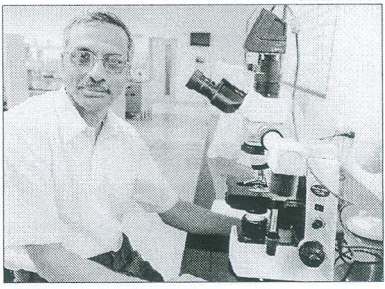
SANDEEP DAUNDKAR



Brain storming

Nishi Kant Subhedar explains how peptides affect the brain

SUNANDA MEHTA

Unlocking the mysteries of the brain and the clockwork perfect communication system by which it functions has been the subject of exhaustive research over decades. Providing vital clues and keys to this intricate and hugely complicated circuit are peptides, particularly neuropeptides and cocaine- and amphetamine-regulated transcript peptide (CART), known to be primarily involved in the regulation of feeding behaviour in all vertebrates including humans. While neuropeptide Y is released when we are starving, and drives us to food, CART has the opposite effect, says Dr Nishi Kant Subhedar, who is researching peptides at the state-of-the-art Indian Institute of Science Education and Research (IISER) in Pune. Subhedar, a professor at the institute, has had his work profusely cited in text-books and published in scholarly journals.

What makes his work on these peptides even more critical and consequential is the increasing realisation that any imbalance in their secretions may give rise to serious pathological conditions like obesity, depression, mania, diabetes and several other central as well as peripheral disorders. Both these peptides may also be involved in other affective conditions like anxiety, depression, memory and learning, says Subhedar.

What are neuropeptides? "Made of chains of amino acids, neuropeptides represent a class of compounds that are found in neurons. They serve as neurotransmitters, and play a very important role in the communication system of the brain," says Subhedar who did his MSc in Zoology from the University of Pune and PhD from Nagpur University. After serving as faculty at the Department of Pharmaceutical Sciences, Nagpur University, he retired as Professor of Pharmacology in 2008. Since then he has been serving as professor at IISER. A Fellow of the National Academy of Sciences, Subhedar is also the president of the Indian Society for Comparative Endocrinology, and president of the Indian Subcontinent Branch of the International Neuropeptide Society.

Subhedar conducted studies on rats and for the first time demonstrated that CART may be mediating anxiety, associated with alcohol withdrawal following addiction. This work was published in Neuropsychopharmacology. Subhedar explains how they studied the involvement of CART in the three distinct anatomical sites in the brain that are known to play a role in precipitating anxiety-like behaviour. Injection of the peptide directly and specifically into these regions of the rat brain generated anxiety in the animal. Alcohol intake for 15 days followed by withdrawal precipitated an anxiety-like response, which was reversed by the injection of anti-CART substances in these anatomical sites. CART content was found to be greatly increased in these anatomical areas following alcohol withdrawal.

According to the scientist, other than brain, peptides are also present in the blood, where they may serve as hormones. Insulin is a classic example. "In the brain, they perform a multitude of actions and interestingly, the same peptide may perform different roles at different sites. For example, neuropeptide Y in the hypothalamus may play a role in the regulation of release of hormones, but in amygdale (yet another part of the brain) it may influence anxiety-like behaviour," he says, adding that since it is believed that not all neuropeptides have been discovered, path-breaking discoveries may be expected in the near future.

Neuropeptide researchers face a lot of challenges. "These neuropeptides, released by one nerve cell, are known to act on other nerve cells via large molecules called receptors. A single neuropeptide may act via many receptors, and each receptor might precipitate a different biological effect. Receptors are important since they can serve as the targets on which the drugs may act. The challenge is to identify these receptors and to figure out the exact physiological or behavioural process they will activate or influence. And since neuropeptides cannot be taken as tablets, we have to come up with non-peptide drugs that will mimic the effect of the neuropeptides and trigger or inhibit the neuropeptide receptors," says Subhedar, who is currently also working on a research project on the involvement of CART in memory and learning funded by the Department of Science and Technology.