

## **"EPITHELIAL SKIN STEM CELLS IN NORMAL HOMEOSTASIS AND IN CANCER"**

by

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## Abstract

In many tissue stem cells divide infrequently and reside in long periods of quiescence, presumably to protect their genome from accumulating genotoxic stress that leads to cancer. To isolate and characterize specific stem cell populations, we devised a mouse transgenic system that allowed us to label skin epithelial cells based on their divisional frequency. This way we identified markers for lineage tracing experiments and characterized the behavior of several epithelial stem cell populations in the hair follicle and inter-follicular epidermis. We demonstrate that early-activated hair follicle stem cells are at the origin of skin epithelial tumors. Furthermore, we find that transcriptional control of early stem cell activation during normal homeostasis (i.e. the transcription factor Runx1) is in fact crucial for both initiation and maintenance of skin epithelial tumors. Finally, we demonstrate that Runx1 coordinates both cell–intrinsic (i.e. lipid metabolism) as well as cell-extrinsic (i.e. remodeling of the stem cell niche components) during activation and implicate Runx1 in human skin and oral epithelium squamous cell carcinoma.

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All are welcome