Researchers tackle protein mechanisms behind limb regeneration

December 14 2009

The most comprehensive study to date of the proteins in a species of salamander that can regrow appendages may provide important clues to how similar regeneration could be induced in humans.

Researchers at the School of Science at Indiana University-Purdue University Indianapolis and colleagues investigated over three hundred proteins in the amputated limbs of axolotls, a type of salamander that has the unique natural ability to regenerate appendages from any level of amputation, with the hope that this knowledge will contribute to a better understanding of the mechanisms that allow limbs to regenerate. Their findings were published online in the journal Biomedical Central Biology on November 30 (*BMC Biology* 7:83, 2009).

"In some ways this study of the axoltol's proteins was a fishing expedition. Fishing expedition can be a derogatory term in biology but for us it was positive, since we caught some important "fish" that enable us to formulate hypotheses as to how limb regeneration occurs," said David L. Stocum, Ph.D., professor of biology and director of the Indiana University Center for Regenerative Biology and Medicine, both in the School of Science at IUPUI, who led the study.

"Comparison of these proteins to those expressed in the amputated frog limb, which regenerates poorly, will hopefully allow us to determine how we might enhance limb regeneration in the frog and ultimately in humans, Dr. Stocum said.

With few exceptions - notably the antlers of moose, deer and their close relatives, the tips of the fingers and toes of humans and rodents, and the ear tissue of certain strains of mice and rabbits - the appendages of mammals do not regenerate after amputation.

Limb regeneration in the axolotl occurs when undifferentiated cells accumulate under the wound epidermis at the amputation site, a process known as the establishment of a blastema. These cells are derived by the reprogramming of differentiated cells to a less specialized state, and from resident stem cells.

"We found proteins that point to several areas that need to be studied closely to give us vital information about the mechanisms that operate to form a blastema that then goes on to regenerate the missing parts of the limb," said Dr. Stocum, an internationally respected cell and developmental biologist who has studied limb regeneration for over three decades.

Investigating the proteins found in the axolotl limb, the researchers noted three findings that appear to have significance in reprogramming cells to grow new limbs:

1. Quantities of enzymes involved in metabolism decreased significantly during the regeneration process.

2. There were many proteins that helped cells avoid cell death. Because amputation is very traumatic, this is critical.

3. A protein which appears to keep cells from dividing until they are fully dedifferentiated and reprogrammed to begin forming a new limb was expressed at high levels throughout blastema formation.

Source: Indiana University School of Medicine