MedicalXpress

Switch off enzyme to control chronic pain, say researchers

January 12 2011, By Paul Cantin

A team of researchers at the University of Toronto has developed a new drug targeted at parts of the brain and spinal cord associated with pain perception, which may more effectively control chronic pain caused by nerve injuries.

In a paper published Jan. 12 in the journal Science Translational Medicine, a team led by Professor Min Zhuo of the Department of Physiology and Centre for the Study of Pain, the Canada Research Chair in Pain and Cognition, showed that a new drug called NB001 produced powerful pain-killing effects in mice and in human neuronal cell lines.

“Acute or physiological pain is necessary for animals and humans to get through daily life. Minor pain alerts the body that something is wrong,” said Zhuo. “On other hand, increased and unmanageable nerve pain, typically described as chronic ‘shooting’ or ‘burning’ sensations, has no survival benefit and is usually caused by severe injury or diseases such as cancer or AIDS.”

Chronic pain one of the most common health problems worldwide. In extreme cases, even the gentle pressure of clothing rubbing against the skin or the bending of a joint can become unbearable. Previous studies have found that chronic pain is not just a prolonged form of acute pain, but arises from distinct changes in synapses, the junctions that permit neurons to pass through to another cell, along sensory pathways in the brain and spinal cord. Unfortunately, most conventional painkillers don’t effectively shut off chronic pain and have a tendency to also attack acute

pain.

In the paper, entitled Identification of an Adenylyl Cyclase Inhibitor for Treating Neuropathic and Inflammatory Pain, the researchers found that pain may be controlled by using NB001 to block a particular enzyme known as type 1 adenylate cyclase, or AC1. That enzyme is mainly produced in the neurons of the spinal cord and front region of the brain during nerve injury. Zhuo and his colleagues previously showed that knocking out the AC1 gene significantly reduced or blocked chronic pain in mice. Yet this time, instead of blocking AC1 in the entire body, the new drug works by only blocking AC1 in specific regions of the brain and spinal cord. The dose of NB001 required for producing analgesic effects is at least 10-50 times lower than current chronic pain drugs in the market.

“The findings suggest that AC1 is critical for various forms of chronic pain, but does not contribute to acute pain. Moreover, unlike other drug targets for chronic pain, AC1 is selectively expressed in neurons and thus is less likely to cause potential side effects in non-neuronal organs such as the heart, liver, and kidney,” Zhuo said.

Provided by University of Toronto