Docket #: S24-375

Repurposing Metformin to Prevent Corticosteroid-Induced Osteonecrosis

Stanford researchers have identified a new therapeutic application for metformin in preventing corticosteroid-associated bone death, or osteonecrosis (ON). Osteonecrosis of the femoral head (ONFH) is a severe bone disease that frequently affects both hips, leading to joint collapse, secondary arthritis and multifocal damage to other joints throughout the body. It primarily afflicts younger patients undergoing long-term corticosteroid therapy for conditions such as leukemia, asthma, and organ transplantation, and there are currently no effective preventive treatments for corticosteroid-associated ON.

In vitro studies have demonstrated that prednisolone, a commonly used and often lifesaving corticosteroid prescribed for a variety of indications, impairs mesenchymal stromal cell (MSC) function by increasing oxidative stress and reducing the cells' ability to form new bone. Such aberrations contribute to poor bone regeneration and heightened susceptibility to necrosis in patients undergoing long-term treatment with corticosteroids. The inventors find that at therapeutic concentrations, metformin successfully counteracts these effects by reducing oxidative damage, restoring osteogenic potential, and enhancing bone mineralization. This discovery suggests that metformin could serve as a protective co-therapy for patients at risk of corticosteroid-induced bone deterioration, enhancing patient quality-of-life and potentially reducing the future need for invasive, costly interventions such as joint replacement.

Stage of Development
Proof of concept — *in vitro* data, with animal studies planned to validate *in vivo* effects.

Applications

- Prevention of corticosteroid-associated osteonecrosis, including ONFH and more widespread multifocal ON (e.g. of the knees, ankles, and shoulders)
- Co-therapy for patients receiving long-term corticosteroid treatment
- Bone health preservation in high-risk patient populations

Advantages

- First potential preventive treatment for corticosteroid-induced osteonecrosis
- Demonstrated ability to effectively restore osteogenic function
- Utilizes an FDA-approved drug, accelerating clinical translation and reducing regulatory obstacles and costs
- May decrease the need for expensive and invasive joint replacement surgeries

Publications

- Cekuc, M.S., Ergul, Y.S., Pius, A.K., *et al.* (2024). Metformin Modulates Cell Oxidative Stress to Mitigate Corticosteroid-Induced Suppression of Osteogenesis in a 3D Model. *Journal of Inflammation Research*, 10383–10396.
- Shinohara, I., Susuki, Y., Murayama, M., *et al.* (in press). Metformin modulates oxidative stress in mesenchymal stem cells *in vitro* and alleviates corticosteroid-induced inflammation and impairment of bone formation. *HSS Journal: The Musculoskeletal Journal of Hospital for Special Surgery*.

Patents

- Published Application: WO2026064173

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