Iron Insights: Unveiling MTB's Strategies

Brief Introduction to Mycobacterium Tuberculosis:
Tuberculosis (TB) is one of the top ten global causes of mortality, it is an infectious disease that spreads through airborne means and is perceived as a leading cause of death from a single infectious agent, placing it above HIV/AIDS (WHO, 2020). The causative agent of tuberculosis (TB) is regarded as the Mycobacterium tuberculosis (MTB) pathogen and is perceived to negatively influence the pulmonary organs. TB is transmitted via airborne means (can be easily spread from one person to another). Additionally, MTB is known to have developed resistance to various drugs that are used to treat TB. Examples of this include extensively drug-resistant TB and multidrug resistant TB, these forms of TB are resistant to several antibiotics. Thus, making treatment difficult. Moreover, treatment is extensive since it typically requires/ consists of having to take antibiotics for several months. Diagnosis for TB is often regarded as 'difficult' since most of the symptoms for TB resemble those of other diseases.

Dr. Mitra and his Research Lab:
Dr. Avi Mitra is a part of the Department of Microbiology and Molecular Genetics at Oklahoma State University. He is an assistant professor with a PhD in Cell & Molecular Biology. His lab primarily focuses on the understanding of how MTB acquires heme iron (a type of iron found within red blood cells of the human body and is termed as heme since it is bound to a molecule known as 'heme' and is part of the hemoglobin protein that is responsible for transporting oxygen from the lungs to the tissues). He explains this in more detail on the Department of Microbiology and Molecular Genetics website, where he writes that in order for a successful colonization to take place within the host, MTB must rely on its iron source (an important nutrient) and since more than 80% of the iron in our bodies is stored within heme, this makes hemoglobin the primary source of this essential nutrient (Mitra, 2019). Dr. Mitra and his research team's goal is to understand how the usage of heme impacts MTB's pathogenicity within the human host. Additionally, they also focus on exploring new molecules that hinder the activity of gram-negative pathogens from obtaining iron, hoping to develop new drugs that prevent iron uptake and impede the multiplication of pathogens within the human host.

Interviewee Dr. Mitra:
For my science journal column interview, I decided to interview Dr. Avi Mitra to gain insight into the research process of MTB. I believe this topic is critical for the public community since it allows them to stay informed about the advancements being made to combat bacterial infections. Thus, shedding light onto public health. Moreover, increasing awareness of the topic may also lead to the support of funding for more research and an increase in public health efforts.

Question 1: Can you give us a brief overview of your research project?
In our lab, we study two different types of lung pathogens, says Dr. Mitra. *"Our lab focuses on trying to understand how these pathogens get iron nutrients from the human body. Just like how the human needs iron for various processes, bacterial pathogens and almost all living organisms*

need iron. When we think of pathogens affecting the human host, we can think of them gaining iron from the human host. If we can understand the different ways that these different pathogens are obtaining iron from the human host, then we can block these processes and essentially starve the pathogen of the essential nutrient. However, blocking the nutrient by itself won't be enough but we can use this strategy alongside pre-existing antibiotics and make them more efficient in killing these pathogens."

Question 2:
What inspired you to pursue this topic?
"I grew up in India, in India TB disease is still very prevalent. Growing up, I had lots of friends and family members who were affected by TB. In the back of my mind, I knew I wanted to do some sort of research with TB. Eventually when I attended graduate school and started developing different types of research skills, I realized this is my opportunity to do something that I've always wanted to do."

Question 3: Were there any unexpected results or challenges you experienced during your research project?
"Yes, that happens all the time. Any kind of biological research (any research in general) has its roadblocks, sometimes even too many roadblocks. For me, one of the biggest challenges in research is that it is a slow process. Everything takes a long time. For example, when we design an experiment, we take a long time in terms of questions like What am I going to do within the next five to six months? And plan things that are down to the smallest detail we can think of. So that if anything unexpected happens, we have a fallback plan to essentially complete the experiment."

Question 4: Can you describe the methods or techniques used in your research in a way that a non-expert audience can understand?
"For all biological processes, whether it's the human host or bacterial pathogens, they are done by proteins. They are the molecules that perform all vital biological processes.
We're trying to identify the proteins used by these bacterial pathogens to get these iron nutrients from the host. To identify this protein we do a lot of different types of genetics, meaning we make mutants to identify proteins that are unable to get iron nutrients and then we do all sorts of biological chemistry to look at the functions of these proteins and how they are able to bring in those iron nutrients from the human host into the bacterial cells."

Question 5: Did your findings lead to any new questions or avenues of research that you plan to explore in the future?
"Our biggest discovery in the last year was that we found some specific proteins that are used by the mycobacterium tuberculosis pathogen for iron acquisition. These proteins that are used by

this pathogen are ONLY found in this pathogen. It is not found in any other bacteria or any other host cells. These specific proteins are so unique that they have (possibly) the biggest potential to be used as drug targets. If it's only found in the pathogen, then we can specifically target the pathogen and not have to worry about any kind of off-target."

Question 6: How do you envision your research changing society or influencing future studies in the field?
"I would say it goes back to the discovery of this protein. As I mentioned earlier, scientific research is slow because it is so hard. First, we must understand how these proteins function. Whenever we develop any kind of drug, the drug targets the proteins. So, to target proteins first, we must understand the structure. Once that is done, we can then make specific types of drugs to block its protein activities. What I am hoping for is that since these proteins are so unique to these pathogens, they will have a significant potential to come up with a completely new type of antibiotic."

Question 7: Lastly, is there anything else you would like the general public to know about your research and its implications?
"One thing I would like the general public to know about research in general is that everything takes time, everything is a painstaking process and takes time. It also involves research to often build upon prior work."

Summary:
TB is a global health issue and a leading cause of death; the infectious disease is caused by MTB which primarily affects the lungs. Since it has developed resistance to multiple antibiotics, it is difficult to treat. Due to this, TB treatment is extensive. However, thanks to researchers like Dr. Mitra and his laboratory, there are ongoing global efforts to control and eradicate TB. Efforts include identifying pathogen mechanisms, developing therapeutic strategies, discovering drug targets, and advancing antibiotic development.

Citations:

Geneva: Global tuberculosis report 2020. World Health Organization; 2020. License: CC BY-NC-SA 3.0 IGO. Retrieved April 10, 2024, from Global tuberculosis report 2020 (who.int)

Mitra, A., Dr. (2019). *Faculty*. Okstate.edu. Retrieved April 12, 2024, from Avi Mitra, Ph.D. (okstate.edu)