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Hair Follicle Stem Cells: Dynamics and Commitment Issues

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Adult stem cells (SCs) function in tissue homeostasis and wound repair. In the hair follicle (HF), slow-cycling, relatively undifferentiated SCs exist within a niche known as the bulge, located below the sebaceous gland in the permanent portion of the outer root sheath (ORS). Hair follicles undergo cycles of growth (anagen), destruction (catagen) and rest (telogen). During hair growth, SCs exit the bulge and migrate downward along the ORS to give rise to transit-amplifying (TA) cells in the matrix, which will differentiate and originate the various layers of the hair and its channel.

Little is known about the properties and fates of ORS cells. They express many of the HF-SC markers, however it is not known whether they possess stemness like their predecessors or if they are committed like their TA progeny. It is also unknown if they survive catagen. If so, it is unknown if they could home back to the bulge and still function as stem cells.

By employing histone and nucleotide double-pulse-chase and lineage tracing, we have defined the point at which SCs become irreversibly committed along a differentiation lineage. We show that upper ORS cells survive catagen. They retain stemness and slow-cycling properties and home back to the bulge niche. They become the primary SCs for the next hair cycle, whereas initial bulge SCs become reserves for injury. Some actively cycling lower ORS cells also survive catagen and home back to the bulge. They lose their ability to proliferate but they serve two essential roles in the stem cell niche: anchoring the club hair and regulating SCs quiescence.

Hsu YC, Pasolli HA, Fuchs E. Dynamics between stem cells, niche, and progeny in the hair follicle. Cell 2011, Jan 7, 144, 92-105.

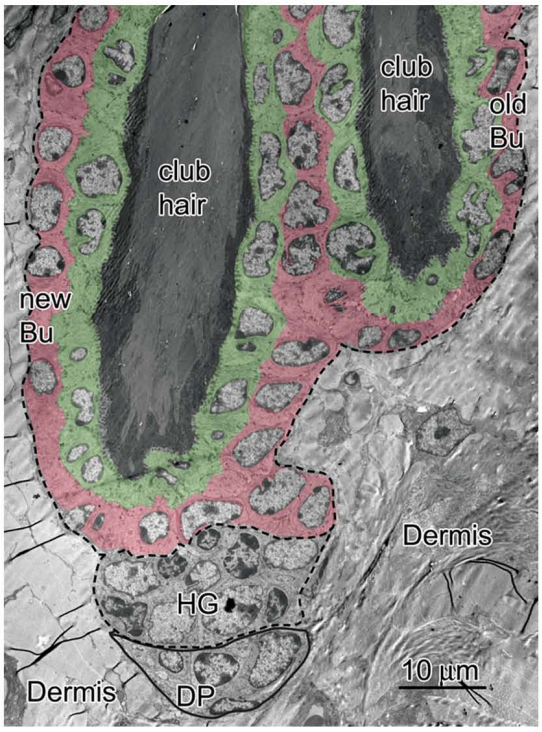

Figure 1: Hair follicle in the resting stage (telogen). The new bulge and the old one (from the previous hair cycle) are depicted, each one with its club hair. Each bulge has two cell layers: the outer layer (in red) which expresses the marker CD34 and the inner layer which is CD34 negative but expresses keratin 6. The CD34-K6+ layer anchors the club hair to the bulge. The new bulge is in contact with the hair germ (HG), which faces the dermal papilla (DP).

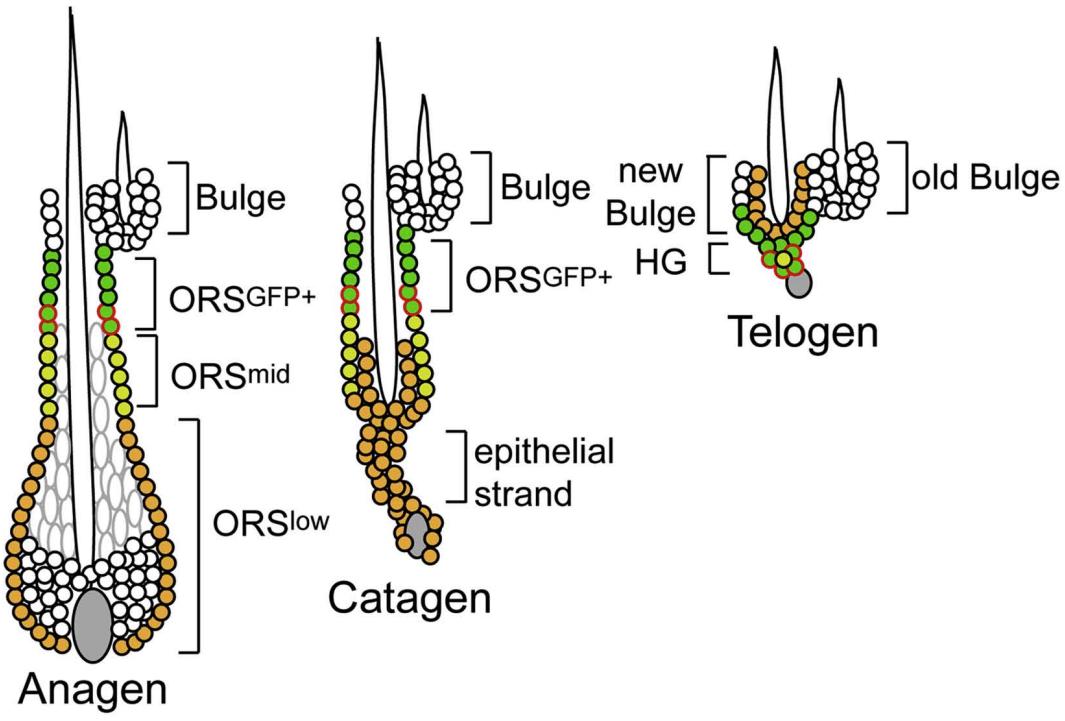

Figure 2. Schematic summarizing how the HG, new bulge and K6+ bulge layer arise. During anagen, HF-SC bulge descendants appear in the single layer of ORS. At full-anagen the ORS can be divided into three segments: ORS^{GFP+}, $ORS^{mid,}$ and ORS^{low}. ORS^{GFP+} cells are the slow-cycling bulge descendants. The upper part of ORS^{GFP+} (green cells with black circles), induce CD34 expression at catagen and contribute substantially to the new bulge. The lower part of ORS^{GFP+} does not express CD34 (green cells with red circles) but rather contributes to the new HG. Most cells in the ORS^{mid} and ORS^{low} zones do not survive catagen. The few surviving ORS^{mid} cells end up as $GFP^{low/neg}$ HG cells, while the surviving ORS^{low} cells home back to the bulge, where they become the K6+ layer. The K6+ bulge cells are not bona-fide stem cells. Instead, they act to anchor the hair and keep the HF-SCs in their quiescent state. Reprinted from Hsu et al, 2011, with permission from Elsevier.

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