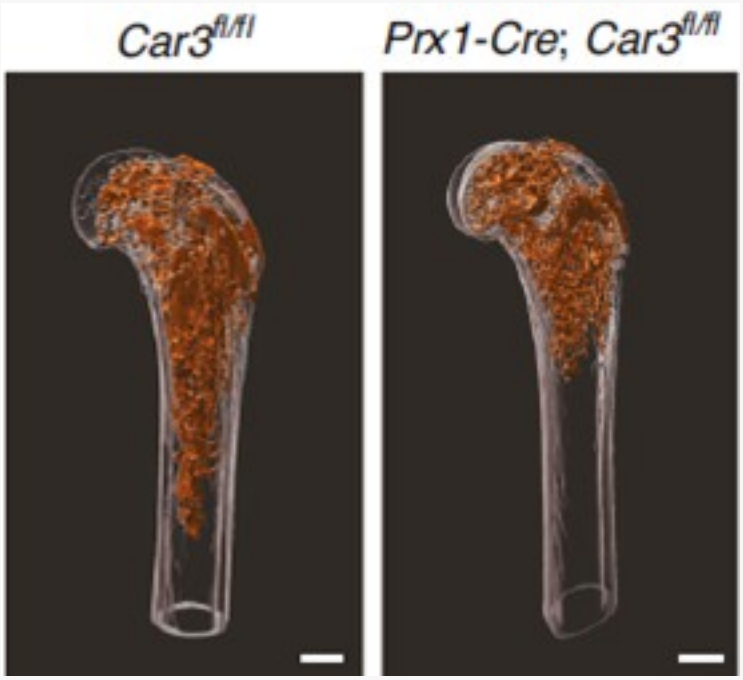
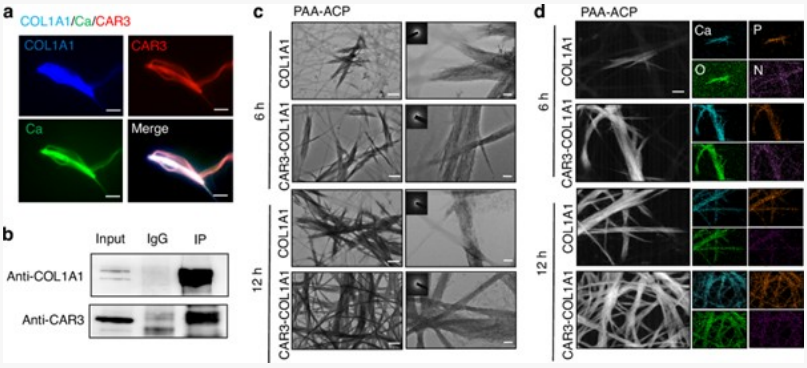
Scientists Uncover Key Protein That Helps Build and Strengthen Bone

New study identifies CAR3 as a key osteoblast protein promoting collagen mineralization, bone formation, and skeletal regeneration



Carbonic anhydrase 3 (CAR3) promotes bone formation and regeneration.



CAR3 protein found to promote collagen mineralization and strengthen bone formation.

CHINA, June 26, 2026 /EINPresswire.com/ -- A recent study identified carbonic anhydrase III (CAR3) as a previously unrecognized protein critical for healthy bone development and regeneration. Using single-cell RNA sequencing, genetically modified mice, and bone repair models, researchers found that CAR3 helps osteoblasts mineralize collagen and strengthen bone tissue by interacting with collagen and bone sialoprotein. Mice lacking CAR3 developed low bone density and impaired bone formation, while CAR3-functionalized scaffolds significantly improved bone healing and regeneration following skeletal injury.

The skeletal system forms the structural framework of the body, with bones providing support, protection, and mobility. Bone tissue is primarily composed of collagen, minerals such as calcium, and specialized non-collagenous proteins that together provide strength and flexibility. Bone health is maintained through the coordinated activity of osteoblasts, the cells responsible for building and mineralizing bone, osteoclasts, which break down bone tissue, and osteocytes, which help regulate bone remodeling. Among these, osteoblasts play a particularly important role in biomineralization, the process through which

minerals are deposited within the collagen framework to form hardened bone tissue. However, the molecular mechanisms regulating osteoblast differentiation and mineralization remain incompletely understood.

Previous studies identified carbonic anhydrase III (CAR3) as a protein associated with osteoblast differentiation, with its expression increasing during osteoblast maturation. However, its precise role in skeletal development and bone formation had remained unclear.

To address this gap, a research team led by Dr. Fangfang Song and Professor Yufeng Zhang from Wuhan University investigated the function of CAR3 in skeletal development using genetically modified mouse models. Their findings were published on May 19, 2026, in the International Journal of Oral Science.

“As osteoblasts have critical roles in skeletal development, we examined the molecular mechanisms involved in osteoblast differentiation, which can potentially aid in developing novel therapeutic strategies for bone disorders,” explained Dr. Song while discussing the motivation behind the study.

The researchers first analyzed publicly available single-cell RNA sequencing datasets from developing mouse cranial bone to examine the spatial and temporal expression of Car3, the gene encoding CAR3. They found that Car3 was highly activated in osteoblast-lineage cells during early embryonic cranial development, particularly between embryonic days 14.5 and 15.5, a period associated with active bone mineralization. In addition to craniofacial bones, Car3 expression was also observed in limb, rib, and spinal bones. Interestingly, while Car3 expression in young mice was closely associated with collagen-producing osteoblasts, its expression shifted toward adipocytes in aged mice.

Further experiments revealed that RUNX2, a master transcription factor involved in bone formation, directly regulated Car3 expression during osteoblast differentiation. The researchers also discovered that CAR3 formed a molecular complex with collagen type I alpha 1 (COL1A1) and subsequently recruited bone sialoprotein (BSP), a key structural component involved in mineral deposition. This ternary complex promoted collagen intrafibrillar mineralization, an essential process for generating strong and properly mineralized bone tissue.

To examine the functional importance of CAR3, the team selectively deleted Car3 in Prx1-lineage skeletal stem cells, which contribute to the development of skeletal and connective tissues. Although early femur development remained largely unaffected, adult mice lacking Car3 showed impaired osteoblast activity, defective collagen mineralization, reduced bone formation, and decreased bone density, highlighting the critical role of CAR3 in maintaining skeletal integrity.

The researchers then explored the therapeutic potential of CAR3 in bone regeneration. In mouse models with bone defects, implantation of recombinant CAR3-functionalized collagen scaffolds significantly enhanced new bone formation, increased bone volume, promoted osteoblast

recruitment, and improved bone matrix mineralization after eight weeks.

Commenting on the potential implications of the findings, Prof. Zhang stated: “Our mouse experiments revealed that application of collagen functionalized with CAR3 promoted bone formation. Thus, the regulatory effects of Car3 on osteoblast differentiation can be harnessed to treat bone disorders.”

Together, these findings identify CAR3 as a previously unrecognized regulator of osteoblast differentiation and collagen mineralization. By clarifying how CAR3 coordinates bone formation and regeneration, the study provides new insights into skeletal biology and highlights the potential of CAR3-based biomaterials and regenerative strategies for treating osteoporosis, fractures, and other bone disorders.

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Reference
Title of original paper: Osteoblast-derived CAR3 synergizing with collagen and bone sialoprotein enhances bone formation
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About Wuhan University
Wuhan University (WHU), founded in 1893, is one of China’s oldest and most prestigious comprehensive universities and is directly affiliated with the Ministry of Education. It is part of China’s “985 Project,” “211 Project,” and “Double First-Class” initiative. Located beside East Lake and Luojia Mountain, WHU is renowned for its scenic campus and strong academic reputation across disciplines including medicine, engineering, sciences, humanities, and law. The university maintains partnerships with 341 institutions across 53 countries and regions. In 2024, WHU ranked 134th in the THE World University Rankings, 89th in ARWU, and 194th in the QS World University Rankings.
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About Dr. Fangfang Song from Wuhan University
Dr. Fangfang Song is a researcher at the Hubei Key Laboratory of Stomatology, School and Hospital of Stomatology, Wuhan University, China. Their research focuses on cell biology, molecular biology, bone tissue engineering, and dental medicine. Dr. Song studies the molecular mechanisms underlying bone metabolism, osteoblast differentiation, and skeletal regeneration, with applications in osteoporosis treatment and regenerative medicine. They have also contributed to research on mesenchymal stromal cells and biomaterial-based therapies for bone and dental tissue repair, and have co-authored numerous peer-reviewed publications in these fields.

About Prof. Yufeng Zhang from Wuhan University

Prof. Yufeng Zhang is a Full Professor at the School and Hospital of Stomatology, Wuhan University, China. His research focuses on functional biomaterials for periodontal regeneration, regenerative dentistry, and the pathogenesis of periodontitis. Prof. Zhang has contributed extensively to research on biomaterial-based strategies for bone and periodontal tissue repair, with a particular interest in skeletal regeneration and oral tissue engineering. He has authored numerous peer-reviewed publications in the fields of regenerative medicine, biomaterials, and oral biology.

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