World TB Day – March 24 is a sober reminder that tuberculosis continues to be a major public health concern. Appreciable advances have been made in our understanding about various facets of tuberculosis in recent times. But the drugs, that we use, are more than 30 years’ old, the vaccine some 80 years’ old, methods for diagnosing active tuberculosis are more than 50 years’ old and the Tuberculin Skin Test (TST) for diagnosing early or latent tuberculosis is 100 years’ old. Scientific and medical journals carry a large number of articles, signalling significant volume of knowledge that is being generated. Why haven’t the scientists been able to give newer tools for the people who need it most? Where have we gone astray?

Scientists engaged in basic and fundamental research work tirelessly at the bench to unravel the mysteries of Mycobacterium tuberculosis mechanisms at cellular and molecular level. Clinicians study how new tools and interventions perform in clinical settings. For quite some time, efforts have been under way to bring the two ends of research spectrum together to translate the knowledge generated in the sophisticated laboratories into tools for use at community level. In recent years, this collaborative spirit has become so much a part of research climate in some areas that translational research is now a buzz word, for example, in cancer research.

Translational research refers to the practice of translating basic science data or discoveries from laboratory bench into clinical applications. It is really about trying to bring together the progress we are making in laboratory, with the progress we are making in the clinics.

In a statement released on the World TB Day, 2005, Anthony Fauci, Director of National Institute of Allergy and Infectious Diseases at the National Institute of Health (NIH) and his colleagues, while highlighting the advancement of new vaccine and drug products in past few years as extraordinary achievement, remind us of the importance being given to translational research. The NIH has given a big boost to translational research. One of the themes in its roadmap is the re-engineering of clinical research enterprise. At the heart of this programme is a collection of new funding mechanisms specially tailored to the process of translational research.

It is not just NIH, but INSERM Trasfert programme of France’s Institut National de la Santé et de la Recherche Médicale (INSERM), University of California San Diego (UCSD) College of Integrated Life Sciences, the National Heart, Lung and Blood Institute’s Programme for Genomic Analysis and Programmes of Excellence in Gene Therapy, and Medical Research Council’s UK Biobank and Stem Cells Cross Research Council Headline Programme are a few of the prominent initiatives launched to increase translational research.

Tuberculosis is also being used as a model for translational research. For example, at Tulane University Medical Centre, USA, a new centre is being established which would build upon seminal findings of researchers and expand the knowledge of mechanisms to develop new therapies.
During the past ten years or so, major progress in the understanding of mycobacterial pathogenesis has been facilitated by sequencing of the genome of *M. tuberculosis*, and development of tools for gene deletion, and for exchange of genes between mycobacteria. Gene knockout technology has generated important insights into the mechanisms of the adaptive immune response of the host, and the central role of the innate immune system in modulating the response.

Through the NIH testing programme, more than 250 TB vaccine candidates have been screened for their ability to protect against *M. tuberculosis* infection in mice and guinea pigs. Examples of some important categories of vaccines include subunits (114), DNA (43), recombinants (29), fusion (27), mutants (25), adjuvants (7), BCG sub-strains (10), and saprophytes (5). A few of the successful candidates identified in the experimental models are now ready for clinical testing.

Although, a few truly novel compounds to treat TB have been introduced into clinical practice in the past 30 years, some promising work has been done on long-acting rifamycins (e.g., Rifapentine, Rifabutin, Rifalazil); fluoroquinolone compounds (e.g., levofoxacin, moxifloxacin, gatifloxacin); oxazolidinone compounds; and nitroimidazopyrans. These drug classes might provide the best means for rapidly improving TB treatment.

So what does it take to successfully translate a potential basic research finding to clinical application?

Translational research involves many constituents in research pipeline. Basic science researchers, clinicians and patients are of course the key players. Co-operation of knowledge managers, public health specialists, epidemiologists, market sociologists, risk analysts, venture capitalists, fund raisers, etc. are equally important. Medical journals are publishing articles stressing the philosophy and practice of translational research.

Are we preparing our researchers of today and of tomorrow to think about their research in different ways? Are we preparing our future researchers in nuances of translational research?

A new culture of cooperation is necessary to make the transfer from research to practice more successful. Research is necessary to achieve understanding but cannot, by itself, put new knowledge to useful applications. The bridge between the worlds of research and practice is difficult to build, but necessary to assure that research has meaningful and specific end points and is designed to prove its effectiveness. Translational research takes fundamental observations and applies them to people, providing an opportunity for integrating theory, research and practice. The immense opportunities and benefits require that we rethink our strategies, construct the bridge, and also locate people with commitment and understanding to travel it.

Translational research is poised to expand very rapidly, especially with the information explosion triggered by genome programmes. Genomics—the systematic identification of all of the genes in a cell through DNA sequencing and bioinformatics analysis—also offers great potential in terms of drug target discovery and development of new antibacterial agents, and the recently sequenced genome of *Mycobacterium tuberculosis* should provide a number of new targets for novel drugs. The objective should be to speed up translation of discoveries arising from structural genomics, post-genome technologies, gene function, gene-environment interactions into a model of delivery that would benefit human health.

Tuberculosis research in India is supported by multiple funding agencies. At times, one agency is
unaware of what the other is funding. We need to set up a Tuberculosis Research Management Forum, which would bring together major funding agencies and major stakeholders. It would not only provide a common platform to share results of research but would be able to facilitate the much needed bridge of translational research in tuberculosis.

Without this bridge, the long journey from bench side to bed side may become longer and the depth of value of our basic scientists may never be realized.

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REFERENCES