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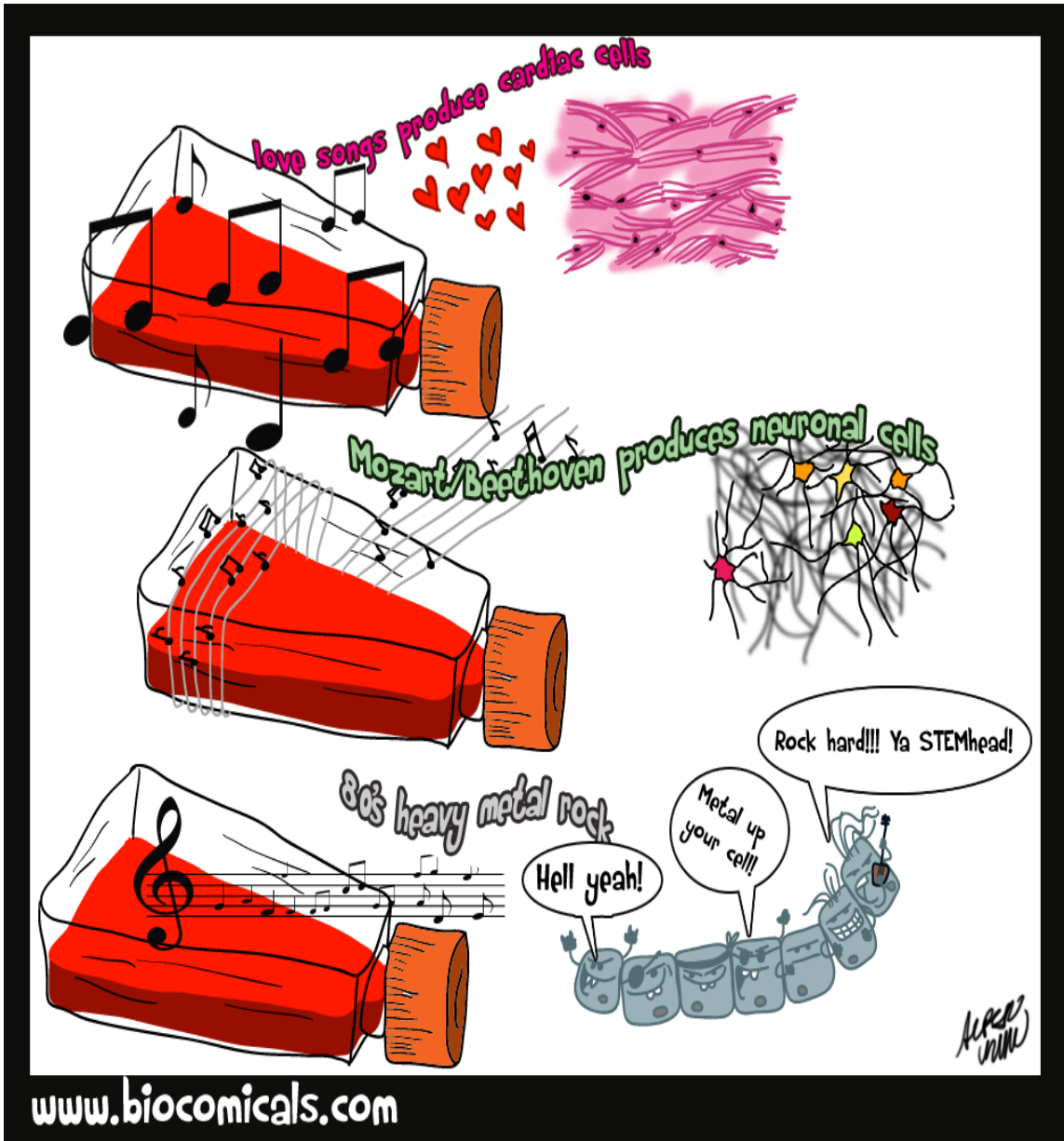
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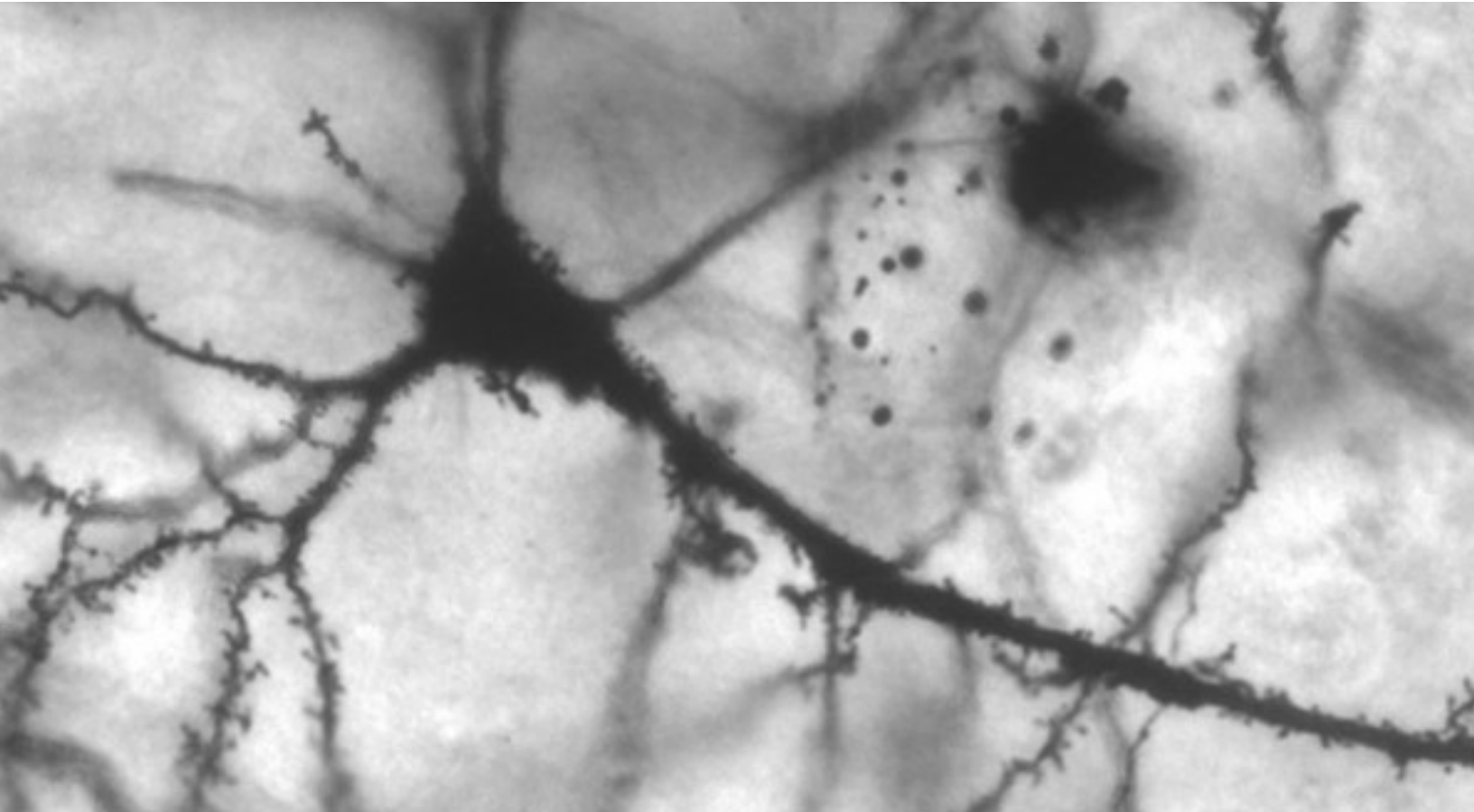
STEM CELLS: SCIENCE AND SOCIETY





# THE BRAIN'S FOUNTAIN OF YOUTH

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*Methoxy Roxy/Wikimedia Commons*

**New neurons.** Cells are constantly being added to the adult brain, and new research shows that factors in the blood can speed up or slow down how many new cells develop.

Dracula may have had it right: Young blood can restore an aging body. Scientists have discovered that blood from a 3-month-old mouse can coax the brain of an older mouse into making new brain cells. The team has not yet identified the rejuvenating factor, but they have found a blood-borne compound that seems to promote brain aging.

As the body ages, the brain gradually becomes more sluggish. Even in people lucky enough to dodge neurodegenerative disorders such as Alzheimer's disease, fewer new neurons are created from stem cells in the brain, and the activity of existing neurons weakens. Neuroscientist Tony Wyss-Coray of Stanford University School of Medicine in Palo Alto, California, suspected that the changes could be mediated by factors in the blood.

Previous research has shown that giving young blood to older mice boosts their immune system and muscle function. Wyss-Coray wondered whether the same might be true in the brain. Although the so-called blood-brain barrier blocks many large molecules from entering the brain from the bloodstream, the

barrier isn't sealed tight everywhere, which might allow some compounds to get through. It's leakiest at places where there are brain stem cells, suggesting that these neuron precursors may have interaction with the circulatory system.

Wyss-Coray's team measured neurogenesis, the creation of new neurons from stem cells, in mice that were 3 months old and mice that were almost 2 years old and considered adults. Then they surgically connected the circulatory systems of pairs of young and old mice. The number of new cells in one region of the brain's hippocampus, related to memory formation, went from fewer than 400 to almost 1000 in the older mice. In the younger mice, it dropped by almost a quarter, the scientists report today in *Nature*. "It worked in both directions," says Wyss-Coray. "The age of the blood has a special effect on the brain."

When the researchers gave young mice daily injections of older blood, not only did neurogenesis decrease, but their learning and memory scores in a water maze test got worse. They made more than twice the number of mistakes in the maze after a day of training and a day of testing.

To isolate the compound responsible for these changes, Wyss-Coray and his colleagues focused on 66 blood-borne chemicals. They identified 17 that increased in concentration as a mouse aged. One of them, a protein called CCL11, was enough to slow neurogenesis when injected into the bloodstream on its own. The researchers haven't yet found a compound that does the reverse—turning up neurogenesis. But finding more neurogenesis in old mice given young blood suggests that it exists.

The findings offer a proof of principle that neurogenesis can be controlled through the blood, a paradigm-shifting idea for treating neurodegenerative disease, Wyss-Coray says. "The big implication here is that we can potentially affect brain aging and degradation, even dementia, by targeting factors in the periphery rather than having to target the brain directly."

Richard Ransohoff, a neuroscientist at the Cleveland Clinic in Ohio, says the new study is a leap toward understanding how neurogenesis is controlled in the adult brain. "I think it's very exciting to know that the aging stem cell population can remain responsive to environmental cues." But more work is needed to fully understand how all the cues work, he says, and whether the findings hold true in people.

"One of the next steps is to take these factors and measure them in aging humans," Ransohoff says. "You might take patients with neurodegenerative diseases and see how the factors are different, or follow how they change over time in people with early cases of disease."

Wyss-Coray plans to start out by analyzing more blood-borne factors in mice. His team is planning a screen of hundreds more factors to see what else may be controlling the aging of the brain.

*"The Brain's Fountain of Youth - ScienceNOW." Science/AAAS | News - Up to the Minute News and Features from Science. American Association for the Advancement of Science, 31 Aug. 2011. Web. 05 Sept. 2011. <<http://news.sciencemag.org/sciencenow/2011/08/the-brains-fountain-of-youth.html>>*

# MOUSE STUDY: NEURON GROWTH IN ADULT BRAIN BUFFERS STRESS

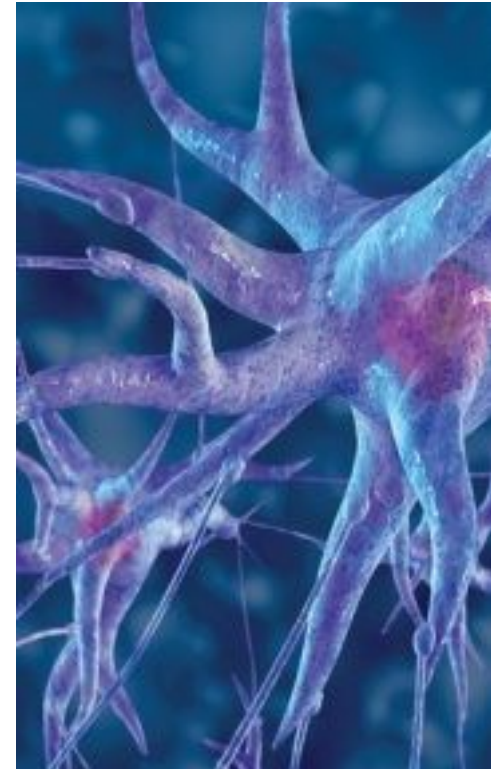
By **TRACI PEDERSEN** *Associate News Editor*

*Reviewed by John M. Grohol, Psy.D. on August 21, 2011*

Stem cells have the remarkable potential to develop into many different cell types in the body during early life and growth. In addition, in many tissues they serve as a sort of internal repair system, dividing essentially without limit to replenish other cells as long as the person or animal is still alive. When a stem cell divides, each new cell has the potential either to remain a stem cell or become another type of cell with a more specialized function, such as a muscle cell, a red blood cell, or a brain cell.

Stem cells are distinguished from other cell types by two important characteristics. First, they are unspecialized cells capable of renewing themselves through cell division, sometimes after long periods of inactivity. Second, under certain physiologic or experimental conditions, they can be induced to become tissue- or organ-specific cells with special functions. In some organs, such as the gut and bone marrow, stem cells regularly divide to repair and replace worn out or damaged tissues. In other organs, however, such as the pancreas and the heart, stem cells only divide under special conditions.

Until recently, scientists primarily worked with two kinds of stem cells from animals and humans: embryonic stem cells and non-embryonic "somatic" or "adult" stem cells. The functions and characteristics of these cells will be explained in this document. Scientists discovered ways to derive embryonic stem cells from early mouse embryos nearly 30 years ago, in 1981. The detailed study of the biology of mouse stem cells led to the discovery, in 1998, of a method to derive stem cells from human embryos and grow the cells in the laboratory. These cells are called human embryonic stem cells. The embryos used in these studies were created for reproductive purposes through in vitro fertilization procedures. When they were no longer needed for that purpose, they were donated for research with the informed consent of the donor. In 2006, researchers made another breakthrough by identifying conditions that would allow some specialized adult cells to be "reprogrammed" genetically to assume a stem cell-like state. This new type of stem cell, called induced pluripotent stem cells (iPSCs), will be discussed in a later section of this document.



In another standard test of depression-like behavior, food was placed in an open, exposed space, and scientists observed whether the mice would venture out to get some food.

Mice that had not undergone any stress responded similarly regardless of whether neurogenesis was intact. However, mice whose neurogenesis had been impaired and had also undergone the stress of being restrained took longer to eat, choosing safety over food. These and other tests suggested that the presence or absence of neurogenesis affected how the mice reacted to stress, regarding both hormonal responses as well as behavior.

Stress is a strong risk factor for depression, but certain individuals seem particularly susceptible to stress while others seem more resilient. This work suggests that adult neurogenesis helps an individual better handle stress. Therefore, stress itself may trigger a cycle that spirals into a declining ability to effectively handle more stress, possibly leading to depression.

Understanding how adult neurogenesis affects the development of depression—and how it works in the actions of antidepressant drugs—can help with the prevention and treatment of depression.

The findings are published in the journal *Nature*.

**Source:** NIMH

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*Pedersen, T. (2011). Mouse Study: Neuron Growth in Adult Brain Buffers Stress. Psych Central. Retrieved on September 21, 2011, from <http://psychcentral.com/news/2011/08/21/mouse-study-neuron-growth-inadultbrain-buffers-stress/28798.html>*