Basics of Ricin

Ricin is a naturally occurring protein derived from castor beans. Because of its extreme toxicity even in small doses, ricin has been used in attempted and successful terrorist attacks across the world, including a political assassination in London in 1978 and a string of incidents in 2003-04 targeting water supplies, the White House, and the United States Capitol building. Ricin represents a significant challenge for security forces because military personnel and counter terrorist forces may be exposed to the toxin during warfare or an attack. An effective vaccine would improve both of the first responders and the victims because it would allow emergency and military personnel to more quickly and efficiently respond to threats.

Mechanism of Toxicity

Ricin enters the cell through the B chain, whose galactose ligands bind to receptors on the cell wall. Once the B chain has been accepted by the cell, the disulfide bond connecting the A and B chain dissolves, releasing the A chain into the cytoplasm. Then, the A chain deactivates a base on RNA through deadenylation, or the process of removing its adenosine. Without functioning ribosomes the cell can no longer produce the proteins it requires to survive, and so it dies.

Structure of Ricin

Ricin is heterodimeric - composed of two distinct chains bonded together. The A chain of Ricin is composed of three domains: characterized by a five-stranded beta sheet, five alpha helices, and a disc-like shape. Gal177 (colored dark salmon) is active site of the A chain and performs deadenylation. The B chain facilitates entry into the cell by binding to surface receptors. The B chain is composed of two nearly identically-folded domains that share high amino acid similarity. Gal264 and Gal267 (colored blue) are the active sites of B chain and facilitate entry into cell. Asp46 and Lys40 (colored red), as well as Asp22 (colored purple) determine epimer-specificity of the domain that contains Gal264; Asn355 (colored gold) and Asp 334 (colored chocolate) determine epimeric specificity of the domain that contains Gal 267. Non-highlighted amino acids in the A chain are colored white; in the B chain they are colored lightblue.

Methods

Racing Against Ricin – The Pressing Search for an Effective Vaccine

**Whitefish Bay SMART Team, Whitefish Bay High School, Whitefish Bay, Wisconsin**

**Members:** Declan Coleman, Evan Davis, Luke Dragseth, Austin Gent, Andrew Janssen, Stephen Koch, Andrew Ramirez, Benjamin Sevart

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**Methods:**
The Whitefish Bay SMART team used IMol molecular modeling software to model the ricin molecule. IMol is a software package which allows researchers to view and edit detailed 3D models of molecules. The Center for BioMolecular Modeling used a ZCorp 3D printer to print the 3D, physical structure of the model.

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**Dangers of Ricin:**
Exposure can occur through inhalation, ingestion; skin and eye exposure are especially dangerous. Symptoms begin 4-24 hours after exposure and include fluid buildup, seizures, respiratory, liver, or kidney failure, and death, which can occur 36-72 hours after exposure. No antidote exists, but medical care can reduce harmful effects. Ricin should be removed from the body as soon as possible, while other care should be given to help breathing, seizures, and low blood pressure. If one knows or suspects they are a victim of ricin poisoning, he or she should remove contaminated clothing, wash themselves with soap and water, rinse their eyes, and seal the clothes in plastic bags. If ingested, one should not vomit or consume liquids. Medical attention should be sought immediately. Methods of detecting ricin poisoning include observation, chemical testing of the suspected ricin, and urine analysis.

**Vaccines:**
Two recombinant vaccines, RVax and RVEc, are in development to protect against ricin exposure. Both are composed of the A chain of ricin with intentional amino acid substitutions that prevent the toxic effects of ricin exposure. RVax is composed of the entire A chain, while RVEc is composed of only part. Based on experimental evidence, RVax is more effective than RVEc because of that structural difference.

**References:**

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**Vaccinology Data:**
Experimental data shows that recombinant vaccines composed of the entire toxin are more effective than partial-length vaccines. Antibodies, which determine resistance to the toxin, are detected at much higher rate in mice given the full-length vaccines. Currently, there are multiple laboratories focused on producing a vaccine to this deadly toxin. They are competitive, but still manage to respectfully coexist, sharing data from studies and at several points publishing papers in collaboration with scientists from other labs.

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**Summary:**
While ricin is feared for its deadly effects, current scientific breakthroughs in the form of RVax and RVEc may reduce the risk of exposure to the poison. These vaccines could be used by security forces or first responders to mitigate the effects of Ricin attacks. While more research is needed, these vaccines represent an exciting new breakthrough in the field of vaccinology.