Emerging Treatment For Insulin Resistance With Snake Venom

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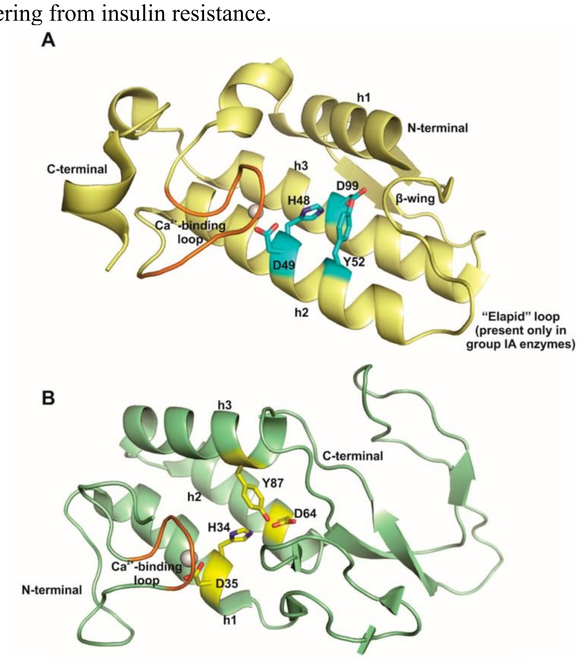
Abstract

The objective of this study is to investigate the enzyme Phospholipase A2 found in snake venom as a treatment for insulin resistant diseases such as Type 2 diabetes, obesity, and cardiovascular disease. Phospholipase A2 works by hydrolyzing the Substitution Nucleophilic Bimolecular (sn-2) ester bond of a/the phospholipid substrate. The sn-2 reaction is a nucleic substitution reaction where a bond is broken and another is formed synchronously. The PLA2 (Phospholipase A2) active site that is responsible for the hydrolysis of sn-2 is located at the bottom of a hydrophobic channel of the C-terminus which has a His-Asp catalytic dyad and a Ca^{2+} atom that is responsible for introducing two water molecules into the active site to start the hydrolysis of the phospholipid. The products of the hydrolysis of the sn-2 ester bond of phospholipid are a free fatty acid and lysophospholipid which increases the body's metabolism by generating energy so that the insulin can be used more efficiently throughout the body and prevents insulin buildup. Because of the increased efficiency of the metabolism caused by the PLA2 this process encourages weight loss and prevents weight gain. This emerging treatment of using a phospholipase found in snake venom can create new life changing therapies for those suffering from insulin resistance.



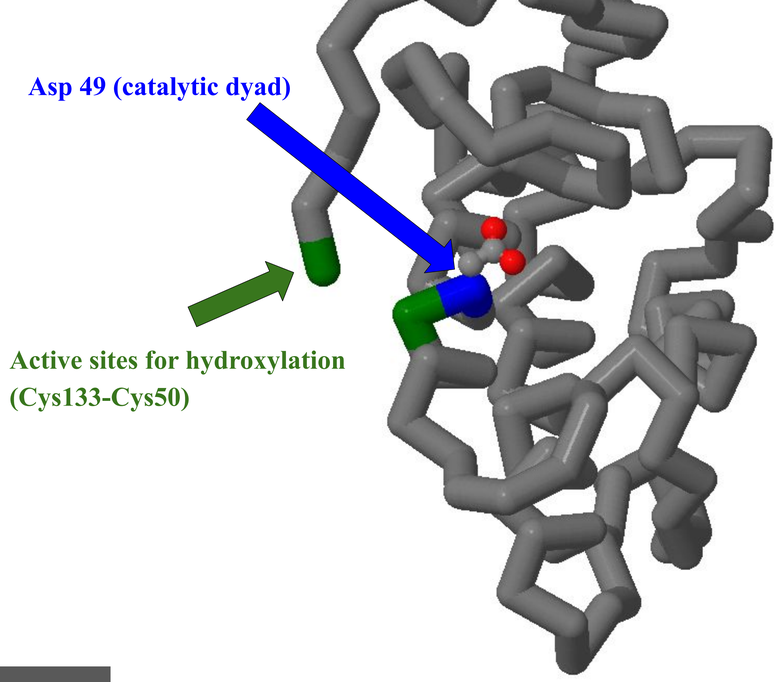
Monocled Cobra (*Naja kaouthia*) Venom

Venoms of snakes of the family Elapidae (including cobras) are predominantly composed of number phospholipases A2 and three-finger toxins. The toxin CTX-I isolated from *Naja kaouthia* snake venom stimulates insulin secretion in a concentration-dependent manner in the absence of glucose when the neurotoxin is shutting down the calcium ions entering into the cells which stops exocytosis and the release of insulin into the bloodstream. This type of insulin secretion modulator is also highly attractive for the treatment of Type 2 Diabetes.

PLA2 and Insulin Resistance

Insulin resistance occurs when the blood stream to absorb the hormone insulin, resulting in increased blood sugar. Insulin is produced by the pancreas to regulate the amount of glucose in the blood. With insulin resistance, the body struggles to regulate blood sugar levels, which is associated with Type 2 diabetes, hypertension, cardiovascular disease, and obesity. PLA2 is an enzyme found in snake venom that can be a therapeutic agent to treat insulin resistance. The process of hydrolysis of the sn-2 ester bond and mediation of lipid signaling increases the efficiency of the metabolism.

PLA2

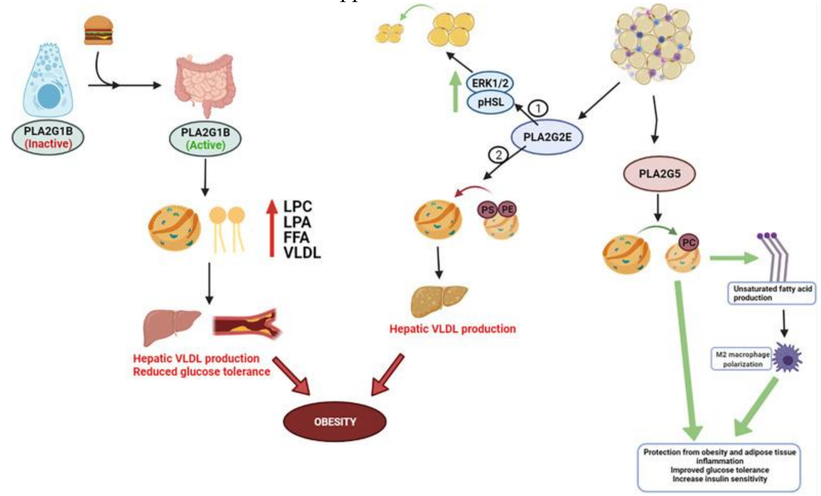


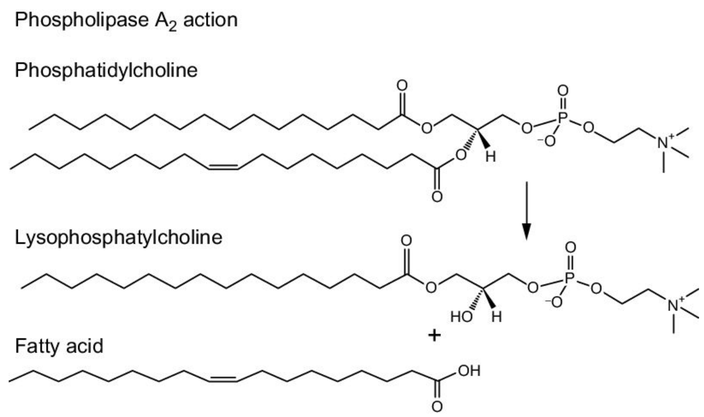
Conclusion

The enzyme PLA2 has a unique ability to create a free fatty acid which works to increase the body's metabolism and result in weight loss. The objective of this study is to investigate the enzyme Phospholipase A2 found in snake venom as a treatment for insulin resistant diseases. This emerging treatment of using a phospholipase found in snake venom can create new life changing therapies for those suffering from insulin resistance.

Applications

Cytotoxic Venom from a Cobra (*Naja kaouthia)* is purified using reversed phase HPLC, creating the by-product of nontoxic PLA2 molecules. Currently scientists are only conducting studies on in vitro rats by injecting the modified snake venom into the mammals with the intention of application in human diseases in the future.





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