

Protein Structure II: Vampire Vengeance-Waning Immunity and Boosters

Framing analogy: The Price of Forgetting

The year is 1790. Two ragged figures blazed across a cornfield toward a dilapidated farmhouse in colonial Vermont. The two men sprinted furiously determined to beat the impending sunrise. Sergiu and Alexandru burst through the door of their safe-house and slammed it shut just as the sun began to break the horizon and its rays began to sneak through cracks in the doors. "Good job making sure the windows were boarded up ahead of time. We were almost toast" gasped Sergiu as he struggled to catch his breath.

Alexandru, panting as well, remarked, "Vampire life has been tough lately. How many weeks have we gone without feeding on a human?"



Sergiu, replied with a sigh, "It has been more than a year, America was supposed to be the land of easy feeding but as soon as the existence of our vampire race was discovered a few years ago we have been hunted nearly to extinction. The humans can recognize us on sight now. We can feed on rats and birds to survive, but really what kind of life is that? To think, I have lived for more than 1,000 years, and I will fade away to nothing in this awful ruin at the edge of a corn field. I saw Charlemagne crowned, the Magna Carta signed, and then of course there were those crusades! Who could forget that?"

Alexandru's face tightened as he came to a startling realization, "Hey Sergiu, I will tell you who could forget all

of those things..... humans born today who never experienced them. In today's world you couldn't find ten people who could tell you the significance of the Magna Carta. For humans most knowledge is lost throughout the ages because what people need to know is driven by the necessities of the time they live in. No one thinks to watch for signs of the black plague anymore; it is nothing more than a scary story now. Our immortality is our advantage. If we lie low for a few hundred years and keep to feeding on rats and birds the humans will forget that we were ever a threat. They will forget what we look like as well as our weaknesses. We will become nothing more than folk tales. One day people will probably even think that we shimmer in the sunlight instead of bursting into flames. When the humans are once again ignorant of our race and lax in their suspicions, we will reemerge and drain this world dry! Let us set a loose date of 2012 to restart the hunt."

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It is October 2012. Brothers Jimmy and Davy Sturgess explore their attic. Jimmy is 10 and Davy is 12-years-old. Their parents have gone out for the evening, and the two boys are home alone. This home has been in their family for 8 generations and contains a number of interesting heirlooms. While the two explored the dark and dusty attic Davy joked, "it is pretty



creepy up here, there are a lot of old things.....just look at this weird book. I am surprised that it still holds together. It is called 'The Guide for Vampire Detection and Hunting by Abraham Sturgess'. Let me read this for a few minutes, it is kind of crazy what people believed in back then!"

Jimmy shivered a little, "I know! If you want crazy just think about all of those brutal murders that are going on all over the state now. How many have taken place? There must have been 10 or 15 murders within the last month alone. All of them take place in homes, whole families killed and torn apart but not one drop of blood at any of the crime scenes. It sounds like some stupid horror movie"

Davy laughed, "Yeah it does. According to this book vampires are bald, tall, have fangs, claws, long pointy ears and all black eyes and you are not

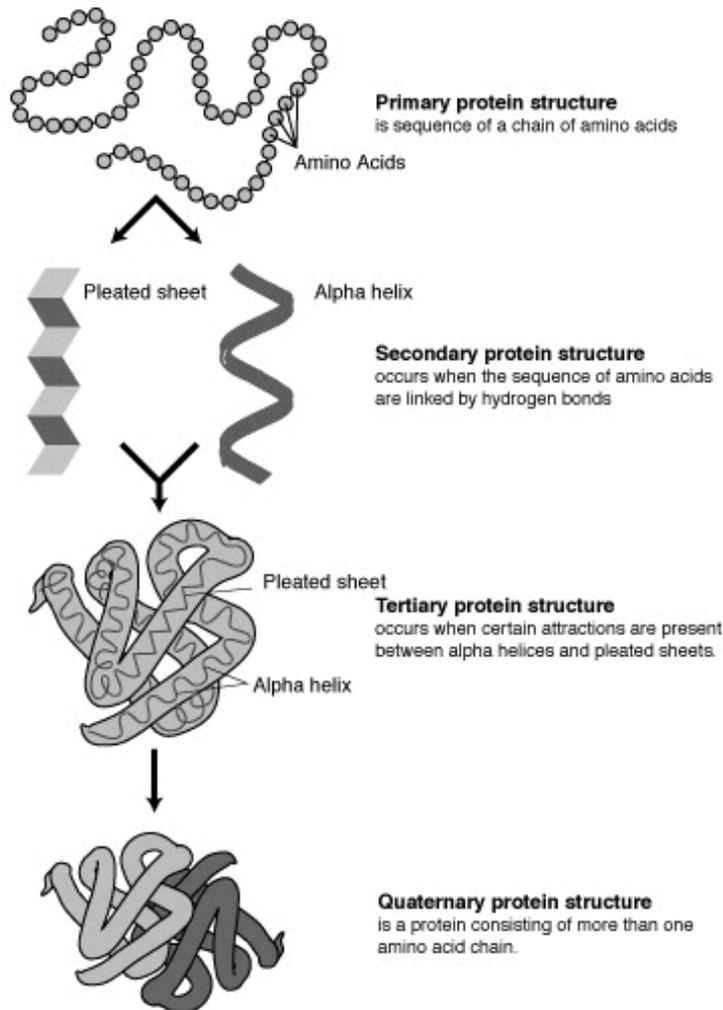
ever supposed to invite them into any building if you want to live. What a joke! Supernatural killing machines constrained by the laws of good manners. Who comes up with this stuff?"

The ring of their door bell interrupts their joking. The two boys run down to investigate, they live in the middle of nowhere so unexpected visitors are not common. Davy glanced out the window next to the front door and saw two tall men in baseball caps and pizza delivery uniforms holding a box of pizza. Davy looked at Jimmy in confusion, "We didn't order anything." Jimmy opened the door and the two, tall, slender men stood still with the brims of their hats hiding their faces. One of them spoke in a low raspy voice, "We had a delivery to make but it turned out that the order was a prank and no one was at the house we were supposed to deliver this pizza to. It was probably just some kids messing around with us. Can we come in to use your phone to call back to our restaurant and update them? You can have this pizza as thanks." As they stepped forward Davy got a better look at them and his heart stopped. Both men had all black eyes, long pointed ears, sharp fingernails, and what looked like tips of fangs poking out of their mouths. They matched the description of vampires he saw in the old book. He was not going to take any chances. Davy pushed Jimmy aside and slammed the door just as the men stepped closer. Davy yelled, "We are not interested! Get out of here! You are not allowed inside!" Jimmy saw how upset that his brother was and knew better then to question him about it, but he secretly thought Davy was being ridiculous. When the boys looked out the window again the men were gone. Both boys were a little shaken by the incident and watched television in their living room uneasily for the next few hours, startled by every sound they heard until they fell asleep on the couch.

The boys were woken up by their parents who hugged them immediately. Their father said, "I am so glad that the two of you are safe! The murderer struck again at a house a few miles from here. They found Mr. and Mrs. Morley dead, drained of blood with a pizza box open on the table."

Scientific Connection:

The two vampires in this story faced a serious problem. Due to their distinctive features



they were detected everywhere they went. This prevented them from catching human prey and frequently endangered their lives. Alexandru and Sergiu realized that if people forgot what vampires looked like then they could hunt again without difficulty. Immortality is a tremendous advantage that vampires have over humans. The two vampires agreed to hide until people forget how to recognize and kill them. Once the vampires believed that humans let their guard down they would strike again.

The vampire plan worked perfectly and when they came out of hiding they were able to feed on a number of families throughout Vermont that could not recognize them for what they were and foolishly allowed them into their homes. The two boys in this story found a vampire detection manual and got a little "knowledge boost" in what physical features to look for. This

recognition is what saved their lives. The Morley family did not have this information and paid for it dearly.

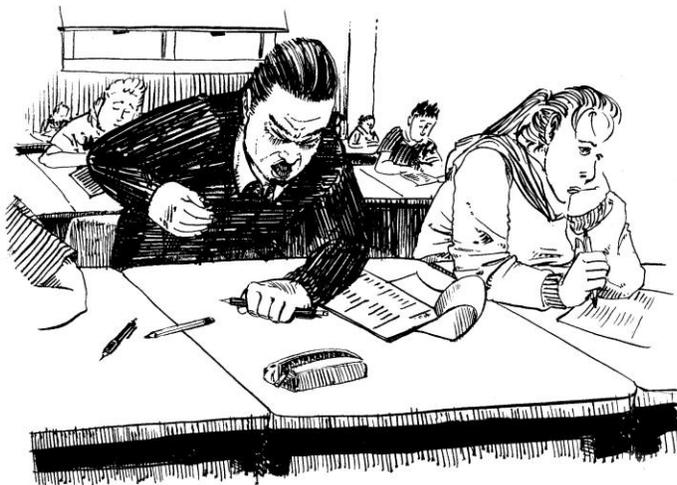
Once the vampires murder enough people their presence will become known once more, they will be recognized and forced into hiding until they are no longer believed to be a threat. This is a cycle of persistence in a predator and apathy in its prey. This is not an uncommon problem for your immune system as well. The bacteria and viruses that cause disease never really go away. They survive by infecting other species like birds and rats just waiting for your immune system to forget what they look like before starting an epidemic again.

Vampires are detected due to distinctive features like pointy ears, long claws, all black eyes, and fangs. These features are vampire “**epitopes**”. **Epitopes** are structural features that the immune system uses to recognize targets that it wants to destroy (**antigens or immunogens**). If something has an epitope that the immune system recognizes as foreign then the immune system will do everything in its power to annihilate that target. The immune system has a “shoot first, shoot again to make sure it is dead, and then ask questions” philosophy. **The majority of antigens are proteins**. The structural features of a protein like the specific arrangement of the amino acid chain in alpha helices or beta sheets (secondary structures) as well as the folding of the protein (tertiary structures) are what make up the epitopes for most antigens. The sequence of amino acids that a protein is made of (primary structure) usually does not contribute to epitopes in living systems because most functional proteins are folded. Epitopes generated from folded structures are known as **conformational epitopes** while unfolded proteins that are in primary structure have **linear epitopes**.

Your body learns to recognize disease epitopes by encountering them either through surviving infections or being shown them ahead of time through vaccination. The immune cells that remember these epitopes are called “**memory cells**”. Unfortunately, these memory cells do not live as long as you do and if you go a long time without encountering the disease again these memory cells die which means that your immune system forgets what the viruses or bacteria that cause the disease look like. This leaves you open for attack like the unfortunate Vermont families in this story.

Decreasing or waning immunity is a huge problem, but just as vaccination shows you disease epitopes ahead of time, a second vaccination given years later to generate more memory cells known as a “booster” can give you additional protection. This is the equivalent of the vampire manual in this story that reminded the boys what vampires looked like. Boosters are very important in preventing diseases that are more terrifying than any vampire.....like whooping cough. I guarantee you would rather let a vampire into your home than let Bordetella Pertussis into your lungs.

Story: The Persistence of Pertussis



“Let me tell you doc, it hurts every time I breathe”, groaned Tim Tyler a 52-year-old public school teacher. In between painful breaths Tim confided, “I am a pretty healthy guy. I know that I have missed several annual appointments, but it is only because I never get sick...until now at least. It all started with a cough. I’ll tell you what, I coughed harder than I ever thought a person could cough. It felt like my head was going to explode with some of them. I felt fine but a few times an hour I would cough real

hard and rapid like a machine gun. When I was done I was all out of breath. I would have to inhale deeply, and it made a sound like a big “whoop”. It went on like this for a couple of weeks, but it still hurts when I breathe. What do you think is wrong?”

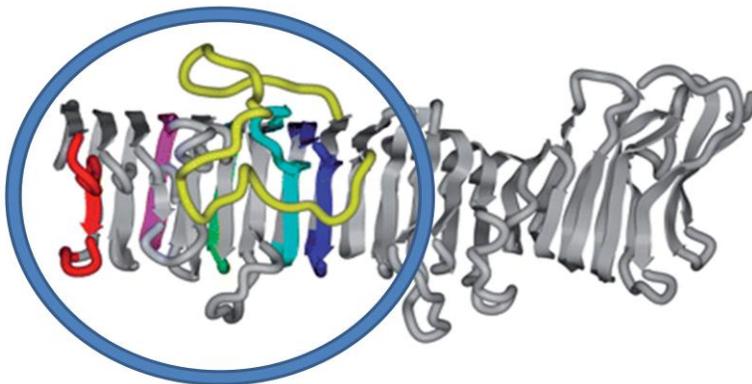
Dr. Morton studied Tim’s X-rays intently, “It looks like you broke a rib on each side of your body! No wonder you are in so much pain. It sounds like you had a case of whooping cough. It is caused by a bacterium called Bordetella Pertussis. When these bacteria get inside of your body they make a poison that causes you to cough hard enough to hurt yourself. If you can even believe it, infected babies younger than 3 months can cough so hard that they actually explode blood vessels in their brains and die. Coughing that hard could easily cause you to break your ribs. Whooping cough was a major cause of childhood death in the past before people began to get vaccinated against it. Unfortunately, it still kills tens of thousands of children every year across the world. It is strange but lately I have been noticing that more and more adults are getting it.

Tim replied, “But, I received all the vaccines I was supposed to as a kid. Shouldn’t I still be protected? I was working with some exchange students from England. I wonder if that had anything to do with it.”

Scientific Explanation:

Whooping cough (pertussis) is a disease that is starting to reemerge in the developed world. Toddlers and school-aged children who received their vaccinations are protected, but there has been an increase in adult infections. Scientists haven't proven why this happens, but one belief(hypothesis) is that while the vaccine trains the body to recognize and eliminate the bacteria, after decades of not encountering them the memory cells die leaving your body susceptible once more. The theory behind encountering it less and less is due to the success of vaccinations. Vaccination helps eliminate the disease in large groups of people so the immune system encounters it less and less in everyday life which creates fewer and fewer memory cells to remember the bacteria’s epitopes. Poor Mr. Tyler was one of these people; he was vaccinated as a young child as were all the other children in his town. Pertussis was a rare

Figure 1. Pertussis Epitopes



disease there and his immune system lost its memory over the years. Unfortunately when he encountered the English exchange students who carried pertussis he ended up getting really sick.

The pertussis vaccination has been so successful that many people think that Whooping Cough is a disease of the past. They

don’t get vaccinated because they don’t think it is a real threat. England has notoriously low vaccination rates for a developed country and as a result the rates of whooping cough are rising

there. Despite our best efforts many diseases never really vanish, they are just lying in wait for us to let our guard down. Their persistence gives them a relative immortality. A solution is to give a pertussis booster vaccine to adults. This has been included with a booster for tetanus that adults are supposed to receive every 5 to 10 years. This booster vaccine would remind the body what the pertussis toxin's epitopes look like to increase its defense against whooping cough. This is why it is important to go to regular doctor's appointments even if you feel healthy because getting booster vaccinations is very important and an easy way to avoid horrible illnesses like whooping cough.

Another current example of this concept is the decrease in children receiving the measles, mumps, and rubella vaccine (MMR) due to fears that this vaccine caused autism. A paper published in 1995(Wakefield et al.) reported a connection between the MMR vaccine and autism which resulted in many parents refusing vaccination for their children. Because cases of measles, mumps, and rubella were not common, many parents felt that there was no longer any risk to their children being infected and saw no harm in refusing vaccinations. Unfortunately most people don't have experience with how sick children with these diseases can get or why millions of dollars were invested in developing vaccines against these diseases in the first place. **The connection between MMR and autism has been demonstrated to be false.** The data presented in the paper, which was pretty suspicious in the first place, was reexamined and there were numerous clues that the primary author may have falsified it in order to gain prestige and make money. As a result the article was pulled from publication 12 years after its initial printing. It is now a classic example of fraud in research but unfortunately it continues to cause significant damage world wide. The fear it inspired led to decreases in vaccination rates and a reemergence of measles, mumps and rubella. These diseases were never gone.....they have just been waiting to strike again.

Take Home Message: alpha helices, beta sheets and protein folding are distinctive structural features of proteins that the immune system uses to recognize threats

Curious? For further reading on this topic take a look at these:

<http://www.ncbi.nlm.nih.gov/pubmed/21422281>

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3088611/?tool=pubmed>

<http://emedicine.medscape.com/article/803186-overview#a0199>

<http://www.time.com/time/magazine/article/0,9171,1960277,00.html>

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2831678/>

<http://www.copakids.com/Pediatric-Health-News/whooping-cough>

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