



SMART Teams 2013-2014

Research and Design Phase

Greenfield High School SMART Team

Dakota Alphin, Andrew Braatz, Katie Cavins, Francis Deleon-Camacho, Srinidhi Emkay, Hannah Flees, Ariel Franitza, Alyssa Gerwig, Elena Groth, L.I. Am Gangland, Alyxx Idell, Logan Klug, Veronica Nakhla, Zoe Osberg, Paige Paniagua, Jessica Wallner

Teachers: Julie Fangmann and Drew Rochon

Mentor: Martin St. Maurice, Ph.D., Marquette University Department of Biological Sciences

The Role of Yeast Urea Amidolyase in Patients with Suppressed Immune Systems

PDB: 3VA7

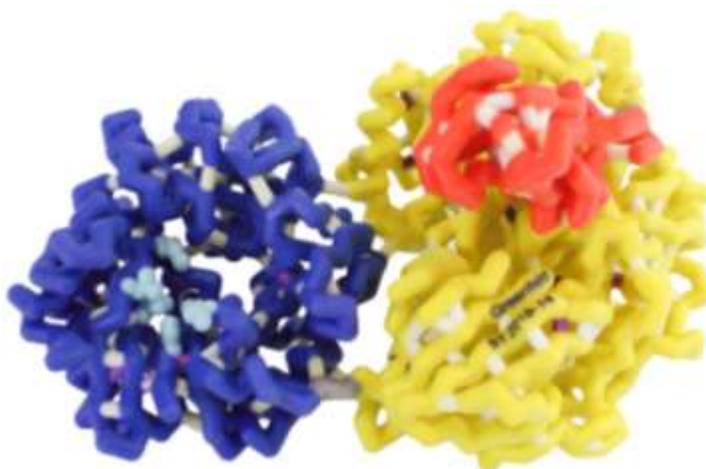
Primary Citation: Fan, C., Chou, D.Y., Tong, L., Xiang, S. (2012). Crystal structure of urea carboxylase provides insights into the carboxyltransfer reaction. *Journal of Biological Chemistry* 287:9389-9398.

Format: Alpha carbon backbone

RP: Zcorp with plaster

Description:

According to Rice University, 70% of people are affected by the infectious fungus *Candida albicans*. The immune system uses T and B cells to stop pathogens. People with suppressed immune systems, such as transplant patients, and AIDs or cancer patients, lack functional T and B cells, and rely on macrophages to destroy *Candida*. *Candida* can kill and exit macrophages due to an enzyme: urea amidolyase (UAL). While in the macrophage, an environmental change causes *Candida* to morphologically switch from a sphere to a structure with hyphae. UAL converts urea to ammonia (NH_3) and CO_2 , creating an environment for hyphae to form, bursting the macrophage. The Greenfield SMART (Students Modeling A Research Topic) Team used 3D printing technology to model UAL. The biotin carboxylase (BC) domain uses energy from ATP cleavage to attach CO_2 to the swinging arm portion, or biotin carboxyl carrier protein (BCCP) domain. The BCCP domain swings across UAL, attaching CO_2 to urea forming allophanate in the carboxyl transferase (CT) domain. Allophanate moves to the allophanate hydrolase (AH) domain, hydrolyzing the allophanate into CO_2 and NH_3 . Increases in CO_2 and NH_3 cause hyphae to form, destroying macrophages and allowing *Candida* to spread. Researchers could block UAL's active sites to prevent *Candida*'s macrophage-killing shape change, preventing systemic candidiasis without damaging human cells.



Specific Model Information:

- The biotin and BCCP domain alpha carbon backbone (residues 1742-1829) is highlighted red.
- The CT domain alpha carbon backbone (residues 1068-1737) is highlighted yellow.
- Amino acids (Tyr1628, Asp1524 and the backbone amide of Gly1636) that interact with urea are highlighted forest green.
- Urea is displayed in ball and stick and colored lime green.
- Amino acids (His829, Asn856, Lys858, Glu896, Glu910 and Arg914) in the BC domain involved in the ATP and biotin binding site are displayed in ball and stick and colored sky blue.
- Glycerol, displayed in ball and stick and colored orange, represents where biotin would bind to the BC domain active site.
- Hydrogen bonds within the beta sheets are colored white.
- Structural supports to stabilize the molecule are colored beige.

<http://cbm.msoe.edu/smartTeams/>

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