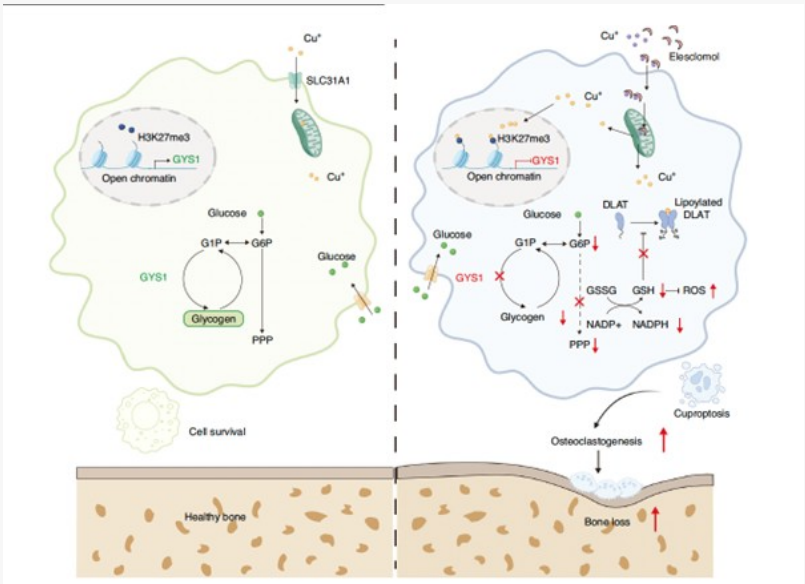
Altered copper metabolism is a crucial factor in inflammatory bone diseases

Researchers find that copper overload in cells suppresses glycogen synthesis and increases inflammatory activity in bones

CHINA, March 5, 2026 /EINPresswire.com/ -- Inflammation of bones is a characteristic of disorders like apical periodontitis. Researchers have found that copper-mediated cell death is an important factor. Copper overload suppresses the production of glycogen and reducing agents, increasing oxidative stress and inducing pro-inflammatory activity in macrophages. Suppressing copper overload and restoring glycogen synthesis are potential therapeutic pathways against inflammatory bone diseases.



Excessive intracellular copper,during inflammatory bone disorders, suppresses GYS1 transcription,affecting glycogen synthesis and impacting macrophage survival. Reducing copper overload and restoring glycogen synthesis is a potential pathway for new therapies.

Inflammatory osteolysis is a condition involving progressive bone tissue destruction and is observed in many well-known skeletal disorders, including rheumatoid arthritis, osteoporosis, and chronic apical periodontitis. This condition is driven by immune hyperactivation, sustained immune responses, and increased numbers of bone-degrading osteoclast cells, which together cause inflammation and weakening of affected bone tissue.

Copper is a vital element for the deposition of collagen in bone tissue, and hence bones contain significant traces of copper. However, excessive cellular copper disrupts glucose and glycogen metabolism pathways and triggers cuproptosis, a form of programmed cell death. Recent studies have found that copper metabolism is altered in the bones of people with arthritis and osteoporosis, suggesting that dysregulated copper levels may contribute to these conditions through cuproptosis.

Could cuproptosis impact bone metabolism and contribute to inflammatory osteolysis? A team of researchers from Wuhan University, led by Professor Lu Zhang, investigated this question by examining signs of cuproptosis and altered glycogen metabolism in bone tissue affected by chronic apical periodontitis in both mice and humans. Their findings were made available online on February 3, 2026, in Volume 18 of the International Journal of Oral Science.

“Emerging studies revealed that glycogen metabolism modulates immune cell functionality, signaling through metabolic intermediates, and energy homeostasis,” said Prof. Zhang, adding, “However, the precise mechanisms by which glycogen metabolism regulates cuproptosis progression remain to be elucidated.”

The team found that cuproptosis was involved in the bone weakening seen in chronic apical periodontitis. Higher amounts of cuproptosis-associated metabolites correlated with greater weakening of jaw bones. More importantly, copper was directly involved in the suppression of Glycogen Synthase 1 (GYS1), an enzyme crucial for converting glucose to glycogen. Copper could bind to histone proteins in chromosomes and silence GYS1 right at the source. When copper overload occurred, cells broke down glycogen into glucose, which they then used for greater energy production. Glucose is also diverted away from the pentose phosphate pathway (PPP), which produces reducing agents that mitigate oxidative stress in cells.

As a result of these changes, disrupting glycogen synthesis increased oxidative damage within cells, ultimately causing cell death. However, suppressing GYS1 had an interesting effect on macrophages—they transformed into osteoclasts and degraded bone tissue. This transformation occurred both under conditions of copper overload and when GYS1 inhibitors were added to bone tissue. In fact, when copper overload was combined with GYS1 inhibitors, cells experienced significantly greater oxidative damage, and more macrophages transformed into osteoclasts.

Conversely, the cuproptosis inhibitor tetrathiomolybdate (TTM) restored GYS1 activity and glycogen synthesis, ultimately reducing bone degradation even when copper levels were elevated. “Collectively, these findings suggest that both copper and GYS1 may regulate inflammatory pathways,” said Prof. Zhang.

These findings highlight copper metabolism as a potential new therapeutic target for inflammatory osteolysis. Inhibition of cuproptosis, restoration of glycogen synthesis and PPP, and disruption of copper-histone interactions represent promising avenues for new therapies against inflammatory bone diseases. Importantly, such copper-targeted approaches could offer safer, long-term relief without the side effects associated with current anti-inflammatory treatments that suppress immune system activity.

“Elucidating the mechanism of action of cuproptosis inhibitors in inflammatory bone diseases and developing therapeutics targeting copper and cuproptosis could provide new directions and strategies for treating inflammatory bone diseases, including rheumatoid arthritis, osteoporosis,

and apical periodontitis," says Prof. Zhang in conclusion.

***

Reference
Title of original paper: Cuproptosis promotes inflammatory osteolysis via GYS1-mediated glycogen metabolism
Journal: International Journal of Oral Science
DOI: https://doi.org/10.1038/s41368-025-00408-1

About Wuhan University
Founded in 1893, Wuhan University is a leading research university located in Hubei province, China. The university offers programs in 13 disciplines, with over 55,000 undergraduate and graduate students enrolled. The university is involved in several national-level education and research programs, pioneering the "Double First-class" initiative and housing 7 National Key Laboratories. Times Higher Education places Wuhan University at a global rank of 122. In addition to its education and research programs, three tertiary hospitals in Hubei are affiliated to the university.
Website: https://en.whu.edu.cn

About Professor Lu Zhang of Wuhan University
Prof. Lu Zhang is a Professor at the Department of Cariology and Endodontics in the School and Hospital of Stomatology, Wuhan University. Prof. Zhang received her doctorate in 2006. Her research focuses on bone homeostasis and metabolism in the mouth and jaw, and she has authored 53 academic publications in this field. Prof. Zhang is on the standing committee of the Division of Endodontics of the Chinese Stomatological Association. In addition to her academic work, Prof. Zhang practices endodontics and cariology at the university's Hospital of Stomatology.

Funding information
This work was supported by the National Natural Science Foundation of China (82370948, 82170941).

Yini Bao
International Journal of Oral Science
+862885546461 ext.
ijos@scu.edu.cn
Visit us on social media:
X

we have missed, please do bring it to our attention. Your help is welcome. EIN Presswire, Everyone's Internet News Presswire™, tries to define some of the boundaries that are reasonable in today's world. Please see our Editorial Guidelines for more information.