Could the ways animals regenerate hair and feathers lead to clues to restore human fingers and toes?

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This summer's action film, "The Amazing Spider-Man," is another match-up between the superhero and his nemesis the Lizard. Moviegoers and comic book fans alike will recall that the villain, AKA Dr. Curt Connors, was a surgeon who, after losing an arm, experimented with cell generation and reptilian DNA and was eventually able to grow back his missing limb. The latest issue of the journal *Physiology* contains a review article that looks at possible routes that unlock cellular regeneration in general, and the principles by which hair and feathers regenerate themselves in particular. The authors apply what is currently known about regenerative biology to the emerging field of regenerative medicine, which is being transformed from fantasy to reality.

The Review is entitled "Physiological Regeneration of Skin Appendages and Implications for Regenerative Medicine" and was written by Cheng-Ming Chuong, Randall B. Widelitz, Ping Wu, and Ting-Xin Jiang of the University of Southern California, and Valerie A. Randall of the University of Bradford. It appears in the current edition of *Physiology*, published by the American Physiological Society.

Review Article

While the concept of regenerative medicine is relatively new, animals are well known to remake their hair and feathers regularly by normal regenerative physiological processes. In their review, the authors focus

on (1) how extrafollicular environments can regulate hair and feather stem cell activities and (2) how different configurations of stem cells can shape organ forms in different body regions to fulfill changing physiological needs.

The review outlines previous research on the role of normal regeneration of hair and feathers throughout the lifespan of various birds and mammals. The researchers include what is currently known about the mechanism behind this re-growth, as well as what gaps still exist in the knowledge base and remain ripe for future research.

The review examines dozens of papers on normal "physiological regeneration"—the re-growth that happens over the course of an animal's life and not in response to an injury. This regeneration takes place to accommodate different stages in an animal's life (e.g., replacing downy chick feathers with an adult chicken's, or replacing the fine facial hair of a young boy with the budding beard of an adolescent), or in response to various environmental conditions (e.g., cats shedding a thick winter coat in the summer heat but re-growing it when the seasons change again, or snowshoe hares switching from brown in the summer to white in the winter for camouflage). These changes seem to respond both to internal cues such as physiology of the hair follicle itself, or external cues such as the environment, but the mechanisms behind these normal alterations are largely unknown. Stem cells inside the follicle prompt hair and feather regeneration, but researchers are still unsure how to guide those cells to form the shape, size, and orientation of these "skin appendages" so that controlled re-growth is possible. Additionally, scientists are still unsure how to re-grow hair on skin in people after severe injuries that lead to scar tissue.

Importance of the Findings

The reviewed studies suggest that while researchers are making headway

in understanding how and why hair and feathers regenerate after normal loss or in response to different life stages, much still remains unknown. This missing knowledge could hold valuable clues to learning how to regenerate much more complicated and valuable structures after loss to injury, such as fingers and toes.

"Using the episodic regeneration of skin appendages as a clear readout, we have the opportunity to understand and modulate the behavior or adult stem cells and organ regeneration at a level heretofore unknown," the authors say.

More information: The study is available online at bit.ly/IGC6mP

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