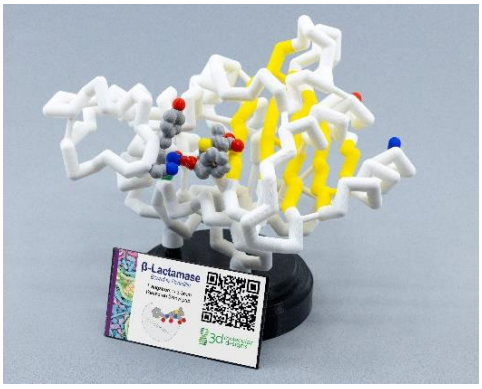
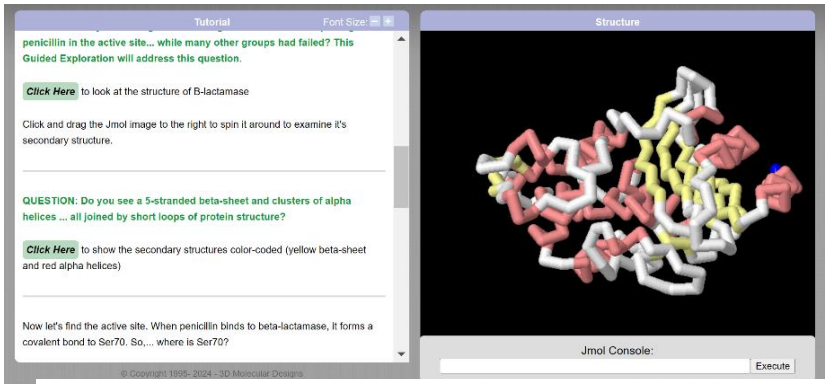
3D-Printed Model of β-Lactamase

Although bacteria have evolved several different mechanisms to develop resistance to antibiotics, one of the most successful strategies has been to produce an enzyme that destroys the antibiotic. This is the case with **β-lactamase** – an enzyme that can bind penicillin and open its 4-atom lactam ring, and in so doing, inactivate it.

This 3D-printed model of β-lactamase is based on the structure described by 5KMW.pdb. The model – and the accompanying Guided Jmol Exploration – tell an interesting story of how one research group was finally able (in 2016) to solve the structure of this protein with penicillin trapped in its active site.





3D Molecular Designs - Beta Lactamase (centerforbiomolecularmodeling.org)

Additional note to teachers:

Never display your art in an art gallery. If you do, your art will be displayed along with hundreds of other art pieces.... all competing for the attention of the gallery visitors. We have a similar problem with the 12 different instructional tools we have created to support our ***Modeling Infection and Immunity*** workshop. In spite of all that competition from the other materials you experienced in that summer course... I hope that some of you will field-test the **β-lactamase physical model** and the **β-lactamase Guided Jmol Exploration** with your students....and provide us with some feedback.

The model and Guided Exploration were NOT designed to directly tell the story of this protein. The story that we want your students to discover is nicely described in a paper by Langan et.al (2016) (see description in the documentation of the Guided Jmol Exploration of β-Lactamase). Many other research groups had been able to solve the structure of this protein prior to 2016 – but none of these structures had a penicillin bound in its active site. So,... how did Langan et.al. finally solve this structure? Our hope is that with this physical model and the accompanying Guided Jmol Exploration your students will understand how this was done.

In a broader sense, this model/Jmol Exploration frames a story about the ***process of science***... how different research groups can all focus on the same topic over a period of many years until finally, enough is known so that one group can achieve the final goal – of seeing penicillin bound in the active site of the enzyme that it is known to inactivate.

BONUS Activity!

If your students work through the Guided Exploration of β-lactamase with the physical model,… here is one more follow-on activity you can have them explore:

The QUESTION is: ***Where did β-lactamase come from?*** It seems improbable that bacteria evolved a β-lactamase that could bind and inactivate penicillin from scratch. It seems much more likely that β-lactamase evolved from a PBP. *I'm not sure that we have explicitly said this before,… but penicillin is actually a structural analog of the stem peptides that the PBP protein crosslinks to stabilize the cell wall*. Therefore, if a cell is looking to evolve a protein that can bind penicillin – it makes sense to start with a PBP that already binds something (the D-Ala/D-Ala peptide at the end of the stem peptides) that is structurally similar to penicillin. ***So,… have your students explore the structure of a PBP to see if they can notice any structural similarities between their β-lactamase and PBP.*** They can do this by loading 1PWC.pdb into the Protein Exploratorium (https://learn.3dmoleculardesigns.com/protein-exploratorium)… and comparing this structure with their β-lactamase model. Features of the PBP that your students should focus on include:

- A 5-stranded beta-sheet. (click the *Color by….secondary structure* button in the Exploratorium, and
- The positions of the N-terminus and C-terminus of the protein relative to the beta-sheet, and
- A serine sidechain just to the left of the beta-sheet.

After your students have made this comparison, you can ask them if they believe this hypothesis that β-lactamase evolved from a PBP.