



SMART Teams 2013-2014

Research and Design Phase

Valders High School SMART Team

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CYP17A1 (Cytochrome P45017)

PDB: 2AAI

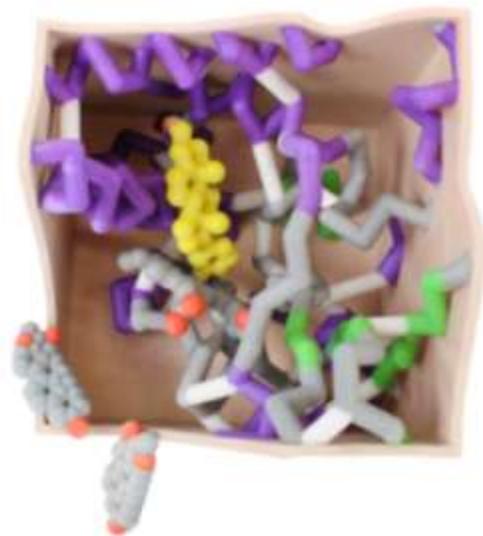
Primary Citation: M. Gregory, P. J. Mak, S. G. Sligar, J. R. Kincaid (2013)
“Differential Hydrogen Bonding in Human CYP17 Dictates Hydroxylation
versus Lyase Chemistry”, *Angew. Chem. Int. Ed.* 52, 5342-5345.

Format: Alpha carbon backbone

RP: Zcorp with plaster

Description:

Inhibiting Cytochrome P45017 (CYP17A1) could prevent androgen synthesis and treat prostate, breast, and other hormone responsive cancers. Cholesterol is the precursor of all steroid hormones including testosterone and estrogen. CYP17A1, an enzyme bound to the membrane of adrenal cells, plays a critical role in the biosynthesis of steroid hormones. This enzyme determines whether corticoids, which control metabolism, or androgens such as testosterone, will form. CYP17A1 catalyzes the hydroxylation of its substrates pregnenolone (PREG) and progesterone (PROG) to form 17-OH pregnenolone (17-OH PREG) and 17-OH progesterone (17-OH PROG), respectively. Most interestingly, it can further process the 17-OH PREG by catalyzing the cleavage of the carbon 17, 20 bond as a next step, which is the first committed step in androgen biosynthesis. While the enzyme can similarly transform the 17-OH PROG, it does so with much lower efficiency, and it is this difference which has attracted the interest of researchers. Attention has been focused on a key amino acid, asparagine 202 (N202), whose amide fragment can provide differential H-bonding interactions with these two substrates. The technique of resonance Raman spectroscopy can provide structural insight into the mechanisms that direct the reaction along a given pathway. Improved structural resolution at the active site of CYP17A1, may help lead scientists to better anticancer drug development. The Valders SMART (Student Modeling A Research Topic) Team used 3D printing technology to model the protein CYP17A1.



Specific Model Information:

- Alpha helices are highlighted in purple.
- Beta sheets are highlighted in green.
- Abiraterone is displayed in ball and stick and colored yellow.
- The heme group is displayed in ball and stick and colored in cpk.
- Asn202, displayed in ball and stick and colored cpk, provides differential hydrogen binding interactions with substrates resulting in two different products, androgens or corticoids.
- Structural supports are colored white.

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

The SMART Team Program is supported by the National Center for Advancing Translational Sciences, National Institutes of Health, through Grant Number 8UL1TR000055. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the NIH.