SMART Teams 2013-2014
Research and Design Phase

Greenfield High School SMART Team

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

PDB: 4ISS

Primary Citation: Fan, C., Li, Z., Yin, H., Xiang, S. (2013). Structure and function of allophanate hydrolase. *Journal of Biological Chemistry* 288: 21422-21432.

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 alpha carbon backbone of Chain A is highlighted in purple.
- The alpha carbon backbone of Chain B is highlighted in hot pink.
- 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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