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CELL POLARITY

Heads or tails?

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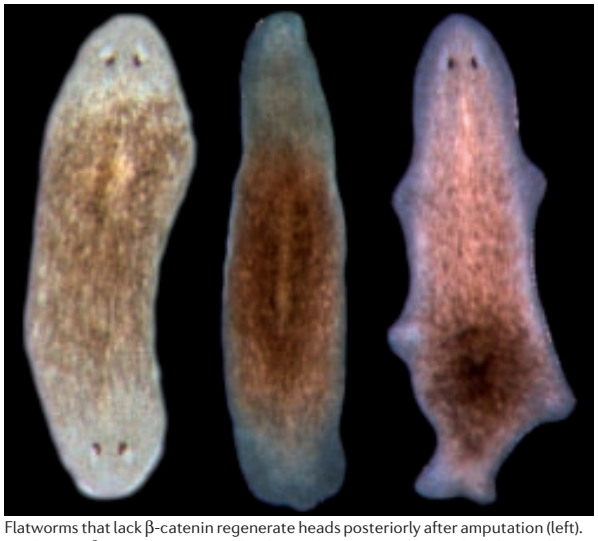
> …the canonical Wnt/β-catenin signalling pathway controls A/P tissue identity during homeostasis and regeneration in flatworms.

Chop the head and tail off a flatworm and a new head grows back where a head should be and a new tail grows back where a tail should be. So, what decides whether it's heads or tails?

Two reports now answer this century-old question. They show that β-catenin, a multifunctional protein that regulates various cellular processes (including proliferation, cell fate specification and differentiation) in both vertebrates and invertebrates specifies and maintains the anterioposterior (A/P) identity of flatworms during regeneration and homeostasis.

As part of a project to systematically analyse the function of signalling pathways in the flatworm *Schmidtea mediterranea,* a group led by Alejandro Sánchez Alvarado cloned and analysed the expression pattern of the core components of the Wnt/β-catenin signalling pathway. Using RNA interference (RNAi), the authors depleted individual pathway components or combinations of components and studied their role during regeneration of the worm head and tail after amputation. They found that animals lacking Smed-β-catenin-1 or Smed-dvl-1 and -2 (the flatworm homologues of β-catenin and its positive regulator dishevelled) formed a head instead of a tail at the posterior wound site. Conversely, depletion of the β-catenin antagonist adenomatous polyposis coli (APC) resulted in animals with two tails. In another, independent study, Christian Petersen and Peter Reddien also identified β-catenin as a determining factor in A/P identity in flatworms.



Flatworms that lack β-catenin regenerate heads posteriorly after amputation (left). Depleting a β-catenin antagonist leads to tail regeneration at both ends (middle). In intact animals, β-catenin elimination yields ectopic heads (right). Image courtesy of K. Gurley, Howard Hughes Medical Institute, University of Utah School of Medicine, Utah, USA.

Next, the two groups performed longitudinal amputation experiments to remove the lateral half of the animals. Normal worms completely regenerated the missing part of the body, but animals in which β-catenin was depleted developed multiple heads along the lateral cut, suggesting that signalling through β-catenin is required to inhibit the head fate regardless of the A/P location of the amputation.

What about intact worms? Is β-catenin important for maintaining polarity and cell fate homeostasis too? The answer is yes: depletion of β-catenin in uninjured animals resulted in the growth of head-like structures.

These experiments suggest that the canonical Wnt/β-catenin signalling pathway controls A/P tissue identity during homeostasis and regeneration in flatworms. The inhibition of the pathway in the anterior region results in the formation of the head, whereas posterior activation determines tail development. The molecular mechanisms that regulate β-catenin activation or repression during this process are still unclear. It will be interesting to investigate if β-catenin has a similar role in the tissues of other animals.

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ORIGINAL RESEARCH PAPERS Gurley, K. A., Rink, J. C. & Sánchez Alvarado, A. β-catenin defines head versus tail identity during planarian regeneration and homeostasis. *Science* 6 Dec 2007 (doi:10.1126/science.1150029) | Petersen, C. P. and Reddien, P. W. Smed-β-catenin-1 is required for anteroposterior blastema polarity in planarian regeneration. *Science* 6 Dec 2007 (doi:10.1126/science.1149943)
FURTHER READING Slack, J. M. W. Metaplasia and transdifferentiation: from pure biology to the clinic. *Nature Rev. Mol. Cell Biol.* **8**, 369–378 (2007)