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Skin and hair: Means to a genetic end

Skin and hair proteins fascinate Elaine Fuchs, Ph.D., who heads the university's Laboratory of Mammalian Cell Biology and Development.

From proteins that act like glue to hold together skin to those that form a tough outer barrier to keep harmful pathogens out and essential fluids in the body, Fuchs's research goal is the same: understand how skin proteins function at the level of the cell. While unraveling the secrets of our body's largest organ, she finds clues to the genetic origins of skin diseases, including cancer.

Fuchs is addressing one of today's crucial biological questions: "What are the amazing properties of stem cells of the body that enable them to develop into tissues and organs?"

Her lab studies how skin stem cells are able to divide and churn out skin cells in a Petri dish, a process used to treat burn victims. "If we understand enough about the biology of skin stem cells, and how they can make both hair and skin, will we be able in the future to coax stem cells of the skin or hair into becoming something that they normally would not become, such as a blood vessel to the heart, neurons for the brain, or pancreatic islet cells?" she asks.

These tissues can be severely damaged by, respectively, heart attack, Alzheimer's and diabetes. If skin stem cells can be persuaded to become other tissues, they could be the basis for new treatments.

Scientists must first thoroughly understand normal stem cells. "There is much promise for stem cells in revolutionizing medicine, but there is so much we must first learn about stem cells before we can reach the stage of even knowing whether this might be possible," she points out.

Unlike other stem cells, skin stem cells can be cultured easily in the lab. With these lab cultures, Fuchs and her research team study stem cells and learn about how they choose between making skin epidermis or making hair. Employing modern molecular biology techniques, the scientists trick stem cells into making one choice — for example, to become hair. The scientists test their findings by introducing small mutations in specific skin genes in laboratory mice. More often than not, this key step has guided them to the genetic bases of human skin disorders.

Fuchs's lab has determined the genetic basis of a type of skin tumor that affects the scalp. The lab hopes to understand the genetics of squamous and basal cell carcinomas, the most common types of human cancers in the world. "Because of their extraordinary self-regenerating properties, stem cells, when gone awry, are the likely cause of many if not most types of human cancers," says Fuchs.

While her goal is to unravel the biology of normal cells, not the causes of skin diseases, Fuchs's results exemplify the unexpected benefits of basic research to medicine as well as science.

Skin cells' durability comes from the protein keratin. This protein also makes up the bulk of hair cells. To switch on hair keratin genes and turn cells into keratin factories, hair precursor cells need a signal to tell them to make a transcription factor between beta-catenin and a partner protein. The hair follicle at right is stained with antibodies to reveal the presence of beta-catenin (lime green). In blue are the cells' nuclei. Beta-catenin normally stays at the cells' borders, but the hair precursor cells (at base) have received their signal and begun to move with their partners to the nucleus.