SMART Teams 2013-2014
Research and Design Phase

Saint Thomas More High School SMART Team

Bradley Drew, Megan Wengelewski, Ben Boren, Matthew Peter, Kelly Howell, Martha Lezama, Carolyn Sikora, Robyn Cabigting, Faith Bowman, Anna Bollis, and Sophia Olmos

Teacher: Kathy Stelling

Mentors: Joseph McGraw, Ph.D., Pharm. D. and Cameron Patterson, Pharm. D. candidate, Concordia University Wisconsin School of Pharmacy

Estrogen Sulfotransferase and Brominated Flame Retardants

PDB: 4JVN

Primary Citation: Gosavi, R.A., Knudsen, G.A., Birnbaum, L.S., Pedersen, L.C. (2013). Mimicking of Estradiol Binding by Flame Retardants and Their Mataboilites: a Crystallographic Analysis. *Environmental Health Perspectives* 121: 1194-1199.

Format: Alpha carbon backbone

RP: Zcorp with plaster

Description:

Hypoplastic left heart syndrome is a disorder of the fetal heart in which the ventricles and aorta are formed improperly. As a result, infants with this condition will die shortly after birth unless they receive immediate surgery. According to the World Health Organization, this syndrome affects about 1 in every 4,000 babies born each year. Further research by Dr. Joseph McGraw and Dr. Andrew Pelech has linked this condition to brominated flame retardants, or BFRs. BFRs are a class of chemicals that have bromine atoms attached to them in a specific sequence. Estrogen sulfotransferase (EST) is a metabolic enzyme that metabolizes various fatty acids, neurotransmitters, and hormones. The Saint Thomas More SMART (Students Modeling A Research Topic) Team modeled EST using 3D printing technology to further investigate the structure-function relationship. One function of EST is to attach a sulfate group to thyroid hormone, thyroxin, in a developing fetus. This process changes the thyroid hormone from a non-polar to a polar substance. The polar form of thyroxine may be absorbed into the fetus and later metabolized back to the thyroid hormone for use in fetal organ development. BFRs can closely mimic thyroxin, which causes EST to attach sulfate groups to BFRs rather than thyroxin itself. However, BFRs do not function in the same way as thyroxin, and adversely sulfation in thyroid hormone metabloism. Further research may result in effective prevention or treatment of fetal developmental disorders such as hypoplastic left heart syndrome.

Specific Model Information:

- The A chain alpha carbon backbone is colored purple.
- Alpha helices within the A chain are colored medium purple.
- The B chain alpha carbon backbone is colored hot pink.
- Beta sheets are highlighted in grey.
- YUG501 (2,6-dibromo-3-(2,4-dibromophenoxy)phenol) is displayed in ball and stick and colored red.
- The amino acids Lys105 (displayed in ball and stick and colored goldenrod), Phe141 (displayed in ball and stick and colored yellow) and His107 (displayed in ball and stick and colored khaki) create the active site that YUG501 binds to.
- The amino acids Lys47 (displayed in ball and stick and colored spring green) and Ser137 (displayed in ball and stick and colored pink) interact with each other to prevent the bridging of oxygen with the PAPs and to regulate the hydrolysis of the PAPs.
- Hydrogen bonds within the beta sheets are colored thistle.
- Structural supports to stabilize the model are colored tan.

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.