# Inhibition of JNK signaling pathway blocks tail and spinal cord regeneration in the Mexican axolotl (Ambystoma mexicanum)

*Nour Al Haj Baddar, MS* [1] • *Randal Voss, PhD* [2]

[1]Department of Biology, University of Kentucky • [2]Department of Neuroscience , University of Kentucky

The Mexican axolotl (Ambystoma mexicanum) is a model organism in biological research because it can regenerate tissues within amputated tails, including the spinal cord. The axolotl embryo tail amputation assay was developed to identify components of cell signaling pathways that regulate regeneration. Jun- N terminal kinases or (JNK) is a highly conserved cell signaling pathway that is known from diverse studies to regulate wound healing and the response to stress, as well as apoptosis, cell proliferation, and tissue patterning. However, it's role in axolotl tail regeneration is unknown. We amputated the distal tail tips of axolotl embryos and immersed them in 5uM SP600125, a JNK inhibitor. Relative to non-treated controls, SP600125 blocked tail and spinal cord regeneration. We then performed a microarray analysis to identify genes that were expressed differently in response to JNK inhibition at 24 hours post amputation (hpa). We found that SP600125 inhibited the expression of genes associated with the immune response and apoptosis. This is consistent with mammalian studies that found a role for JNK in neuronal migration, apoptosis and regeneration. Interestingly, genes responsible for proximal-distal patterning during appendage outgrowth were also down-regulated by SP600125. Further, genes coding for extracellular matrix proteins and muscle-specific proteins were significantly up-regulated in SP600125 treated embryos suggesting disruption of tissue remodeling and histolysis, an important process during regeneration. Our findings show that JNK activity is required for successful axolotl tail regeneration and suggest JNK signaling to have a phylogenetically conserved role during tissue regeneration.