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Industry thrust is key to battle against TB

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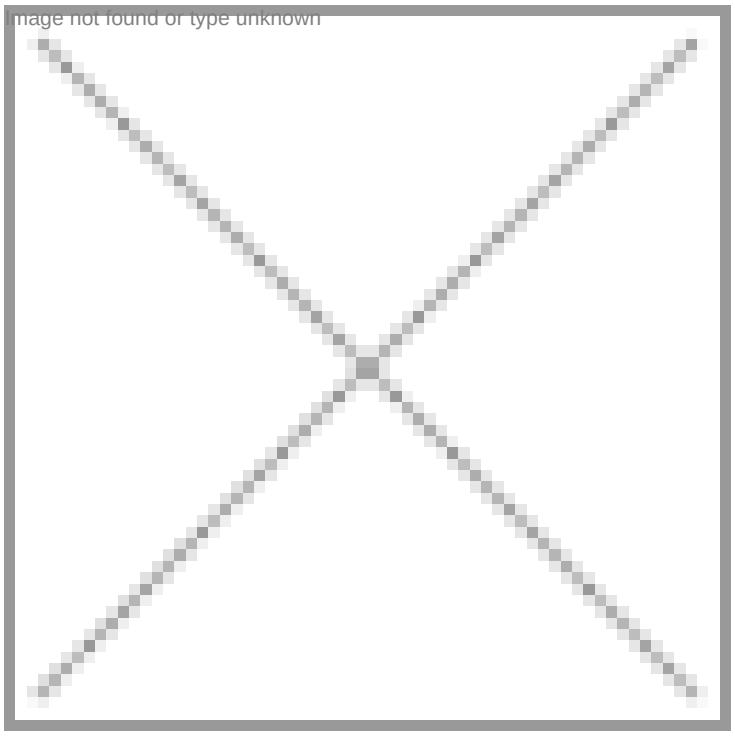

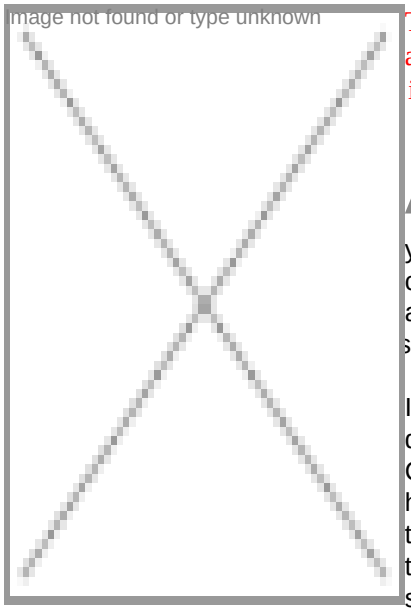

The number of TB infected people and deaths is growing year-on-year in India. However, a major portion of the research in this area is conducted within government-funded is yet to actively participate in such projects

Although India has a long history of tuberculosis (TB) research, the disease continues to remain a major health issue in the country. According to statistics from the World Health Organization (WHO), India accounts for one-fifth of the global TB cases. Each year, nearly two million people in India contract TB, of which around 870,000 are infectious cases. It is estimated that annually around 330,000 Indians die due to TB. Lack of availability of TB drugs, high costs of treatment with the few drugs that are available and s of the disease are the primary reasons.

In addition to this, the emergence of multi-drug resistance TB (MDR-TB) and extensively drug resistance TB (XDR-TB) have caused significant concerns in eradicating the disease. Conventional market-based patent incentives are ineffective in addressing the public health needs in developing countries, with only one percent of the newly developed drugs targeting neglected diseases. New, highly potent and fast acting drugs with short treatment regimen are essentially required for treatment of tuberculosis, which has seen a slow pace. According to reports, between 1975 and 2004, only three out of 1,556 new chemical entities arrived in the market for TB treatment.

Pioneering studies from India demonstrated the efficacy and safety of domiciliary treatment, the necessity of direct

observation of treatment, the feasibility of case detection through sputum smear microscopy in primary healthcare institutions, and the effectiveness of intermittent short-course chemotherapy. These findings laid the foundation for the Directly Observed Treatment Short course (DOTS), which has been adopted by nearly 150 countries. Today, India has the second-largest and the fastest-growing DOTS program in the world.

While a chunk of basic research is currently being conducted within the realms of academic institutions and government-funded research institutes, companies in India are still apprehensive about allocating their R&D budgets for TB. Dr KK Bhutani, officiating director, National Institute of Pharmaceutical Education and Research (NIPER), Mohali, says, â€œThere is TB research happening in India and I know of around 52 research institutes conducting groundbreaking research in the country.â€?

Despite the grim situation, industry experts are positive that given the presence of a fast growing life sciences industry, India has a huge potential in leading TB research. Dr Lucica Ditiu, executive secretary, Stop TB Partnership, comments, â€œThe challenge is clearly huge, but India is rising in the global health arena. The country is moving towards universal access to quality TB care. It has the world's fastest growing pharmaceutical industry and huge potential to become a global frontrunner in biotech, medical and public health research.â€?

Is the focus of companies changing?

Companies are yet to purge the 'commercialization' bug out of their system, opine industry observers. This is the root cause for them to keep distance from TB research. â€œCompanies in India are following the model of their counterparts in the West - of looking at return on investments. I know of innumerable small R&D labs who came up with innovative molecules in TB but then dropped them due to this business outlook,â€? says Dr Ashok Vaidya, research director, Kasturba Health Society, Mumbai, and director, clinical pharmacology, BSES MG Hospital, Mumbai. Above all, TB drugs coming under the ambit of the drug price control has proved to be a major dampener for TB research in the country.

â€œThe industry follows a formula of 10 is to 90, which means putting 90 percent of their revenues for only 10 percent of the diseases. Nobody today gives any importance to neglected diseases. India does not have a dearth of R&D funds but a lack of initiation in TB research,â€? says Dr K Satyanarayana, scientist G, Indian Council of Medical Research, New Delhi.

Few players in the field

Due to the prevalent situation in the country, there are companies who are taking novel steps towards TB research, including Lupin Pharma and AstraZeneca Pharma India among others.

AstraZeneca rolled out ambitious plans in TB. Its discovery research center in Bangalore is part of their global infection innovative medicines unit, focused on TB research and other diseases that are found primarily in the developing world. The team is collaborating with leading names in their respective fields to meet this objective. Mr Anandh Balasundaram, managing director, AstraZeneca Pharma India, earlier said to BioSpectrum, â€œWe have delivered a candidate drug to treat TB in both its drug-sensitive and drug-resistant forms, which also offers the potential to shorten the duration of therapy. The compound is in phase II clinical trials. In addition to TB research, the team supports our antibacterial discovery efforts in close collaboration with colleagues at AstraZeneca's R&D site in Massachusetts, US.â€? An investment of $22 million has been made in the TB research center in Bangalore.

Global Alliance for TB Drug Development (TB Alliance) and AstraZeneca announced in 2010 that they had entered into a research collaboration agreement to accelerate discovery, development and clinical use of drugs against TB, including drug resistant strains of the disease. The joint portfolio will be resourced by a core group of scientists based at AstraZeneca's TB research center in Bangalore with expertise and funding from both organizations. Promising compounds identified in this collaboration will also be tested in combination with other therapies as part of the critical path to TB drug regimens, a cross-sector initiative intended to speed TB drug regimens for patients who need them.

Lupin has been at the forefront of the Indian anti-TB market, commanding a large market share in the segment. It is one of the leading global manufacturers of rifampicin, besides being the largest manufacturer of ethambutol. Lupin also collaborated with the Council of Scientific and Industrial Research (CSIR) in the development of anti-TB drug candidate sudoterb (LL 3858), which is now in the clinical trials stage. The novelty of this drug is that it will potentially bring down the treatment time to two-to-three months while the normal treatment time is six months. In the past, Cadila Pharmaceuticals also collaborated with the CSIR to develop a drug called risorine.

Another prominent sub-segment within the field of TB is the diagnostics market. The importance of this segment has fueled interest in the light of a large number of undiagnosed population in India for TB. Most of the existing testing products for TB (in-vitro diagnostics market) is mainly imported, making treatment an expensive process for the common masses. There is thus an urgent need for domestic indigenous companies to come up with innovative diagnostic solutions making treatment

affordable. Although it is difficult to size this market, a preliminary study by Mckinsey suggested that the annual TB diagnostics market in India might be worth $100 million, although there is uncertainty surrounding the estimates from the private sector, which does not report TB-related statistics. Companies that are pursuing this domain include Tulip group, Span Diagnostics, Bigtec and Achira Labs. In February 2012, Avesthagen signed a memorandum of understanding (MoU) with CosmosID, a US-based company, for collaborating to correctly diagnose and therapeutically manage tuberculosis treatment. Avesthagen and CosmosID will pool their expertise to identify the particular TB strain and thereby support proper treatment. The collaboration is expected to result in a new method for developing diagnostic kits for rapid screening of patient samples.

Government initiatives

Open Source Drug Discovery (OSDD), which is a first-of-its-kind government initiative, was launched in September 2008 by the CSIR. It is a $35 million collaborative research effort that focuses primarily on TB. The vision of OSDD is to provide affordable healthcare to the developing world by providing a global platform where scientists can collaborate and collectively solve complex problems associated to discovering novel therapies for neglected tropical diseases such as TB, thus accelerating research for TB drugs. To achieve this goal, OSDD aims to reduce the risks in the discovery stage by facilitating collaborations between scientists, doctors, technocrats and students through a collaborative platform.

Research Institute	Work Conducted in TB
National Institute for Research in TB, Chennai	1. Randomized clinical trial to study the efficacy and tolerability of three-times-a-week gatifloxacin and moxifloxacin, containing regimens in the treatment of sputum positive pulmonary TB 2. Randomized clinical trial to study the efficacy and tolerability of three and four month moxifloxacin containing regimens in the treatment of sputum smear positive pulmonary TB 3. HIV vaccine study
National Tuberculosis Institute, Bangalore	1. Study on the status of pulmonary TB patients put on treatment under the Revised National Tuberculosis Programme in Bangalore Mahanagara Palike. 2. Study on treatment outcome of smear positive pulmonary TB patients treated under the Revised National Tuberculosis Control Programme. 3. Study on surveillance of drug resistance in the district of Mayurbhanj,Orissa; Hooghly, West Bengal; and Nagaon, Assam.
Co-ordinated research between the International Center for Genetic Engineering and Biotechnology, New Delhi; University of Delhi, South Campus, New Delhi; Acharya Narendra Dev College, University of Delhi, New Delhi; Sri Venkateswara College, University of Delhi, New Delhi; Institute of Mathematical Sciences, Chennai; and Central Jalma Institute for Leprosy and other Mycobacterial Diseases, Agra	The major focus is to identify antigens or combination of antigens that can potentially be used as vaccine candidates against TB alongwith identification and validation of genes involved in the pathogenesis of Mycobacterium tuberculosis, which are essential for the survival of pathogen in the host. Identification of new drug targets and understanding of the mechanism(s) of pathogenesis will also be carried out. The system biology of the Mtb-macrophage interaction will be studied by combining mathematical modeling with experimental approaches
ILS Institute of Tuberculosis and Respiratory Diseases, New Delhi	1. Assessment of the Revised National Tuberculosis Control Programme Strategy and FNAC diagnosis (at two weeks) and six months duration of treatment for peripheral tubercular lymphadenitis 2. Identification of biomarkers and pathogen regulated targets for tuberculosis infection 3. Role of suppressors of cytokine signaling during Mycrobacterial tuberculosis infection 4. Validation and clinical studies for method for diagnosis of tuberculosis by smear microscopy, culture and polymerase chain reaction using processed clinical samples and kit thereof
All India Institute of Medical Sciences (Biotechnology), New Delhi	1. Molecular pathogenesis with reference to dormancy adaptation of Mycobacterium tuberculosis 2. TB Inhibitor discovery and development 3. Deciphering host-Mtb interactions 4. Developing a tool box for the diagnosis of tuberculosis

CSIR's Open Source Drug Discovery Initiative	It is a global platform where scientists can collaborate and collectively work to solve the complex problems associated with discovering novel therapies for neglected tropical diseases like TB, thus accelerating research for TB drugs. To achieve this goal, OSDD aims to reduce the risks in the discovery stage by facilitating collaborations between scientists, doctors, technocrats and students through a collaborative platform
National Institute of Pharmaceutical Education and Research, Mohali	1. Novel aza-aromatics for tuberculosis activity against Mycobacterium tuberculosis 2. Determination of the role of acute-phase reactants in the interaction of Mycobacterium tuberculosis with macrophages in vitro

The latest development on this front is the release of its 'Connect 2 Decode' (C2D) project to re-annotate biological and genetic information relating to the Mycobacterium tuberculosis (Mtb) genome. C2D's findings may help to reveal the previously undiscovered details of TB, resulting in development opportunities for urgently needed new TB drugs in India and other developing countries. This is the first time that a comprehensive mapping of the Mtb genome has been made publicly available. Under the C2D project, researchers and students pooled their time and skills using online tools to provide insights into 4,000 genes of the deadly pathogen. The researchers also mapped the genes as they relate to functional interactions and pathways. Their work is held in a shared database, which the OSDD will share through a globally accessible database with any research institutions involved in TB research through its open portal. The gene map is similar to a Google map or a Wikipedia article that can be modified and updated as new information emerges on the features of the genome.

â€œWe need to have a balanced view between health as a right and health as a business. It is because there has been imbalance in this view that diseases like TB, with high mortality but low profitability, are neglected by the current system of pharmaceutical research,â€? says Dr Samir K Brahmachari, director-general, Council of Scientific and Industrial Research (CSIR). â€œAs virtually no new TB drugs have been developed since the 1960s, the OSDD's model in particular holds great promise for the scientific community by stimulating the development of better drugs and diagnostics for patients.â€?

India is very much on the agenda of the Stop TB Partnership. â€œIn late August, we joined a meeting in Bangalore on the development of new diagnostics. In the same month we organized meetings with the government to discuss global TB drug shortages and to launch a new guide on the research needed to improve the quality and reach of TB care,â€? confirms Dr Lucica Ditiu. The Stop TB Partnership was established in 2000 to realize the goal of eliminating TB as a public health problem and, ultimately, to obtain a world free of TB. It comprises a network of international organizations, countries, donors from the public and private sectors, governmental and non-governmental organizations. Its secretariat is hosted by the WHO at Geneva and from there, it has been transforming the fight against TB in more than 100 countries.

Furthermore, WHO India has provided technical support to the Revised National Tuberculosis Control Programme in its research activities with Tuberculosis Research Center, Chennai, and with other agencies and in the surveys to assess the impact of different TB control measures. It also provides technical support to the National TB Institute in operational research and impact assessment surveys.

In conclusion, it can be said, that while the government is playing a proactive role in bolstering TB research, the industry needs to chalk out models wherein a balance between business and needs of the public at large is maintained. Prospective areas of research now include vaccines and diagnostics tools for TB.

Nayantara Som in Mumbai, (with inputs from Rahul Koul in New Delhi)