



Westosha Central High School SMART Team

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Blood in the Eye, Diabetes; You Give VEGF a Bad Name

PDB: 5T89

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Format: Alpha carbon backbone

RP: Zcorp with plaster

Description:

The WHO estimates that in 2014, 422 million adults were living with diabetes, a condition which limits blood flow to the small blood vessels of the eye. To restore blood flow, the body triggers angiogenesis, or the growth of new blood vessels, using vascular endothelial growth factors (VEGF) and the VEGF receptor (VEGF-R). Blood vessels created by VEGF-R signalling are weak and leak blood and fluid into the back of the eye, causing diabetic retinopathy and eventually blindness. The VEGF-R is a dimer and each monomer is composed of seven extracellular domains and an intracellular kinase domain. Dimerization of the receptor occurs after binding VEGF, causing the correct positioning of the kinase domain to begin a signal cascade that stimulates the growth of endothelial cells into new blood vessels. Domains 1-3 are responsible for binding VEGF, with the amino acids Q263, F292, V278, R224, N259, R261, R280, Q284, and N290 forming the binding pocket for the VEGF. Domains 2-7 are responsible for the dimerization and activation of the VEGF-R. The amino acids R351, K393, A381, K379, E513, K517, T455, S346, A434, K433, and Q429 in domains 4 and 5 form homotypic interactions and control the VEGF-R activation. The Westosha Central High School SMART (Students Modeling A Research Topic) team has designed a model of VEGF-R to study structure-function relationships. Although VEGF-R inhibitors are widely used to treat diabetic retinopathy, they are extremely expensive and not effective in all patients. Elucidation of VEGF-R's targeting and activation could lead to more effective inhibition of angiogenesis, thereby preserving vision in diabetic patients.



Specific Model Information:

Amino acid side chains involved:

- Gln263, Phe292, Val278, Arg224, Asn259, Arg261, Arg280, Gln284, and Asn290 are the residues that VEGF binds to - springgreen
- Arg351, Lys393, Ala381, Lys379, Glu513, Lys517, Thr455, Ala434, Lys433, and Gln429 are involved in the activation of the receptor. – cyan

Highlighted protein structures:

- VEGF is colored gainsboro
- Monomers of VEGF-R are color deeppink and steelblue
- Hydrogen bonds are colored pink

Supporting Features:

- Struts are colored white

CBM SMART Teams Website:

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