



HAIR DISORDERS

PATHOMECHANISM OF PERMANENT HAIR LOSS AFTER CHEMOTHERAPY: PRIMING MOBILIZATION AND DEPLETION OF HAIR FOLLICLE STEM CELLS

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The maintenance of genetic integrity is critical for stem cells to ensure homeostasis and regeneration for extended periods. Little is known about how adult stem cells respond to irreversible DNA damage, resulting in loss of regeneration in humans. Here, we established a permanent regeneration loss model using cycling human hair follicles treated with alkylating agents: busulfan followed by cyclophosphamide. Using this model, we investigated the cellular mechanisms by which hair follicle stem cells (HFSCs) lose their pool. Histologically, the bulb, which is rapidly proliferating zone, immediately underwent massive destructive changes. However, the bulge, where quiescent HFSCs located, showed unexpected proliferation after busulfan, then underwent large-scale apoptosis by following cyclophosphamide. HFSC proliferation was activated through the PI3K/Akt pathway, and depletion was driven by p38-dependent cell death. Our findings indicate that priming mobilization causes adult stem cells lose their resistance to DNA damage, resulting in permanent loss of regeneration after alkylating chemotherapy.

