Scientist Unraveling Mystery of Treating Chronic Pain

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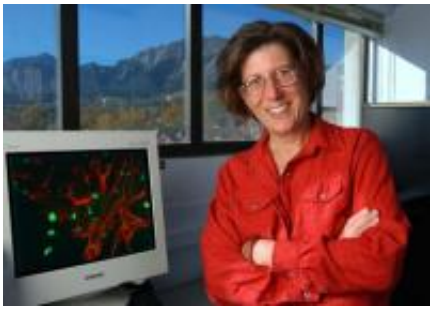

Linda Watkins

(PhysOrg.com) -- Successfully treating chronic pain with opioids such as morphine -- minus the side effects -- may soon become a reality, bringing relief to millions of people who suffer from debilitating pain, according to Distinguished Professor Linda Watkins of the University of Colorado at Boulder.

Watkins and her colleagues in CU-Boulder's psychology and chemistry and biochemistry departments are working to develop new drugs that enhance the ability of opioid drugs to treat pain, while decreasing their negative side effects such as tolerance, dependence and addiction. They are collaborating with researchers at the University of Adelaide in Australia and the National Institute on Drug Abuse in Bethesda, Md.

Recent work by Watkins, a neuroscientist, and others has shown that

glial cells in the central nervous system act as key players in pain enhancement by exciting neurons that transmit pain signals. They also found that glial cells hinder the ability of opioids to suppress pain.

Now they believe they have figured out how morphine affects glial cells and neurons. "We've found that different receptors are involved in how morphine suppresses pain through its actions on neurons versus how morphine activates glial cells," Watkins said. "What this means is that you should be able to separate the suppressive effects of morphine -- its pain-reducing effects through its action on neurons -- from all of its bad effects when it excites glial cells."

A paper on the topic was published online in August in the journal *Brain, Behavior and Immunity*.

Under normal circumstances glial cells are thought to be like housekeepers, said Watkins. They essentially clean up debris and provide support for neurons.

"What's become evident is that glial cells have a Dr. Jekyll and Mr. Hyde personality," Watkins said. "Under normal circumstances they do all these really good things for the neurons, but when they shift into the Mr. Hyde formation they release a whole host of chemicals that cause problems like neuropathic pain and other chronic pain conditions."

The challenge was to figure out how to let morphine do its work on the neurons, without alerting the glial cells, which are known to suppress morphine's ability to kill pain, she said.

To keep the glial cells quiet, the team used a type of drug called naloxone to turn off what is called a toll-like receptor, which is found only on glial cells and not on neurons. Doing this blocks morphine's effects on glia but not on neurons, resulting in effective pain relief

without addiction and other side effects.

The team found a particular receptor, called TLR4, not only is important in driving pain but also detects all clinically relevant classes of opioids.

"So if you block this receptor, this should not only block chronic pain, but also make opioids work much better by suppressing pain, while avoiding the bad actions of glial cell activation," Watkins said.

Millions of Americans suffer from chronic pain, a debilitating condition that makes it extremely painful to do anything from taking a shower to putting on a shirt. Chronic pain is different from pain associated with an injury such as a broken bone, which goes away when the injury heals. Cancer and AIDS patients and others with nerve damage suffer from chronic pain, even though no bodily source of the pain can be identified.

Provided by University of Colorado