



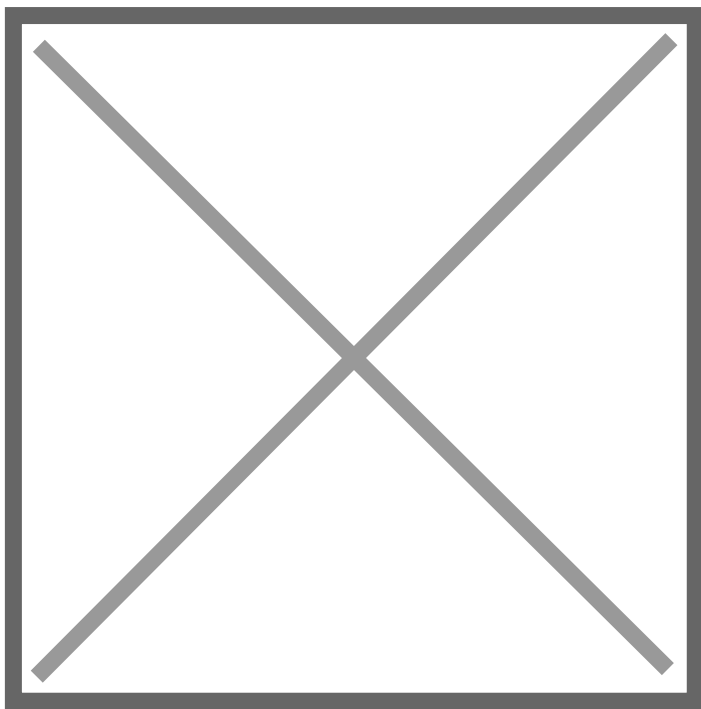
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Indian researchers discover a new anti TB molecule

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In a joint public-private partnership project between the Council of Scientific and Industrial Research (CSIR) and Lupin laboratories Mumbai, researchers have discovered a new anti-tubercular molecule for the treatment of tuberculosis (TB). This development has enthused the entire research community as the molecule, LL 4858-SUBOTERN, has the potential to not only treat tuberculosis effectively but also reduce the treatment time significantly.

The Institutional Partners

1. International Centre for Genetic Engineering and Biotechnology (ICGEB), New Delhi.
2. Bose Institute (BI), Kolkata
3. Central Drug Research Institute (CDRI), Lucknow
4. Centre for DNA Fingerprinting and Diagnostics (CDFD), Hyderabad
5. Indian Institute of Chemical Technology (IICT), Hyderabad
6. Indian Institute of Science (IISc), Bangalore
7. Institute of Genomics and Integrative Biology (IGIB), New Delhi
8. National Chemical Laboratory (NCL), Pune
9. National Institute of Immunology (NII), New Delhi
10. Regional Research Laboratory (RRL), Jammu
11. University of Hyderabad

Lupin Laboratories, Mumbai, partnered with CDRI, NCL, IICT and University of Hyderabad in achieving this breakthrough.

Announcing the breakthrough, Kapil Sibal, minister for science and technology, said, "This is the first success achieved in developing a new therapeutic molecule for tuberculosis since the last discovery of Rifampicin in 1963. All over the world, work has been going on to reduce the TB treatment time from the current level of six to eight months and there has been no success. The Indian breakthrough makes it possible by clearing the total infection in two months only."

The molecule, which works through combination therapy, is compatible with the present drugs, is less toxic and can prevent the recurrence of disease. It fits well into the present four-drug therapy by replacing one or two drugs from the present cocktail. Significantly the new molecule is also effective against multi-drug resistant strains of tuberculosis.

The genesis

This success story can be traced back to 2001, when the CSIR through the New Millennium Indian Technology Leadership Initiative (NMITLI) scheme supported the project entitled "Latent M. tuberculosis: New targets, drug delivery systems and bio-enhancers and therapeutics". The objectives of the project were to improve current treatment by shortening total duration of treatment and address the problems of multi-drug resistance and latent tuberculosis infection. In order to achieve these objectives, a three-pronged strategy was employed viz. development of new drugs including identification of new targets, new drug delivery systems and application of bio-enhancers as an adjunct to chemotherapy. A network of 11 leading CSIR research institutions and Lupin as industrial partner in "public-private partnership" mode was put in place to achieve these objectives. Lupin invested about Rs 11 crore and CSIR put in Rs 9 crore in the project.

Along with the Central Drug Research Institute, Lucknow, the Indian Institute of Chemical Technology, Hyderabad, the National Chemical Laboratory, Pune and the University of Hyderabad, Lupin was involved in the designing and synthesis of the new molecule, whereas seven other institutes were engaged in research on bioenhancers and identification of new targets

The regulatory studies on the new pharmacophore have been completed and the molecule has been tested on mice and guinea pigs and proved to be highly effective. An Investigational New Drug (IND) application running into 2903 pages has been filed. Once the IND is cleared by the Drugs Controller General of India (DCGI), the molecule will undergo phase I, II and III clinical trials in human subjects. These trials are expected to take about four to five years and if they are successful, the

new drug will be introduced into the market.

Rolly Dureha

Important tree genes mapped

Researchers in Sweden and the US have released a new database of many of the important genes in a tree genome. This collection of genes includes a large proportion of those expressed during tree growth. Just as Arabidopsis is the most commonly studied plant in the world with respect to molecular genetics, poplar is the most commonly studied tree.

The database describes about 102,000 sequences of the most commonly expressed genes in the genus *Populus*, which includes cottonwoods and aspens. In living organisms, the genes that are "expressed" are only a fraction of the total DNA in cells. But they are most important to determining an animal or plant's function—in the case of a tree, forming its bark, leaves, roots and wood and enabling it to respond to environmental stresses. The database was produced by a research group in Sweden with collaboration by researchers at Oregon State University (OSU).

The study also compared many of these gene sequences to those found in Arabidopsis, and found that nearly all the genes were functionally common between the two, even though they have been separated by about 100 million years of evolution and look completely different. Arabidopsis is the most frequently used plant in the world for basic genetic research on plant structure and function and being able to compare its genetics to those of a tree is expected to speed genetic research with trees. According to the researchers, this also indicates that the large majority of transfers of genes between widely separated plant species via genetic engineering would not produce novel characteristics, but simply modify existing genetic characteristics.

"There is still an enormous amount we do not know about the genetic function of trees at the most basic levels, but advances such as this will narrow the gap between the scientific research we can undertake with trees and the studies that are possible with traditional model plant species, such as rice, corn, and Arabidopsis," said Steven Strauss, a professor of forest science at OSU.

Trees, which are among the most ancient of plant life forms, also have a very complex genetic makeup that so far has resisted many of the traditional genetic research techniques that are used with other plants, which have short life cycles.

The new study, along with advances that are expected soon to describe the entire *Populus* genome DNA sequence, will help scientists find specific genes in a matter of minutes using computational approaches. "Such discoveries would take decades or centuries prior to these databases. Once you know a lot of gene sequences and can study thousands of genes at a time, you can start to really explore how trees might respond on a basic genetic level to such stresses as drought, exposure to cold, and pest attack," said Strauss.

Ultimately, the researchers believe that a more comprehensive understanding of tree genetics should allow controlled gene transfer, both as a research and biotechnology tool.

Source: Oregon State University

Vanillin may treat sickle cell disease

Vanilla, a popular ice cream flavoring, fudge and cake-frosting agent, may have potential uses as a medicine. Recent laboratory research has indicated the possibility that a form of vanilla may become a drug to treat sickle cell disease. This was concluded after experiments in which specially bred mice received a compound that turns into vanilla in the body, survived five times longer than mice that did not receive the chemical. All the mice were subjected to low oxygen pressure, a condition that causes their red blood cells to form the hazardous sickle shape. Results of the study, led by research hematologist Toshio Asakura, of The Children's Hospital of Philadelphia, have appeared in the June 2004 issue of the British Journal of Haematology.

It had been known for 30 years that vanillin, the compound that gives the vanilla bean its flavor, protects red blood cells with sickle cell disease. However, this effect previously occurred only in test tubes, because vanillin normally breaks down in the digestive tract before reaching the bloodstream.

Scientists at Medinox, a San Diego-based biotechnology company, developed a variant of vanillin called MX-1520, chemically modifying it to resist degradation by the digestive system. MX-1520 is a prodrug-a compound that becomes an active drug (in this case, vanillin) in the body.

Dr Asakura and his team tested MX-1520 in transgenic sickle mice-animals with red blood cells containing human sickle hemoglobin, similar to the defective blood cells in people with sickle cell disease. The researchers found that most of the MX-1520 turned into vanillin in the mice, where it interacted with sickle hemoglobin and inhibited the formation of rigid sickled cells.

A gene mutation causes red blood cells to become stiff and sickle-shaped, damaging and obstructing blood vessels. The disease may cause severe pain, stroke, anemia, life-threatening infections, and damage to the lungs and other organs.

"The results of the study indicate that further study of the vanillin prodrug MX-1520 is warranted, but the compound has not yet been studied in any patients. Patients with sickle cell disease should also be aware that this study does not imply that eating food products currently containing vanilla will benefit patients, because most vanilla is destroyed in the stomach and does not reach the bloodstream," said Dr Asakura.

Source: The Children Hospital of Philadelphia