

Limb Regeneration



Topics:

Skin

Muscle

Bone

Axolotls

Stemcells

Limb

Regeneration

There is a lot that goes into limb regeneration, but for humans it is currently an impossible task.



So we are going to talk about the organ systems in the human arm and how other species regrow limbs.

By Iliamna O'Malley




What is skin?

The skin is made up of three layers and each layer has an important function.

The three layers are:

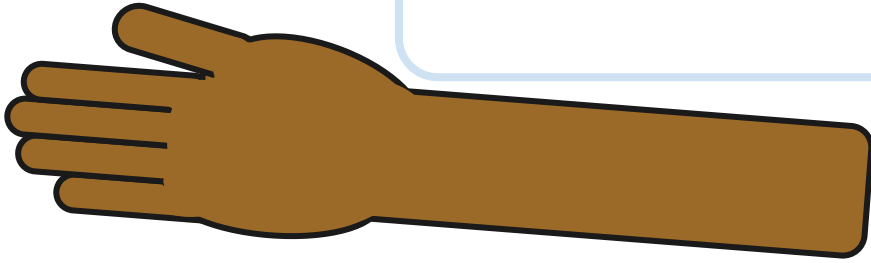
- The Epidermis
- The Dermis
- The Hypodermis



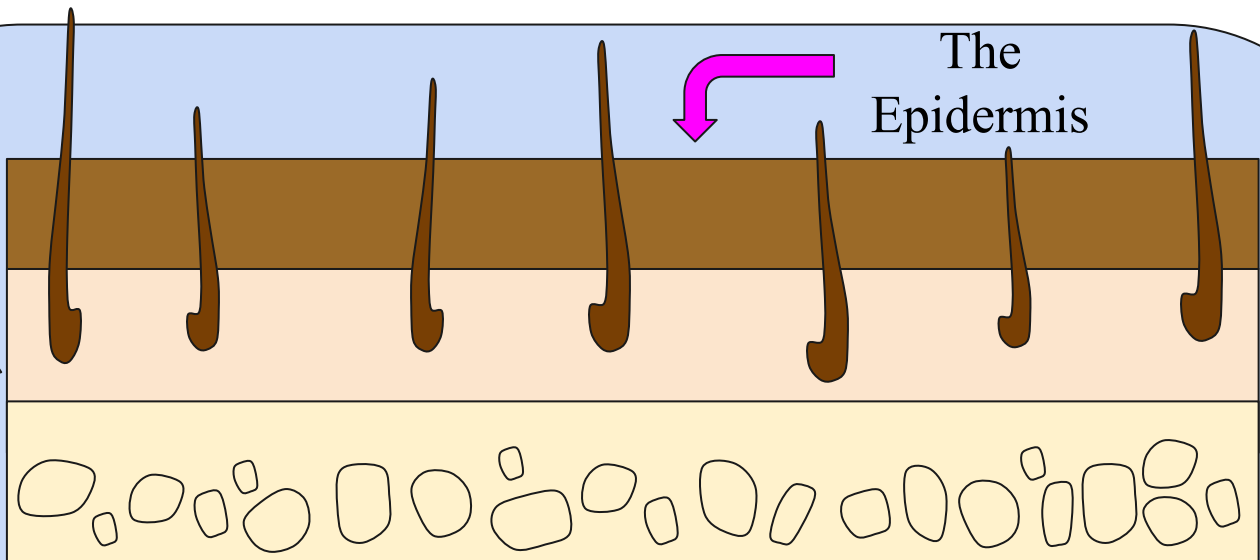
The skin is actually the body's largest organ! It has a job to cover the entire body in order to protect you.

Epidermis - Dermis - Hypodermis

The Epidermis is the outermost layer of your skin. It is the skin you see on your arm and where the color of your skin is!



Underneath the Epidermis is the other two layers of the skin, the Dermis and the Hypodermis.



The Dermis is the second layer of the skin, it is right under the Epidermis. This has blood and lymph vessels, nerves, sweat glands, and other structures. Your hair grows from here!

The hypodermis is also called the subcutaneous layer. This is a layer directly below the dermis and has the job to connect the skin to the fibrous tissue of the bones and muscles. Fat lives here.



What is Muscle?

There are actually three main types of muscle tissues!

- Skeletal
- Cardiac
- Smooth Muscle

Muscles main job for your body is to help with movement.

What is Bone?

Bone is actually a tissue, but Bones are organs!

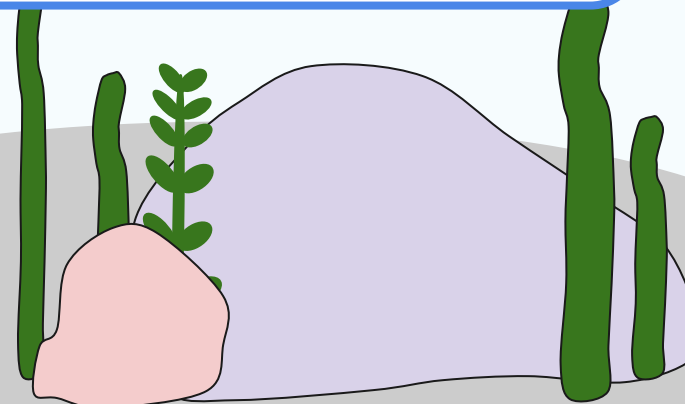
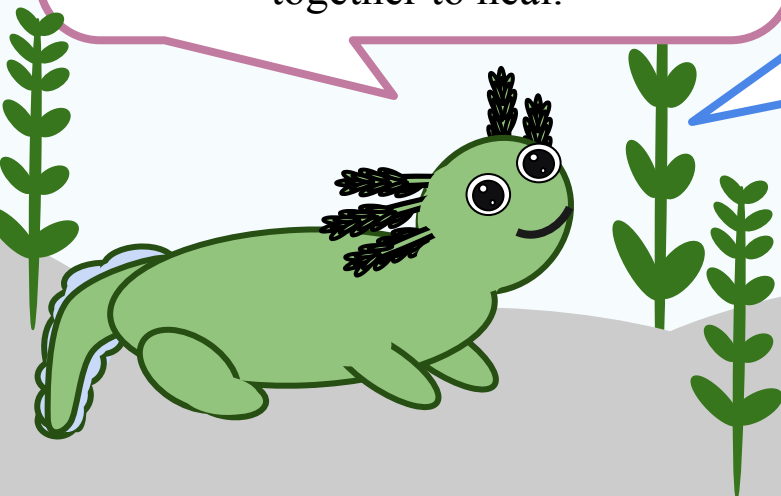
-Bones provide support and protection for the body and organs.

The structure of bones is dependent on the type of bone. Bones work together with muscles to help you move.

The body is a lot more complicated than this, but we are not here to talk about every little thing.

What I want to do is talk to you about how those three systems work together to heal.

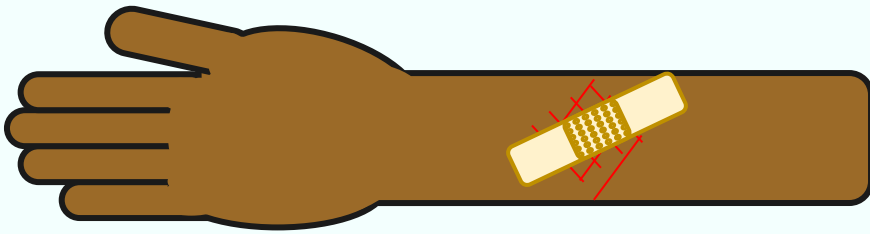
I am an axolotl, and you may have seen others like me in this book. We heal differently than you do, unlike you I can actually regrow limbs!





Your body replaces the cells in the epidermal layer of your skin constantly.

Let's talk about your arm for an example. Your arm is constantly touching things, rubbing against things, getting cuts or scrapes, or taking even more serious damage.



Do to all of this the cells on the surface of your skin need to be constantly replaced. This is achieved because of how the Epidermis layer functions. The cells in the Epidermis have layers, and those cells divide from the bottom of this layer and move up to replace old cells.

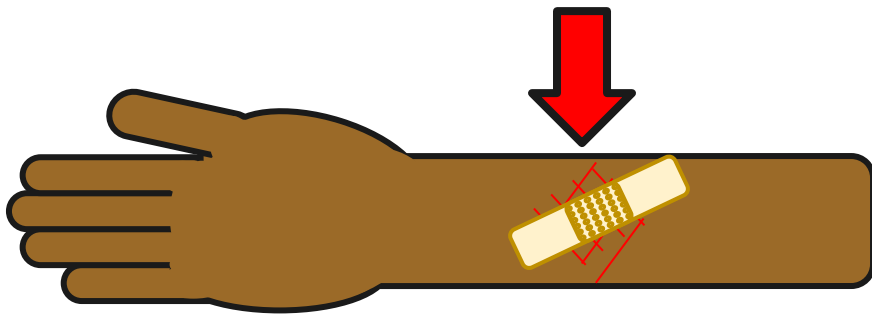
When you get a small cut or injury your cut will heal by eventually fully replacing the missing or dead cells.

So what happens when you have a serious injury? Like a missing arm?

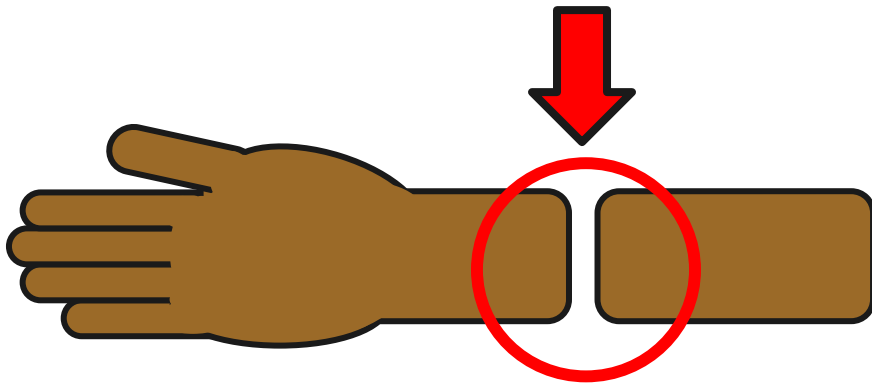


There are five different systems in this region of the arm. The Integumentary, Skeletal, Cardiovascular, Muscular, and Nervous system.

Let's say that right where the bandaid lays is where the arm is severed at. It is after your elbow, but before your wrist.



This section of the arm is called the forearm!



In this area of the forearm there are layers of skin, muscle, and bone, along with some nerves and blood vessels.



Organ Systems In The Forearm:

Integumentary: This system is the outermost layer of your body, the skin, hair, nails, and glands.

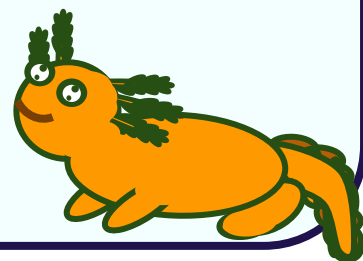
Cardiovascular: This system is your heart and blood vessels.

Muscular: This system is made of the skeletal, smooth, and cardiac Muscles.

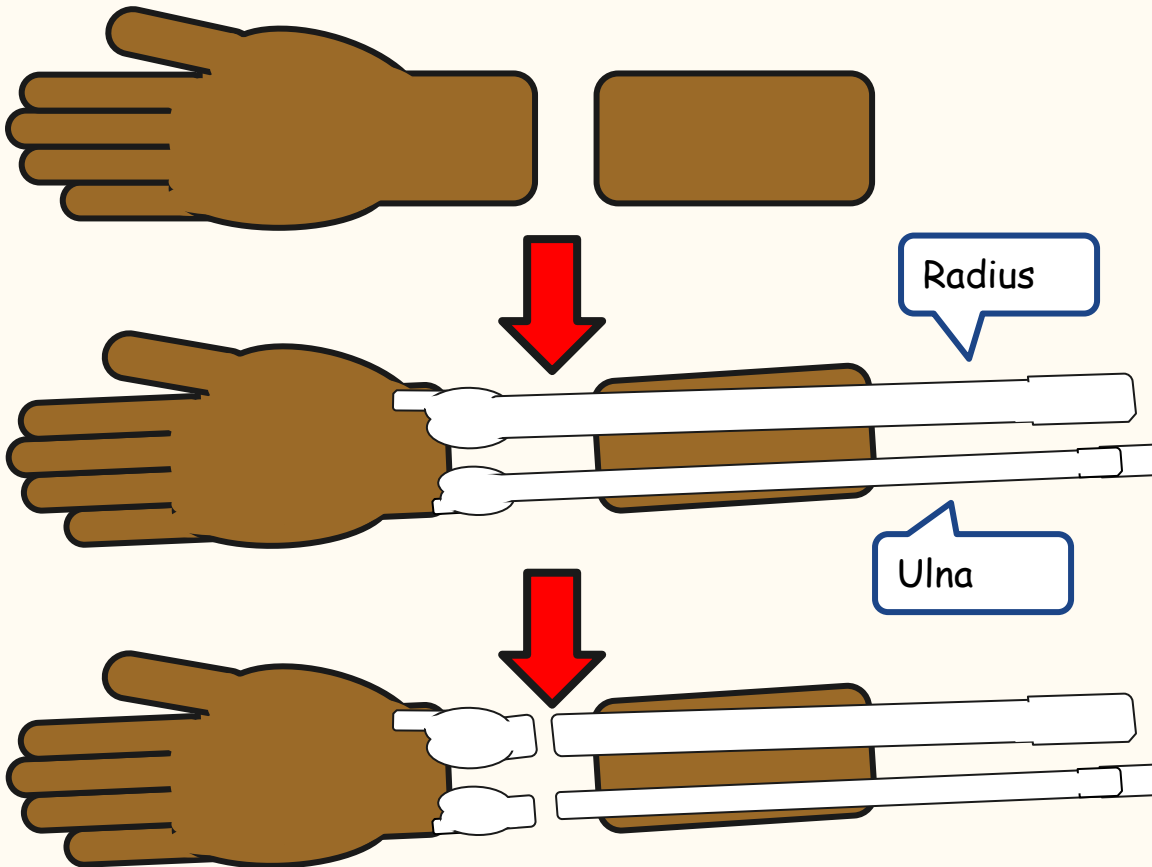
Skeletal: This system is the bones and cartilage in your body.

Nervous: This system is your brain, spinal cord, and all your nerves.

Did you know that as a baby you have around 260 bones in your body, but as an adult you only have around 206?



When this arm is severed it has been cut through all those organ systems. In order for an arm to heal, it either needs to be reattached at every system, as we cannot regenerate limbs.



There are two bones that have been cut, the Radius, and the Ulna

There are four main parts when it comes to bone repair:

Step 1: A hematoma forms at the break.

Step 2: The internal and external calli form.

Step 3: The cartilage of the calli is then replaced by trabecular bone.

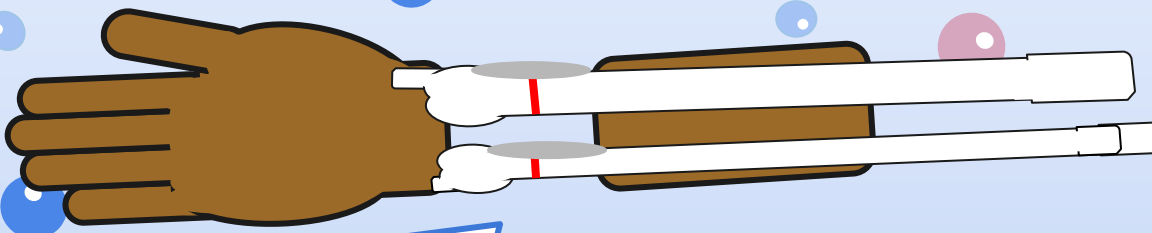
Step 4. The bone undergoes remodeling.

In order for the bones to heal they have to have supporting plates attached to them on each side. This helps them heal straight.



Resource: Page 240

Senior Contributing Authors. (2013). Anatomy & Physiology. Retrieved June 17, 2022, from <https://assets.openstax.org/oscms-prodcms/media/documents/AnatomyandPhysiology-OP.pdf>

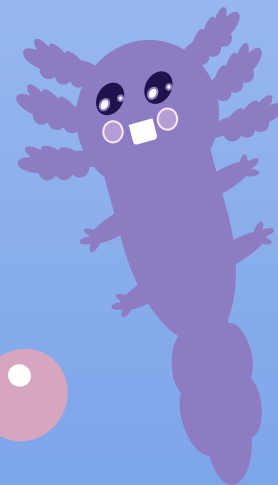


Once plates have been placed, the bone can begin to properly heal. When this bone heals, it is actually undergoing a kind of reconstruction.

The process broken bone undergoes:

- Chondrocytes from the endosteum create a internal callus. They do this by secreting a fibrocartilaginous matrix between the two ends of the broken bone. While they do that the the periosteal chondrocytes and osteoblasts create an external callus of hyaline cartilage and bone around the outside of the break.
- Then over time the osteoclasts resorb the dead bone. Osteogenic cells become active, divide, and then differentiate into osteoblasts. The cartilage in the calli is replaced by trabecular bone due to the endochondral ossification process.
- The internal and external calli come together and compact bone replaces spongy bone at the outer margins of the fracture. This is when healing is considered complete.

That was a lot of big words, but in short the bone forms new bone over time by the bone-forming osteoblasts. During this healing process the osteoclasts resorb dead bone. So the body is able to add new bone and take away dead bone!



Muscles

There are three layers of muscles in the forearm, the superficial layer, the intermediate layer, and the deep layer. The superficial layer: flexor carpi ulnaris, flexor carpi radialis, palmaris longus, and the pronator teres.

Intermediate layer: The flexor pollicis, the flexor digitorum superficialis, and the flexor digitorum profundus.

Deep layer: Pronator quadratus

“The pronator quadratus (PQ) is a quadrilateral muscle located on the volar surface of the distal forearm...”
(Snelling, 2021)

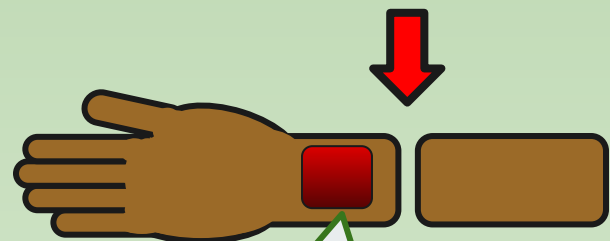
How the pronator quadratus functions is it produces forearm pronation by acting on the proximal radioulnar joint. This makes the head of the radius pivot around the ulna.

This action is turning your palm posteriorly or inferiorly. This action is aided by the pronator teres and the brachioradialis muscles in your forearm.

There are a lot of muscles here so we are going to focus on one in particular, the pronator quadratus.



The reason we are talking about this muscle in particular is because the injury we are talking about would directly affect it.



The pronator quadratus would be in this area, next to the wrist. So where the arm is severed would disconnect that muscle, and area, from the rest of the forearm.

Resource: Page 246

Senior Contributing Authors. (2013). *Anatomy & Physiology*. Retrieved June 17, 2022, from <https://assets.openstax.org/oscms-prodcms/media/documents/AnatomyandPhysiology-OP.pdf>

Citation:

Snelling, P. J., Keijzers, G., & Ware, R. S. (2021). *Point-of-care ultrasound pronator quadratus hematoma sign for detection ...* *Journal of Ultrasound in Medicine*. Retrieved June 14, 2022, from <https://research-repository.griffith.edu.au/bitstream/handle/10072/408221/Snelling475123-Accepted.pdf>

Veins

There are two main veins in the forearm, the superficial veins and the deep veins.

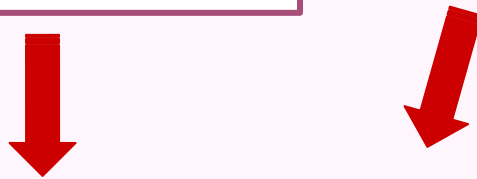
Superficial veins: The cephalic and basilic veins.

Deep veins: The radial, ulnar and the anterior and posterior interosseous veins.

Nerves

There are three main nerves that are in the forearm, the median, ulnar, and radial nerves.

The ulnar nerve in particular has the function to provide motor nerves to part of the forearm and a majority of the hand.



So why is this important?

Just like muscles, the veins and nerves in your arm need to be reattached one by one. Once the bone is reattached, the rest of the organ systems need to be reattached one by one.

Did you know that in order to see your veins they can use imaging devices to make it easier?

“For vein localization, transillumination, photoacoustic and near infra-red (NIR) imaging techniques are widely used.”
(Shah, 2010)



Resource: Page 246

Senior Contributing Authors. (2013). Anatomy & Physiology. Retrieved June 17, 2022, from <https://assets.openstax.org/oscms-prodcms/media/documents/AnatomyandPhysiology-OP.pdf>

Citation:

Z. Shah *et al.*, "Deep Learning-Based Forearm Subcutaneous Veins Segmentation," in *IEEE Access*, vol. 10, pp. 42814-42820, 2022, doi: 10.1109/ACCESS.2022.3167691.

Axolotl Regeneration

Hi!



So what does this have to do with me? Well, I am an axolotl! Unlike you, I have the ability to regrow limbs, so noone has to reattach my arm if it gets cut off!

Axolotl's regeneration involve stemcells and their ability to have the cells at the injury site to revert back to stem cells.



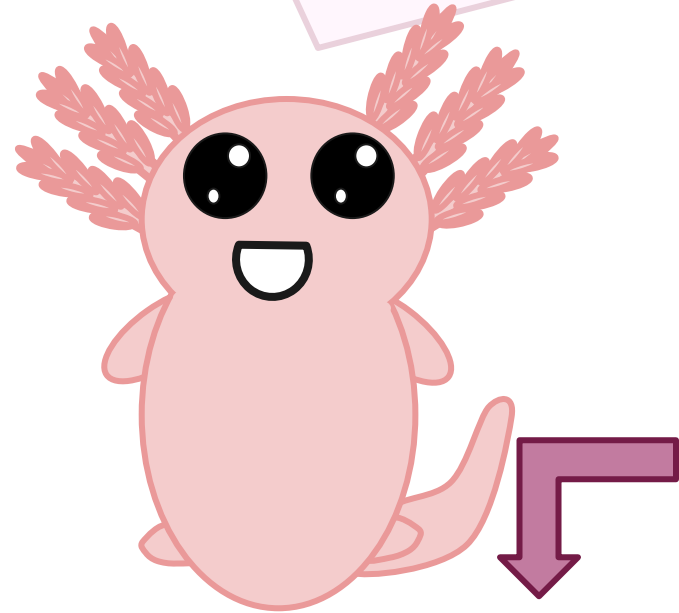
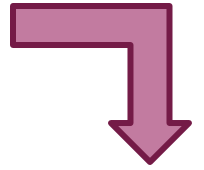
There are only a few certainties when it comes to how axolotl's regenerate limbs, one necessary thing is the fibroblast growth factors. "Signaling mediated by members of the fibroblast growth factor (Fgf) family is necessary for normal limb development and for limb regeneration in the salamander *Ambystoma mexicanum* (axolotl)..." (Glotzer, 2022)

So when I lose a limb, my body is able to work hard and regenerate the lost limb. So there is no need for me to keep the cut off part, I will just get a whole new one!

Citation:

Glotzer, G. L., Tardivo, P., & Tanaka, E. M. (2022, May 19). *Canonical Wnt Signaling and the regulation of divergent mesenchymal FGF8 expression in axolotl limb development and regeneration*. eLife. Retrieved June 17, 2022, from <https://elifesciences.org/articles/79762>

There is a wonderful article that explains how my body works called, Canonical Wnt signaling and the regulation of divergent mesenchymal Fgf8 expression in axolotl limb development and regeneration, and it talks all about what my body does!



“When a limb amputation is performed, anterior cells express *Amex.Fgf8* and posterior cells express *Amex.Shh*, initiating a positive feedback loop in which *Amex.Fgf8* and *Amex.Shh* reciprocally maintain each other’s expression: prolonged expression of both signaling molecules sustains blastema growth and limb regeneration.”
(Glotzer, 2022)

“Limb regeneration in the axolotl proceeds through the formation of the blastema, a structure that resembles the limb bud, both at the morphological and transcriptional level... In both the axolotl limb blastema and limb bud, *Amex.Fgfs 8, 9, and 17* are expressed in the mesenchymal compartment, unlike in other vertebrates, while *Amex.Fgf4* transcription is negligible or absent...Restriction of *Amex.Fgf8* expression to the mesenchymal compartment is to our knowledge unique to the salamander limb, where it serves a crucial role in connecting positional identity with growth and patterning during limb regeneration.”
(Glotzer, 2022)

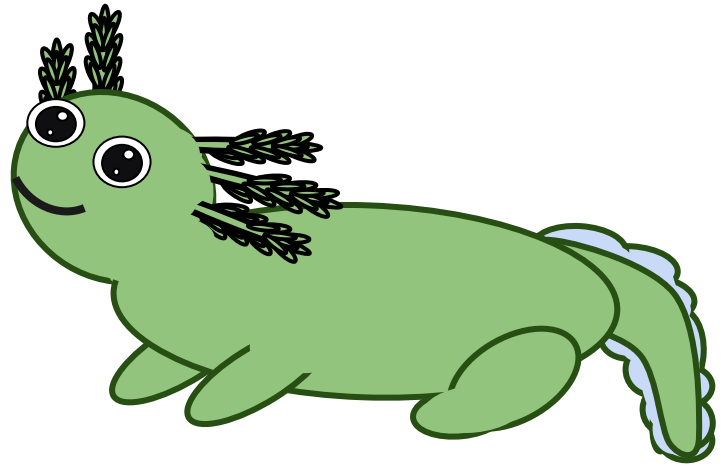
I know, a lot of big words, but what it is saying is that I am unique and my body is able to perform extra steps to force my cells to regenerate my limb!

Citation:

Glotzer, G. L., Tardivo, P., & Tanaka, E. M. (2022, May 19). *Canonical Wnt Signaling and the regulation of divergent mesenchymal FGF8 expression in axolotl limb development and regeneration*. eLife. Retrieved June 17, 2022, from <https://elifesciences.org/articles/79762>

Right now the main focus on me is my stem cells and my blastoma! My blastomas are cells that are known as regeneration-competent limb progenitor cells. Blastomas can be derived from abnormal stem cells. My limb regeneration cells can be called limb blastoma stem cells. Stem cells are important because these cells are capable of evolving into many different types of specialised cells. Which is why it is so amazing that when I lose a limb, somehow my body evolves the cells at the wound into a regenerative cell. So I grow my limb back!

So be safe out there because if you lose an arm, you will need surgery to reattach it!



Biggest takeaways:

- The human body is complicated, but unable to regenerate limbs.
- The forearm has many organ systems, all working together to keep your arm functioning.
- Each system needs to be physically reattached in order for your forearm to work again.
- Axolotl's are able to regenerate limbs due to their body's functions and stem cells.

Thank you for reading my book!

The human system is a lot more complicated than it is described in this book, I encourage you to research it more because it is fascinating!

Citations:

Glotzer, G. L., Tardivo, P., & Tanaka, E. M. (2022, May 19). *Canonical Wnt Signaling and the regulation of divergent mesenchymal FGF8 expression in axolotl limb development and regeneration*. eLife. Retrieved June 17, 2022, from <https://elifesciences.org/articles/79762>

Senior Contributing Authors. (2013). Anatomy & Physiology. Retrieved June 17, 2022, from <https://assets.openstax.org/oscms-prodcms/media/documents/AnatomyandPhysiology-OP.pdf>

Snelling, P. J., Keijzers, G., & Ware, R. S. (2021). *Point-of-care ultrasound pronator quadratus hematoma sign for detection ...* Journal of Ultrasound in Medicine. Retrieved June 14, 2022, from <https://research-repository.griffith.edu.au/bitstream/handle/10072/408221/Snelling475123-Accepted.pdf>

Z. Shah *et al.*, "Deep Learning-Based Forearm Subcutaneous Veins Segmentation," in *IEEE Access*, vol. 10, pp. 42814-42820, 2022, doi: 10.1109/ACCESS.2022.3167691.

Z. Shah, et al. (2010). *Deep learning-based forearm subcutaneous veins segmentation*. IEEE Xplore. Retrieved June 14, 2022, from <https://ieeexplore.ieee.org/document/9758711>

Resources:

Senior Contributing Authors. (2013). Anatomy & Physiology. Retrieved June 17, 2022, from <https://assets.openstax.org/oscms-prodcms/media/documents/AnatomyandPhysiology-OP.pdf>