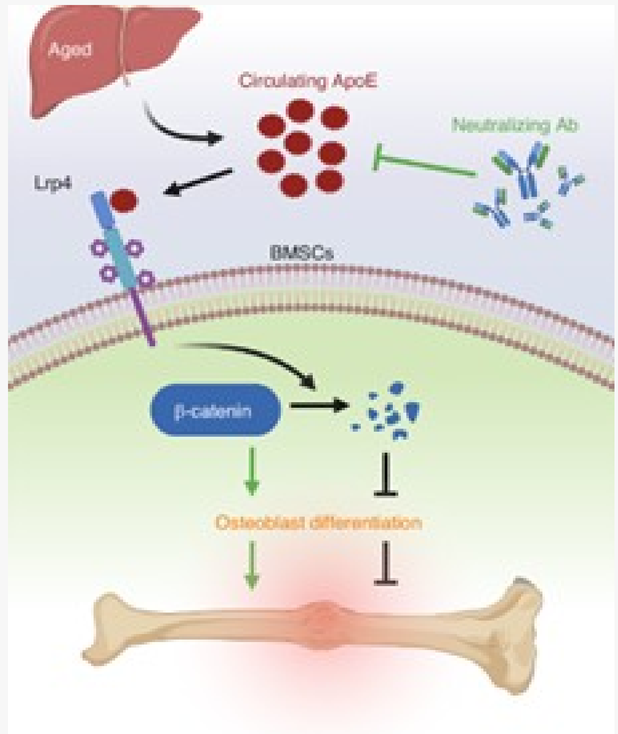
A Non-invasive Therapeutic Strategy for Improving Bone Healing in Aged Patients

Scientists show that neutralizing liver-derived ApoE protein reverses age-related delays in bone fracture healing



How elevated ApoE from the aged liver disrupts Lrp4–β-catenin signaling in bone marrow stromal cells, suppressing osteoblast differentiation and bone repair.Neutralizing antibodies block ApoE activity, restore β-catenin signaling and promote effective fracture healing.

CHINA, February 11, 2026 /EINPresswire.com/ -- Bone fractures heal more slowly with age, increasing health risks for older adults. A new study reveals that rising levels of the liver-produced protein apolipoprotein E (ApoE) interfere with bone repair by suppressing osteoblast activity. Using aged mouse models and human cells, scientists showed that neutralizing circulating ApoE restores bone formation and accelerates fracture healing. The findings highlight a promising noninvasive therapeutic strategy to improve bone healing in the elderly.

Bone repair is a tightly coordinated biological process that relies on stem and progenitor cells to rebuild damaged bone tissue. In younger individuals, these cells rapidly differentiate into osteoblasts—the bone-forming cells that generate new mineralized tissue. With aging, however, this process slows dramatically. Clinicians have long observed that fractures in older adults heal more slowly and are often associated with impaired recovery; however, the molecular signals driving this decline have remained unclear. Understanding why bone regeneration falters with age is critical amid global population aging and rising fracture-related disability.

Against this backdrop, in a new study, researchers have identified apolipoprotein E (ApoE), a protein produced primarily by the liver, as a key systemic inhibitor of bone repair during aging. The team found that circulating ApoE levels increase with age and interfere directly with signaling pathways required for osteoblast formation. By blocking ApoE activity, they were able to restore bone regeneration and significantly improve fracture healing in aged animal models. Their findings were made available online on January 22, 2026, in Volume 14 of the journal Bone Research.

The study was led by Associate Professor Gurpreet Singh Baht from the Department of Orthopaedic Surgery at Duke University, USA, along with Postdoctoral Associate Dr. Mingjian Huang and Ms. Kristin Molitoris, Research Technician, from the Duke Molecular Physiology Institute, USA.

To uncover how aging alters bone repair, the researchers used mouse models of fracture healing combined with molecular, cellular, and histological analyses. They compared young and aged mice to track differences in systemic factors, stem cell behavior, and bone regeneration outcomes. Their experiments revealed that elevated ApoE in older mice suppressed β-catenin signaling in bone marrow stromal cells—a pathway essential for osteoblast differentiation. Without this signal, progenitor cells failed to mature properly, stalling the repair process at an early stage.

Crucially, the researchers demonstrated that ApoE exerts its inhibitory effect by interacting with the Lrp4 receptor on bone marrow stromal cells. This interaction disrupts downstream β-catenin activity, effectively placing a molecular "brake" on bone formation. When ApoE-neutralizing antibodies were administered, β-catenin signaling was restored, osteoblast differentiation resumed, and fracture healing improved markedly. "Aging doesn't just slow bone repair—it starts to turn it off through systemic signals," explains Dr. Baht. "By blocking ApoE, we were able to release that brake and allow healing to proceed."

The impact of ApoE neutralization was striking. Aged mice treated with ApoE-blocking antibodies formed larger, more robust calluses and showed improved bone bridging at fracture sites compared to untreated controls. Importantly, the regenerated bone more closely resembled healthy repair seen in younger animals, suggesting that the intervention did more than simply accelerate healing—it restored quality regeneration. "What surprised us was how reversible the process turned out to be," notes Dr. Baht. "Even in aged animals, bone-forming cells retained their regenerative potential once the inhibitory signal was removed."

Beyond fracture healing, the findings highlight the liver's unexpected role in regulating skeletal repair. While bone biology has traditionally focused on local signals at the injury site, this study underscores the influence of circulating factors produced by distant organs. The identification of ApoE as a systemic suppressor of bone regeneration opens new avenues for treating age-related skeletal fragility. Therapies that target circulating inhibitors, rather than bone cells themselves, may offer safer and more effective strategies for older patients.

The researchers were motivated by a growing clinical challenge: fractures in elderly patients are associated with longer hospital stays, higher complication rates, and reduced independence. Current treatments focus largely on surgical fixation, with limited options to enhance biological healing. By revealing a modifiable molecular pathway that links aging, liver function, and bone repair, the study offers hope for therapies that actively restore regenerative capacity rather than simply managing its decline.

Together, these findings redefine how aging influences bone repair and identify ApoE as a promising therapeutic target. Neutralizing age-elevated systemic inhibitors could transform fracture care for older adults, reducing nonunion risk and improving recovery. As populations age worldwide, strategies that restore the body's natural regenerative programs may play a critical role in preserving mobility and quality of life.

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Reference
Title of original paper: Neutralizing hepatic apolipoprotein E enhances aged bone fracture healing
Journal: Bone Research
DOI: 10.1038/s41413-025-00489-y

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About Associate Professor Gurpreet Singh Baht

Dr. Gurpreet Singh Baht is an Associate Professor in the Department of Orthopaedic Surgery at Duke University, Durham, NC, USA, and a member of the Duke Molecular Physiology Institute. He earned his Ph.D. from Western University, Canada, in 2009. His research focuses on bone health, particularly the molecular and cellular mechanisms regulating fracture repair during aging, with the goal of informing aging-related therapies. With advancing age, tissue regeneration declines, resulting in delayed bone healing and abnormal tissue deposition in older individuals. He employs mouse models and tissue culture systems to identify key biological drivers of skeletal repair and regeneration.

Funding information
G.S.B. was supported by a Borden Scholars award, Duke Claude D. Pepper Older Americans Independence Center Pilot Award (P30AG028716), and by the NIH/NIA (R01AG081393).

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