# Stress makes your hair go gray

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Those pesky graying hairs that tend to crop up with age really are signs of stress, reveals a new report in the June 12 issue of *Cell*.

Researchers have discovered that the kind of "genotoxic stress" that does damage to DNA depletes the melanocyte stem cells (MSCs) within hair follicles that are responsible for making those pigment-producing cells. Rather than dying off, when the going gets tough, those precious stem cells differentiate, forming fully mature melanocytes themselves.

Anything that can limit the stress might stop the graying from happening, the researchers said.

"The DNA in cells is under constant attack by exogenously- and endogenously-arising DNA-damaging agents such as mutagenic chemicals, ultraviolet light and ionizing radiation," said Emi Nishimura of Tokyo Medical and Dental University. "It is estimated that a single cell in mammals can encounter approximately 100,000 DNA damaging events per day."

Consequently, she explained, cells have elaborate ways to repair damaged DNA and prevent the lesions from being passed on to their daughter cells.

"Once stem cells are damaged irreversibly, the damaged stem cells need to be eliminated to maintain the quality of the stem cell pools," Nishimura continued. "We found that excessive genotoxic stress triggers differentiation of melanocyte stem cells." She says that differentiation

might be a more sophisticated way to get rid of those cells than stimulating their death.

Nishimura's group earlier traced the loss of hair color to the gradual dying off of the stem cells that maintain a continuous supply of new melanocytes, giving hair its youthful color. Those specialized stem cells are not only lost, they also turn into fully committed pigment cells and in the wrong place.

Now, they show in mice that irreparable DNA damage, as caused by ionizing radiation, is responsible. They further found that the "caretaker gene" known as ATM (for ataxia telangiectasia mutated) serves as a so-called stemness checkpoint, protecting against MSCs differentiation. That's why people with Ataxia-telangiectasia, an aging syndrome caused by a mutation in the ATM gene, go gray prematurely.

The findings lend support to the notion that genome instability is a significant factor underlying aging in general, the researchers said. They also support the "stem cell aging hypothesis," which proposes that DNA damage to long-lived stem cells can be a major cause for the symptoms that come with age.
In addition to the aging-associated stem cell depletion typically seen in melanocyte stem cells, qualitative and quantitative changes to other body stem cells have been reported in blood stem cells, cardiac muscle, and skeletal muscle, the researchers said. Stresses on stem cell pools and genome maintenance failures have also been implicated in the decline of tissue renewal capacity and the accelerated appearance of aging-related characteristics.

"In this study, we discovered that hair graying, the most obvious aging phenotype, can be caused by the genomic damage response through stem cell differentiation, which suggests that physiological hair graying can be triggered by the accumulation of unavoidable DNA damage and DNA-

damage response associated with aging through MSC differentiation," they wrote.

Source: Cell Press (news : web)