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Branching from nerve to skin: neurofibroma microenvironment & novel epithelial stem cells

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Neurofibromatosis type I (NF1) is an autosomal dominant genetic disorder affecting one in every 3,000 newborns. Individuals with NF1 are predisposed to tumors, and neurofibroma is the most prevalent among them. By employing genetically-engineered mouse models, we explored the tumor microenvironment of neurofibroma. Our results showed that neurofibroma development is facilitated by *Nf1* heterozygous tumor microenvironment. However, *Nf1* heterozygosity impairs the malignant transformation of neurofibroma. This is important evidence showing that the genetic status of microenvironmental cells can influence tumor cell progression and transformation. While studying neurofibroma, we serendipitously observed a striking hair graying phenotype in mice. This discovery led us to identify transcription factor Krox20 as a new lineage marker for hair shaft progenitor cells whose stem cell factor expression is indispensable for melanocyte maturation and hair pigmentation. Our recent data further suggested that epithelial Krox20+ cells are indeed a novel population of universal epidermal stem cells that can give rise to both hair follicle and skin in the epidermis. Epidermal Krox20+ cells are essential for normal skin and hair development, and Krox20 protein participates in hair regeneration and wound healing. Krox20 is the first identified stem cell lineage that can give rise to all the keratinocytes constituting the epidermal structure during homeostasis.

"Life was like a box of chocolates. You never know what you're gonna get."

~ Forrest Gump