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Amentadione is a new modulating agent for osteoarthritis in an ex-vivo co-culture preclinical assay

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Introduction: Osteoarthritis (OA) is a whole-joint disease where inflammation interplays with extracellular matrix mineralization in a cycle that leads to its degradation. The lack of effective preventing treatments and disease modifying agents, demands new therapeutic targets and development of effective drugs. Amentadione (YP), a meroditerpenoid extracted from the alga *Cystoseira usneoides* was previously shown to have anti-inflammatory and antioxidant activities [1]. The main purpose of this study was to develop a close-to-the-in-vivo OA model, to evaluate the potential and mode of action of novel therapeutic agents. Also, we aim to evaluate the potential of YP as a novel therapeutic agent for OA, using the developed 3D OA model.

Materials and methods: Monocultures of articular cells [2], cartilage ex vivo explants and co-cultures of cartilage explants with synoviocytes, were treated with YP and subjected to inflammatory/mineralizing conditions. OA gene markers and inflammatory mediators were analysed by qPCR and ELISA. Histological evaluation of cartilage explants was performed by von Kossa/hematoxylin and Alcian blue staining.

Results: YP was shown to reduce the inflammatory response in the articular primary cell system when subjected to mineralizing and inflammatory conditions. After establishment and characterization of an ex vivo OA co-culture model, YP was confirmed to be able to reduce the expression of OA gene markers of inflammation, cell differentiation, and matrix degradation (COX-2, IL-6, Col10, Runx2, MMP3) following stimulation with hydroxyapatite and IL1-b.

Discussion and conclusions: YP pre-treatment of OA culture model systems resulted in a significant downregulation of inflammatory, differentiation, and extracellular matrix-related genes and reduced the levels of inflammatory cytokines. These results clearly indicate a protective effect of YP on cartilage degradation with high potential for OA therapeutic application.

KEYWORDS Amentadione (YP); osteoarthritis (OA); inflammation; calcification; co-culture

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