INTRODUCTION

- *Ambystoma mexicanum*, or the Mexican axolotl mole salamander, retains the ability to regenerate any of its four, well-defined limbs throughout its lifespan.
- Although limb regeneration has been widely studied in the axolotl, little is known about the intrinsic repair or regeneration capabilities of the articular cartilage.

Objective

Our objective in this study was to investigate the utility of the axolotl as a vertebrate model to study the repair of large articular cartilage defects.

Hypothesis

We hypothesized that these amphibians possess the intrinsic ability to fully repair large full thickness lesions in the articular cartilage of the distal femur.

MATERIALS AND METHODS

- Major articular cartilage defects continuing to the level of the metaphysis were made at 4 months of age by resection of either the lateral or medial condyle of the distal femur (Figure 1).
- After surgery, the joint was closed with 10-0 suture.
- At 8, 12, 18 and 24 weeks post surgery, hind limbs were collected, fixed, de-calcified and embedded in paraffin.
- Two limbs from each collection point were sectioned at 10 µM and stained with Hematoxylin and Eosin (H&E).

RESULTS

- Axolotl Femorotibial Joint Anatomy

  - In the axolotl femorotibial joint, we observed the presence of a cellular tissue in the intra-articular space between joint surfaces of the femur, tibia, and fibula (Figure 2).
  - The identity of this tissue is unknown and we have chosen to refer to it as the interzone tissue.

  Figure 2. Anatomy of the axolotl femorotibial joint including the interzone tissue

- Articular Cartilage Repair Response

  - At all post-surgical collection points, the defect was filled with a cellular repair tissue (Figure 3).
  - During early time points, cells closest to the joint surface were morphologically similar to those within the interzone tissue.
  - As time from surgery increased, these cells appeared to be progressively replaced by chondrocytes.
  - By 24 weeks post surgery, cartilaginous tissue almost completely filled in the surgical defect and restored the distal femur structure in the area where the hemicondyle had been removed.
  - Essentially complete restoration of the distal femur anatomy was confirmed at 48 weeks.

DISCUSSION

- These results suggest that the axolotl is able to repair large, surgically induced full thickness articular cartilage lesions without formation of a blastema.
- We believe that some of the cells participating in the repair process originate from the interzone tissue, which potentially could represent an axolotl homologue to meniscal, synovial membrane, or perichondrial tissue in mammals.
- Additional studies of this interzone tissue may provide new information about articular cartilage repair mechanisms in vertebrates that for some reason are no longer fully functional in mammals.