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New function for telomerase?

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Telomerase promotes proliferation of resting stem cells through a mechanism that does not involve the extension of chromosomal telomeres, researchers report in *Nature* this week.

"This is a completely new function for telomerase that gives us new insight into stem cells and cancer," Steven Artandi of Stanford University, the study's senior author, told *The Scientist*.

It had generally been thought that the only function of telomerase was to promote telomere extension, but in recent years evidence has started to accumulate suggesting that the enzyme promotes the development of cancer, and that it might have roles other than synthesizing telomere repeats. In spite of this, some researchers have remained skeptical.

In an attempt to clarify this issue, Kavita Y. Sarin of Stanford University and a team of researchers turned to the mouse hair follicle, an organ that harbors stem cells and cycles between a telogen (resting) phase and an anagen (growing) phase. They built transgenic mice in which they could control the expression of TERT–the protein component of telomerase–using a tetracycline regulatory system.

When the researchers switched TERT on, the overexpressed protein promoted the transition from telogen to anagen through precocious activation and proliferation of quiescent stem cells in the hair follicle. This caused strong hair growth, making the mice shaggy. "We saw these incredibly profound effects that would never have been expected in the context of the previously understood function of telomerase," said Artandi.

In another experiment, the authors used mice that completely lacked TERC—the RNA portion of telomerase that enables the enzyme to make telomere DNA. Remarkably, the effects of TERT remained in the absence of TERC.

"This study extends the range of functions of telomerase beyond what was previously understood. It's the clearest demonstration of something that has been accumulating for a while," said Elizabeth H. Blackburnof the University of California, San Francisco, who was not involved in the study.

"The fact that they could see the effects on the stem cell proliferation when the TERT protein was overexpressed in the absence of the RNA component says that this has nothing to do with making telomeres longer, or even probably to do with telomeres," said Blackburn, who wrote a News and Views article that accompanies the paper.

"I think it's a very nicely conducted study and it has very provocative conclusions," said Elaine Fuchs of Howard Hughes Medical Institute, who did not participate in the research. "The experiment in the TERC-no situation is key. If the effects of TERT were due to telomerase activity, the absence of TERC should have obliterated it, but it didn't. The authors did show that it obliterated the telomerase activity. That's what I love of this paper: they did all the right controls. However, I think the verdict is still out, until we know what the function of TERT is."

Jerry W. Shay, of the University of Texas Southwestern Medical Center at Dallas, who was not part of the research team, agreed that the studies provide additional evidence for a role of telomerase

independent of telomeres maintenance, but he also said he believed that the verdict is not conclusive. "Overexpressing a transgene, in this case telomerase, with a strong promoter could be indirectly causing the effect. For example, insertional mutagenesis or very high levels of the TERT protein could somehow protect stem-like cells from differentiating or undergoing apoptosis, thus allowing cells to stay in anagen longer and thus affecting hair growth. The study would have been even more significant if the findings were observed with levels of TERT protein in a TERC-deficient strain that were similar to those found in normal tissues."

For Blackburn, this work has an interest that goes beyond the academic. "This is a commentary on the human mind. We discovered telomerase purely as a DNA synthesizing enzyme, and people still believe that this is the enzyme's only function. I'm just amazed that people lock themselves into dogma so quickly."

References

1. K.Y. Sarin et al., "Conditional telomerase induction causes proliferation of hair follicle stem cells," *Nature*, 436:1048-52, August 18, 2005. doi:10.1038, [http://www.nature.com]

2. Steven Artandi , [http://hematology.stanford.edu/research/artandi_lab.html]

3. J. Perkel, "Telomeres as the key to cancer," *The Scientist*, May 27, 2002., [http://www.the-scientist.com/2002/5/27/38/1]

4. J.W. Shay, W.E. Wright, "Does telomerase moonlight?" *The Scientist*, 19:18, February 28, 2005., [http://www.the-scientist.com/2005/2/28/18/1]

5. Elizabeth H. Blackburn, [http://biochemistry.ucsf.edu/~blackburn/aboutdrblackburn.html]

6. E.H. Blackburn, "Shaggy mouse tales," *Nature*, 436:922-3, August 18, 2005., [http://www.nature.com]

7. Elaine Fuchs, [http://www.hhmi.org/research/investigators/fuchs_bio.html]

8. Jerry W. Shay, [http://www.swmed.edu/home_pages/cellbio/shay-wright/index.html]