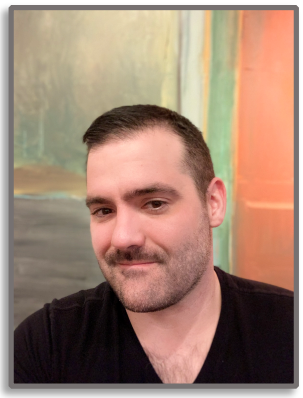

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Awakening the Regenerative Potential of the Mammalian Retina

Dr. Ross Poché is an Associate Professor in the Department of Molecular Physiology and Biophysics at Baylor College of Medicine. His lab utilizes mouse genetics and molecular biology to study the transcriptional and metabolic regulation of retinal development and regeneration. Additionally, to better understand the dynamic nature of the developing retina and the pathological consequence of specific genetic alterations, his lab has developed live, fluorescent microscopy imaging techniques. The lab's long-term goal is to use this multidisciplinary approach to gain significant insight into retinal development, disease, and regeneration to restore sight.

Abstract: In response to retinal damage, the Müller glial cells (MGs) of the zebrafish retina have the remarkable ability to undergo a cellular reprogramming event in which they enter the cell cycle and divide asymmetrically thereby producing multipotent retinal progenitors capable of regenerating lost retinal neurons. However, mammalian MGs do not exhibit such proliferative and regenerative ability. We have identified Hippo pathway-mediated repression of the transcription cofactor YAP as a core regulatory mechanism that normally blocks mammalian MG proliferation and cellular reprogramming. MG-specific deletion of Hippo pathway components Lats1 and Lats2, as well as transgenic expression of a Hippo non-responsive form of Yap (Yap5SA), resulted in dramatic Cyclin D1 upregulation, loss of adult MG identity, and attainment of a highly proliferative, progenitor-like cellular state. Together, our results reveal that mammalian MGs may have latent regenerative capacity that can be stimulated by repressing Hippo signaling. To fully unlock that potential, current efforts are focused on using adeno-associated viral transduction to transiently bypass the Hippo pathway as a means to temporarily reprogram MGs to a progenitor state that is then capable of differentiating into new retinal neurons.

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