Forsyth scientists discover early key to regeneration

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Science may be one step closer to understanding how a limb can be grown or a spinal cord can be repaired. Scientists at The Forsyth Institute have discovered that some cells have to die for regeneration to occur. This research may provide insight into mechanisms necessary for therapeutic regeneration in humans, potentially addressing tissues that are lost, damaged or non- functional as a result of genetic syndromes, birth defects, cancer, degenerative diseases, accidents, aging and organ failure. Through studies of the frog (Xenopus) tadpole, the Forsyth team examined the cellular underpinnings of regeneration.

The Xenopus tadpole is an ideal model for studying regeneration because it is able to re-grow a fully functioning tail and all of its components, including muscle, vasculature, skin, and spinal cord. The Forsyth scientists studied the role that apoptosis, a process of programmed cell death in multi-cellular organisms, plays in regeneration. The research team, led by Michael Levin, Ph.D., Director of the Forsyth Center for Regenerative and Developmental Biology, found that apoptosis has a novel role in development and a critical role in regeneration. According to Dr. Levin, "Simply put, some cells have to die for regeneration to happen."

The findings will be published in the January 1, 2007 issue of *Developmental Biology* (v301i1). "We were surprised to see that some cells need to be removed for regeneration to proceed," said Ai-Sun Tseng, Ph.D. the paper's first author. "It is exciting to think that someday this process could be managed to allow medically therapeutic

regeneration."

In the context of efforts to understand biophysical controls of regenerative processes, The Forsyth Center for Regenerative and Developmental Biology investigated the dynamics of cell number control in the regenerating tail bud. Previous research in the field has shown that one mechanism by which cell number is controlled is by programmed cell death, which has been shown to be involved in sculpting of growing tissue in a number of developmental systems including heart, limb and craniofacial patterning. This study shows that despite the massive tissue proliferation required to build the tail, an early apoptotic event is required for regeneration.

Normal regeneration of the tail includes a small focus of apoptotic cells; when apoptosis is inhibited during the first 24 hours, regeneration cannot proceed and the growth of nerve axons becomes abnormal. Later inhibition of apoptosis has no effect, suggesting that the programmed death of a specific cellular component is a very early step in the regeneration program. One possible model is that tissues normally contain a population of cells whose purpose is to prevent massive growth in the region surrounding them. Future work by the Levin group will identify the cells that must die, in order to try to understand the signals that cells utilize for growth control.

Source: Forsyth Institute