Scientists make major discovery to advance regenerative medicine

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Scientists at Forsyth may have moved one step closer to regenerating human spinal cord tissue by artificially inducing a frog tadpole to re-grow its tail at a stage in its development when it is normally impossible. Using a variety of methods including a kind of gene therapy, the scientists altered the electrical properties of cells thus inducing regeneration. This discovery may provide clues about how bioelectricity can be used to help humans regenerate.

This study, for the first time, gave scientists a direct glimpse of the source of natural electric fields that are crucial for regeneration, as well as revealing how these are produced. In addition, the findings provide the first detailed mechanistic synthesis of bioelectrical, molecular-genetic, and cell-biological events underlying the regeneration of a complex vertebrate structure that includes skin, muscle, vasculature and critically spinal cord.

Although the Xenopus (frog) tadpole sometimes has the ability to re-grow its tail, there are specific times during its development that regeneration does not take place (much as human children lose the ability to regenerate finger-tips after 7 years of age). During the Forsyth study, the activity of a yeast proton pump (which produces H+ ion flow and thus sets up regions of higher and lower pH) triggered the regeneration of the frog's tail during the normally quiescent time.

This research will be published in the April issue of *Development* and will appear online on February 28, 2007.

According to the publication's first author, Dany Adams, Ph.D., Assistant Research Investigator at the Forsyth Institute, applied electric fields have long been known to enhance regeneration in amphibia, and in fact have led to clinical trials in human patients. "However, the molecular sources of relevant currents and the mechanisms underlying their control have remained poorly understood," said Adams. "To truly make strides in regenerative medicine, we need to understand the innate components that underlie bioelectrical events during normal development and regeneration. Our ability to stop regeneration by blocking a particular H+ pump and to induce regeneration when it is normally absent, means we have found at least one critical component."

The research team, led by Michael Levin, Ph.D., Director of the Forsyth Center for Regenerative and Developmental Biology has been using the Xenopus tadpole to study regeneration because it provides an opportunity to see how much can be done with non-embryonic (somatic) cells during regeneration, and it is a perfect model system in which to understand how movement of electric charges leads to the ability to re-grow a fully functioning tail. Furthermore, said Dr. Levin, tail regeneration in Xenopus is more likely to be similar to tissue renewal in human beings than some other regenerative model systems. The Forsyth scientists previously studied the role that apoptosis, a process of programmed cell death in multi-cellular organisms, plays in regeneration.

Michael Levin, PhD. is an Associate Member of the Staff in The Forsyth Institute Department of Cytokine Biology and the Director of the Forsyth Center for Regenerative and Developmental Biology. Through experimental approaches and mathematical modeling, Dr. Levin and his team examine the processes governing large-scale pattern formation and biological information storage during animal embryogenesis. The lab investigates mechanisms of signaling between cells and tissues that allows a living system to reliably generate and maintain a complex morphology. The Levin team studies these processes in the context of

embryonic development and regeneration, with a particular focus on the biophysics of cell behavior.

Source: Forsyth Institute