Skin Regeneration in the African Spiny Mouse: A Brief Overview

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The African spiny mouse, *Acomys,* is a mammal with the unique ability to regenerate its skin. Compared to a typical lab mouse (*Mus*), the *Acomys* has weaker skin, distinct inflammatory responses, and complete reconstruction after wounding. The African spiny mouse's skin and hair regeneration response improves its survival prospects when predators attack.

While the African spiny mouse's regenerative response to wounds is its most well-known characteristic, the mouse's uniquely weak dermal structure minimizes the initial injury. Research shows that the amount of elastin on *Acomys* skin is similar to that of *Mus* skin (Seifert et al., 2017). However, the *Acomys*' large spiny hairs take up much of the total skin area and interrupt the elastin formation. This structure provides more flexible damage reduction than the fracture plates used by lizards and other autotomizing creatures. Testing was conducted to quantify the skin stress tolerance in both mouse types. Results showed that the *Acomys* skin was extremely weak and brittle, tearing under $1/20^{th}$ of the load that the *Mus* could handle (Seifert et al., 2017). Therefore, when a predator grasps at the spiny mouse, the predator is left holding only that skin and hair follicles while the mouse scampers away.

Once the skin has been punched, the *Acomys* immune response is markedly different from the *Mus*. Neither species alters their behaviors in response to the injury, resuming regular activities, such as eating. Both mice experience an influx of neutrophils in the days following the incident. However, the *Acomys* neutrophils levels were approximately half that of the *Mus* and declined at a faster rate (Simkin et al, 2017). These immune cells are restricted to the outside of the *Acomys* blastema. The *Mus* neutrophils infiltrate the granulation tissue. Conversely, another type of immune cell, the macrophage, is much more present in the *Acomys* than the *Mus*. Chemiluminescence testing showed that the *Acomys* had higher levels of macrophages. Like neutrophils, macrophages are present around but not inside the *Acomys* blastema (Simkin et al, 2017). In a subsequent experiment, *Acomys* mice were injected with a liposome that depleted macrophage levels. The treated mice did not start closing the wound until two weeks after the final injection. The regeneration process was disabled, no longer forming the blastema or rebuilding the epithelium. Therefore, the macrophage is essential to the *Acomys* wound closure ability, which helps start the wound regeneration process (Simkin et al, 2017).

This response was explored by other researchers who tracked ear hole punch recovery for the two species, removing 30 to 40% of the skin in each ear. The experiment compared the changes daily for the first two weeks, weekly until all the *Acomys* healed, and a few months after recovery (Santos et al., 2015). Both species underwent mild inflammation, shed necrotic skin, and re-epithelialized in the first week. Over the course of the second week, the *Mus* started laying down collagen in the wound area. By day 14, the *Acomys* open hole was smaller than the original wound perimeter. On day 21, hair follicles were observed in the Acomys regrowth area. Over the following weeks, these processes continued, and the hole shrank further. Fifty-six days after the initial punch, the *Acomys* wound had completely healed while the *Mus* hole was still 4 mm in diameter. After analyzing the regenerated tissue, the dermis, epidermis, immature collagen, follicles of pigmented hair, and sweat glands were identified. Additionally, fluorescence was used to identify a capillary network and nerves. The mice appeared to retain full sensory and movement capabilities in the wounded area. Five months after the initial injury, the researchers observed that the collagen matched the surrounding uninjured areas and noted varying presences of muscle fibers in the individual *Acomys* mice. The regenerated ear tissue is nearly indistinguishable from uninjured surrounding tissue (Santos et al., 2015).

As a result of its damage minimization techniques and unique immune response, the *Acomys* has a restored dermis, pigmented hair follicles, muscles, and sweat glands (Santos et al., 2015). Most *Acomys* research is conducted using ear hole punches, which are an imperfect stand-in for skin customization on the rest of the body. Given that human wound recovery resembles the *Mus* more than the *Acomys*, further research is needed into how these *Acomys* skin regeneration techniques could be applied to human medical research and healing technology.

References

Brant, J. O., Lopez, M., Baker, H. V., Barbazuk, W. B., & Maden, M. (2015). A Comparative Analysis of Gene Expression Profiles during Skin Regeneration in *Mus* and *Acomys*. *PLoS ONE*, *10*(11), e0142931.

Santos, D. M., Rita, A. M., Casanellas, I., Ova, A. B., Araújo, I. M., Power, D., & Tiscornia, G. (2015). Ear wound regeneration in the African spiny mouse *Acomys cahirinus*. *Regeneration*, *3*(1), 52–61.

Seifert, A. W., Kiama, S. G., Seifert, M. G., Goheen, J. R., Palmer, T. M., & Maden, M. (2012). Skin shedding and tissue regeneration in African spiny mice (*Acomys*). *Nature*, *489*(7417), 561–565.

Simkin, J., Gawriluk, T. R., Gensel, J. C., & Seifert, A. W. (2017). Macrophages are necessary for epimorphic regeneration in African spiny mice. *eLife*, *6*.