

# SMART Teams 2014-2015

## Research and Design Phase

### Cudahy High School SMART Team

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### Think Pink: The Role of Cytochrome Aromatase in Estrogen Production and Breast Cancer Risk P450

**PDB:** 4kq8

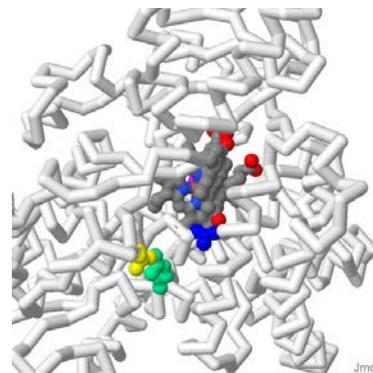
**Primary Citation:** : Mak P., Luthra A., Sligar S. and Kincaid J. (2014). Resonance Raman Spectroscopy of the Oxygenated Intermediates of Human CYP19A1 Implicates a Compound I Intermediate in the Final Lyase Step. *Journal of the American Chemical Society* (136): 4825-4828

**Format:** Alpha carbon backbone

**RP:** Zcorp with plaster

#### Description:

According to the American Cancer Society (2012), postmenopausal women with high levels of endogenous hormones have about twice the risk of developing cancer compared to women with the lowest levels. A key protein for estrogen biosynthesis from androstenedione (AD), and possibly linked to development of breast cancer, is cytochrome P450 aromatase (CYP19A1) found in adipose breast tissue. CYP19A1 converts AD to an aromatic C18 estrone through two consecutive hydroxylations at the C19 methyl group and catalyzing a third lyase step, culminating in cleavage of the C10–C19 bond of the C19-aldehyde, with concurrent aromatization of the A ring of the steroid framework. AD is attracted to the active site by Arg192, Asp309, and Glu483. A heme group, bound in the CYP19A1 active site by Cys437, is responsible for these 3 oxidation steps. The key residues were modeled by the Cudahy SMART (Students Modeling A Research Topic) Team using 3D printing technology. The heme group binds molecular oxygen and then forms strong oxidizing intermediates that achieve these difficult oxidation reactions. The resonance Raman technique provides detailed structural insight into these important but unstable heme intermediates. Gaining an understanding of the reaction mechanism of CYP19A1 is important. If it can be learned how CYP19A1 functions, a suppression treatment to disable local estrogen production in breast adipose tissue by CYP19A1 could be developed by scientists to control estrogen levels, possibly reducing tumor growth or diminishing the risk of development of breast cancer.



### Specific Model Information:

- Glu483 (Yellow), Arg192 (Medium Spring Green), Asp309 (Blue) are key amino acids which attract the substrate, androstenedione, to cytochrome P450 aromatase for conversion to estrone.
- Cys437 (Magenta) is the residue which attracts the heme group to the cytochrome P450.
- The heme group (CPK) performs the hydroxylations and lyase of the C19 methyl group resulting in cleavage of the C19 methyl group and the formation of an aromatic ring in the A ring of the steroid.
- Androstenedione (CPK) is the substrate converted to estrone.
- The backbone is white.

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

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