Newly identified stem cells in sweat glands: roles in homeostasis and wound repair

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Eccrine sweat glands perform a vital function by controlling body temperature in hot climates and during exercise. Despite their abundance (3 to 4 million in the human body) and critical role for survival, they have seldom been extensively studied. Using mouse as a model, our lab has succeeded in identifying the stem cells from which sweat glands initially develop as well as stem cells that regenerate adult sweat glands. By devising a strategy to purify and molecularly characterize the different kind of stem cell populations, we have studied how these populations respond to tissue homeostasis and to different types of injuries and how sweat glands differ from their close relatives, the mammary glands.

Sweat glands are quiescent during normal homeostasis and after epidermal injury. When each sweat gland population was selectively targeted for diphtheria toxin-induced cell death, surviving glandular cells proliferated and sweat production was restored, thereby exposing their regenerative potential.

When purified sweat gland stem cells were grafted onto cleared mammary fat pads, they were able to regenerate de novo sweat glands. Intriguingly, when cells were grafted onto cleared pads of lactating mice, they generated structures that began to express milk, while still retaining some sweat gland features. These findings tell us that sweat gland stem cells can “remember” who they are but also adopt new identities in other environments. Our findings can now be used to explore the roots of some genetic disorders that affect sweat glands, as well as ways to potential means to treat them.

Figure 1. (A) Diagram showing orifice and intraepidermal portion of a sweat duct, which extends from epidermis (Epi) into dermis and terminates in a coiled, secretory gland. (B) Semithin section of paw skin showing sweat glands. Boxed area is enlarged in (C), an electron micrograph of a coiled duct, displaying myoepithelial (Myo) and luminal (Lum) cells.

Figure 2. Purified Progenitors from Sweat Ducts and Glands Exhibit De Novo Tissue Morphogenesis and Maintain Their Identity when Engrafted into Some Foreign Microenvironments. (A) Immunofluorescence for ATP1a1 (sweat gland-specific marker) and milk protein (mammary gland-specific marker) in de novo glandular structures from transplanted FACS-purified K14H2BGFP sweat gland myoepithelial cells. Scale bars, 10 μm (C) Ultrastructure analysis of de novo glandular structure within host mammary fat pad 10 weeks after transplanting donor K14H2BGFP+ myoepithelial cells. GFP+ glandular structures were identified by correlative immunofluorescence and TEM. I: Example of glandular structure. Cells are organized around an open lumenal space. Boxed areas are enlarged in II and III. Scale bar, 10 μm. II: Myoepithelial cell (Myo) beside a luminal cell (Lum). Boxed areas are magnified in insets. Boxed area (a), myoepithelial cell attachment to basement membrane (arrowheads). Boxed area (b) shows dense actin filament bundles within myoepithelial cytoplasm. Scale bar, 500 nm. III: Luminal cells within gland. Note numerous apical microvilli (Mv). Intercellular junctions are boxed, showing desmosome (De) and tight junction (Tj). Scale bars, 500 nm