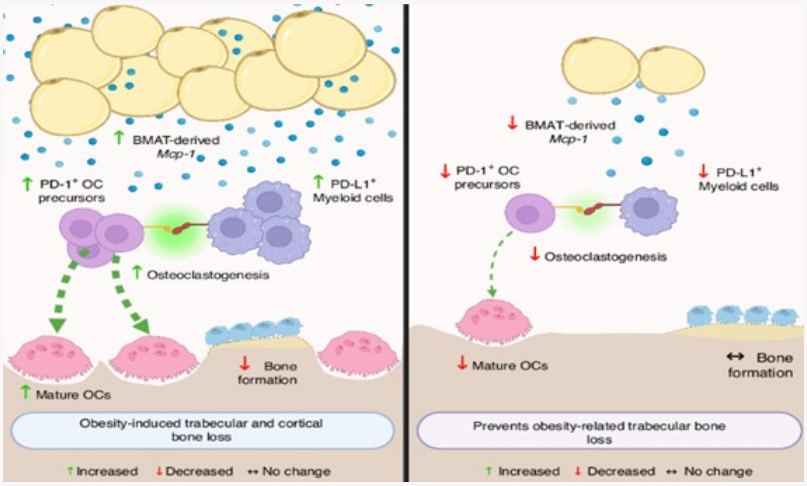
How Bone Marrow Fat Drives Immune Suppression and Bone Loss in Obesity

Researchers reveal how bone marrow fat reprograms immune signaling to promote osteoclast activity and weaken bones



Schematic diagram illustrating how expansion of bone marrow adipocytes in obesity increases MCP-1 signaling, promotes PD-L1+ immunosuppressive myeloid cells, and enhances osteoclastogenesis, leading to bone loss.

SICHUAN, CHENGDU, CHINA, April 24, 2026 /EINPresswire.com/ -- Researchers reveal how bone marrow fat reprograms immune signaling to promote osteoclast activity and weaken bones

Obesity alters bone health not only through increased body weight but also by reshaping the bone marrow environment. Researchers show that expansion of bone marrow fat promotes immunosuppressive PD-L1 signaling, which enhances osteoclast formation and accelerates bone loss. By reducing bone marrow fat in mice, they reduced immune suppression and improved bone structure. These findings uncover a new mechanism linking metabolism, immunity, and skeletal health, offering potential therapeutic targets for obesity-related bone disorders.

Bone health has traditionally been viewed as benefiting from higher body weight, with increased mechanical loading thought to strengthen bones. However, recent research challenges this notion, showing that obesity can negatively impact skeletal integrity. One key factor gaining attention is bone marrow adipose tissue, a specialized fat depot within bones that plays an active role in metabolic and immune regulation. Despite its importance, how this fat contributes to bone loss in obesity has remained unclear.

To address this challenge, a team of researchers led by Dr. Clifford J. Rosen, MD, Senior Scientist and Dr. Sergey Ryzhov, PhD, Researcher, both working at the Center for Molecular Medicine, MaineHealth Institute for Research, Scarborough, ME, USA, investigated how bone marrow fat influences immune function and bone remodeling in obesity. Using diet-induced obese mouse

models, cellular co-culture systems, and genetic depletion models, the team examined interactions between bone marrow adipocytes, immune cells, and osteoclast precursors. Their findings were published on March 20, 2026, in Volume 14 of the journal Bone Research.

The researchers found that obesity leads to a rapid and sustained expansion of bone marrow fat. This expansion altered the molecular profile of adipocytes, increasing the production of signaling molecules such as MCP-1, which recruits and reshapes myeloid immune cells. As a result, there was a marked increase in PD-L1-expressing myeloid cells within the bone marrow. These cells suppressed T-cell activity, creating an immunosuppressive microenvironment that disrupted normal immune balance. Importantly, these PD-L1+ cells not only suppressed immune responses but also directly influenced osteoclast development.

At the same time, this altered immune signaling had a direct impact on bone remodeling. The study revealed that PD-L1-expressing myeloid cells interact with PD-1 receptors on osteoclast precursors, promoting their differentiation into mature osteoclasts. This process significantly increased bone resorption, leading to reduced trabecular and cortical bone volume. Notably, blocking the PD-1/PD-L1 pathway during early stages of osteoclast formation reduced both the number and activity of these bone-resorbing cells, highlighting its critical role in osteoclastogenesis. Dr. Rosen explained, “We discovered that bone marrow fat is not simply a passive tissue but actively reshapes immune signaling in ways that accelerate bone loss in obesity.”

To further confirm these findings, the researchers used a genetically modified mouse model lacking bone marrow adipocytes. These mice showed reduced levels of MCP-1, fewer PD-L1+ immune cells, and a significant decrease in osteoclast precursors. Importantly, this led to improved bone structure and reduced bone resorption, even under obese conditions. These results demonstrate that bone marrow fat plays a central role in driving both immune suppression and bone degradation.

Dr. Ryzhov added, “This immune checkpoint pathway, known for regulating T-cell responses, also directly drives osteoclast formation, revealing a completely new link between immunity and skeletal health.”

Beyond the mechanistic insights, the study highlights important implications for human health. In the short term, it suggests new strategies to protect bone health in individuals with obesity by targeting bone marrow fat or immune checkpoint pathways. It may also provide insights into why obesity is associated with impaired immune responses, such as reduced vaccine effectiveness and increased infection risk.

In the long term, these findings could influence therapeutic approaches across multiple fields. Since PD-1/PD-L1 inhibitors are already used in cancer treatment, this research suggests potential future exploration of repurposing such therapies to address bone loss and metabolic disorders. It may also encourage collaborations between immunologists, endocrinologists, and

bone researchers to explore integrated treatment strategies.

Ultimately, this study redefines the role of bone marrow fat as a key regulator of immune and skeletal health. By uncovering how it drives immunosuppression and osteoclast activity, the research provides a foundation for developing innovative therapies aimed at reducing obesity-related bone loss and improving overall health outcomes.

Reference
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Dr. Sergey Ryzhov, MD, PhD, is a Faculty Scientist III and Co-Director of the Myocardial Biology & Heart Failure Research Lab at MaineHealth Institute for Research, Scarborough, USA. He is part of the Center for Molecular Medicine and affiliated with the University of Maine's Graduate School of Biomedical Science and Engineering. He earned his PhD from Siberian State Medical University in 1999 and completed postdoctoral training at Vanderbilt University. His research explores immune–cardiac cell interactions during heart recovery, focusing on myeloid cell function, tissue regeneration, and neuregulin signaling. He has authored 129 publications with over 4,600 citations globally.

About Dr. Clifford J. Rosen

Dr. Clifford J. Rosen is an Associate Director of the Center for Clinical and Translational Science and a senior scientist at the MaineHealth Institute for Research, Scarborough, Maine, USA. He is also a Professor of Medicine at Tufts University School of Medicine. A globally recognized expert in bone biology, Dr. Rosen has authored over 650 peer-reviewed publications. He has led numerous NIH-funded clinical trials and served on the FDA Advisory Panel on Endocrinologic and Metabolic Drugs. As former president of the American Society for Bone and Mineral Research, his work focuses on skeletal metabolism, stem cell biology, and marrow adipogenesis.

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