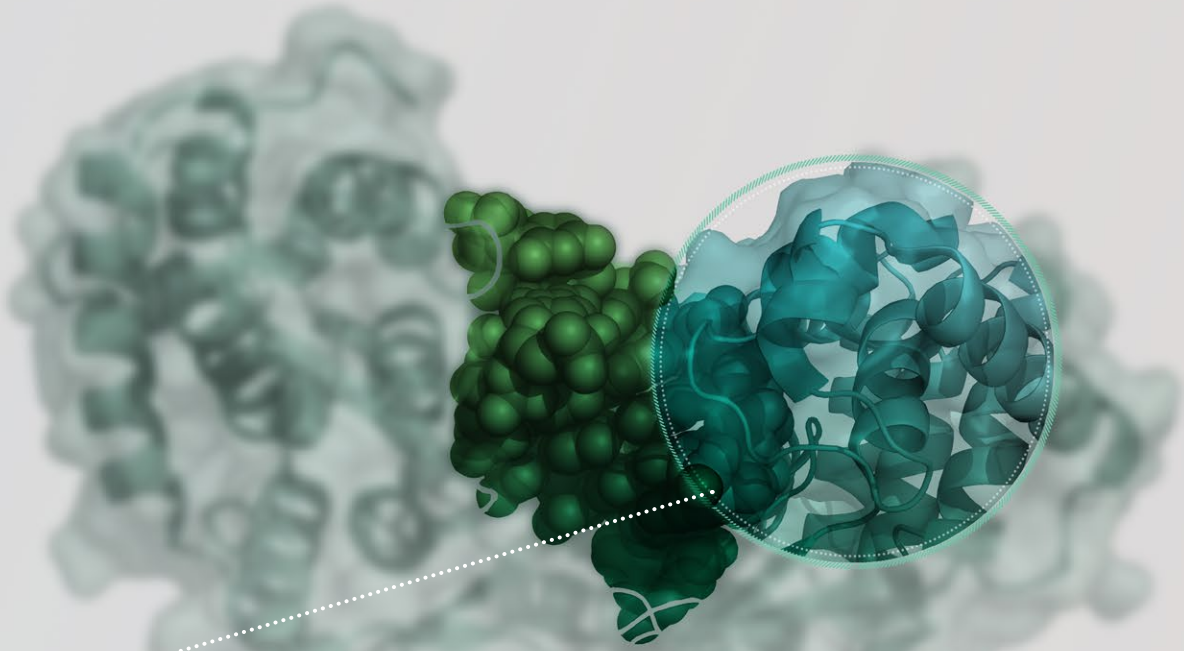
BERYLLIUM DISCOVERY

Your Preferred Discovery Partner

Premium Gene-To-Function Services

GENE TO PROTEIN | **STRUCTURE GUIDED LEAD DISCOVERY** | **FUNCTIONAL BIOLOGY**



Structural Biology

Proven expertise in *de novo* structure determination:

- Clear insight into Mechanism of Action
- Validate targets, generate and optimize lead therapeutics
- Structural insight to protein-protein, protein-ligand, and protein-nucleic acid interaction

Structure-guided solutions for your drug discovery programs

BE4.COM

COLLABORATE@BE4.COM

Working with Beryllium

- Construct design and expression optimization
- Protein purification
- Protein complex crystallization
- X-ray screening and dataset collection
- Structure determination

4-12 MOS

DELIVERABLE
Fully annotated Protein Data Bank-coordinate and structure factor files

+ OVER 900
Structures deposited into the Protein Data Bank as part of the SSGCID structural genomics collaboration by Beryllium scientists.

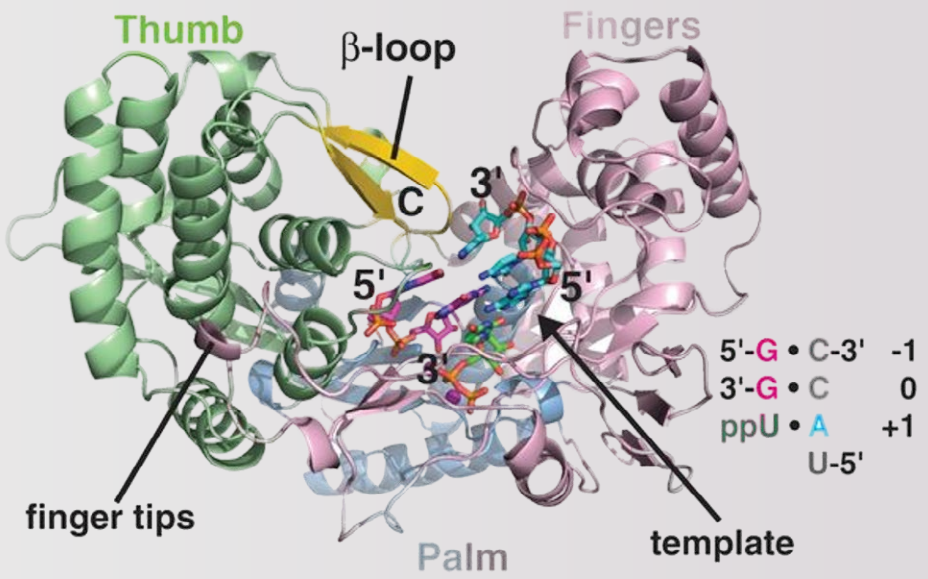
+ OVER 1000
proprietary structures delivered to clients covering many protein classes.

SCIENTIFIC CASE STUDY

Collaboration with Pharmasset (Gilead acquisition)

Pharmasset required a partner to determine the mechanism of action of an important new oral hepatitis C virus (HCV) drug to understand how it would synergistically interact with other drugs on the market and in development.

First HCV NS5B ternary complex (2.0 Å resolution, PDB 4WTL):



EXPERIENCE/INSIGHT:

Beryllium set out to obtain structures of HCV NS5B polymerase bound to RNA and incoming nucleotides to understand:

- Structural changes required for activation of the polymerase.
- Binding of native substrates and nucleotide analog inhibitors (NAI) to active NS5B polymerase complexes.

SOLUTION:

Beryllium determined a series of crystal structures of stalled polymerase ternary complexes with enzymes, RNA templates, RNA primers, incoming nucleotides, and catalytic metal ions during both primed initiation and elongation of RNA synthesis.

- The crystal structures capture a number of key steps throughout the catalytic pathway including the two slow steps and have allowed Beryllium to propose a more complete catalytic pathway for HCV polymerase.
- Beryllium obtained elongation phase ternary complexes with NAIs including the metabolite of the FDA approved drug sofosbuvir. These structures showed differences in the active site which demonstrated why sofosbuvir is distinct from native substrates or other nucleotide analog inhibitors in development.

These results have been published in Science (Appleby, T.C. et al. 2015, 347, 771)