MedicalXpress

Dallas doctor finds the root of balding and graying hair and is working on treatment

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When the mice went gray and bald, the doctor knew he was onto something.

For more than 10 years, Dr. Lu Le had studied cells and genes, hoping to understand the roots of cancer and further the search for a cure.

Instead, in his lab at UT Southwestern Medical Center, he discovered something unexpected - a chemical and biological process that could explain gray hair and bald heads in people.

Science often works this way. A search in one direction leads to an entirely different discovery in another. For Le, baldness and graying weren't concerns of his research. And yet, there they were, gray and bald mice inside his lab.

"We accidentally, serendipitously, discovered the cell that directly gives rise to hair. That was new," said Le, associate professor in the department of dermatology with the Harold C. Simmons Comprehensive Cancer Center.

Now Le, who at 46 has a few flecks of gray in a full head of black hair, is hoping to create a topical compound or other remedy that could turn back the clock on thinning and graying hair.

"That's within the realm of possibility," Le said, "and we're working in the lab to do that for that next step."

There are no guarantees; any remedy is likely to take years of careful lab work.

ACCIDENTAL DISCOVERY

Le's research had focused on how cancer begins - in particular with tumors that grow on nerves in a disorder called neurofibromatosis. He and his team would remove different proteins in the tumors to better understand how they formed.

That's when Le discovered the role a protein called KROX20 plays not just in nerve development but in hair color and growth.

The KROX20 protein turns on in skin cells that develop into shafts of hair. These cells then produce a protein called stem cell factor (SCF) that is essential for hair color. When that SCF protein was deleted from mice in KROX20 cells, their hair turned gray and then white. And when the scientists deleted the KROX20 cells, the mice turned bald.

"The mice turned gray and then completely white. That was unexpected," Le said.

But science requires results to be repeated. And that's what Le has been doing since he made his discovery about two years ago.

"The first thing we do in science is to repeat it, to make sure it's true," Le said. "Every single time, consistently, we got the same result. You rarely have a piece of data where it repeats every single time."

RESULTS WENT VIRAL

The results were published in May in Genes & Development, a peer-reviewed scientific journal. The story immediately attracted tens of

thousands of page views and readers on the journal's website and was picked up by news sites around the world.

"I can tell you that it was amazingly well-read in a short period of time," said Terri Grodzicker, editor of Genes & Development.

Fellow scientists also commended the work of Le's team.

"This is an exciting and novel development of great significance," said Dr. Luis Garza, an associate professor of dermatology at Johns Hopkins School of Medicine.

Such unexpected discoveries aren't entirely by accident, Garza said, quoting Louis Pasteur's famous saying: "Chance favors the prepared mind."

It is not simply chance, Garza said, "but careful, observant scientists who made this work a success."

VIETNAM REFUGEE

For Le, the discovery is the pinnacle of an unlikely career, one that might never have happened for a man who came to America as a teenage refugee.

Le was born in 1971 in Vietnam, near My Lai, three years after the notorious massacre of hundreds of civilians in that village by U.S. troops.

Le's father had worked on America's side during the war. When it was over, Le had little choice but to leave his homeland.

"There was no future for us at that time after the war, when North

Vietnam took over the South," Le said. "Our only option was farming."

He decided to escape, setting out as a teenager on a dangerous ocean journey on a tiny fishing boat propelled by a motorcycle engine.

"I didn't know how to swim. I could have died," he said.

Instead, he made it to a refugee camp in Thailand, then to the Philippines and finally to the home of relatives living in Long Beach, Calif.

Le credits the work ethic he learned at a young age to his success in science. He attended high school from 8 a.m. to 3 p.m. and then worked at McDonald's from 5 p.m. to midnight. With no buses running that late, he had to run home about five miles through dangerous neighborhoods.

It's an experience he recently repeated with his three young children. "I made them walk from that McDonald's to where I used to live - although not in the middle of the night," he said. " I hope they learned something. It's a life lesson."

In Long Beach, McDonnell Douglas (now part of Boeing) had plants that built aircraft, and Le became interested in aerospace engineering. But at UCLA, he got a job in a research lab and fell in love with the work.

In addition to being a scientist specializing in tumor development in the nervous system, Le also has a medical degree and is a board-certified dermatologist. That made him well-qualified to grasp the significance of what was happening when his lab mice turned bald and gray.

Scientists already knew that stem cells contained in a bulge area of hair follicles were involved in making hair and that SCF was important for hair color, said Dr. Le.

What they learned was what happens after those stem cells moved down to the base, or bulb, of hair follicles. They discovered how the KROX20 protein switches on in cells that develop into a hair shaft and produce SCF protein required for hair color.

INSIGHTS INTO AGING

Because graying and thinning hair are predictable signs of growing old that ultimately affect all humans, the study provides insights on aging in general, Le said.

Throughout history, the quest to understand what causes hair loss and why hair turns gray "has been a topic of considerable interest," Le said. "We all want that youthfulness," he said.

Le and his team will now try to determine if what he found applies to humans. That is, they will try to determine if the KROX20 cells and the SCF protein diminish as people age, leading to graying and hair thinning as well as male pattern baldness.

MILLION-DOLLAR QUESTION

The million-dollar question - whether baldness and loss of hair color is reversible - is a long way from being answered. However, with the new discovery of the hair shaft producing cells, it is possible, Le said.

Le's working theory is to see if he can restimulate the stem cells in the hair follicle into hair-producing cells and grow hair again.

"I think that is the biggest implication of the discovery here," he said.

He will also try to restore the color-producing protein (SCF) into these hair cells. "If we can find a way to reintroduce this SCF back, we can

have the color back," he said. "We have a lot of work to do."

Hundreds of millions, if not billions, would eagerly welcome his results. No pressure, though.