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Epithelial Stem Cell Niche in Skin: Ultrastructural Insights

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Skin epithelium exhibits a remarkable turnover which is accelerated in case of injury. To accomplish this process, skin maintains a reservoir of multipotent stem cells (SCs) critical for replenishing and keeping the balance of cells within the tissue. Skin SCs reside in a special niche, a region in the hair follicle known as the bulge. Follicles periodically undergo cycles of growth (anagen), destruction (catagen), and rest (telogen). The bulge or SC niche is located in the zone between noncycling and cycling segments. The entire follicle (see figure A) is surrounded by a basal lamina (BL), which is surrounded in turn by a dermal sheath. The bulge also likely receives inputs from sensory nerve endings and blood vessels, which encase this region. Bulge SCs give rise to transit-amplifying matrix cells, which proliferate and then differentiate to produce the hair shaft and the channel that surrounds it. Matrix cells are surrounded by a pocket of specialized mesenchymal cells, the dermal papilla (DP), with potential hair growth inductive properties.

Recently, the Fuchs lab has been able to isolate an enriched bulge cell population from skin and demonstrated their self-renewal capacity *in vitro* and their multipotency *in vivo*, providing definitive evidence for bulge cells as SCs [1-2]. We have now examined the ultrastructure of the cell populations in the stem cell niche and its interaction with the dermal papilla under quiescent (telogen) and activated (early anagen) states. As recently described [2], our studies showed two populations within the bulge: one that maintains the BL contact through abundant hemidesmosomes and another which is suprabasal. There are no significant differences in the ultrastructure of nuclei and cytoplasm between both populations. The basal bulge population is in close contact with the DP (at telogen) and with nerve terminals and dermal sheath cells at any moment of the hair cycle. Both basal bulge and dermal sheath cells exhibit numerous small plasma invaginations (caveolae) that are known to participate in intercellular signal transduction. No mitosis were detected in the bulge area, while they were frequently seen in the hair germ at the onset of anagen.

These studies now open the door for employing ultrastructural analyses to examine closely the cellular interactions in skin SCs to gain additional insights into their proliferation and differentiation.

[1] Tumbar T, Guasch G, Greco V, Blanpain C, Lowry WE, Rendl M, Fuchs E. Science. 2004 Jan 16;303(5656):359-63. Epub 2003 Dec 11.

[2] Blanpain C, Lowry WE, Geoghegan A, Polak L, Fuchs E. Cell. 2004 Sep 3;118(5):635-48.

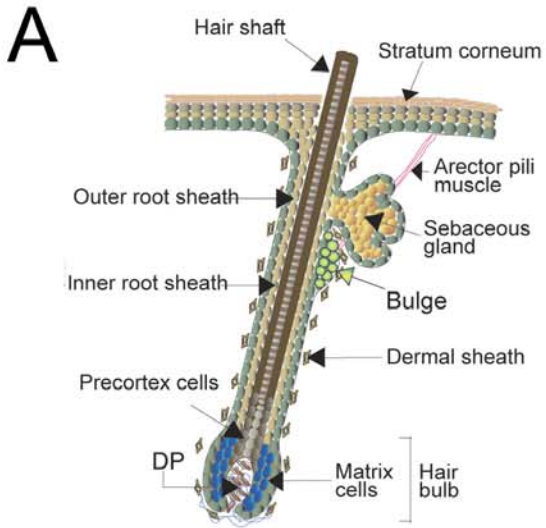

Fig. A: The hair follicle. Skin multipotent stem cells reside in the hair follicle, in a region known as the bulge, located below the sebaceous gland (SG) and at the juncture of the arector pili muscle. Bulge stem cells give rise to transit-amplifying matrix cells, which proliferate and then differentiate to produce the hair shaft and the channel that surrounds it. Matrix cells (Mx) are surrounded by specialized mesenchymal cells, the dermal papilla (DP). Courtesy of Dr. Geraldine Guasch, The Rockefeller University.

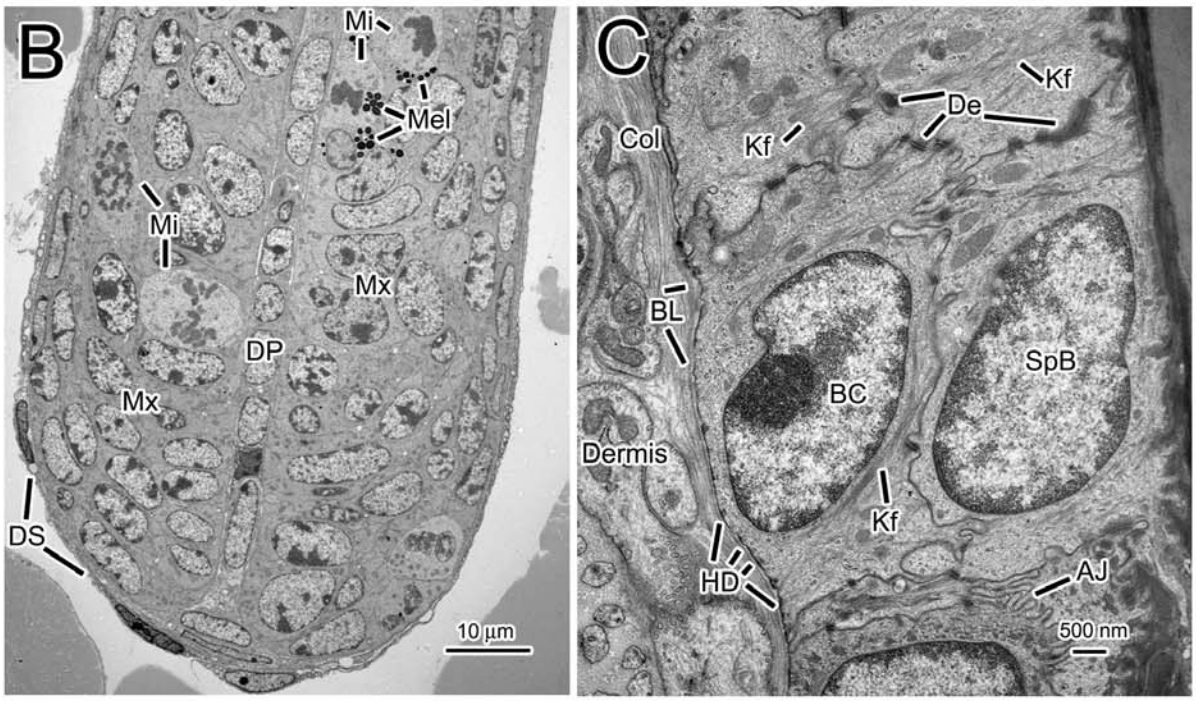

Fig. B. The hair bulb. Sagital section. Note mitosis (Mi) in Mx cells. Note also central strand of DP. Mel: melanin granules.Fig. C. The bulge .contains two distinct cell populations, the basal cells (BC) that keep contact with the BL through numerous hemidesmosomes (HD) and the suprabasal cells (SpC). Note the presence of desmosomes (De), adherens junctions (AJ) and keratin filaments (Kf) in both BC and SpC. Col: collagen fibers.

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