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RESEARCH NEWS

SEPTEMBER 03, 2004

Stem Cells Renew Hope for Fading Hair Follicles

Howard Hughes Medical Institute (HHMI) researchers have isolated stem cells from the skin of mice and shown that they have the power to self-renew and differentiate into skin and functioning hair follicles when grafted onto mice. The findings mean that the human equivalent of these stem cells—which scientists are also trying to isolate—could ultimately be used to regenerate skin and hair, the researchers said.

Stem cells—isolated from embryos or from adult tissue—are immature progenitor cells with the capability to differentiate into a variety of specialized cells that form tissues and organs. Scientists are working toward using stem cells to grow mature specialized cells that could regenerate damaged or diseased skin, brain, heart or other organs. The new findings constitute another step toward understanding how to mimic the chemical signals that the cells require to differentiate into mature tissues, according to Howard Hughes Medical Institute investigator Elaine Fuchs. Fuchs and colleagues at The Rockefeller University published their findings in the September 3, 2004, issue of the journal *Cell*.

According to Fuchs, previous studies in her laboratory and others suggested that a structure called the bulge, which is located within each hair follicle, might contain stem cells. Those studies hinted that the stem cells might provide the source of both new skin and hair follicles.

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> **- Elaine Fuchs**

“However, two major questions remained,” said Fuchs. “One was whether there was a single type of multipotent stem cell within the bulge, or a bag of different kinds of stem cells—some of which could repopulate the epidermis and others that could produce hair follicles.

“The second major question was whether these cells were capable of undergoing self-renewal. And of particular interest to clinicians was whether they could undergo division in a lab dish and still have the capability to perform either epidermal repair or hair-follicle generation.”

To answer those questions, Fuchs and her colleagues first isolated stem cells from the bulge by fusing antibodies to characteristic cell surface molecules.

“An important aspect of this paper was that we found we could isolate and characterize these cells by taking advantage of the cell-surface markers that we had previously identified from molecular profiling experiments,” said Fuchs. “We can now utilize similar methods to begin to compare mouse and human skin stem cells.”

The scientists' analyses of the biochemical characteristics of the isolated mouse stem cells revealed that the bulge contained two distinct populations of stem cells. One type, called “basal” cells, is active during early development. In contrast the “suprabasal” cells appear only after the first hair generation cycle. This distinction offers biologists an opportunity to compare the two groups of cells, in terms of the control that the bulge exerts over their proliferation and differentiation.

Despite the fact that the stem cells expressed many different genes, both populations were capable of self-renewal when grown in culture, said Fuchs. The researchers also found that both types of cells—even after being cultured—produced hair follicles when grafted onto the skin of a strain of hairless mice.

“I think clinicians will be interested in the fact that both of these populations can produce hair follicles after culture,” said Fuchs. “Previously, researchers have done similar transplant experiments with dissected parts of the hair follicle. And, while they've had evidence that hair follicle structures were forming, they didn't see generation of hair.

“In contrast, in our experiments, we saw quite a density of hairs, in some cases at a density that's very similar to that of normal mouse fur,” said Fuchs. “While we are not yet able to achieve such density a hundred percent of the time, the fact that we do get such density in some cases tells us that the system is working well. We just need to tweak it to the point where we can get such results consistently,” she said.

Importantly, said Fuchs, the stem cells they isolated showed a molecular signature of gene activity that demonstrates their “stemness.” Such characteristics, she said, represent the beginning of a broader effort to compare the genes activated in many stem cell types, to understand the factors that control their proliferation and differentiation.

“The information that we have now on the 'stemness' genes is allowing us to narrow in on some of the similarities among stem cells of the body,” she said. “I believe this profiling information will ultimately give us some very good clues as to how stem cells respond to various external cues. And this information will help us understand how we can coax stem cells down one specific lineage or another in culture.”

The findings also emphasize the promise that such studies hold for the treatment of such skin disorders as ulcers or injury, as well as the generation of hair follicles from stem cells, she said.