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Bliss Magella, Robert Mahoney, Mike Adam, S. Steven Potter

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Reduced Abd-B Hox function during kidney development results in lineage infidelity

Bliss Magella, Robert Mahoney, Mike Adam, S. Steven Potter*

Division of Developmental Biology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH 45229

*Corresponding author: Steve.Potter@cchmc.org

Abstract

Hox genes can function as key drivers of segment identity, with Hox mutations in *Drosophila* often resulting in dramatic homeotic transformations. In addition, however, they can serve other essential functions. In mammals, the study of Hox gene roles in development is complicated by the presence of four Hox clusters with a total of 39 genes showing extensive functional overlap. In this study, in order to better understand shared core Hox functions, we examined kidney development in mice with frameshift mutations of multiple Abd-B type Hox genes. The resulting phenotypes included dramatically reduced branching morphogenesis of the ureteric bud, premature depletion of nephron progenitors and abnormal development of the stromal compartment. Most unexpected, however, we also observed a cellular level lineage infidelity in nephron segments. Scattered cells within the proximal tubules, for example, expressed genes normally expressed only in collecting ducts. Multiple combinations of inappropriate nephron segment specific marker expression were found. In some cases, cells within a tubule showed incorrect identity, while in other cases cells showed ambiguous character, with simultaneous expression of genes associated with more than one