A whole lotta axolotl to love

Filed to Random Walk

Posted by Shawnna Buttery | Published February 10, 2017, 09:00

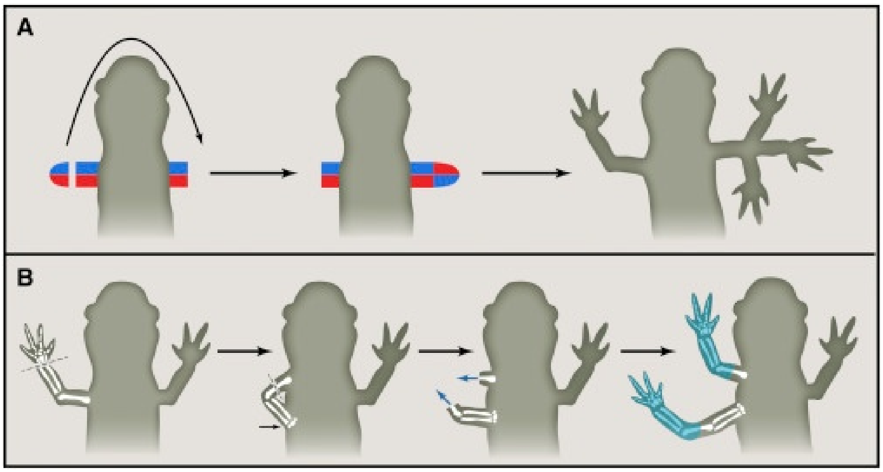
The cover of the January 17 issue of *Cell Reports* is graced by a cute little amphibian called axolotl, also known as the Mexican salamander (*Ambystoma mexicanum*). This adorable creature led me down an internet rabbit hole to discover more about the science behind this fascinating model organism.

The name axolotl has its origins in Aztec mythology: Xolotl was the god of death and lightning who guided the sun through the underworld each evening. The story goes that Xolotl became paranoid that the other gods were plotting to kill him, so he morphed into an axolotl to hide in Lake Xochimilco near Mexico City. This mythology is satisfying for its explanation of the limited ecological range of this unusual animal, but in reality amphibians are often found in a very specific habitat because they require relatively stable temperatures and both wet and dry environments.

Unfortunately for the axolotl (as well as other amphibians), these limitations make them more susceptible to habitat loss. Population growth and development of Mexico City, coupled with the introduction of non-native fish during an attempt at fish farming, led to the decline of its populations in the wild. It certainly didn't help that the meat is said to be delicious. Today, the axolotl is listed as critically endangered, with very few remaining in the wild.

Luckily, the axolotl population is thriving in the laboratory. It has been used for research since 1864 and has become a popular model organism due to its ease of breeding (especially in comparison with other salamanders) and its large embryos (allowing for easy imaging and manipulation). Axolotl is also unusual for its neoteny, which means it keeps its larval traits into adulthood. Metamorphosis into a salamander is rare for an axolotl, but it can be induced by treatment with iodine or with the thyroid hormone thyroxine. Most salamanders express this hormone, which the axolotl has lost; interestingly, axolotl still has the hormone receptors, which explains why it can respond to added thyroxine. Comparing the frequency of metamorphosis in wild-caught versus domesticated stocks suggests that captive axolotls are now fully neotenic due to artificial selection.

Perhaps axolotl's most interesting feature to scientists is its power of regeneration and healing. Like other amphibians and reptiles, axolotl can easily and repeatedly regenerate its limbs, tail, jaw, skin, and even spinal cord and brain. Amazingly, the process seems to be independent of where the limb is cut, and the animal can regenerate the same limb perfectly multiple times without any scarring at the site of amputation. Axolotls can also receive transplanted organs, limbs, and even heads without any loss of function or any problem with rejection. Scientists hope to dissect how axolotl performs these amazingly robust feats of regeneration, with the ultimate goal of applying these lessons to human regenerative medicine.



Limb regeneration in the salamander was first observed by Italian scientist Lazzaro Sallazani over 250 years ago. Some of the initial experiments on the process of regeneration read like the lab notes of a mad scientist. As detailed in a Leading Edge Review in *Cell*, if you graft regenerating tissue from the right arm to the left arm, you can induce an extra limb to form. You can also make a circular arm if you cut the limb and reattach it to the body; amazingly, the arm will grow in the correct polarity—forming an upper arm instead of a lower arm.

After the basic phenomenon of limb regeneration was described, scientists started to figure out the specifics of the regeneration pathway. Immediately after amputation, the immune system activates to mount a basic injury response. A few hours after the injury, a variety of cells from the adult tissue above the amputation site start to grow and proliferate, forming a structure called the blastema; the blastema continues to grow and differentiate, eventually forming the various types of cells that are required to make a complete limb.

What is the source of the cells that form the blastema? A recent resource article in *Developmental Cell* adapted "brainbow," a multi-color cellular imaging approach, to address this question. The technique, which the authors cleverly re-named "limbow," allowed them to visualize the different types of cells within the connective tissues (e.g., skeletal, muscle, skin) as they moved from the formed limb into the blastema. They identified the types of tissues that formed the blastema, showing that each tissue cell type had a characteristic dynamic and movement pattern, and found that the time and place of migration determines the cell fate in the blastema, such that fast movers are preferentially selected to form the blastema.

A complementary study using multi-color imaging to visualize tail regeneration in zebrafish was recently published in *Current Biology* suggesting that these approaches may be the start of single-cell resolution imaging in a complex event like regeneration (for more, see the recent *Cell Stem Cell* Forum piece). Evidently, the *Developmental Cell* staff was also charmed by the axolotl—this resource is on the November 21 cover!

The *Cell Reports* resource that brought me to this point comes from Jessica Whited's lab. (I recommend checking out this fun and informative interview she did with Carl Zimmer for STAT news in 2016.) A major limiting factor in axolotl research is the large size of the axolotl genome: at 32 gigabases of DNA, it is 10 times the size of the human genome. Whited's group performed a genome-wide expression analysis of a number of axolotl tissues, including the regenerating limb. Their transcriptome identified different genes that were enriched or repressed in particular tissues during limb regeneration. This resource can be a useful data set to look for other tissue-enriched or tissue-repressed RNA transcripts, which will help guide future studies.

The ultimate goal of these studies is in human regenerative medicine: being able to turn on limb regeneration or even improve healing ability, reduce scarring, and limit transplant rejections would be incredibly useful in the clinic. Once we understand the specifics of how limb regeneration occurs in a model organism, scientists might be able to trick a mammal into regenerating an amputated limb.

The idea isn't that crazy, really! Humans and some other mammals can regenerate small portions of amputated fingers as long as a portion of the nail remains, suggesting that humans might have this ability locked away. Of course, we are still a long way away from this goal, but the amazing axolotl can help us get there.

Axolotl is just one of the many fascinating model organisms used by scientists to answer questions in their field. If you want to learn more, check out this review in *Trends in Cell Biology* or follow the link below.

Posted by

Shawnna Buttery

Shawnna (@yeastgrrl) joined the *Cell Reports* team as a Scientific Editor in August 2016. She previously worked for Elsevier's BBA journals. Her training in the laboratory was in cell biology, studying the cytoskeleton in worm sperm as a grad student and in budding yeast as a postdoc. When she isn't reading science, she enjoys bike commuting, running, playing board games, and attempting to read the entirety of the internet. You can find more of her writing on her personal blog, Science Types.

0 Comments

First Name*

Yan

Last Name*

Song

Email*

leafsong@gmail.com

Industry

Comment*