

Brg1 governs a positive feedback circuit in the hair follicle for tissue regeneration and repair

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Hair follicle stem cells (bulge cells) are essential for hair regeneration and early epidermal repair after wounding. Here we show that Brg1, a key enzyme in the chromatin-remodeling machinery, is dynamically expressed in bulge cells to control tissue regeneration and repair. In mice, sonic hedgehog (Shh) signals Gli to activate *Brg1* in bulge cells to begin hair regeneration, whereas Brg1 recruits NFκB to activate *Shh* in matrix cells to sustain hair growth. Such reciprocal Brg1–Shh interaction is essential for hair regeneration. Moreover, Brg1 is indispensable for maintaining bulge cell reservoir. Without Brg1, bulge cells are depleted over time, partly through the ectopic expression of a cell cycle inhibitor p27^{Kip1}. Also, bulge Brg1 is activated by skin injury to facilitate early epidermal repair. Our studies demonstrate a molecular circuit that integrates chromatin remodeling (Brg1), transcriptional regulation (NFκB, Gli), and intercellular signaling (Shh) to control bulge stem cells during tissue regeneration.

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