Ancient gene gives planarians a heads-up in regeneration

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A seldom-studied gene known as notum plays a key role in the planarian's regeneration decision-making process, according to Whitehead Institute scientists. Protein from this gene determines whether a head or tail will regrow at appropriate amputation sites.

Since the late 1800s, scientists have been fascinated by the planarian's amazing ability to regenerate its entire body from a small wedge of tissue. Whitehead Member Peter Reddien and former postdoctoral fellow Christian Petersen recently found that the Wnt pathway—an ancient signaling circuit that operates in all animals—inhibits head regeneration at wound sites in the tiny flatworms. Intriguingly, Petersen and Reddien also noticed that wounding triggers activation of a Wnt gene at injury sites that normally regenerate a head, suggesting that something else must determine whether a wound makes a head or a tail.

In a paper published in the May 13 issue of *Science*, authors Christian Petersen and Peter Reddien describe how the gene notum acts at head-facing (anterior) wounds as a dimmer switch to dampen the Wnt pathway and promote head regeneration. When the head or tail of a planarian is cut off, Wnt is activated. This Wnt activity turns on notum, but only at anterior-facing wounds. In a feedback loop, notum then turns Wnt down low enough that it can no longer prevent a head from forming. In tail-facing wounds, however, notum is not activated highly, a condition that promotes tail regrowth.

"These results suggest that animals 'decide' what needs to be regenerated,

in part, by using cues that indicate axis direction with respect to the wound," says first author Petersen, who is a former postdoctoral fellow in the Reddien lab and currently Assistant Professor of Molecular Biosciences at Northwestern University. "It's telling us that for the head/tail decision, proper regeneration requires sensing and responding to tissue orientation at wound sites."

Petersen and Reddien are intrigued by this new role for notum. Like the Wnt signaling pathway, notum is highly conserved throughout species, from sea anenomes to fruit flies to humans, but little is known about its roles in biology. Because both notum and the Wnt signaling pathway are so evolutionarily ancient, their interaction in planarians may indicate a relationship that is important in other animals as well.

"We anticipate that this phenomenon of feedback inhibition regulating the levels of Wnt activity will be seen broadly in other biological contexts," says Reddien, who is also an Associate Professor of Biology at MIT and a Howard Hughes Medical Institute (HHMI) Early Career Scientist. "Wnt signaling is so broadly studied and important in biology, including for tissue repair and regeneration. notum isn't really on the map for the broad roles Wnt signaling plays in tissue repair, but this work demonstrates the central role it can play."

More information: "Polarized activation of notum at wounds inhibits Wnt signaling to promote planarian head regeneration", *Science*, May 13, 2011.

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https://phys.org/news/2011-05-ancient-gene-planarians-heads-up-regeneration.html