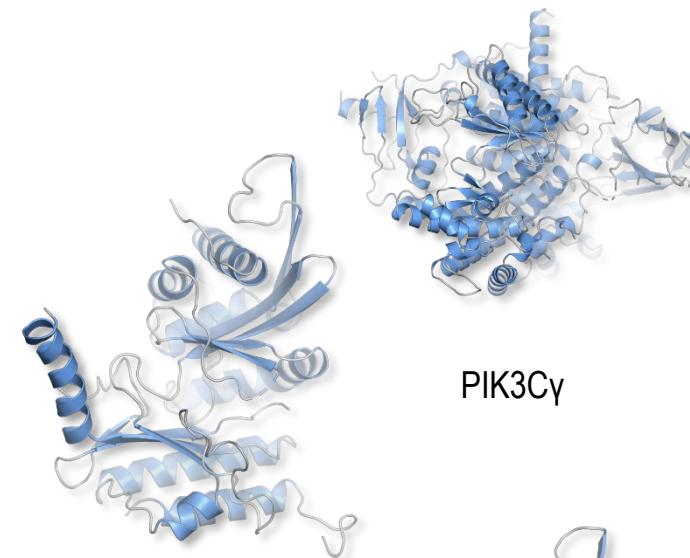
Phosphatidylinositol Kinases

PIK3C α , PIK3C α -PIK3R1, PIK3C γ , PIP4K2A, PIP4K2B, PIP4K2C

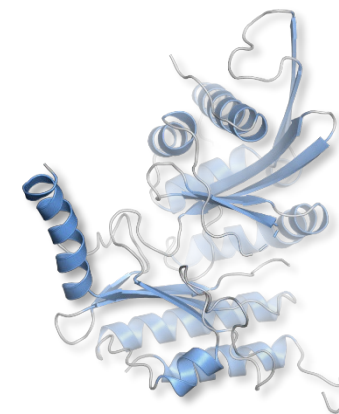
- Experience in the production of various phosphatidylinositol kinases for biophysics and structural biology
- Established MST, nanoDSF and SPR assays for biophysical screening and characterization of compounds
- Successfully structurally characterized examples:
 - PIK3C α – WT, E542K, E545K, H1047R
 - PIK3C α -PIK3R1 – WT, E542K, E545K, H1047R
 - PIK3C γ
 - PIP4K2A
 - PIP4K2B
 - PIP4K2C
- Over 70 structures of phosphatidylinositol kinases determined with orthosteric and allosteric inhibitors



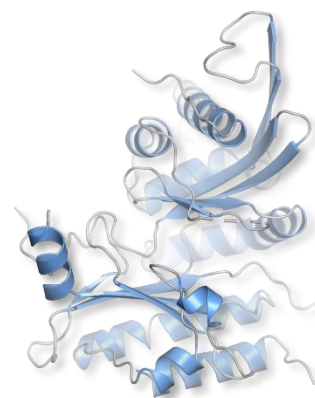
PIK3C α -PIK3R1



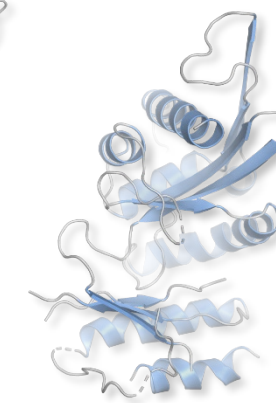
PIK3C γ



PIP4K2B



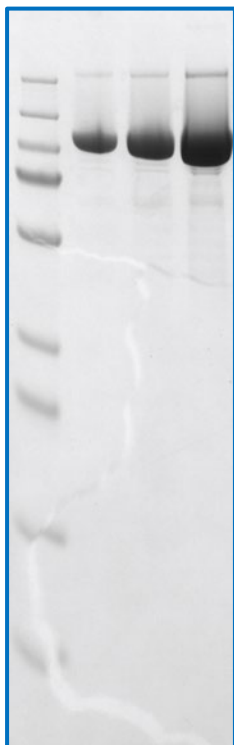
PIP4K2A



PIP4K2C

Off-the-Shelf Structural Biology Constructs

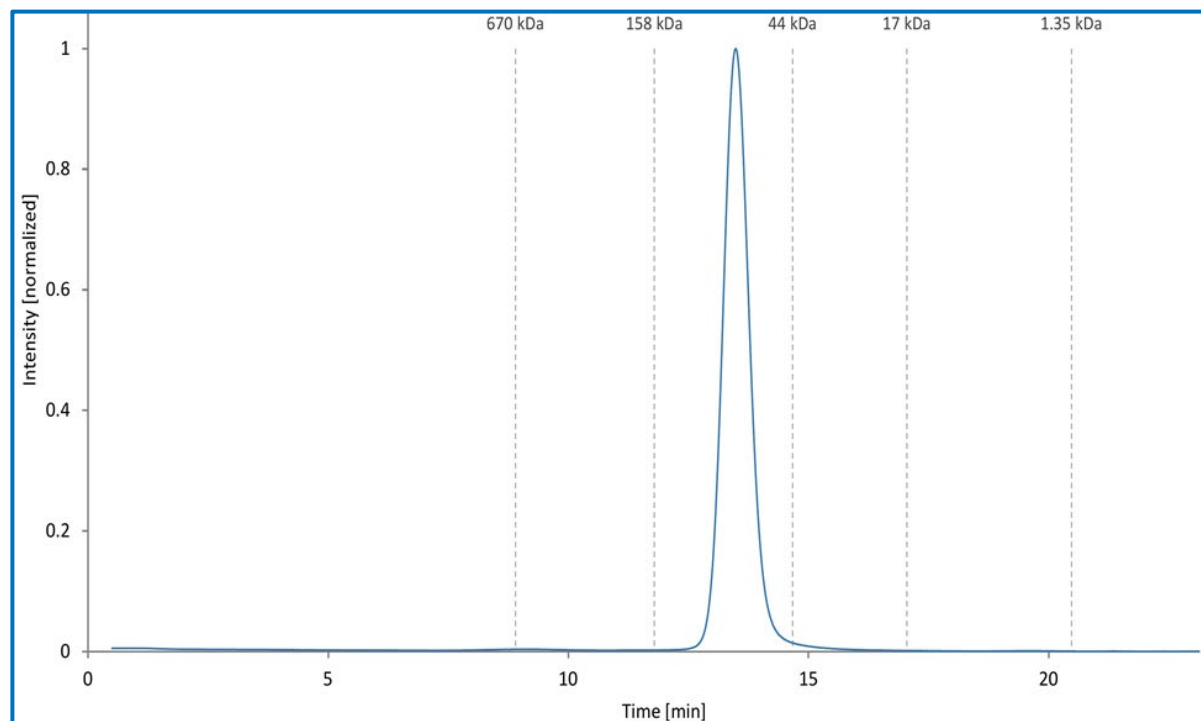
SDS-PAGE



- 10% Tris-Glycine gel
- Reducing condition
- Coomassie stained

Lane	Quantity
1	Marker
2	1 μ g
3	2 μ g
4	5 μ g

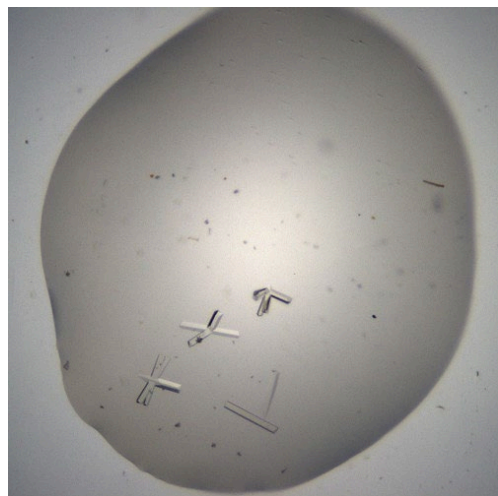
aSEC Chromatogram



- Column: S200 increase 10/300
- Running buffer corresponds to storage buffer
- Retention time of globular standard proteins is indicated by dotted lines

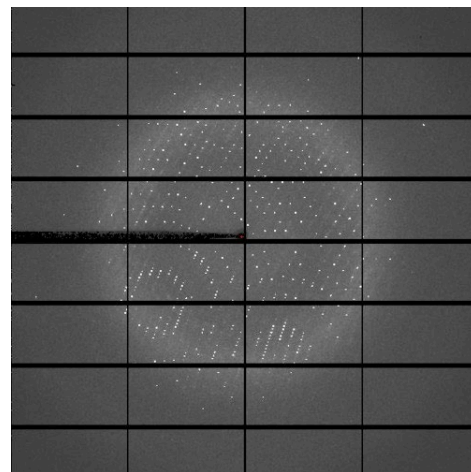
Off-the-Shelf Structural Biology Constructs

Crystallization



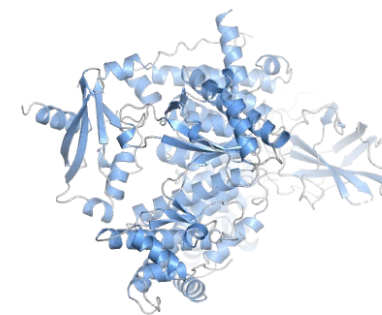
- Representative crystals of PIK3CA^{H1047R} (Construct CPX19)

Data Collection



- Representative diffraction pattern of PIK3CA^{H1047R} (Construct CPX19)

Overall Structure

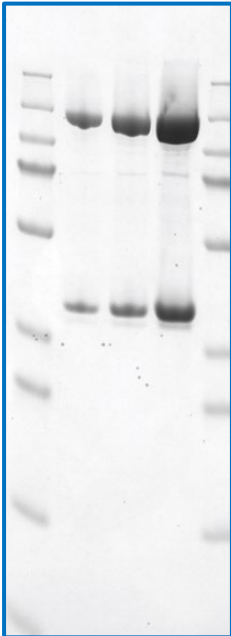


- Overall structure of PIK3CA^{H1047R} (Construct CPX19)

PIK3C α -PIK3R1

Off-the-Shelf Structural Biology Constructs

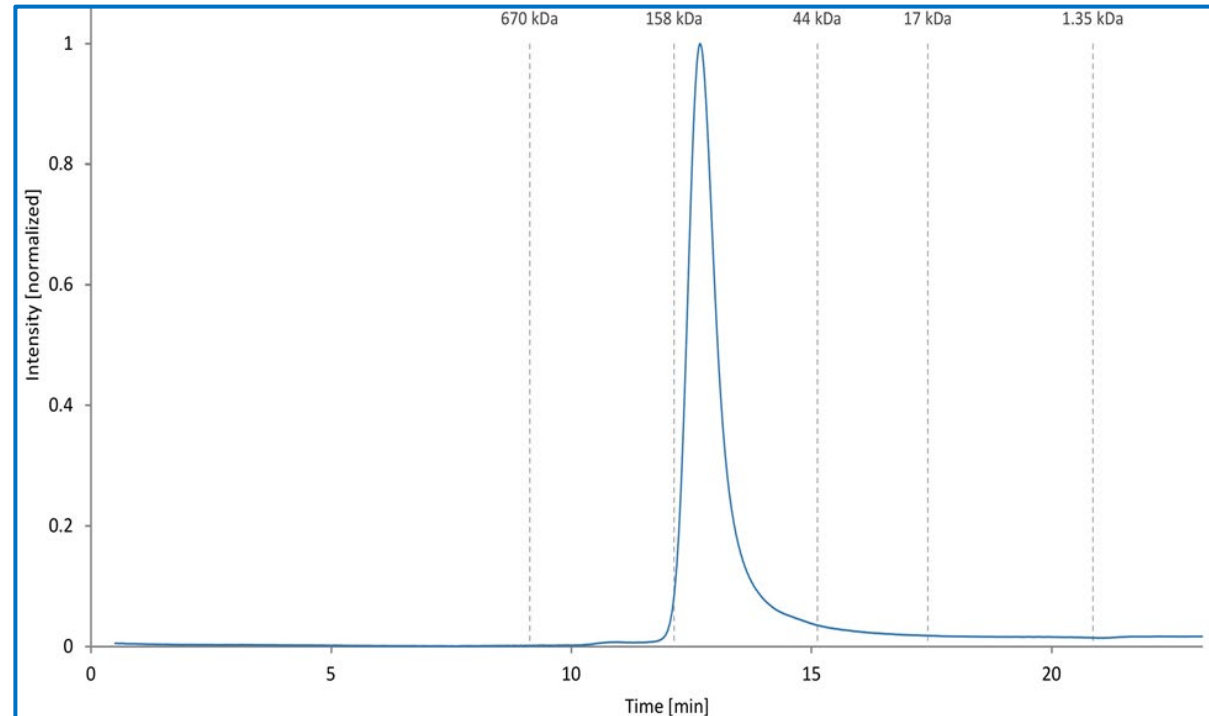
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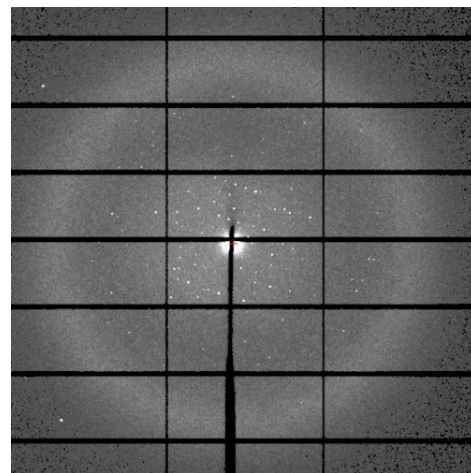
Off-the-Shelf Structural Biology Constructs

Crystallization



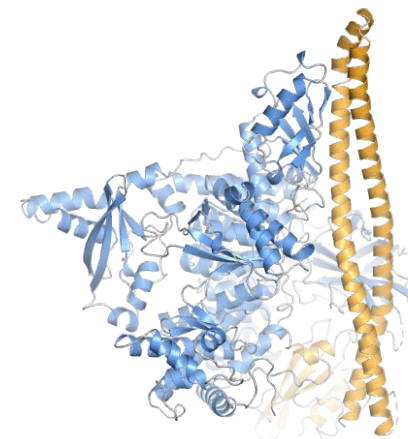
- Representative crystals of PIK3CA^{H1047R}-PIK3R1 (Construct EPV26) in complex with STX-478 and Inavolisib (GDC-0077)

Data Collection



- Representative diffraction pattern of PIK3CA^{H1047R}-PIK3R1 (Construct EPV26) in complex with STX-478 and Inavolisib (GDC-0077)

Overall Structure



- Overall structure of PIK3CA^{H1047R}-PIK3R1 (Construct EPV26) in complex with STX-478 and Inavolisib (GDC-0077)

Broad Range of Off-The-Shelf Targets

Kinases	AMP kinase, BRAF, BTK, CDC7-DBF4, CDK1-CKS2-CCNB1, CDK2, CDK2-CCNA2, CDK2-CCNE1, CDK6, CDK9-CCNT1, CDK12-CCNK2, CK1a, CK1d, EGFR, FGFR2, FGFR3, FGFR4, IRAK3, IRAK4, JAK1, JAK2, JNK1, JNK2, JNK3, KIT, LCK, MAP4K1, MKNK2, PIK3C α , PIK3C α -PIK3R1, PIK3C γ , PIP4K2 α , PIP4K2 β , PIP4K2 γ , PKA, PKM2, PKR, RSK1, SIK3, SRC, TYK2, WEE1
Proteases	3C-like protease (SARS-CoV-2 and Norovirus), Cathepsin K, Cathepsin S, MALT1, USP7, USP21
Targeted Protein Degradation	CRBN, DDB1, SKP1-SKP2, SKP1-SKP2-CKS1, VHL-Elongin B-Elongin C
Histone Modification	BRD4, BRD9, CREBBP, HDAC2, HDAC7, HDAC8, JMJD2C, JMJD2D, MLLT1, NSD1, PRMT5-WDR77, SIRT2
Innate Immunity	cGAS, STING
Nuclear Receptors	ER α , GR, ROR γ
Nucleic acid binding proteins	APOBEC3B, cGAS, PARP1, SMARCA2, SND1, STAT6, WRN

Over
150
Targets

Complete **XPRESS** Portfolio available on our website

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