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Zebrafish as an animal model to study renal regeneration after acute kidney injury

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Acute kidney injury (AKI) is a devastating and often lethal condition in which kidney nephron cells are destroyed by damage from ischemia or toxin exposure. While nephron epithelial cells can regenerate after some forms of damage, there is a poor understanding of the cellular and molecular events that mediate nephron regeneration. The zebrafish is an attractive and viable system to study the molecular pathways responsible for nephron regeneration, as its nephrons are simple, yet they maintain the biological complexity inherent to that of higher organisms including mammals. Previous studies have demonstrated that gentamicin-based chemical injury in zebrafish mimics human AKI, but detailed analysis of the cellular events associated with damage was not reported. We generated a novel toolkit of cellular and molecular protocols to perform this analysis in the zebrafish. Next, we extensively characterized the cellular changes resulting from gentamicin injury in the adult zebrafish using our platform of histology and immunohistochemistry techniques. This work has established the timing of renal cell death after injury, identified proliferative compartments within the kidney, and led to the assessment of gene expression changes associated with the regenerative response of proliferating cells. Taken together, these data have provided a greater understanding of the full cycle of regenerative events. Insights from this work can be applied in future translational studies toward the design of chemical genetics screens in the adult and/or embryonic zebrafish to identify renal regeneration pathways and provide novel insights into the signals that orchestrate kidney epithelial regeneration.

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