Adult hair follicle stem cell compartment changes in androgenetic alopecia demonstrate maintenance of progenitor stem cells with loss of descedant CD200high A6 integrin-high expressing cells

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The status of adult stem cell compartments in tissue specific disease has not been thoroughly addressed. We tested the hypothesis that hair follicle stem cells might be depleted in androgenetic alopecia (AGA), which is characterized by drastic miniaturization of the hair follicle. To compare hair follicle stem cell numbers between paired hairs and bald scalp samples from the same individuals, we used flow cytometry to quantify cell cycle, cell size, and expression of CYTOKERATIN 15 (KRT15), FOLLISTATIN (FST), CD200 and alpha-6 integrin. We found a gradient of stem cell characteristics, as defined by a high degree of KRT15 and FST expression, cellular quiescence and small cell size. This gradient is not grossly altered between paired hairs and bald scalp, and stem cells are maintained in bald scalp. However, a specific CD200 high alpha-6-integrin high population, which has characteristics of early stem cell progeny, is lost in bald scalp. Consistent with the loss of the immunosuppressive CD200 protein, and based expression profile demonstrates significant increases in inflammation associated genes in androgenetic alopecia. Previous reports of CD200 loss leading to alopecia in mouse models suggest that AGA may be exacerbated or caused by CD200 downregulation in the human hair follicle stem cell compartment.

BMP activity defines refractory and competent hair follicle populations during the propagation of regenerative waves

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Hair cycle can be regulated by molecular oscillation within the follicle (autonomously) or by dynamic changes in the inter-follicular environment (non-autonomously). While human hair follicles largely cycle autonomously, cycling of mouse hair follicles is affected by the status of adjacent follicles. Thus hair cycle progression can advance like a transverse wave on the surface of the skin. Observations of the dynamic hair cycle domains on the skin of wild type and Mx2Δ/i-mice show that each hair cycle domain is made of an initiation site, a propagating wave, and boundaries. Analyses of patterns of wave propagation and boundary formation led us to identify a novel stage in telogen. In the first stage of telogen, hair follicles are refractory to the anagen spreading wave, thus forming a sharp domain boundary. Refractory telogen becomes competent to respond to anagen initiation signals after Bmp 2/4 loss. Hair plucking can induce anagen in competent follicles, but not refractory ones. In Krt14-NOG mice there is drastic shortening of the refractory telogen, and last anagen re-entry. Individual follicle cycles faster and the wave dynamics of follicle populations are altered. Transplantation of a piece of Krt14-NOG skin to normal skin microenvironment results in restoration of Bmp signaling activity and refractory telogen. Our data identifies two new stages of telogen, refractory and competent. They are defined by the ability of telogen follicles to re-enter anagen, and based on the on-off switch of BMP2/4 expression within and around the follicle. This study presents a novel population approach to the study of hair cycling, and gives a more systematic and integrative explanation to the hair follicle behaviors observed in classical literatures.

Reactive oxygen species (ROS)-mediated androgen-inducible TGF-β1 regulation in dermal papilla cells

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Intracellular signaling roles of reactive oxygen species (ROS) generated in response to androgen hormone in hair follicle dermal papilla cells are not well assessed. To assess the contribution of ROS in androgen induced increase of TGF-β1 secretion, we stably transfected DP-6 cells with a reporter containing the androgen response element (ARE) and promoter from TGF-β1. In the presence of androgen, increased ARE activity and TGF-β1 expression were observed. To determine the role of reactive oxygen species (ROS) in androgen-induced TGF-β1 regulation, we assessed the effect of antioxidants and reactive oxygen species scavengers. Our results show that antioxidants and reactive oxygen species scavengers inhibit TGF-β1 induction in androgen positive cells. We suggest that antioxidants could be one of the candidates to control androgen-mediated pattern hair loss.