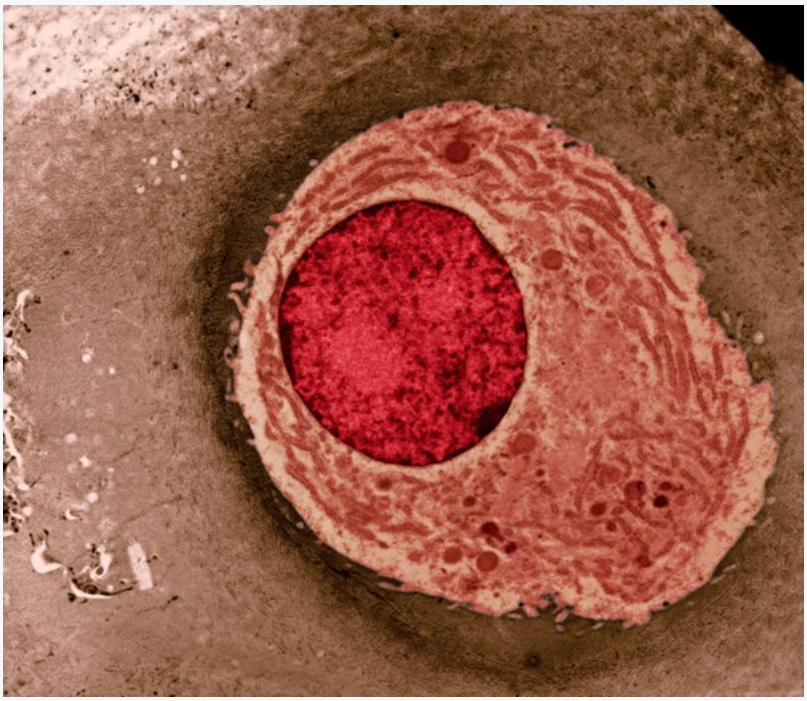
Cartilaginous cells regulate growth and blood vessel formation in bones

Research finds subtypes of chondrocytes that transform into bone growth, repair and vascularization, regulating classes



Mice deficient in hypertrophic chondrocytes were smaller, with shorter, malformed, and poorly vascularized bones

CHINA, December 12, 2025 /EINPresswire.com/ -- Hypertrophic chondrocytes are deeply involved in the growth of mammalian bones. Researchers find that these cells transform into multiple functional cell types, including those responsible for lengthening bones, maintaining the periosteum, and promoting the invasion of blood vessels that supply newly formed bone. Thrombospondin-4, a key signaling molecule produced by these cells, drives blood vessel formation. These findings open new avenues for enhancing bone repair and healing injured bones.

Normal, regulated growth of skeletal bones is a crucial part of the growth of mammals. This is a complex process involving the growth of cartilaginous cells or chondrocytes, their transformation into bone-building cells or osteoblasts, and the formation of new blood vessels to supply the newly formed bone tissue.

While osteoblasts evolve from a variety of progenitor cells, over 60% of osteoblasts in mammals originate from one class called hypertrophic chondrocytes (HCs). HCs are versatile cells involved in a variety of bone growth and maintenance tasks, including healing injuries and normal blood vessel formation. However, the specific mechanisms behind how HCs carry out these tasks are not known.

A team of researchers has studied the roles HCs play in bone growth in mice. Professor Liu Yang and Dr. Chao Zheng from the Fourth Military Medical University, China, led this research effort.

The team's findings were published in Volume 13 of the journal Bone Research on November 10, 2025.

Having previously studied how HCs can transform into bone tissue, the team looked at the new forms HCs take through various stages of bone growth. First, the team created transgenic mice with the selective deletion of HCs. Compared to normal mice, these HC-ablated mice were smaller, with shorter limbs, rounded skulls and malformed backbones. Their long bones, like the femur, had fewer blood vessels.

"[HC-ablated] mice displayed a dwarfism phenotype, impaired trabecular bone structure, and prolonged healing of drill-hole injuries, underscoring an essential role of HC lineage extension in bone development and repair," remarked Prof. Yang.

Next, the team studied the gene expression patterns of HCs to understand their transformational pathways. Eight pathways led to bone marrow formation; one led to bone formation. Within the bone formation pathway, the team found seven subtypes. Their expression patterns suggested that:

- Three subtypes were related to bone formation
- One subtype was involved in cartilage formation
- One subtype was involved in the periosteum layer that surrounds the bone surface
- One subtype formed skeletal stem cells
- One subtype regulated the formation of new blood vessels inside the bone. The team called these cells pro-angiogenic descendants or PADs

The team analyzed proteins secreted by PADs to identify which ones induced blood vessel formation. "We pinpointed factors such as Vegfa, Thbs4, Fn1, Cxcl1, Col6a1, and Col1a2, secreted by PADs to signal endothelial cells," said Dr. Zheng, adding "Our further results indicated that PADs likely communicated with endothelial cells through the Thbs4-(Cd36/Cd47) pathway."

Previous studies have shown that Thrombospondin 4 or Thbs4 is highly potent at inducing blood vessel formation in many other tissues. The team found that supplementing Thbs4 increased blood vessel formation and healing in foot bones taken from HC-ablated mice.

Summarizing these findings, Prof. Yang says, "Collectively, the present study demonstrates a critical role of HC descendants in bone growth and injury repair by secreting THBS4 to regulate angiogenesis. These findings also shed translational insights that could be leveraged to enhance bone injury repair of bone and treat defective angiogenesis." She adds that further research is needed to fully understand how PADs regulate blood vessel formation, including the roles of other signaling factors that PADs secrete.

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Reference
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About Fourth Military Medical University, China
Founded in 1941, the Fourth Military Medical University is one of the foremost medical research and training universities in Shaanxi province, China. The university offers both undergraduate and postgraduate education for doctors and nurses, as well as many postdoctoral research programs. Several civilian and military medical research programs are housed in Fourth Military Medical University. Since 2017, it is also one of the constituent institutions of the new Air Force Medical University.
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About Professor Liu Yang from Fourth Military Medical University
Dr. Liu Yang is a Professor in the Department of Orthopaedics at Xijing Hospital, Air Force Medical University (formerly Fourth Military Medical University), Xi'an. Her research centers on bone biology and skeletal disorders (e.g. osteoporosis, osteoarthritis, intervertebral disc degeneration), with her name listed on the editorial board of the journal Bone. She appears to be active in bone-related basic and translational research at a major orthopaedic hospital in China.

About Dr. Chao Zheng from Fourth Military Medical University
Dr. Chao Zheng is a researcher affiliated with the Fourth Military Medical University, where he contributes to advancing medical science through ongoing work in his specialty area. His research focuses on applying modern biomedical approaches (including osteoarthritis and bone maintenance) to improve diagnosis and treatment strategies.

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