Hair Today Gone Tomorrow?

Teasing out details of hair growth.

By Damaris Christensen

From the strength-giving locks of the biblical Samson to the elaborate updo of a geisha and the neon, spiked styles of punk rockers, hair remains an important part of a person's self-image and one of the most obvious forms of self-expression.

People may cut their hair, dye it, perm it, and style it. But unless they resort to wigs and hair transplants, they are stuck with the quantity of hair that nature gives them—and takes away. That fact of life becomes especially vexing when people lose their hair to chemotherapy, diseases that attack hair follicles, or simply aging. And there are few options for hirsute women, who have an overabundance of hair and may even grow beards.

At the moment, scientists don't fully understand the molecular orchestrations that underlie hair growth. That hasn't stopped them from providing a few drugs for hair-related problems. The two medications now available to treat hair loss, known commercially as Rogaine and Propecia, were developed after researchers fortuitously observed hair growth as a side effect of drugs designed for treating hypertension and enlarged prostates. Likewise, the only drug on the market that slows hair growth came as a spin-off of a search for an anticancer drug.

In the past few years, however, researchers have begun to tease out the molecular signals that cause hair to grow and fall out. Unraveling such signaling, they hope, will lead to new ways of addressing the needs of people with either too little hair or too much.

"Hair disorders aren't necessarily important from a life-or-death situation ... but we are defined by how we look, in terms of gender and of youth," says Ricardo Azziz, a specialist in hair disorders at the University of Alabama at Birmingham. "Our job is not only to make people survive but to give them a better quality of life."

Whether it's the light, downy hair on a woman's arm, the short, curly hairs on a man's chest, or the longer hairs on either gender's head, each hair grows from a tiny, cell-lined skin indentation called a follicle. By adulthood, the skin hosts all of the follicles it ever will have naturally.

A hair follicle consists of three concentric cylinders. The central cylinder, the hair fiber, is created by the rapid growth and death of cells at the follicle base, which make proteins such as keratin. The outermost cylinder is known as the outer root sheath, a structure that separates the hair follicle from the surrounding skin. The middle cylinder, the inner root sheath, shapes and guides the hair as it grows outward. A person's hair will be straight if this middle cylinder is round and will be curly if the cylinder is flattened.

An eyebrow hair grows slowly and falls out after just a couple of months. In contrast, a hair on a person's head can extend many feet long because the follicles there stay in the growth stage for 6 to 10 years.

One theory has it that such long-term growth cycles operate on an internal clock that's independent of the seasons or temperature. Some scientists suggest the timer is set by the dermal papilla, a structure containing dividing cells at the base of the hair follicle. Others argue that the clock controlling hair growth is part of a bulge lying just to the side of the hair follicle. Still others doubt whether this timer exists at all.

Over the past 50 years, scientists have

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that they encode cause the cells to initiate hair formation – for example, by producing keratin.

Further evidence for the importance of the Wnt pathway emerged when Fuchs' group created genetically engineered mice that couldn't degrade betacatenin. This essentially made the cells behave as though they were constantly bombarded with Wnt signals. These mice developed new hair follicles as adults and so sported lush coats. As the mice aged, however, they also developed benign lumps resembling human scalp tumors.

Fuchs and her colleagues have altered different factors in the Wnt signaling pathways to coax precursor cells in hair follicles to specialize into either skin cells or the cells that make up the hair follicle and a nearby gland. The researchers described these findings in the July 1 *Genes and Development*. The implication, Fuchs says, is that Wnts play an important role in hair cycling, as well as in the development of hair follicles.

The same caution must be applied to potential treatments based on Wnts and beta-catenin as to those based on PTHrP. Animal studies have linked Wnts and abnormal amounts of betacatenin to the growth of malignant tumors of the colon, liver, breast, and reproductive tract.

To develop treatments for hair disorders while minimizing cancer risk, Fuchs suggests supplying Wnts in a pattern that mimics nature's precisely controlled delivery. Alternatively, effective treatments might come from interfering with steps in the Wnt cascade other than beta-catenin.

New molecular signals for hair growth and cycling are being uncovered on a regular basis. "We're living in a golden age of hair research," says Cotsarelis. "We know so much more than we did 5 years ago ... but there are still many unanswered questions."

The connections between cancer cells and hair cycling may not be surprising since both involve systems of rapidly dividing cells, notes Barbara M. Mathes of Bristol-Myers Squibb in Princeton, N.J. Mathes ran the clinical trials of Vaniqa, a drug that slows hair growth by interfering with the formation of amino acids needed for cell growth. The drug was originally developed as an anticancer treatment.

"If we can figure out the molecular links [between cancer and hair cells], we can learn a lot about manipulating cell cycles ... and the consequences of such manipulation," she says. That could be useful in developing safe, new drugs for hair disorders.

Meanwhile, on a more fundamental level of science, a growing number scientists are beginning to look at hair as an accessible model for various biological processes, such as organ development and communication between different kinds of cells.

Fuchs predicts that within a few years, despite the complexity of molecular signals involved, researchers will understand what compounds control the regular progression of hair follicles from growth to regression to rest and back again.

"It's like putting together a puzzle," she says. "In the early stages of trying to understand a molecular process, or put together a thousand-piece puzzle, it seems hopeless because there are so many pieces. But as you put together more of the puzzle, it actually gets easier to see patterns."