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Lineage Tracing Sonic Hedgehog-Expressing Cells in Adrenal Glands in Post-Weaning Mice

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The Sonic Hedgehog (Shh) gene expressed in the subcapsular cortical region of the adrenal gland has been found to play a role in adrenal gland development. The Shh(+) cell population at the fetal stages contributes to different cortical layers in the adrenal gland. However, the (1) capability of these cells after weaning and (2) how soon they can renew the adrenal cortex in the postnatal stages is not fully understood. Here, we conducted a lineage tracing experiment to track Shh(+) cells and cells descended from them in post-weaning mice to ultimately better understand the processes of adrenal cortex renewal and remodeling over time in young adult mice.

This experiment used the NuTRAP; Shh-Cre-ERT2 mice as the Shh-reporter mouse model. This tamoxifen-inducible mouse model allows us to specifically target and label Shh-expressing cells and all descendant cells with green fluorescence. Tamoxifen was given at postnatal days (P) 22, P24, and P26 to enable the Cre recombinase activity driven by the Shh promoter. Adrenal glands were then analyzed after two and four months. This lineage tracing experiment found that Shh(+) cells and their descendant cells reached the margin of the Cyp2f2(+) cortical zone in 2 months and the cortical-medullary boundary in 4 months. This finding indicates that the Shh(+) cell population in post-weaning mice can proliferate, differentiate, and eventually renew the entire adrenal cortex over a four-month period of time.

Understanding the adrenal cortex's renewal rate helps us design our follow-up study to test the capability of Shh(+) cells in adult mice at different ages and how their potency changes overtime at the 'omic' level. Because this NuTRAP;Shh-Cre-ERT2 mouse model also allows us to isolate cell-type-specific DNA/RNA, we can further decipher

the underlying gene/pathways which control this progenitor cell population of the adrenal gland cortex.

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