

## **"Special primates pave way to cures for aging, surging Boomer generation"**

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What's the nation to do about its 78 million baby boomers who are living longer than preceding generations, but suffering from age-related illness in the process?

The short answer: stem-cell science and marmoset monkeys.

Ranked No. 1 on Time magazine's Top 10 Scientific Discoveries for 2007 (just ahead of human genome mapping), stem-cell science took off like a rocket in November when Japanese and American researchers independently rebuilt skin cells to resemble embryonic stem cells without the use of embryos.

This latest development of induced pluripotent stem cells, or iPSCs for short, is unprecedented.

The phenomenon has spread to San Antonio. At the University of Texas Health Science Center's Sam and Ann Barshop Institute for Longevity and Aging Studies, Drs. Suzette Tardif, associate professor of the Department of Cellular and Structural Biology; Steven Austad, professor of the Department of Cellular and Structural Biology; and Arlan Richardson, director and senior research scientist of the Barshop, are developing a colony of marmoset monkeys in part to assist in aging research aimed at reprogrammed stem cells.

The monkey population is planned to mirror American society in which the oldest animals outnumber the youngest. Keeping the primates pathogen-free is critical, Tardif says. "These animals offer unique opportunities to show whether pathogen-free cells from older primates can be reprogrammed and used to treat degenerative diseases in both younger and aging ones. The goal is to help people get to old age without disease."

Abetting the three, Dr. Peter Hornsby, professor of the Department of Physiology at the Barshop, is growing marmoset skin cells in his lab and studying how to reprogram them to iPSCs. He plans to transplant the stem cells into a special breed of lab mice that have no immune system to see whether the cells function as intended. Minus immunities, the mice will not reject the implanted cells.

If tests with the mice prove successful, Hornsby will move on to the marmosets. "The great thing about the marmosets is that we will be able to take skin cells from one individual marmoset, reprogram them and then transplant them back into the same individual. As primates, marmosets are the ideal pre-clinical model for personalized

medicine for humans," he says.

In each successive phase of the research, the steps are basically the same for the mice, the marmosets and eventually, the human subjects.

"It is for people we're developing these therapies of 'personalized medicine,'" Hornsby says. "Say you want to develop cells to repair a heart muscle damaged by heart attack. We first work with mice as test organisms. If it works safely in mice, we move on to primates, knowing all along the idea is eventually to translate our successful research to human patients."

Researchers hope personalizing patients' medical care using their own cells will ease suffering and increase success with organ transplants and diseases of the heart, nerves or brain, for example, and lead to a better quality of longer life.

Making medicine personal at the cellular level is expected to reduce or perhaps eliminate the immune system's rejection of implants, thereby also eliminating the need for lifelong medication now typically prescribed to patients to counteract rejection.

At the Barshop, marmoset monkeys play the star role in stem cell research for good reason.

As primates, marmosets are among the species that most closely resemble humans in physiological makeup and cellular behavior. Never mind that they typically weigh less than a pound and have tails the length of their 9-inch-long bodies. At the cellular level, they're a lot like people and are thus, ideal subjects.

In fact, marmosets and humans share many characteristics. Both have large brains compared to the size of their bodies. Both are diurnal, meaning they are awake during the day and asleep at night, and both share the same sleeping patterns.

In addition, marmoset monkeys' reproductive processes are identical to humans, and the females are sensitive mothers. Both humans and marmosets are flexible in behavior. "Their similarities make marmosets of great interest particularly to our studies related to human memory or cognition," adds Tardif.

"Stem cell therapy will be particularly important to the field of aging because major age-related diseases affect tissues like the brain or heart, which are unable to replace cells that die," Richardson says. "Stem cell therapy gives us a potential tool to replace dead cells."

Tardif's and Hornsby's studies will focus initially on therapies for Parkinson's disease. "Parkinson's is a defect in one small piece of the brain where cells die," Hornsby explains. "If we could implant the right kind of cells into the dead area, then we could restore that piece of the brain."

Diseases such as Alzheimer's and other forms of dementia are likely targets for stem cell study in the future, but pose special problems, Hornsby notes. "Rather than cells dying in one particular piece of the brain, as with Parkinson's, they die all over the place, which makes it significantly more difficult to target. The memory also is involved, so more functions of cells are involved, and that makes it more complicated as well."

The discovery of reprogrammable cells is revolutionary, but also preliminary. Scientists at the Barshop speculate this first round of research may eventually lead to cures for age-related illness and help reduce suffering associated with aging. But it does not point toward a fountain of youth.

"Stem cell therapy will not change the aging process," Hornsby asserts. "A sci-fi view would be that you'd have to replace every stem cell with new stem cells in order to stop aging. Currently there is no way to do that, and why would anyone want to live forever? Right now, we have people dying of real diseases. Today, this is where we are focused."

Healthier lifestyles and advances in preventative medicine notwithstanding, millions of older people are pouring into healthcare systems with age-related ailments, and more are sure to come. Meanwhile, a significantly smaller and unsuspecting society of younger adults will soon face a day when they will have to cope and care for a disproportionate number of elders who are living longer than ever before in the history of humankind.

At least for today, great hope appears to stem from marmoset monkeys and the science of regenerative medicine under study at the Barshop.

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