Naturally produced protein could boost brain repair

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(Medical Xpress) -- Scientists from the Medical Research Council (MRC) have discovered that a protein produced by blood vessels in the brain could be used to help the brain repair itself after injury or disease.

The protein, called Betacellulin (BTC), was found to boost brain regeneration in mice by stimulating the organ's stem cells to multiply and form new nerve cells. The findings, published in the journal *PNAS*, suggest that BTC could enhance future regenerative therapies for conditions such as stroke, traumatic brain injury and dementia.

Although most nerve cells (neurons) in the adult brain are formed in the womb and soon after birth, new neurons continue to be generated throughout life by stem cells. These neural stem cells are housed in two small 'niches' of the brain and supply new neurons to the olfactory bulb, responsible for our sense of smell, and the hippocampus, which is involved in forming memories and learning.

The niches produce a range of signals that control how fast the stem cells divide and the type of cell they become. Stem cells in these areas normally produce neurons, but in response to a brain injury such as stroke they tend to produce more so-called glial cells, leading to the formation of scar tissue.

Dr Robin Lovell-Badge from the MRC's National Institute for Medical Research (NIMR), who led the research, said:

“The stem cell niches in the brain are not fully understood, but it appears that many factors act in concert to control the fate of the stem cells. We believe these factors are finely balanced to control precisely the numbers of new neurons that are made to match demand in a variety of normal circumstances.

“But in trauma or disease, the stem cells either can’t cope with the increased demand, or they prioritise damage control at the expense of long-term repair. We hope that our new findings can add to the arsenal of exciting approaches coming out of stem cell biology that might eventually lead to better treatments for damaged brains.”

The researchers studied the effects of BTC, which is produced by cells in the blood vessels within the stem cell niches, on the rate of neuron formation in mice. They found that BTC signals to both the stem cells and to dividing cells called neuroblasts, triggering their proliferation.

When extra Betacellulin was given to the mice, there was a significant increase in both stem cells and neuroblasts in their brains, leading to the formation of many new neurons. In contrast, when mice were given an antibody that blocks BTC activity the production of new neurons was suppressed.

As BTC leads to the production of new neurons, rather than glial cells, this protein could improve the effectiveness of regenerative medicine treatments aimed at repairing damage to the brain.

Professor Jim Smith, Director of the NIMR, said:

“Regenerative medicine has the potential to unlock new treatments for many human diseases that currently have no effective cures. This study is an important step towards our goal of moving beyond the replacement of tissues and organs to the exploitation of the intrinsic repair and

regenerative potential of the human body."

This work is still far from the clinic as further experiments are needed to explain the normal role of BTC in the brain and to explore in animals the effects of BTC on damaged brains alone, or together with transplanted neural stem cells.

More information: The research, "Betacellulin promotes cell proliferation in the neural stem cell niche and stimulates neurogenesis" by Maria-Victoria Gomez-Gaviro et al, is published in the *Proceedings of the National Academy of Sciences*.

Provided by Medical Research Council