Bioelectricity Regulates Regeneration in Vertebrate Eyes

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Regeneration is a complex process that allow injured tissues to be repaired in some animals. However, animals vary in their regenerative ability so an important goal in regeneration is to define a common mechanism. Recent studies have shown spaceflight causes injury to eye tissues, potentially causing long-term vision problems for astronauts. Therefore, investigating the mechanism to allow injury repair minimizes long-term health risk. The clawed frog *Xenopus laevis* displays a remarkable ability to regenerate many injured tissues, including eyes. The vacuolar (V)-ATPase H^+ pump regulates bioelectrical signaling in cells and is expressed during eye development. Its activity is also required for limb regeneration. To investigate if V-ATPase participates in eye regeneration, we use the *Xenopus* eye regeneration model. Previously, we demonstrated that *Xenopus* embryos rapidly regenerated functional eyes within 5 days. Molecular inhibition of V-ATPase blocked eye regeneration, indicating that V-ATPase is required for this process. The block of eye regeneration with V-ATPase inhibition was due to decreased eye stem cell proliferation. Expression of a yeast H^+ pump restored eye regeneration in the absence of V-ATPase activity. This data suggested that the H^+ pump function of V-ATPase is sufficient to initiate regeneration. Overall, our results showed V-ATPase is required for eye regeneration through regulating stem cell proliferation. Further study of V-ATPase may lead to new strategies for developing regenerative therapies.