Hair-GEL online tool gives bird's eye view of hair follicle formation

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Credit: Laura Tiitto/public domain

A new online database will empower researchers exploring how hair follicles and the surrounding skin develop, according to an article published recently in the journal *Developmental Cell*. The work is central to understanding the interactions between stem cells and their environment - or "niche cells" - during fetal development, and will

specifically facilitate future attempts to make skin grafts with functional hair follicles or to regenerate lost hair in patients.

"The new tool and our initial analyses take a molecular snapshot of stem cells and niche cells as they interact to form hair follicles," said senior study author Michael Rendl, MD, Associate Professor in the Department of Developmental & Regenerative Biology, and an investigator within the Black Family Stem Cell Institute, Icahn School of Medicine at Mount Sinai. "We know these cells are important for coordinating hair growth, but we don't know how they communicate on a molecular level to achieve such a complex process. Our goal in publishing this database is to construct a launching pad for future studies that will clarify the role of all signals driving this developmental program - with the ultimate goal of transitioning this knowledge to the clinical setting."

Playfully titled Hair-GEL (gene expression library), the database relies on the fundamental genetic principle that a blueprint for developing tissues is encoded by genes that are differentially activated in specific cell types. Gene expression is the process where information stored within DNA is converted (transcribed) into related molecules called RNAs, which are in turn used to synthesize proteins that make up a cell's structures and signals. A transcriptome is the set of all RNA molecules present in one cell type, and therefore a readout of which genes are expressed and which proteins are active and imparting functionality in that cell type.

Using next-generation RNA-sequencing, the research team compared transcriptomes in embryonic skin cells to uncover hundreds of genes that are active as skin develops, including those that guide the formation of hair follicles.

"While this work provides the first high-resolution molecular study of hair follicle precursor cells, its true power comes from analyzing these

cells in the context of the entire developing skin," said lead study author Rachel Sennett, who recently defended her PhD thesis as part of Mount Sinai's MD/PhD program.

"Crosstalk" in Embryonic Skin

As hair follicles form, many other cells in the local environment simultaneously coordinate epidermal and dermal maturation, pigment cell migration, nerve cell distribution, and more. By comparing the genome-wide RNA-sequencing analysis of distinct cell types isolated from embryonic skin, the research team uncovered unique genes associated with each one. These aptly named "gene signatures" in turn reveal the messages specific cell types send and receive as they communicate and cooperate to form skin and all of its complex compartments.

Importantly, prior studies have defined gene signatures of stem cells and niche cells in adult hair follicles, and the authors of this current study look for common genes in their embryonic counterparts. Such genes could represent core factors that establish stem or niche cell identity and activity, and could be useful to promote hair growth in a clinical setting. The authors additionally confirm the activity of defined signaling pathways, known to be important in diverse developmental programs, but for the first time pinpoint cells throughout the skin that take part in these molecular conversations. Finally, they highlight the widespread activation of signals previously defined by their role in axon guidance signaling, which could have a heretofore unrecognized role in directing the large scale cellular rearrangements important for functional skin development.

The team is sharing all data in an interactive, searchable Hair Gene Expression Library website (Hair-GEL.net) that offers sequencing information on the stem cells and niche cells that interact to build hair

follicles. Researchers can query any gene of interest to see if it is present and/or specifically expressed in any one of the distinct cell types that compose embryonic skin.

More information: Rachel Sennett et al. An Integrated Transcriptome Atlas of Embryonic Hair Follicle Progenitors, Their Niche, and the Developing Skin, *Developmental Cell* (2015). DOI: 10.1016/j.devcel.2015.06.023

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