There are no short-cuts in research: Dr. Amit K Pandey

Dr. Amit Kumar Pandey, an Assistant Professor at THSTI, Faridabad, talks about what fascinates him about his research and the lessons he learned along his scientific journey. He is a myco-bacteriologist and works towards understanding the biology of mycobacterial persistence.

Welcome, Amit, and thanks for talking to SciSpeak.

Ankita: Can you tell our readers what your research is about and what you do in your lab?

Amit: My research interest revolves around understanding one of the most tenacious bacterial pathogens ever known to humankind - *Mycobacterium tuberculosis* (Mtb). It causes tuberculosis (TB) in humans predominantly attacking the lungs (pulmonary tuberculosis). Mtb is also capable of infecting other human organs/tissues like Lymph nodes, Bone tissue, Brain, Eyes, spinal cords, reproductive organs etc (extra-pulmonary tuberculosis). Sadly, India accounts for a fifth of the number amounting to approximately 300,000 deaths.

My lab is currently working to shorten the current extended tuberculosis therapeutic regimen. Our hypothesis is that this extended drug regimen is majorly triggered by the presence of a drug-tolerant, non-replicating and metabolically less active subpopulation of Mtb called "persisters". An extended therapeutic regimen thus ensures prolonged exposure and efficient killing of the persister population generated inside the host during the course of the disease progression.

We have some clue as to how the persisters are generated. Data from our lab indicates that the generation and enrichment of the persisters inside the host are intricately linked to a complex interplay between the host and the pathogen. How the pathogen thrives inside the host depends on the availability and utilization of various nutrients it derives from the host during the course of the infection. Our goal is to identify and target some of the proteins critical for the generation and maintenance of persisters inside the host. This will ensure a better and faster clearance of the bacteria from the host. Targeting persisters, we believe, will eventually shorten the duration of tuberculosis treatment. The hope is to bring a paradigm shift in the different intervention strategies currently being followed globally against tuberculosis [smiles].

Ankita: Well, fingers crossed! What is it about your research that you are most fascinated by?

Amit: I find it very fascinating that a pathogen identified in 1882 is still throwing us surprises every day. The fact that we are used to waving a white flag and are at peace with this state of an uneasy truce in our fight with *Mtb* is interesting. Mtb has learned to be at ease and replicate, inside the very cells that are supposed to kill and for decades - this intrigues me. Unlike other bacterial pathogens, Mtb does not secrete any canonical known virulence factors (exotoxin and endotoxin) and is yet considered as one of the "smartest" and the "deadliest" bacterial pathogen ever to inhabit this planet. Scary, may be, but fascinating indeed.

Ankita: So, how do you design novel intervention strategies against "persisters'?

Amit: The objective is to identify critical proteins and pathways present in the pathogen and the host, essential for the generation and enrichment of persisters inside the host. We first identify potential targets. Then, develop a program that will help us screen novel compounds, eventually inhibiting the activity of the identified target/s. Based on the inhibition pattern in terms of their efficiency, few of these selected molecules are tested to check their ability to prevent the generation of persisters in an animal model. This requires us to develop both *in vitro* and *in vivo* models of persistence generation and an efficient high-throughput assay system to screen potential inhibitors persister generation as a proof-of-concept.

Ankita: When you look back at your scientific trail, what would you say were the most valuable lessons professionally and personally?

Amit: Professionally, I believe the most important lesson that I have learned over the years; unfortunately, the hard way is **"Plan your experiments well"** and **"There are no short-cuts in research."** Scientifically, I enjoy doing hypothesis-based science. I keep it very simple; I challenge my hypothesis daily and if I fail, I know that I am on the right track. This motivation keeps my lab and me going.

Personally, working with an extraordinarily slow-growing bacterium that divides once in 24 hrs (most bacteria have a doubling time of 20-30 mins) develops a unique attribute in your personality, something that is very precious - **"perseverance."** There's no getting away from that.

Ankita: How does a typical day of a myco-bacteriologist look?

Amit: I plan ahead of time. The average time for getting any meaningful data from our experiments is roughly a month; we usually do not wait for the results; we just repeat the investigation before we move on to the next. If required, we modify the protocols and always ensure that our data is authentic and reproducible. I spend a very significant proportion of my time mentoring researchers working in my lab. We mainly discuss and analyze raw data and usually work on a proposed hypothesis. Interestingly, one of our favorite pastimes of the day is our "**troubleshooting sessions**." I believe this is the time when all of us learn the most.

I also spend some amount of my time giving 'marketing lessons' to my students. I make them understand the importance of selling their research stories to the world and help them hone their presentation skills, making it accessible to a wide range of audiences for intense scientific and social impact.

Ankita: What is your favorite fact about tuberculosis most people don't know?

Amit: This is a tough one. Co-evolution with humans for centuries has given this pathogen enough time to decipher and neutralize all possible combinations of host-mediated assault inflicted during the progression of the disease. This has reached an extent where we allow the bug to stay put inside us for decades, fooling our surveillance system to believe that it is one of our own. To my understanding, sooner or later, this is something that we all have to grapple with. What I have learned is we need to quickly realize that the conventional approaches are not helping us move forward. We need to start working on unconventional methods in ways that are fundamentally different and disrupting.

Ankita: As a mentor guiding Ph.D. students, what would be your tips and advice for new Ph.D. students out there?

Amit: Do not push yourself hard. If you think you do not belong here, quit, and do things that you enjoy doing. You certainly would need loads of sincerity, perseverance, and hard work.

Ankita: Do you take an interest in science communication? What do you think about how important it is?

Amit: Science communication occupies a central role in my lab and teachings. A scientist has to deal with a complex hypothesis and equally complicated experiments and results. Conveying your thoughts and ideas, when faced with such situations, becomes very challenging. Not able to freely articulate your thoughts could let you down despite having a good understanding of the subject. A lot of this is rooted in the vast cultural and lingual diversity we have in our country. We have accepted English as the preferred language for communication, and most of our students find this very challenging, especially those who have done their schooling in regional languages. I firmly believe having a dedicated language section helping the student develop their vocabulary, oratory and writing skills is the need of the hour and will go a long way in improving the quality of science communication in India.

Ankita: How do you encourage your students to participate or engage in science communication?

Amit with his team at THSTI

Amit: I believe lab meetings provide a very open and comfortable platform for students to nurture their oratory and presentation skills. Similarly, we have developed Ph.D. courses that require students to submit assignments, thereby providing enough opportunity to hone their writing skills. I believe more needs to be done in very informal settings, and students should be encouraged to attend such programs.

Ankita: At last, any message that you would want to give to researchers out there during this challenging time of pandemic worldwide? What change would mean to your research post-pandemic?

Amit: This might sound clichéd, but challenges and opportunities are inseparable and hence always seen together. The current situation has thrown massive responsibility in terms of our

contribution towards the existing problems, like developing quick, cost-effective, and efficient diagnostics to prevent community spread or development of an efficient intervention strategy against this virus.

More importantly, we should start thinking about having a full-proof plan in place in terms of predicting the future occurrence of such unfortunate events. A big shoutout to my scientific colleagues, who believe they have been left out and are not able to contribute scientifically. My advice for them would be to start working on ideas that they think would help save lives just in case we end up seeing ourselves under similar situations. On a lighter note, I believe there is no shortage of opportunities to help, and you can always volunteer and contribute your time and energy towards fulfilling your social obligations by helping out people in need.

Ankita: Thank you, Amit.