

## Imtech develops novel clot-buster for thrombolytic therapy

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*Nostrum Pharmaceuticals will carry out clinical development of CSSK*

Coronary artery disease (CAD) is a rampant problem worldwide and the current rate of CAD-based deaths is increasing at a particularly alarming rate.

Though clot-buster drugs such as tissue plasminogen activator (tPA) Urokinase (UK) and Streptokinase (SK) have revolutionized the treatment of myocardial infarction in recent years, the quest for an affordable, better clot-busters with fewer side effects and greater target specificity has remained a big challenge worldwide.

The Institute of Microbial Technology (Imtech), Chandigarh, a constituent laboratory of the Council of Scientific & Industrial Research (CSIR), has been working in this direction and has developed a novel clot-buster for thrombolytic therapy. This Clot Specific Streptokinase (CSSK) is an engineered protein produced by recombinant DNA technology. The cDNA coding for Streptokinase has been fused with the cDNA of another naturally occurring human blood protein. The resulting hybrid protein is a product that has a very high affinity for the blood clot while it does not have any plasminogen lysis property. However, upon binding to the blood clot protein fibrin, the hybrid protein is lysed into its individual component proteins. As a result, streptokinase is released and is active only in the vicinity of the blood clot. Therefore, the common problem of blood thinning associated with Streptokinase due to general and widespread plasminogen lysis in the blood that can cause severe bleeding and hence death in some cases, will be avoided when CSSK is used. Imtech has already obtained a European patent for this

molecule, and the Indian and US patents are pending.

Now this therapeutic protein has been licensed to Nostrum Pharmaceutical, a privately held company based in Edison, New Jersey, USA, that develops and commercializes products using novel drug delivery systems for generic and branded pharmaceuticals in the US. Nostrum will develop this therapeutic protein in association with Symmetrix Pharmaceuticals, an affiliate of Nostrum Pharmaceuticals and carry out clinical development and commercialization of the novel clot-busting therapeutic protein.

Symmetrix, was founded by Dr Yatindra Prashar, a renowned biotechnologist and scientific co-founder of Gene Logic, a Gaithersburg, Maryland based biotech company.

Once developed, the CSSK will have a great potential both in the developing countries and the worldwide markets.

Expressing happiness over this technology licensing tie-up, Kapil Sibal, Cabinet Minister for science and technology, opined that the research being carried out by many of the R&D institutions in India are now coming at par with those from globally recognized companies. Sibal was particularly happy to note that the tie-up represented a "brain gain" for India.

Dr Nirmal Mulye, president and founder of Nostrum Pharmaceuticals, said, "The development of CSSK is the result of remarkably ingenious protein engineering research at Imtech and we are very excited about taking this therapeutic protein into clinical development since CSSK works in a highly clot-specific manner and hence overcomes the major problem of blood thinning that is otherwise associated with Streptokinase".

Lauding Imtech for this achievement, Dr RA Mashelkar, director-general, CSIR, said, "This development represents a paradigm change in the working of government sector Indian R&D labs from primary basic research driven programs to the ones which can be commercially exciting as well. Dr Girish Sahni, director, Imtech said, "Nostrum, a technology-driven company has the focus and agility of a small company, and access to intellectual and financial resources to pursue clinical development of a molecule that has a huge commercial potential in the market worldwide".

Sharing financial details of the technology licensing agreement, Dr Sahni said, "The agreement involves payment of \$100,000 initially to Imtech, apart from several milestone payments and other royalties at different levels".

Nostrum has plans to launch the product in India to start with. The product launch would take about three years, during which the required regulatory approvals would be obtained.

Rolly Dureha

### **Treating depression may raise anxiety levels**

A novel research conducted by scientists at the National Center for Biological Sciences (NCBS) has shed new light on the recent clinical reports of patients who suffer from high levels of anxiety when they are subjected to anti-depressant treatment.

A team of scientists led by Dr Sumantra Chattarji discovered that a molecule called brain-derived neurotrophic factor (BDNF), found naturally in the brain is responsible for neural changes associated with chronic stress. More specifically, it is a protein which has activity on certain neurons of the central nervous system and the peripheral nervous system; it helps to support the survival of existing neurons, and encourage the growth and differentiation of new neurons and synapses. In the brain, it is active in the hippocampus, cortex, and basal forebrain—areas vital to learning, memory, and higher thinking.

Animal studies and test tube (in vitro) models have shown that certain neurotrophic factors like BDNF are capable of making damaged nerve cells regrow and reduce depression. Because of this capability, these factors represent exciting possibilities for reversing a number of devastating brain disorders, including Alzheimer's disease, Parkinson's disease, Lou Gehrig's disease, and HD.

Major depression and other chronic stress related disorders, like post traumatic stress disorder (PTSD), cause change in the physical structure of the brain. In order to survive and make connections, neurons require support from the BDNF molecule. Scientists observed that both physical and behavioral changes are attributed to the lack of support from this BDNF molecule. Scientists at the Yale University first suggested this neurotrophic hypothesis.

To further test this neurotrophic hypothesis, Dr Sumantara Chattarji and colleagues investigated the role of BDNF molecule in depression using genetically engineered mice. In their test, the level of BDNF was increased in the mice and also they were subjected to a battery of behavioral and morphological analysis to determine their response to stress.

The researchers found that BDNF acted as an antidepressant and also prevented damage in the hippocampus. However, the enhanced levels of BDNF molecule increased anxiety and also increased connections between neurons in the amygdala that plays an important role in processing emotional information.

The researchers suggest that BDNF's action on different brain regions not only serve as a useful model to help explain the reason why some antidepressants increase anxiety but also opens up the possibility of discovering new effective drugs for countering the debilitating effects of stress disorders.