Young Blood May Hold Key to Reversing Aging

Two teams of scientists published studies on Sunday showing that blood from young mice reverses aging in old mice, rejuvenating their muscles and brains. As ghoulish as the research may sound, experts said that it could lead to treatments for disorders like Alzheimer's disease and heart disease.

"I am extremely excited," said Rudolph Tanzi, a professor of neurology at Harvard Medical School, who was not involved in the research. "These findings could be a game changer."

The research builds on centuries of speculation that the blood of young people contains substances that might rejuvenate older adults.

In the 1950s, Clive M. McCay of Cornell University and his colleagues tested the notion by delivering the blood of young rats into old ones. To do so, they joined rats in pairs by stitching together the skin on their flanks. After this procedure, called parabiosis, blood vessels grew and joined the rats' circulatory systems. The blood from the young rat flowed into the old one, and vice versa.

Later, Dr. McCay and his colleagues performed necropsies and found that the cartilage of the old rats looked more youthful than it would have otherwise. But the scientists could not say how the transformations happened. There was not enough known at the time about how the body rejuvenates itself.

It later became clear that stem cells are essential for keeping tissues vital. When tissues are damaged, stem cells move in and produce new cells to replace the dying ones. As people get older, their stem cells gradually falter.

In the early 2000s, scientists realized that stem cells were not dying off in aging tissues.

"There were plenty of stem cells there," recalled Thomas A. Rando, a professor of

neurology at Stanford University School of Medicine. “They just don’t get the right signals.”

Dr. Rando and his colleagues wondered what signals the old stem cells would receive if they were bathed in young blood. To find out, they revived Dr. McCay’s experiments.

The scientists joined old and young mice for five weeks and then examined them. The muscles of the old mice had healed about as quickly as those of the young mice, the scientists reported in 2005. In addition, the old mice had grown new liver cells at a youthful rate.

The young mice, on the other hand, had effectively grown prematurely old. Their muscles had healed more slowly, and their stem cells had not turned into new cells as quickly as they had before the procedure.

The experiment indicated that there were compounds in the blood of the young mice that could awaken old stem cells and rejuvenate aging tissue. Likewise, the blood of the old mice had compounds that dampened the resilience of the young mice.

Amy J. Wagers, a member of Dr. Rando’s team, continued to study the blood of young mice after she moved in 2004 to Harvard, where she is an associate professor. Last year, she and her colleagues demonstrated that it could rejuvenate the hearts of old mice.

To pinpoint the molecules responsible for the change, Dr. Wagers and her colleagues screened the animals’ blood and found that a protein called GDF11 was abundant in young mice and scarce in old ones. To see if GDF11 was crucial to the parabiosis effect, the scientists produced a supply of the protein and injected it into old mice. Even on its own, GDF11 rejuvenated their hearts.

Dr. Wagers and her colleagues wondered whether GDF11 was responsible for the rejuvenation of other tissues. In the current issue of the journal Science, they

report an experiment on skeletal muscle in mice. They found that GDF11 revived stem cells in old muscles, making old mice stronger and increasing their endurance.

At Stanford, researchers were investigating whether the blood of young mice altered the brains of old mice. In 2011, Saul Villeda, then a graduate student, and his colleagues reported that it did. When old mice received young blood, they had a burst of new neurons in the hippocampus, a region of the brain that is crucial for forming memories.

In a study published Sunday in the journal Nature Medicine, Dr. Villeda, now a faculty fellow at the University of California, San Francisco, and his colleagues unveiled more details of what young blood does to the brains of old mice.

After parabiosis, Dr. Villeda and his colleagues found that the neurons in the hippocampus of the old mice sprouted new connections. They then moved beyond parabiosis by removing the cells and platelets from the blood of young mice and injecting the plasma that remained into old mice. That injection caused the old mice to perform far better on memory tests.

Dr. Wagers's team has been investigating a specific region of the brain involved in perceiving smells.

In a second study in Science, the team reported that parabiosis spurred the growth of blood vessels in the brain. The new blood supply led to the growth of neurons and gave older mice a sharper sense of smell.

After linking the GDF11 protein to the rejuvenation of skeletal muscle and the heart, Dr. Wagers and her colleagues studied whether the protein was also responsible for the changes in the brain. They injected GDF11 alone into the mice and found that it spurred the growth of blood vessels and neurons in the brain, although the change was not as large as that from parabiosis.

"There's no conflict between the two groups, which is heartening," said Dr.

Richard M. Ransohoff, director of the Neuroinflammation Research Center at the Cleveland Clinic.

Dr. Ransohoff and others hope the experiments on mice will lead to studies on people to see if the human version of GDF11, or other molecules in the blood of young people, has a similar effect on older adults.

“We can turn back the clock instead of slowing the clock down,” said Dr. Toren Finkel, director of the Center for Molecular Medicine at the National Heart, Lung and Blood Institute. “That’s a nice thought if it pans out.”

This reversal could occur throughout the body, the new research suggests. “Instead of taking a drug for your heart and a drug for your muscles and a drug for your brain, maybe you could come up with something that affected them all,” Dr. Wagers said.

But scientists would need to take care in rejuvenating old body parts. Waking up stem cells might lead to their multiplying uncontrollably.

“It is quite possible that it will dramatically increase the incidence of cancer,” said Irina M. Conboy, a professor of bioengineering at the University of California, Berkeley. “You have to be careful about overselling it.”