

Planaria: A window on regeneration

We humans prefer to avoid getting our limbs cut off. Once your arm is gone, that's it. But life's different for a salamander. Lose a leg? Grow a new one. The same thing happens for starfish, lobsters, and a surprising number of other animals. Snails can even regrow their heads—imagine what the world would be like if humans could do that.

But we can't. Nor can we grow new limbs or even fingers. That's why some scientists are studying animals that can regrow body parts, that is, regenerate. Regeneration is fueled stem cells, cells with the ability to become other types of cells. Scientists hope that learning more about stem cells in other organisms will help us make regeneration possible in humans.

Regeneration in nature

Humans aren't completely without regenerative talents. We heal from wounds and surgeries and we're always creating new skin, new blood, and new linings for our stomachs, intestines and lungs. To a certain extent, our livers can even regenerate after they've been damaged. Amazingly, liver donors can offer up half of their organ and regrow the removed portion. (People have known about these qualities since ancient times. The myth of the Greek god Prometheus says that his liver regenerated every day after eagles ate it as part of a punishment by Zeus.)



Humans' ability to regrow their livers has been known since ancient times. This statue shows the Greek god Prometheus who, as myth tells it, regenerated a new liver after an eagle ate part of it each day. (Photo: Jastrow, Wikimedia Commons)

Many different kinds of animals show some form of regeneration, though most of them are limited to the sort a lizard is capable of, like regrowing a lost tail. A cockroach can regrow a new limb, for example, but the limb itself (thankfully) can't generate a new cockroach. Scientists call this *unidirectional regeneration*. A few animals with relatively simple body plans, however—hydras, sea stars, and anemones among them—demonstrate *bidirectional regeneration*; in other words, they can go both ways. Cut a hydra in half, and you'll get two hydras. Cut it into four pieces, and you'll get four. But few animals can equal the regenerative magic of the common, pond-dwelling planarian.

Meet the almost-immortal planarian

Many people make their acquaintance with a planaria and its regenerative capacities when they cut one up in biology class. Planaria are tiny flatworms that live in freshwater and marine environments, and on plants throughout the globe. A single one can be cut into hundreds of pieces and each will grow back into a whole planarian—a remarkable feat.



Planaria species *S. mediterranea* and *D. dorocephala* swimming together.

Planarians (and other bi-directionally regenerating animals) can use this capability to reproduce asexually, and, in effect, clone themselves. Because of this remarkable ability, one planarian and its genome can be created over and over, giving it a sort of immortality. Just how old is the oldest planaria? No one really knows.

Scientists have recently learned that planaria are full of cells similar to stem cells. These cells are ready at any time to transform into whichever specific type of cell a planaria needs in order to regenerate lost tissue. The ability of these cells to become whatever tissue the body needs is very similar to the capacity of embryonic stem cells in humans and other vertebrates. This similarity makes planaria very interesting to scientists, and their simple bodies and few tissue types make them relatively easy to study. Interestingly, the planarian's stem-cell like cells are distributed throughout their bodies in great numbers, which helps lend them their amazing regenerative qualities.

Any way you slice it

Planarian regeneration stands out for its dramatic scope, its rapid pace, and the mechanisms that make it possible. And not only can the pieces of a sliced-up planarian each grow into a new flatworm, but regeneration happens quickly: It only takes a week or two for each piece to turn into a miniature version of the original flatworm.

Planaria can also work a sort of magic trick while regenerating: Imagine you're nothing but a tail trying to regrow a head. How will you eat? Or what if you're a head with no gut to digest things? The answer is that planaria *feed off themselves*. As a head grows back, for example, cells in the tail end will self-destruct and provide the regenerating animal with the energy needed to survive. Over time, the tail portion will shrink—to a proportion that exactly matches that of the head it's regenerating. Once it's whole again, it will begin to feed and grow back to a normal size. How it manages to do this proportion-readjustment trick is one of the questions researchers are trying to answer.

How do they do it?

Exactly how planarians work their regenerative magic is the million-dollar question that scientists would love to answer. Researchers have an inkling of some of the genes involved, but the picture is far from clear. What they do know is that the progress of regeneration can be followed by looking at certain features as they develop.

When a planarian loses its head (or its tail, or other chunk of itself), a regeneration blastema will begin to form at the site of the wound. The blastema is an area of whitish cells that are in an embryonic-like state, filled with stem cells that are able to become any of a number of kinds of cells. Over time, these cells will divide, more and more of them will differentiate, and the form of the missing body part will take shape. If scientists could understand how such cells get activated to make more of themselves, or to become the appropriate new cell types, they might learn how to trigger such responses in humans, allowing us to regrow our own tissues under certain conditions. There



Both the head and tail have been removed from this planaria, *S. mediterranea*. This species is often used for research. Both ends of the animal will grow back in just eight days.

are many theories as to how planarians regenerate, but for the moment, we are far from understanding it—and even farther from knowing how to harness the potential in ourselves.

Genes in common

Humans may not look much like flatworms, but there's a surprising overlap between our genome and that of a planarian due to our distant yet common past. At least one of the genes we share is expressed in both planarian and human stem cells and is likely to be involved in regeneration. The planarian form is called *piwi* (pronounced PEE-wee), and the human form is known as *hiwi*. It turns out that planarian *piwi* is important for making stem cells that will divide to produce new, properly functioning daughter stem cells. In humans, the *hiwi* gene is expressed in sperm and eggs, as well as in some stem cells like those that generate new blood cells. Could it be part of a potential mechanism to trigger our own stem cells into action? The answer to that isn't yet clear—we still know very little about the fundamental biology of our own stem cells. Sharing many of our genes and masters of an art that is one of the most impressive in the living world, planaria offer a great model to learn from.

Regeneration and inheritance

In the late 1800s, Thomas Hunt Morgan, the researcher who brought us fruit fly genetics, began his study of inheritance by looking at regeneration in planaria. The subject drew his interest because it formed a problem in a theory of inheritance



put forth by German biologist August Weismann. Weismann's idea, known as the *germ plasm theory*, postulated that each individual cell inherits only what material it needs to become a certain kind of cell. In other words, skin cells would contain only the material for skin cells, and so on. If this were true, Morgan argued, then regeneration wouldn't be possible, and the headless body of a planarian wouldn't be able to regenerate a brain.

We know today, of course, that all cells in an organism inherit the same complement of genetic material, and that stem cells drive the regeneration process. Those facts were unknown in the 1890s, though, and regeneration continued to baffle Morgan until he turned his attention to the fruit flies that made him famous. But his work wasn't for naught: He published an informative volume on regeneration as well as discovering that he could cut the flatworm into a maximum of 279 pieces—and each one would grow into a new planarian.