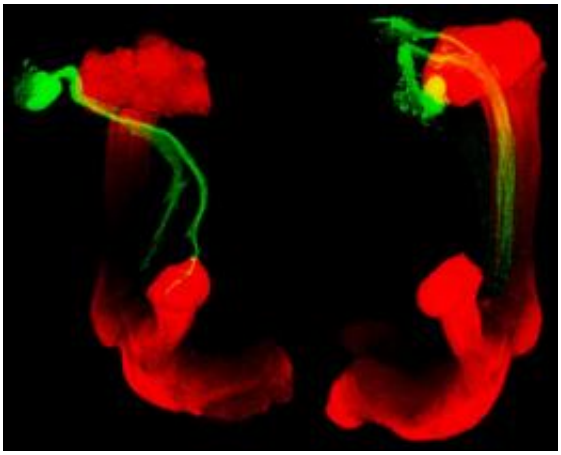
Insulin-like signal needed to keep stem cells alive in adult brain

March 25 2010, By Robert Sanders



Mushroom bodies (red), which are the center of learning and memory in the brain, from two adult fruit flies. Normally, new neurons do not appear in the adult mushroom body. UC Berkeley biologists altered neural stem cells to allow them to persist for at least a month in the adult brain, and to give rise to newborn nerve cells (green) that send out axons to other areas of the mushroom body, just like normal neurons. (Sarah Siegrist/UC Berkeley)

(PhysOrg.com) -- University of California, Berkeley, biologists have found a signal that keeps stem cells alive in the adult brain, providing a focus for scientists looking for ways to re-grow or re-seed stem cells in the brain to allow injured areas to repair themselves.

The researchers discovered in fruit flies that keeping the insulin receptor revved up in the brain prevents the die-off of neural stem cells that

occurs when most regions of the brain mature into their adult forms. Whether the same technique will work in humans is unknown, but the UC Berkeley team hopes to find out.

"This work doesn't point the way to taking an adult who has already lost stem cells and bringing them back mysteriously, but it suggests what mechanisms might be operating to get rid of them in the first place," said Iswar K. Hariharan, UC Berkeley professor of molecular and cell biology. "Plus, if you were able to introduce neural stem cells into an adult brain, this suggests what kinds of mechanisms you might need to have in place to keep them alive."

Hariharan noted that other researchers have gotten neural stem cells to persist by blocking genes that cause them to die. Yet this alone does not produce healthy, normal-looking neural stem cells that can make mature neurons. The UC Berkeley team's new finding shows that it also is necessary to provide an insulin-like signal. If stopping neural stem cell death is analogous to taking your foot off the brake, then providing an insulin-like signal is like stepping on the gas, he said. Both are essential.

Hariharan, post-doctoral researcher Sarah E. Siegrist and their colleagues published their findings today (Thursday, March 25) in the online version of the journal Current Biology. Their report will appear in the journal's April 13 print edition.

Most areas of the adult mammalian brain and fruit fly brain are devoid of neural stem cells, the only cells able to generate full-fledged neurons. Presumably, Hariharan said, the lack of neural stem cells is why the injured brain is unable to replace dead neurons.

In the new study, Siegrist showed that the stem cells present in the pupal stage of fruit flies are gone in the adult brain because they die off, rather than merely mature into neurons. The stem cells that persisted the longest were in the mushroom body, a region of the fly brain responsible

for memory and learning that, in some ways, is like the hippocampus in humans.

In subsequent experiments, she attempted to prevent the death of neural stem cells in fruit flies by genetically blocking a process called programmed cell death (apoptosis). While this allowed the stem cells to survive longer, the cells were small and did not make many neurons. In fact, Siegrist said, they showed signs of impaired growth, suggestive of insulin withdrawal.

She then tried various genetic manipulations to mimic an insulin-type signal, this time using mutant fruit flies with their apoptosis genes also blocked. Amazingly, the neural stem cells persisted for at least a month and even generated many mature, apparently normal, nerve cells.

"These neural stem cells seem to behave properly, they express the proteins that you expect neural stem cells to express, they look like their normal counterparts, and most importantly, they spin off cells which become normal mature nerve cells that put out processes (axons) that, in some cases, seem to go where normal processes go," Siegrist said. "We don't know whether these cells function normally or whether they are electrically active. At least it is encouraging that we can get nerve cells made in a part of the (fruit fly) brain that normally cannot make nerve cells in the adult brain."

"Sarah had to do two manipulations together to keep these neural stem cells alive, and neither worked alone," Hariharan said. "One was to keep the insulin signal on, and one was to block programmed cell death. Each improved things a little bit, but when you did the two together, the neural stem cells survived for a month, at which time they were throwing off mature neurons or normal looking neurons that sent out processes."

Siegrist plans to continue her search through mutant fruit flies to find

other genes that improve survival in the mushroom body and allow stem cells in other areas of the fly brain to persist. She also plans collaborations to explore similar mechanisms in mammals, to see if analogous manipulations could keep neural stem cells alive in the mammalian brain.

"In fruit flies, pathways downstream of the insulin receptor are important in keeping these neural stem cells alive," Siegrist said. "Mammals have the same genes downstream of their insulin receptors, so we may find the same response to insulin or insulin-like growth factors in mammals."

Provided by University of California - Berkeley

Citation: Insulin-like signal needed to keep stem cells alive in adult brain (2010, March 25) retrieved 3 May 2024 from https://phys.org/news/2010-03-insulin-like-stem-cells-alive-adult.html