Title: Phospholipase A_2

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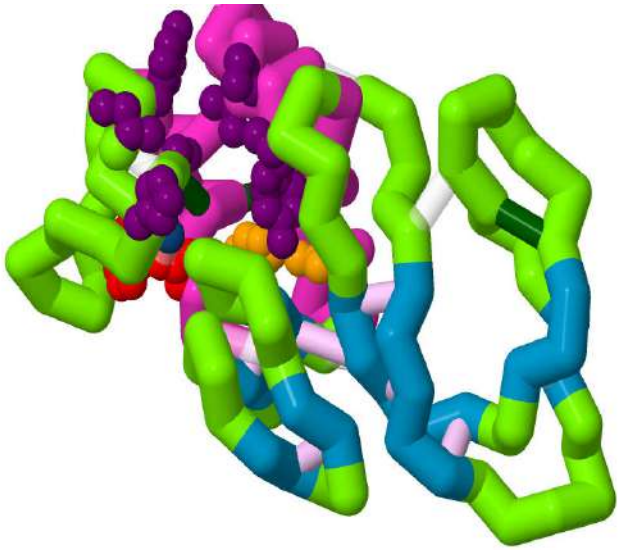
Each year, fifty to one hundred people die of bee stings, and countless others suffer the adverse effects of allergic responses such as pain, swelling, or anaphylactic shock. These physiological responses occur in rapid succession and are facilitated by enzymes present in bee venom. One of the multiple components that initiate these responses is Phospholipase A_2 (PLA_2), an enzyme modeled by the DC Everest SMART Team (Students Modeling A Research Topic) using 3D printing technology.

On the border between all cells and their surroundings is a bilayer of phospholipids. This boundary, thanks to its electrical nature, effectively regulates intracellular composition and protects cells from invading pathogens and other harmful components--two fundamental requirements for a cell's survival, which is why PLA_2 can have such an impact.

The enzymatic function of PLA_2 is to cleave the 2-ester bond of phospholipids. In other words, this enzyme hydrolyzes the bond connecting one of the two fatty acids to the glycerol of the phospholipid head. By degrading the phospholipids, PLA_2 enables the other bee venom components to rapidly penetrate the interior of cells, resulting in a quicker and more efficient dispersion throughout the body. Furthermore, hydrolyzing this specific bond releases arachidonic acid, triggering the archidonic acid pathway that can cause severe inflammatory responses and clot formation. Additionally, it has been shown that PLA_2-mediated phospholipid hydrolysis and subsequent release of arachidonic acid initiates the events of an apoptotic cascade, further assisting bee venom's penetration into the body.

The secreted PLA_2 found in bee venom is Ca^{2+} dependent, meaning it can only function in the presence of calcium ions. Amino acids of the interfacial binding surface (Ile1, Tyr3, Cys9, His11, Thr56, Arg57, Leu59, Val83, Met86, Tyr87, and Ile91) and calcium binding residues (Trp8, Gly10, Gly12, and Asp35) work together to simultaneously hold the calcium ions and water molecules while also destabilizing the ester bond of the phospholipids enough to induce the exchange of electrons that causes the bond to break. More specifically, the active site, His34, in conjunction with Asp35 in the calcium binding cage, contributes an electronegative oxygen leaving an unstable electric potential that must be neutralized and thereby stabilized by Asp64.

Every living cell in the human body is encased in a phospholipid bilayer which, when broken, proves invariably lethal for the cell. Not only does PLA_2, the most abundant enzyme in bee venom, break apart the most basic components of this protective barrier, but the byproducts of its enzymatic activity wreak havoc in other similarly unpleasant ways, both creating and facilitating the undesirable side effects characteristic of bee stings.



Model Description

Structure	Color Code	Color Name
General Backbone	[127, 255, 0]	Chartreuse
Beta Pleated Sheets	[0, 154, 205]	Deep Sky Blue
Alpha Helices	[255, 51, 204]	Hot Pink
His34, Asp64		Orange
Ile1, Tyr3, Cys9, His11, Thr56, Arg57, Leu59, Val83, Met86, Tyr87, Ile91		Purple
Trp8, Gly10, Gly12, Asp35		Red
Calcium Ion	[16, 78, 139]	Dark Dodger Blue
Hydrogen Bonds	[255, 204, 255]	Pink
Disulfide Bonds	[0, 100, 0]	Dark Green

Bibliography

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