

Cell Signaling in Planarian Regeneration and Scaling



Animals capable of tissue regeneration can perfectly re-establish their form after diverse injuries, suggesting that systems enabling robust tissue patterning could be central for regenerative ability. Planarians have emerged as a powerful model organism to study wholebody regeneration mediated by adult pluripotent stem cells. Our studies have used the planarian Schmidtea mediterrantea to identify the cell signaling and regulatory principles that allow restoration of a body axis truncated by injury. Using the head-to-tail body axis of planarians as a model, we identified a canonical Wnt/beta-catenin signaling pathway mediated by asymmetric expression of the Wnt inhibitor notum that responds to tissue orientation at the wound site and polarizes the identity of the axis termini in regeneration. Downstream of this early decision step, a specialized stem-cell-dependent pathway is responsible for the differentiation of a signaling center that drives head outgrowth after decapitation. These and other injury-induced responses intersect with constitutive cues that define axis regionalization and enable reversible body scaling over a wide range, and the reestablishment of their domains likely accounts for the cessation of regenerative outgrowth. The ability of mature organs to absorb migratory progenitors buffers against alterations to body-wide patterning that occur after amputation, allowing seamless integration of preexisting and new tissues. Together, these analyses seek to uncover the factors and regulatory logic underlying regenerative growth.

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