SMART Teams 2014-2015 Qualification Phase

Brookfield Central High School SMART Team

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ACEing Radiation Protection: The Role of ACE Inhibitors in Mitigation of Radiation Damage

PDB: 1O86

Primary Citation: Primary Citation: Ramanthan Natesh, Sylva L. U. Schwager, Edward D. Sturrock & K. Ravi Acharya. (2003). Crystal Structure of the Human Angiotensin-converting Enzyme-Lisinopril Complex. *Letters to Nature* 421: 551 – 554.

Format: Alpha carbon backbone

RP: Zcorp with plaster

Description: In 2001, the United States suffered a major terrorist attack that took the lives of thousands. There is a small, but real, risk of radiological attack or nuclear accident in the future. In addition, exposure of normal tissue to radiation poses a risk to cancer patients undergoing radiotherapy, as radiation induces the production of collagen. Grants were provided to our mentor to research ways to mitigate the harmful effects of radiation. Studies on radiation effects on rats have found that increased collagen is found in the interstitial space of the lungs, which limits free exchange of oxygen and carbon dioxide. Angiotensin Converting Enzyme (ACE) converts angiotensin I into angiotensin II, which binds to fibroblast receptors in to produce collagen. By inhibiting the ability of ACE to convert angiotensin I into angiotensin II, the fibroblasts cannot produce the same levels of collagen. As a result, oxygen and carbon dioxide are more easily exchanged in the lung after damages from radiation. The effects of lisinopril, an ACE inhibitor, on the collagen buildup in the lungs have been observed in rats 7 months after exposure to radiation. Understanding the collagen synthesis pathway by studying ACE and its inhibitors may lead to the production of an efficacious treatment for radiation exposure that can be given after exposure to radiation. The Brookfield Central High School SMART (Students Modeling a Research Topic) Team used the PDB file 1O86 to create a 3D model of the protein ACE and investigate the interaction between ACE and the inhibitor lisinopril to better understand its molecular functions. Research was supported by grants from NIH/NIAID RC1 AI81294 and U01 AI107305.

Specific Model Information:

- Alpha helices are colored midnightblue
- Beta sheets are colored orchid
- Tyr224, His353, Ala354, His383, Glu384, His387, Glu411, Lys511, His513, Tyr520, Arg522, and Tyr523 are colored cpk
- Lisinopril is colored yellow
- Zinc is colored green
- Chlorine is colored lime
- Hbonds are colored orchid
- Struts are colored papayawhip
- Unstructured alpha carbon backbone is colored palegoldenrod

Specific Amino Acids:

- Tyr224, His353, Ala354, His383, Glu384, His387, Glu411, Lys511, His513, Tyr520, Arg522, and Tyr523 are amino acids in the active site that bind lisinopril to ACE
- Zinc is involved in active site
- Chlorine is involved in active site

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

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