New treatment could improve care for two bone diseases

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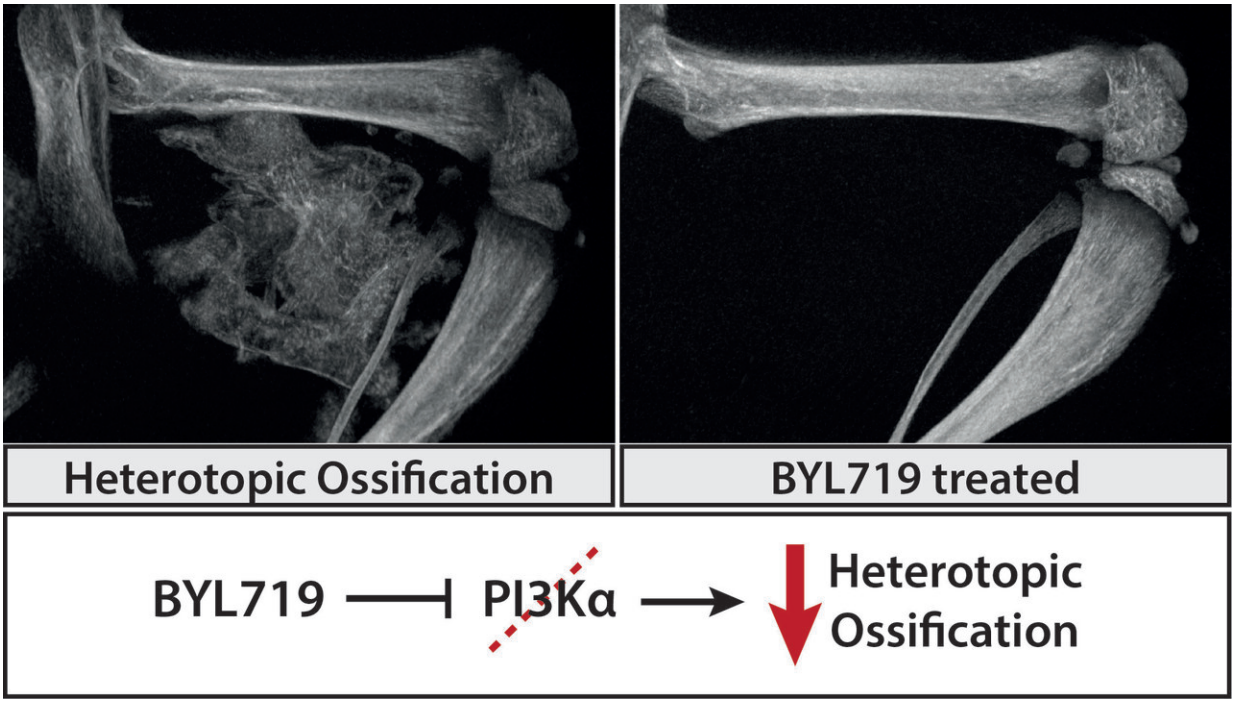

Ectopic bone formation (left) and no bone formation after treatment with BYL719 (right). Credit: Dr. Francesc Ventura

Researchers from the Bellvitge Biomedical Research Institute (IDIBELL) and the University of Barcelona (UB) have described the ability of an inhibitor of the PI3Kα (BYL719) to block the ectopic bone formation in mice. This could lead to improve the treatment of two pathologies: heterotopic ossification and fibrodysplasia ossificans

progressiva (FOP, a rare bone disease). The study was led by Dr. Francesc Ventura, head of the Cell Signaling and Bone Biology group.

Heterotopic ossification (OH) consists in the appearance of ossifications in inappropriate places (ectopic formation), such as tendons, muscles, and connective tissue. For this pathology there are risk factors such as prolonged immobility, spinal injuries, burns, hip operations, and muscle traumas. "Despite knowing this we still do not have a full understanding of the causes and the most appropriate treatment for the disease," says Dr. Francesc Ventura.

On the other hand, the FOP is a rare disease very similar to OH, but has its origin in a genetic mutation. FOP patients have mutations in the gene encoding a bone growth factors receptor (BMPs), the ACVR1. The disease is gradually induced by episodes of inflammation that eventually result in the progressive formation of bone in muscles, tendons, and ligaments. These ossifications reduce drastically the mobility and life expectancy of those affected. There is currently no treatment for this disease.

"What we have observed in this study is that, in stem cells cultures and in preclinical models of the disease, the BYL719 inhibitor prevents the ectopic bone formation induced by mutations in ACVR1," explains Dr. Ventura. The BYL719 inhibitor was approved by the FDA last May for its use in patients with metastatic breast cancer. Therefore, there is a large amount of information about the use of BYL719 in humans. "In this study we have shown that it can also play an important role in the ossification and treatment of these bone diseases," adds Ventura.

More information: José Antonio Valer et al. Inhibition of phosphatidylinositol 3-kinase α (PI 3Kα) prevents heterotopic ossification, *EMBO Molecular Medicine* (2019). DOI: 10.15252/emmm.201910567

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