HARVARD UNIVERSITY
From the Harvard University Gazette, January 4, 2005

Researchers discover why we go gray

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Researchers now know what makes mice and, presumably, humans, turn gray. That knowledge may someday make it possible for humans to maintain their natural hair color for a lifetime.

Scientists have stumbled on the reason our hair turns gray as part of their search for new treatments for a deadly form of skin cancer. What they have learned has implications for growing old and for fighting other forms of malignancy.

People turn gray, they found, when certain adult stem cells gradually die off. The stem cells provide a continuous supply of other, pigment-producing cells that give your hair its natural color. These same types of pigment cells, called melanocytes, can become cancerous in melanoma, the lethal form of skin cancer that killed about 8,000 people in the United States alone during the past year.

"Preventing the graying of hair is not our goal," says David E. Fisher, a Harvard Medical School scientist who directs the Program in Melanoma at Dana-Farber Cancer Institute in Boston. "Our goal is to prevent or treat melanoma. We would love to identify a signal that would make melanoma cells stop growing."

Fisher and his team have done this, at least in a laboratory dish, they report in the December issue of the science journal Cancer Cell.

Working together for the past two years, the team uncovered a protein called CDK2, which the cancer cells cannot live without. Find a way to block the activity of CDK2 and melanoma cells should stop growing. That's the hope.

"Drugs that inhibit CDK2 already exist," Fisher notes. So he hopes that his team's research will quickly lead to trials of the drug with patients.

Many cancer drugs have unpleasant, even debilitating side effects, but this should be less of a problem with a CDK2 inhibitor. Many adverse side effects come from drugs that kill healthy cells along with cancer cells. But normal cells don't need this protein to survive; it's only the tumor cells that can't do without it.

"In theory, we could control the cancer with a drug that may have little toxic effect on the rest of the body," Fisher explains.

A hairy connection

Melanocytes of a different type live in hair follicles. These are stem cells that produce neither color nor cancer on their own but regularly give rise to color-making cells. These latter cells work their way to the bottom of hair follicles where they transfer pigment to growing hair, giving it hue and tint.

Melanocyte stem cells were discovered by Emi Nishimura in 2002 in Japan. Now an instructor at Harvard Medical School, she worked in the Fisher team on the gray-hair experiments. Using mice, then human hair samples, the team found that, as both aged, the number of stem cells decreased. There is a clear correlation between the loss of these cells and the loss of color. The researchers, who include Scott Granter, a Harvard pathologist, report their findings in the Dec. 24 issue of Science.

Right now, this new view of old hair isn't expected to make hair dyeing a thing of the past. But Fisher thinks there is future hope of maintaining natural hair color for a lifetime. "I have little doubt that this could eventually happen," he says. "Now that we know where to look, it should be just a matter of time until strategies are devised to control our hair color."

Drugs being tested

Meanwhile, Fisher's team is working hard on ways to deprive skin cancer cells of the CDK2 they need to live. The protein apparently is a key part in the machinery that controls the capacity of melanoma cancer cells to make more copies of themselves.

A drug or drugs that inhibit CDK2 activity may therefore shut down the frenzied overgrowth of cells that characterizes malignant melanoma, a disease believed to be caused by overexposure to ultraviolet rays from the sun.

Fisher notes that such drugs are already being tested on other types of cancer by a few pharmaceutical companies. He has notified them of his findings and expects tests with melanoma patients to begin soon. "The next step is to get CDK2 blockers into patients as quickly as possible," he says. He hopes that this can be done within months rather than years.

The American Cancer Society estimates that more than 55,000 people in

this country developed malignant melanoma in 2004 and that number will be even higher next year. If melanoma cells are not removed early enough by surgery, it can spread beyond further effective treatment.

While any drug testing goes forward, Fisher and his colleagues will continue laboratory research to learn exactly how melanocyte stem cells die as they age. Such information may be useful for many kinds of aging studies because stem cells that keep all tissues and organs going - hearts, brains, and blood - also "turn gray" with age. "So this work might help identify signals that control these other types of aging," Fisher speculates. "That's an open and intriguing possibility."

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