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## Our closest worm kin regrow body parts, raising hopes of regeneration in humans

Michelle Ma  
News and Information



What if humans could regrow an amputated arm or leg, or completely restore nervous system function after a spinal cord injury?

A new study of one of our closest invertebrate relatives, the acorn worm, reveals that this feat might one day be possible. Acorn worms burrow in the sand around coral reefs, but their ancestral relationship to chordates means they have a genetic makeup and body plan surprisingly similar to ours.



An intact, live acorn worm. The head is on the far left, and the worm will be cut in the middle. *Shawn Luttrell/University of Washington*

A study led by the University of Washington and published in the December issue of the journal *Developmental Dynamics* has shown that acorn worms can regrow every major body part — including the head, nervous system and internal organs — from nothing after being sliced in half. If scientists can unlock the genetic network responsible for this feat, they might be able to regrow limbs in humans through manipulating our own similar genetic heritage.

"We share thousands of genes with these animals, and we have many, if not all, of the same genes they are using to regenerate their body structures," said lead author *Shawn Luttrell*, a UW biology doctoral student based at *Friday Harbor Laboratories*. "This could have implications for central nervous system regeneration in humans if we can figure out the mechanism the worms use to regenerate."

The new study finds that when an acorn worm — one of the few living species of hemichordates — is cut in half, it regrows head or tail parts on each opposite end in perfect proportion to the existing half. Imagine if you cut a person in half at the waist, the bottom half would grow a new head and the top half would grow new legs.

After three or four days, the worms start growing a proboscis and mouth, and five to 10 days after being cut the heart and kidneys reappear. By day 15, the worms had regrown a completely new neural tube, the researchers showed. In humans, this corresponds to the spinal cord and brain.

After being cut, each half of the worm continues to thrive, and subsequent severings also produce vital, healthy worms once all of the body parts regrow.

"Regeneration gives animals or populations immortality," said senior author *Billie Swalla*, director of *Friday Harbor Laboratories* and a UW biology professor. "Not only are the tissues regrown, but they are regrown exactly the same way and with the same proportions so that at the end of the process, you can't tell a regenerated animal from one that has never been cut."



The tail end of the worm after being cut. The boxed area indicates where the worm will grow a new head. *Shawn Luttrell/University of Washington*



A close-up view of the cut site and tail end of the worm the day it was cut. *Shawn Luttrell/University of Washington*



Five days after being cut. A rudimentary head, including the mouth and proboscis, has formed. *Shawn Luttrell/University of Washington*



Fifteen days after being cut. A more developed head and neural tube have formed. The worm's nervous system and organ functions are restored. *Shawn Luttrell/University of Washington*

The researchers also analyzed the gene expression patterns of acorn worms as they regrew body parts, which is an important first step in understanding the mechanisms driving regeneration. They suspect that a "master control" gene or set of genes is responsible for activating a pattern of genetic activity that promotes regrowth, because once regeneration begins, the same pattern unfolds in every worm. It's as if the cells are independently reading road signs that tell them how far the mouth should be from the gill slits, and in what proportion to other body parts and the original worm's size.

When these gene patterns are known, eventually tissue from a person with an amputation could be collected and the genes in those cells activated to go down a regeneration pathway. Then, a tissue graft could be placed on the end of a severed limb and the arm or leg could regrow to the right size, *Swalla* explained.

"I really think we as humans have the potential to regenerate, but something isn't allowing that to happen," *Swalla* said. "I believe humans have these same genes, and if we can figure out how to turn on these genes, we can regenerate."

Regeneration is common in many animal lineages, though among the vertebrates (which includes humans) it is most robust in amphibians and fish. Humans can regrow parts of organs and skin cells to some degree, but we have lost the ability to regenerate complete body parts.

Scientists suspect several reasons for this: Our immune systems — in a frenzy to staunch bleeding or prevent infection — might inhibit regeneration by creating impenetrable scar tissue over wounds, or perhaps our relatively large size compared with other animals might make regeneration too energy intensive. Replacing a limb might not be cost-effective, from an energy perspective, if we can adapt to using nine fingers instead of 10 or one arm instead of two.

The researchers are now trying to decipher which type of cells the worms are using to regenerate. They might be using stem cells to promote regrowth, or they could be reassigning cells to take on the task of regrowing tissue. They also hope to activate genes to stimulate complete regeneration in animals that currently aren't able to regrow all tissues, such as zebrafish.

Co-authors are *Kirsten Gotting* of *Stowers Institute for Medical Research*, and *Eric Ross* and *Alejandro Sánchez Alvarado* of both the *Stowers Institute* and the *Howard Hughes Medical Institute*.

This research was funded by the *National Institutes of Health*, *Howard Hughes Medical Institute*, the *Seeley Fund for Ocean Research on Tetiaroa* and a *National Science Foundation* graduate fellowship.

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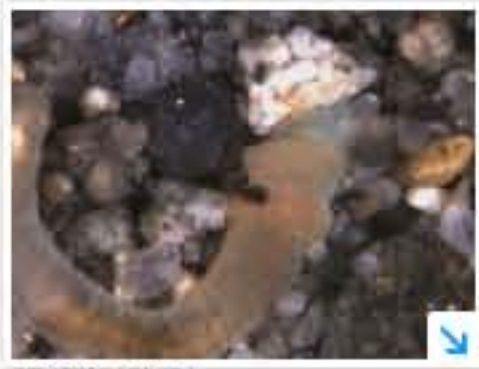
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## Worms could someday help humans regrow body parts



Researchers at the University of Washington hope the next big breakthrough could be to use worms to re-grow body parts.

Dan Cassuto, KING 11:33 PM, PST November 30, 2016



(Photo: KING)



You have more in common with worms than you think.

Researchers at University of Washington's Friday Harbor Lab are studying a certain kind of worm's genes in the hopes humans could learn something from them.

Acorn worms from the Pacific Ocean are capable of regenerating body parts and organ systems.

"These animals are fairly closely related to us," said Shawn Luttrell, a Ph.D. candidate who is mapping out the worm's DNA.

The worms share many genes with humans.

Researchers hope to understand how the worms use their DNA to regrow body parts and if humans could someday do the same thing.

"Interestingly, when you cut these animals in half -- imagine cutting yourself in half -- they will re-grow everything on the top, and regrow everything on the bottom," said Luttrell, who collected the worms from Hawaii and other islands in the Pacific.

"Is it probable we're going to regrow a head? Probably not. But, we could have more extensive nervous system regeneration," said Luttrell, who says science could someday understand how to regrow nerves or body parts, such as fingers or toes.

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'Regeneration gives animals...immortality.'

29/11/2016 11:48

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 **Sophie Gallagher**    
Life Writer at The Huffington Post UK

Scientists are using "immortal" worms to learn how humans could regrow limbs after amputation or restore nervous system function after a spinal injury.

To look at an acorn worm, you wouldn't guess that they were one of our closest invertebrate relatives, but they actually share thousands of genes with humans.



SHAWN LUTTRELL/UNIVERSITY OF WASHINGTON

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Shawn Luttrell, a lead author on the paper, said: "We have many, if not all, of the same genes they are using to regenerate their body structures."

In theory this similar genetic makeup means that we should be able to achieve similar functionality. But that isn't the case.

Acorn worms are able to magically regrow every major body part – including the head, nervous system and internal organs.

Cut them in half, and within 15 days they have replaced their mouth, nose, heart, kidneys, and have even developed a new neural tube (the precursor to a central nervous system).

Billie Swalla, from the University of Washington, said: "Not only are the tissues regrown, but they are regrown exactly the same way and with the same proportions so that at the end of the process, you can't tell a regenerated animal from one that has never been cut."

Obviously for humans, full limb regeneration is still the stuff of sci-fi dreams.

Although we are able to regrow parts of organs and skin cells to some degree, there is something acting as an invisible roadblock to full regrowth. The team says this may be our immune system creating scar tissue, or our size making regrowth too energy consuming.

But the new research suggests that if they are able to unlock the genetic network responsible in acorn worms – in particular a 'master gene' - they might be able to manipulating human genetics to match.

When these gene patterns are known, tissue from a person with an amputation could be collected and the genes in those cells activated to go down a regeneration pathway. Then, a tissue graft could be placed on the end of a severed limb and the arm or leg.

"This could have implications for central nervous system regeneration in humans if we can figure out the mechanisms the worms use to regenerate," said Luttrell.

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UW News

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KOMO Radio's Herb Weisbaum interviews Billie Swalla, professor of biology and director of UW's Friday Harbor Labs, about a new study exploring limb regeneration.

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