

## Existing TB treatments take too long to be effective'

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Microbial geneticist Dr Gyanu Lamichhane of the Johns Hopkins Center for Tuberculosis Research is one of the foremost authority in tuberculosis reseach in the world. He has received many awards, including the \$1.5 million New Innovator Award-2011, and a grant worth \$100,000 from the Bill & Melinda Gates Foundation in 2009 and has also been featured as one of the 36 best and brightest in America by Esquire magazine.

Dr Lamichhane discovered the key role of enzyme L, D-transpeptidase in forming chemical linkages inside the protective cell wall in Mycobacterium tuberculosis, the bacterium responsible for TB diseases. Dr Lamichhane, in an interview with *BioSpectrum*, speaks about his research work and on the progress of TB research in India.

#### **Can you tell us about the tuberculosis-related research activities going on in your institute?**

There are numerous researchers at my institute, Johns Hopkins University, who work on TB research. In summary, our focus spans both basic science and clinical research of TB. Basic science research spans study of how Mycobacterium tuberculosis grows and causes the disease and how it can be killed. We use both in vitro and animal models to study new candidate drugs for treatment of TB. Clinical research involves large clinical trials of new diagnostics and new drugs for evaluation in TB patients.

#### **What makes tuberculosis so difficult to tackle?**

Multiple issues associated with TB make it a difficult disease to work on. The first is that it is an infectious disease that is

airborne and, therefore, it is quite resource-intensive to start a research lab or project to study the disease. Second, the bacterium grows very slowly in the lab making it both time and resource-intensive to study it. Third, the lack of good and readily accessible in vitro and animal models of TB make it difficult to simulate TB in humans.

**What do you think are the three most significant achievements and successes made by you in the battle against TB?**

My group focuses on studying the essential genes or enzymes and metabolites of *Mycobacterium tuberculosis* and the metabolism of the peptidoglycan layer. Our findings include identification of genes essential for growth of *Mycobacterium tuberculosis* in vitro and in vivo. More recently, we have studied and reported on the requirement of a novel enzymes, namely LD-transpeptidases, for biosynthesis of the peptidoglycan layer. This enzyme activity is required for the pathogen to cause TB. We are thinking and working hard and, hopefully, we will be able to come with more significant achievements in the future.

**What are the major hindrances faced by you while doing TB research until date?**

I am in an academic setting. This means, I am very well suited to undertake creative research but in a rather small group setting. When we find something that requires a setting that is both labor and resource-intensive (for example, to synthesize and screen a large number of compounds to develop a new drug), we are not able to do this readily. In addition, there is a large amount of administrative work that I have to do to run my research program, which is the least suitable way to use my time and, therefore, slows the scientific research.

**What are the programs in your pipeline? What are your objectives for the future?**

I have only two research programs, including identification and characterization of novel essential genes of *Mycobacterium tuberculosis* and developing a drug to target the peptidoglycan layer of *Mycobacterium tuberculosis*.

**What are your views on the tuberculosis-related R&D, activities and trends in Asia?**

Asia has tremendous potential to do TB-related R&D. It has both financial and intellectual resources.

**What are the most important concerns that continue to be associated with the treatment and drug development of TB?**

My most important concerns are that the existing treatment of TB takes too long for it to be effective. Also, we need new drugs to treat infections that are resistant to existing drugs. Furthermore, development of new drugs requires both intellectual capacity (expertise), will power and commitment from funding bodies.

**You have been bestowed several honors over the years. What do you have to say regarding these?**

I am honored for the support. I am glad to be working on a disease that is a major global public health issue and on scientific puzzles that would be exciting to solve. Please note that TB is an infectious disease that anyone can get by being physically close to an individual who is infected. Almost all individuals who develop TB get it because they happen to be in the wrong place or are not informed or because preventative measures were not in place. In other words, a person who gets infected did not do anything wrong to get infected. Therefore, it is our common responsibility to understand and work towards helping someone whose condition is not of his or her own making. Anyone or any group that develops new diagnostics or preventative measures and cures will make a tremendous contribution to human health.