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Zebrafish model of acute kidney injury sheds new light on cyst formation in ADPKD

Studies of kidney development and repair after injury are difficult in mammals due to complex architecture of metanephric kidney and the inherent difficulty of in vivo imaging in mammals. Transparent zebrafish larvae have simple pronephric kidneys that closely resembles mammalian nephron in segment identity and arrangement. This vertebrate model allows direct in vivo visualization of kidney development and repair after injury. We developed a novel assay of Acute Kidney Injury (AKI) in GFP transgenic zebrafish larvae using violet laser ablation. This technique allows us to directly visualize the sub-cellular, cellular and organ-level interactions driving kidney injury and repair. For example, by using this technique, we showed that collective cell migration is the primary repair mechanism after AKI. It had been recently proposed that rapid cyst induction in conditional mouse models of ADPKD requires a "third hit", and that AKI serves this role. The suggested interpretation of the interaction between AKI and cyst formation is that injury induces proliferative response in kidney epithelia, thus promoting cyst progression. By utilizing our novel zebrafish model of AKI we show that kidney obstruction and not increased cell proliferation is the driving force leading to rapid cyst initiation after injury. We also show that PKD2 mutant zebrafish demonstrate slower resolutuon of transient cysts after acute injury when compared to control siblings. This findings shed new light on the nature of the "third hit" suggested by inducible mouse models of ADPKD.

Biography

Alex Vasilyev received his PhD and MD degrees from Rosalind Franklin University of Medicine and Sciences. He then completed his Residency training in Anatomic Pathology at the Massachusetts General Hospital and a Research Fellowship in Renal Pathology. He became an Instructor in Pathology at the Massachusetts General Hospital/Harvard Medical School, and later, he started as an Assistant Professor in Biomedical Sciences at the New York Institute of Technology, College of Osteopathic Medicine. He studies kidney development, regeneration and pathophysiology using zebrafish as a model.

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