3 proteins may play important role in nerve-cell repair

April 11 2007

Some mature brain cells can grow new extensions when the amount of three particular proteins on their surface increases, a new study shows.

The research examined three related receptor proteins, called GPR3, GPR6 and GPR12, on nerve cells in the brains of rats.

When researchers increased the amount of the three proteins, the cells grew extensions that were up to three times longer than those on nerve cells with normal levels of the proteins, and the extensions grew four to eight times faster than in control cells.

"Our findings suggest that these three proteins could be important targets for treating stroke, brain and spinal cord injuries and also neurodegenerative diseases," says principal investigator Yoshinaga Saeki of the Ohio State University Medical Center.

The study is published in the April 6 issue of the *Journal of Biological Chemistry*.

Increased amounts of the proteins were associated with a significant rise in the level of an important signaling molecule inside the nerve cells called cAMP. This molecule plays a key role in regulating nerve-cell growth, differentiation and survival, and the regeneration of long parts of the cell called axons that carry the nerve impulses.

Levels of cAMP drop in mammalian nerve cells as they mature, and this

is thought to explain, in part, why mature nerve cells cannot regenerate damaged axons.

"Our findings provide additional evidence that cAMP plays an important role in axon growth and suggest that these receptors are likely to play a major role in regulating cAMP production in nerve cells," says Saeki, an associate professor of neurological surgery and chief of Ohio State's Dardinger Laboratory for Neuro-oncology and Neurosciences.

In this study, first author Shigeru Tanaka, a postdoctoral fellow in Saeki's laboratory, and his colleagues used nerve cells obtained from the brain tissue of rats and mouse neuroblastoma cells growing in culture to learn more about the three proteins and their involvement in cAMP regulation.

The researchers added additional copies of the three genes to the cells to increase the levels of the proteins, and then used a laboratory technique called RNA intereference to turn off production of the proteins.

Of the three molecules, GPR3 was the most abundant in the nerve cells, while GPR12 was the most potent at stimulating growth of the nerve extensions. The study showed that blocking GPR3 greatly slows the growth of the nerve extensions. The researchers reversed this effect by restoring either GPR3 or GPR12 in the cells.

High levels of the three proteins were also linked to higher levels of cAMP, with GPR6 and GPR12 increasing the level twofold to threefold.

"Taken together," Saeki says, "our findings indicate that these three proteins improve growth of neuronal extensions even in the presence of inhibitory molecules, and we are very keen to find out whether the approach can be translated in preclinical animal models of stroke or spinal cord injury."

Source: Ohio State University