Researchers unveil the role of primary cilia in facilitating cartilage regeneration after growth plate fractures

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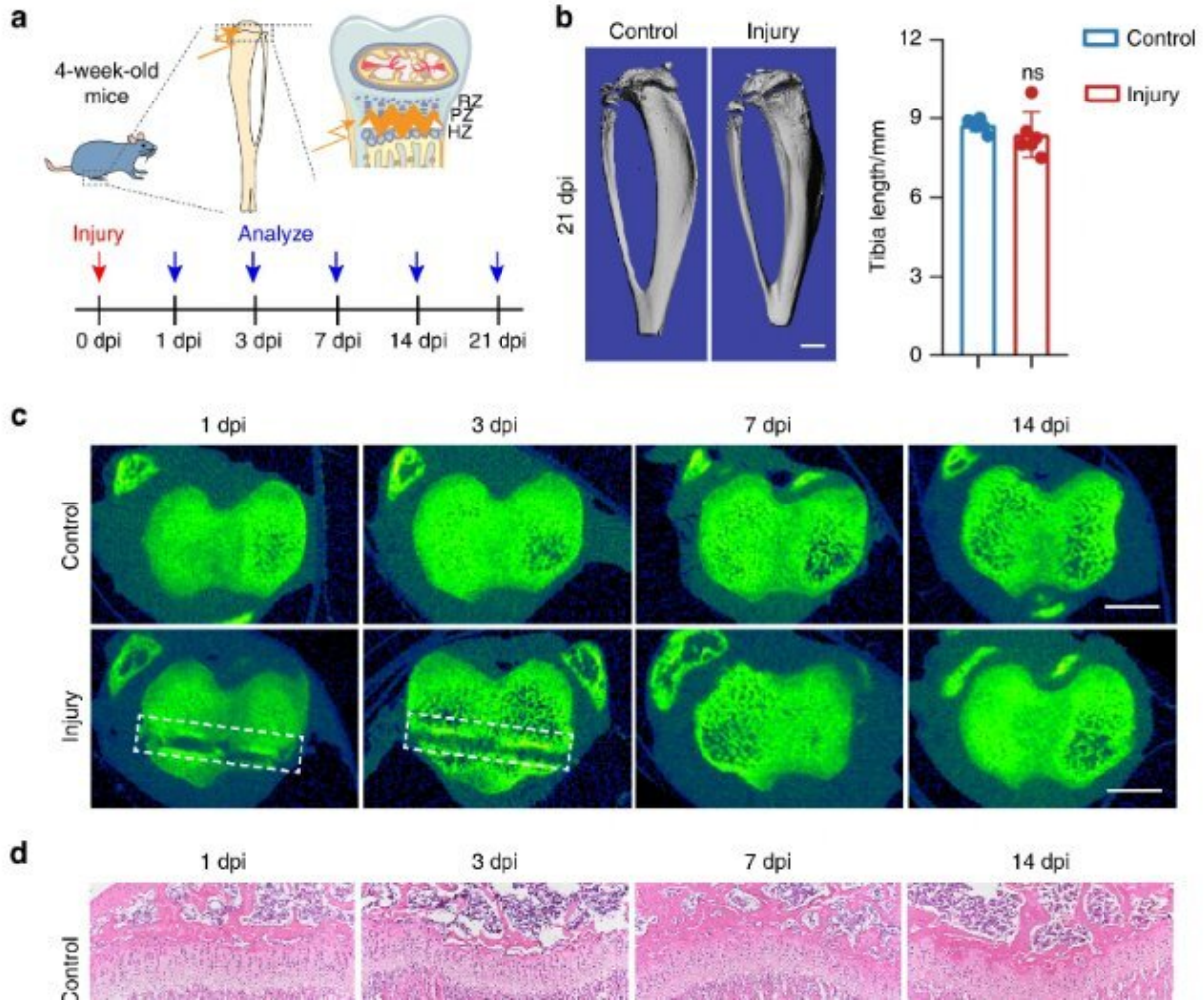

a Schematics of injury model in the tibia growth plate. b Micro-CT images and quantifications of control and operated tibia length at 21 days post-injury (dpi). n

= 6. Scale bar, 1 mm. c Representative micro-CT images of control and operated tibias at 1, 3, 7, and 14 dpi, viewed from the transverse plane. Scale bar, 1 mm. d Representative H&E staining of control and operated tibias at 1, 3, 7, and 14 dpi. Scale bars, 100 μm. e Immunofluorescence staining for collagen type II (COL II) of control and operated tibias at 1, 3, 7, and 14 days after GP injury. Scale bars, 100 μm. The error bar represents the standard deviation of the mean. ns, no statistical significance. Credit: *International Journal of Oral Science* (2023). DOI: 10.1038/s41368-023-00223-6

Growth plates (GP), situated at the ends of long bones in children, supply chondrocytes necessary for bone growth. Damage to the growth plate due to fractures often results in arrested bone growth, making it a significant cause of skeletal disorders in children. However, a small percentage of these injuries astonishingly manage to heal themselves, a phenomenon that had remained a mystery until now.

In a new study published in *International Journal of Oral Science*, Yao Sun from Tongji University and other researchers identified that primary cilia, cellular sensory organelles enriched with receptors for organ developmental signaling pathways, play a critical role in this self-healing mechanism.

Primary cilia, specifically those associated with chondrocytes in resting and proliferating zones of the growth plate, have been discovered to be dynamically ciliated during growth plate repair. The loss of ciliation in aged cells was observed, suggesting that primary cilia play a crucial role in chondrogenesis and growth plate development. At the heart of this process is the Hedgehog (Hh) signaling pathway, which is crucial for chondrocyte differentiation and growth plate maintenance.

It was observed that the activation of Hh signaling in the injured growth plate could trigger the activation of chondrocytes, thereby promoting

cartilage repair. Disruption of the ciliary gene resulted in disorganized growth plate structure and severe bone development arrest, further affirming the crucial role of cilia in growth plate repair.

Moreover, it was found that the application of Smoothened agonist (SAG), which activates ciliary Hh signaling, significantly accelerated the repair of the growth plate after injury. Interestingly, Hh signaling also played a part in promoting the healing of growth plate injury, with the upregulation of Hh signaling by SAG further inhibiting the formation of bony structure in other intractable growth plate injuries. Importantly, through their study, the researchers demonstrated the dynamic ciliation of newly formed chondrocytes during GP regeneration.

The findings suggest that a targeted therapeutic approach could be developed to stimulate the Hh-cilia-Gli1 axis, promoting the repair of growth plate defects more effectively. This validation of the role of primary cilia in growth plate regeneration post-injury not only reveals new mechanisms of how cilia maintain growth plate functions but also opens up new avenues for combating growth plate injury.

These revelations could prove invaluable for the treatment of children suffering from growth plate fractures, potentially rescuing them from enduring skeletal disorders. However, further studies will be needed to construct viable therapeutic strategies based on these insights.

More information: Dike Tao et al, Primary cilia support cartilage regeneration after injury, *International Journal of Oral Science* (2023). DOI: 10.1038/s41368-023-00223-6

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