Hartford Union High School SMART Team

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"Bond … One Bond": The Biological Blowtorch and Other Reactive Players in CYP17 Catalyzed Production of Androgens

PDB: 3RUK

Format: Alpha carbon backbone

RP: Zcorp with plaster

Description:

Prostate cancer makes up 4.7 percent of all cancer related deaths. The exact cause of prostate cancer is unknown, but researchers have identified the leading risk factors, including excess testosterone in the body. Early treatments to reduce testosterone levels in patients involved surgical procedures. A particular heme-containing enzyme, known as CYP17, converts cholesterol-derived hormones into androgens including testosterone. $Fe(III)$ is a key part as all reactions occur within this heme group. Pharmacological efforts, such as the drug abiraterone, decrease the efficiency of CYP17 catalysis and may present a valid treatment option for prostate cancer patients. Further efforts would be facilitated by gaining a better understanding of the mechanisms of CYP17 in the presence of its natural substrates, 17-OH progesterone and 17-OH pregnenolone. This enzyme generates an androgen precursor by catalyzing two sequential chemical conversions, the second one by an unknown process, which has been difficult to track. Using rapid-freezing, γ-ray exposure and Raman spectroscopy, the key reaction intermediates in this process are trapped and structurally defined. The Hartford Union SMART (Students Modeling A Research Topic) Team modeled the enzyme CYP17A1 with 3-D printing technology. Research efforts involving CYP17 could assist pharmaceutical companies in the development of treatments for prostate cancer.
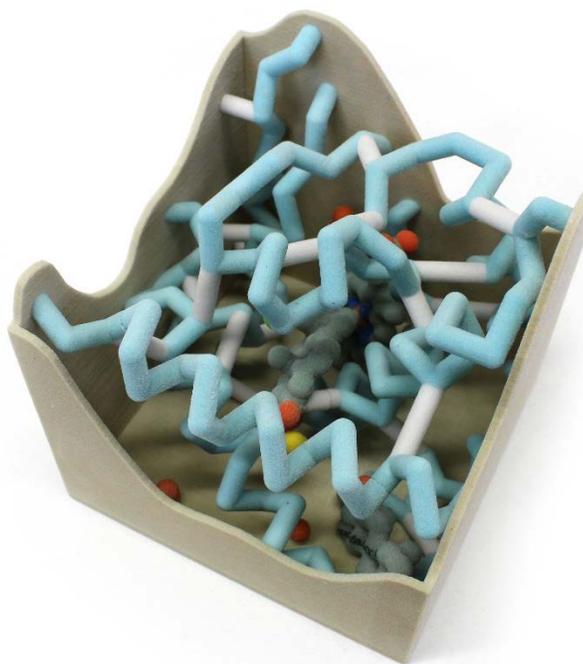
Specific Model Information:

- We chose to use an active box because the active site we are viewing is in a small section a huge protein (226,827.26) it seemed like a waste to print the whole protein.
- We are showing that CYP17 turns cholesterol into various antigen
    - That is why we are using different substrates to show the fact that it makes a various number of androgens
- The backbone is colored lightblue
- The struts are colored aliceblue
- We highlighted four amino acids: Asn202, Ala105, Cys442, and Glu305
- We highlighted Asn202 because it provides H-binding to the substrates
- We colored Asn202 the yellow
- We highlighted Ala105 because it mediated unwanted 16-hydroxylase
- Ala105 is colored lime
- We highlighted Cys442 because it connect the heme with the protein
- Cys442 is colored turquoise
- We highlighted Glu305 because the mutation of this residue to E305G causes loss of 17 ,20-lyase activity
- Glu305 is colored magenta