LIZARD TAILS *hold* HIDDEN SECRETS

1. WHAT WE KNOW

Lizards have the ability to self amputate when they are trying to sneak away from a predator. This means that when a predator pulls on the tip of a lizard's tail they are able to fracture off their tail. Lizards have intervertebral autotomy where the tail breaks in between two vertebrae. By doing this lizard's are able to get away from their predators quickly and when their tail comes off it actually is able to wiggle and serves as distraction giving the lizard more time to escape. However after they lose their tail the lizard is able to regenerate a new tail, but it is not a perfect replica. Current research shows that the lizard is able to regrow cartilage, but they are not able to make bone. Dr. Alibardi, an associate professor in the biology department at the University of Bologna, writes that lizards are able to regenerate cartilaginous tails but when it comes limb regeneration cells will proliferate for about two to three weeks, but then it stops due to an inflammatory response which is not seen in the lizard tail. Other research has been conducted to stimulate limb regeneration by implanting nervous tissues or growth factors on the lizard limb, however ultimately scar tissue develops and stops limb regeneration. There currently is a plethora of research on regeneration that looks into the different signaling pathways so that tail regeneration can be extended to both lizard and human limbs. Keep reading to learn more!

Image source

Image source

Image source

2. CURRENT RESEARCH

Lizards have this cool ability to regrow their tails, which is something humans can't do after an injury. Scientists are curious about how lizards manage this, so they studied the genes and cells involved. They found that when a lizard loses its tail, special cells called fibroblasts kick into action. These fibroblasts have specific genes, like spp1+ and sulf-1, that trigger the growth of new cartilage, allowing the tail to regrow.

To understand this process, scientists looked at the RNA (a type of genetic messenger) in the cells of regenerating lizard tails. They compared two main types of cells, fibroblasts, and phagocytes. Fibroblasts are like construction workers; they get activated by the spp1+ gene and produce cartilage with the help of sulf-1 gene. Phagocytes, on the other hand, assist by turning on certain genes in fibroblasts, starting a signaling pathway called Hedgehog that contributes to the regrowth of new cartilage to make the tail.

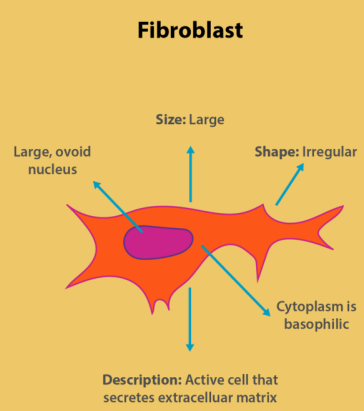


Image source

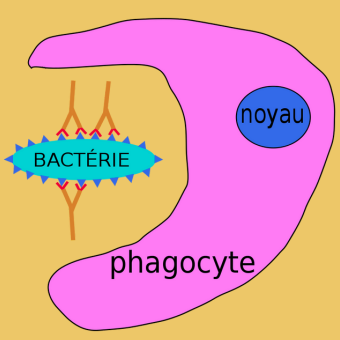


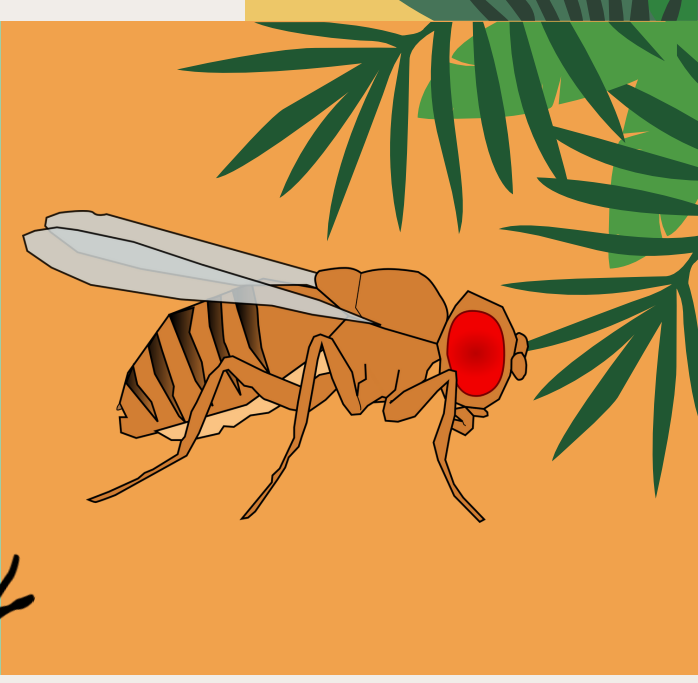
Image source

BUT WHAT EXACTLY IS HEDGEHOG SIGNALING AND HOW DOES IT ALLOW THE LIZARD TO REGROW A NEW TAIL?

WHAT EVEN is HEDGEHOG SIGNALING

1. WHERE DOES THE NAME COME FROM?

The gene was found in mutant drosophila embryos that had a spiky appearance that looked just like a hedgehog.



2. WHAT DOES IT DO?

the pathway serves as a messaging system that helps the lizard's body grow properly by providing the cells with instructions telling them how to form different body parts and develop correctly.

3. HOW DOES IT WORK?

Stimulated by: increasing concentrations of sonic hedgehog (Shh), a hedgehog protein that are released when the body is in need of tissue development

Regulated by: expression of the Sulf1 gene

Inhibited by: Patched (Ptch) protein, it has receptors for Shh allowing it it inhibited the Smoothened (Smo), the protein that transmits the hedgehog signal

4. HOW DOES CARTILAGE FORM?

Fibroblasts and phagocytes lead to cartilage formation. There are two genes controlling fibroblast activation in the tail only.

spp1 gene activates fibroblasts and forms the blastema, a small stump that houses cells resembling the original limb bud, from which the new tail emerges

sulf1 gene activates fibroblasts to become cartilage under the control of hedgehog signaling

WHAT THEY FOUND & WHAT IT MEANS

Scientists wanted to figure out which chemicals were important to tail regeneration in lizards. They took the cells from a donor lizard and then treated them with a bath of either the chemical PBS or Clodronate Liposome and labeled them with markers that they could see under a microscope.

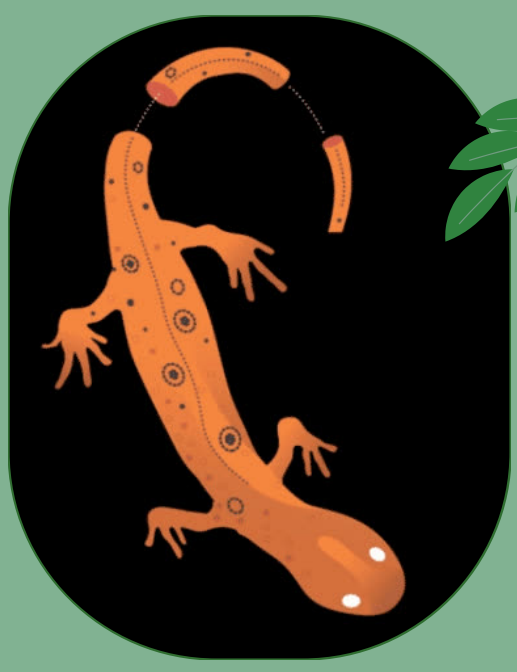


Image source

They found that PBS was important for growth when they returned the cells to a recipient lizards. This technique was also used to check whether an amputated leg cell could also help regenerate a tail, but they found that this is not able to occur. But it doesn't end there!

MORE REGENERATION RESEARCH

Image Source

SKELETON GROWTH

On their own lizards are able to regenerate their tail after amputating it, but it is solely made of cartilage but that's not as good as the original tial they had! However some amazing work has been done Dr. Thomas Lozito and his lab at the University of Southern California Keck School of Medicine. They have been able to create lizard tails that have dorsoventral patterning. This is a fancy way of saying that the lizard tails now have nervous and skeletal tissue on the top, or the dorsal side, and there is cartilage on the lower side, or the ventral side. This is the first time a research lab has been able to create this patterning. Normally when lizards lose their tails, they can grow them back, but the new tails aren't exact copies of their old ones. The new tails have tubes inside called ependymal tubes, which are very similar to the tubes in their tails when they were babies.

These tubes in the new tails make something called cartilage, which is the tissue that makes up humans ears and nose. But here's the big thing: in the new tails, this cartilage doesn't grow in the same way as it did when the lizards were babies.

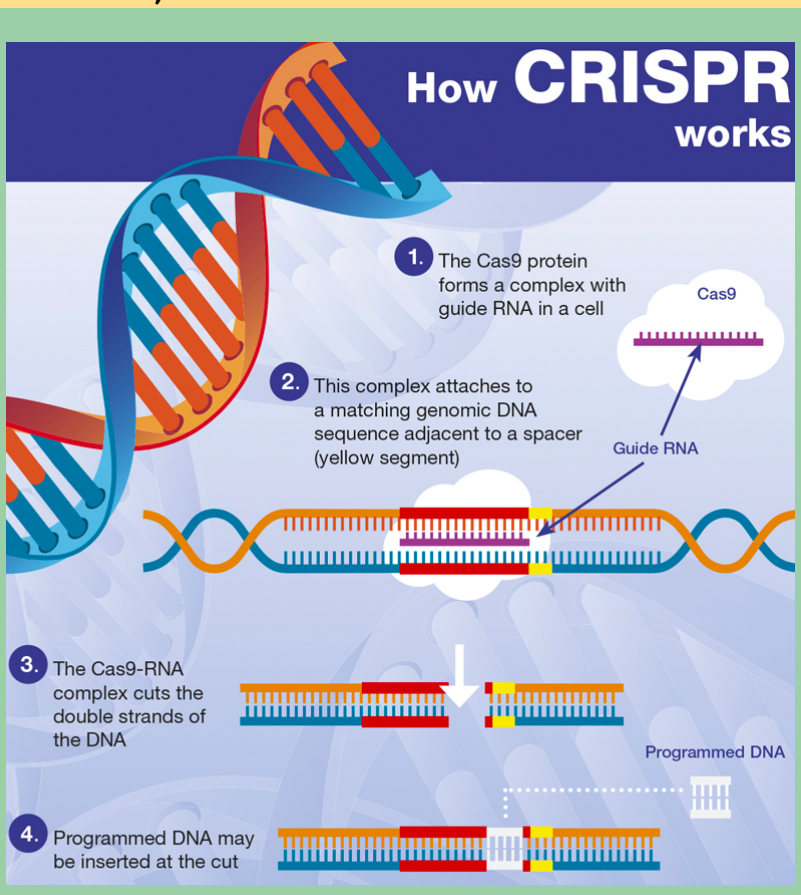


Image Source

Regenerated tail in the green anole lizard

Image Source

There are special cells called neural stem cells inside these tubules. These cells are important because they help make different parts of the lizard's tail. When they studied these cells from baby lizards, they found that if they changed some genes in the neural stem cells using CRISPR, which is a tool used to modify DNA, the new tail that grows back in an adult lizard is different as it doesn't make cartilage in the same way.

This discovery is fascinating because it shows that by changing these special cells from a baby lizard and then implanting them into adult lizards, scientists may be able to help make new tails look practically identical to the original ones. If this is the case then there is the possibility of bone regrowth in a lizard's tail which would be a huge milestone for regenerative medicine research. If this is able to be applied to humans there is the chance that we could regenerate bone and a variety of other tissues after an accident which could eliminate the need for prosthetics and increase the quality of life for many people

Image Source

WHAT ARE *some* TRANSLATIONAL APPLICATIONS?

1. REGENERATIVE MEDICINE

In humans after an injury our body responds by initiating an inflammatory response which helps to get necessary white blood cells to the site to reduce the spread of infection however that prevents regeneration ability because scar tissue grows. As the research advances, they are looking for ways to activate the specific hedgehog signaling pathway in humans so that we can regenerate our own tissues

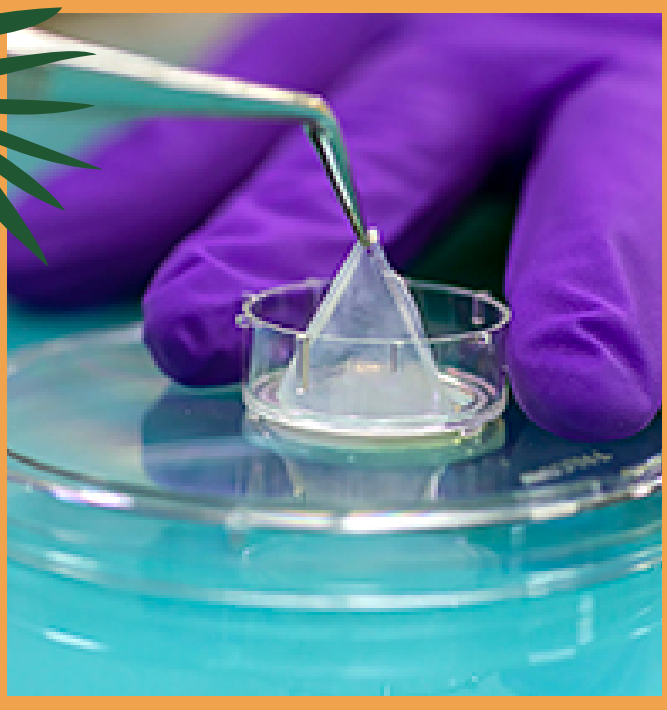


Image source

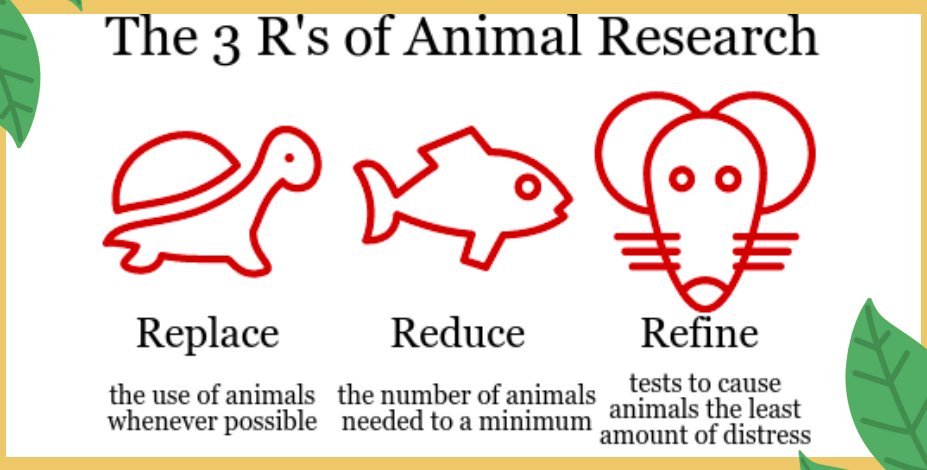


Image source

2. TISSUE ENGINEERING

In the field of research there are three R's that every researcher is thinking about in the back of their mind. They are replace, reduce and refine. Replace means to try to not use animals whenever possible. Reduce means to limit the number of animals used in a study. Refine means to ensure that you are using methods that cause animals little stress. However since lizards can regenerate tissue, scientists are looking at ways to make synthetic tissue that grows in petri dish which knocks out the need for an animal model and takes care of all three of the R's of research

3. WOUND HEALING

Lizards are able to initiate the wound healing cycle much faster than humans for a variety of reasons. After losing their tail the healing process is initiated to protect against infection to keep moisture. This helps to decrease blood loss and increase their chance of survival in the wild and allow for a new tail to grow back because of their quickly dividing stem cells.

Image source