

U-M scientists trigger new hair growth in mice

University of Michigan graduate student David Van Mater knew something strange was going on when he noticed stubble on the shaved skin of experimental mice in his laboratory. Instead of the tumors he had originally expected to see, the mice were growing hair.

Van Mater had stumbled on the discovery that beta-catenin ("bay-tuh-kul-TEEN-in"), a signaling protein involved in embryonic development and several types of cancer, also triggers changes in adult mouse hair follicles that lead to the growth of new hair.

The discovery by Van Mater and U-M scientists Drs. Frank T. Kolig, Andrzej A. Dlugosz and Eric R. Fearon will be published in the May 15 issue of *Genes & Development*.

"Other researchers have shown that beta-catenin and other genes in the Wnt ('wint') pathway are important for normal development of hair follicles in embryos and after birth," says Dlugosz, an associate professor of dermatology in the U-M Comprehensive Cancer Center. "What's new about our study is the finding that a brief activation of beta-catenin in the resting hair follicles could be enough to trigger the complex series of changes it takes to produce a normal hair."

The original purpose of the research study was to learn how the Wnt signaling pathway and beta-catenin are involved in cancer development, according to Fearon, the Emanuel M. Maltel Professor of Oncology in

the U-M Cancer Center.

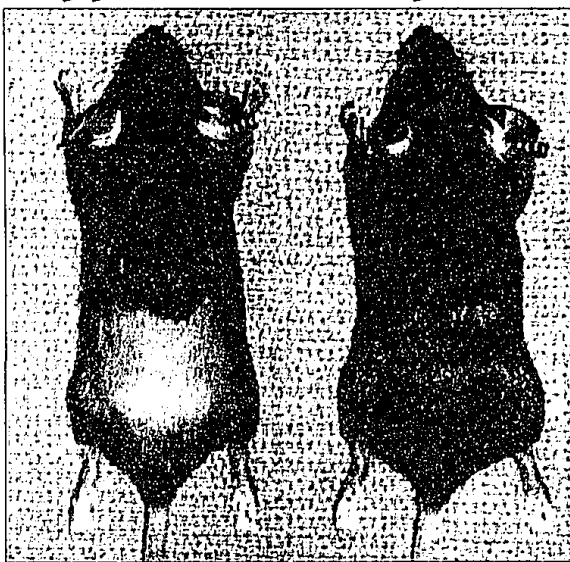
"Beta-catenin carries signals from growth factors called Wnts to the cell's nucleus," Fearon says. "If beta-catenin expression in the cell isn't adequately controlled and regulated, it changes normal patterns of gene expression. This can lead to several types of cancer, especially colon cancer."

STUDY

The study used genetically altered mice developed in the U-M Transgenic Animal Model Core. By adding a packaged set of genes called a construct to fertilized mouse eggs, U-M researchers created a new strain of transgenic mice with an inducible form of beta-catenin in their skin cells and hair follicles.

Van Mater induced beta-catenin signaling activity by applying a chemical called 4-OHT to shaved areas on the backs of the transgenic mice, and matched control mice with normal beta-catenin genes. This chemical turned on the beta-catenin in the skin and hair follicles of the transgenic mice. The plan was to use 4-OHT to turn on beta-catenin activity in the transgenic mice until skin tumors developed, and then turn off beta-catenin activity to see if the tumors disappeared.

"But we never saw tumors - just massive hyperplastic growth of hair follicle cells," Van Mater says. The scientists also noticed other skin changes that suggested an exaggerated



Mice treated with a protein grow new hair.

growth phase of the hair cycle. Dlugosz suggested applying 4-OHT just once, instead of every

day, and to do it during the hair follicles' resting phase or telogen.

"Hair follicles are like a mini-organ in the body," explains Van Mater, a graduate student in

the U-M Medical School's Medical Scientist Training Program. "Unlike most organs in the adult body, hair follicles go through regular cycles of growth, regression and rest. They are able to regenerate completely during each growth phase. Previous studies have suggested that a Wnt signal might be the switch that drives resting hair follicles into the active growth phase. By treating the transgenic mice with a single application of 4-OHT, we hoped to mimic the effect of a short pulse of Wnt expression in normal mice."

So Van Mater started over - applying 4-OHT just once to the shaved backs of transgenic mice and normal mice during the telogen phase of the hair cycle. Fifteen days later, the transgenic mice needed another shave, but there were no signs of new hair growth on the control mice.

Our findings suggest some potential strategies for inducing hair growth, but it is premature to think these results will lead to new approaches for treating common male-pattern baldness," Dlugosz cautioned. "Many hair follicles in bald and balding men are greatly reduced in size, so merely reactivating hair growth would not produce a normal hair. Also, activation of beta-catenin in the body would need to be tightly regulated, since uncontrolled beta-catenin activity can lead to tumors of hair follicle cells or tumors in other sites, such as the colon, liver or ovary."

HYPOTHYROIDISM

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said. "In pregnant women on thyroid hormone, the need increases significantly in the third month of pregnancy. Retrospective studies have been done which tested IQs of babies. Of 1,000 women, 64 were hypothyroid, and those women's infants had significantly decreased IQs."

"The main test we use (to diagnose hypothyroidism) is (a) pituitary (function) test, (which tells whether) there is or is not enough thyroid hormone there. Most endocrinologists treat hypothyroidism with one of four synthetic products containing thyroxine (T4), a hormone secreted by the thyroid," said Taylor, who doesn't treat people with low to normal thyroid levels because he believes "the tests are too sensitive."

CHOLESTEROL PROBLEMS

Contrary to popular belief, Taylor said hypothyroidism does not cause people to gain massive amounts of weight, though there may be some weight gain. In addition to the symptoms listed above, the specialist in hormone disorders also sees patients experience leg cramping without apparent cause.

Taylor adds, "If your cholesterol is elevated, you should be certain it's not thyroid-related. I have had patients whose cholesterol was over 400 to under 200 with treatment."

Dr. David Brownstein, medical director for the Center for Holistic Medicine in West

Bloomfield has authored the book, *Overcoming Thyroid Disorders*, (Medical Alternatives Press, West Bloomfield, Mich.) and calls the prevalence of hypothyroidism "staggering."

In addition to diagnostic blood tests, Brownstein also employs basal temperature readings and clinical presentation. "Relying solely on blood tests will miss 30 percent in blood tests with hypothyroidism," said Brownstein, who believes 40 percent of the U.S. population suffers from hypothyroidism, many undiagnosed.

Brownstein also believes hypothyroidism "may be implicated in two epidemic diseases, chronic fatigue immune deficiency syndrome and fibromyalgia, and he often utilizes thyroid replacement hormone for these disorders with reported success. He also said a low level of thyroid hormone may be the culprit in many cases of infertility."

Brownstein explained that the thyroid gland produces two major hormones: Thyroxine (T4) and Triiodothyronine (T3), both of which influence the "energy work" of the cells in all of the body's organs. When there are adequate amounts of these chemicals, the body functions normally, but if the levels are too low, the body's metabolism reflects this with a slower rate.

While many practitioners diagnose hypothyroidism on the basis of the TSH test (thyroid-stimulating hormone), Brownstein said it is possible for a person to have normal T4 and TSH levels while the T3 level is low.

"Many people do not ade-

quately convert T4 into T3 and thus will be hypothyroid even though the TSH test falls within the normal range."

One of Brownstein's patients with hypothyroidism is Tracy Green, who said her treatment of liver-cleansing regimen, dietary changes, and hormone replacement quickly "made a difference. Within a week, I was 70 percent better."

Green's problem was finding the right doctor; she visited eight doctors before finding Brownstein and treatment that was effective.

As a result of her experience, Green began a support group in 1999, which grew from an initial membership of seven people to over 500 members at present. Meetings usually include professional speakers, and doctors also frequently attend "figuring out what thyroid patients have been telling them for years," said Green. Linda Alvarado attends the Plymouth support group and said, "Being around people who actually understand is one of most relieving aspects of the group."

The group meets the second 2nd Monday of the month at the Plymouth Library at 6:30 p.m. Guest speakers begin at 7:00 p.m. There is no charge.

For more information about Tracy Green's thyroid disorders support group, visit mthyroid@yahoo.com

<http://www.endocrineweb.com/hypot.html>

<http://www.lib.uiowa.edu/hardin/mh/hypothyroidism.html>
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