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Beneficial effects of PACAP in osteoarthritis cartilage. An "in vivo" and an "in vitro" morphological and biochemical study

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Osteoarthritis (OA); the most common form of degenerative joint disease; is associated with variations in pro-inflammatory growth factor levels; inflammation and hypocellularity resulting from chondrocyte apoptosis (1). Pituitary adenylate cyclase-activating polypeptide (PACAP) is a neuropeptide endowed with a range of trophic effects in several cell types; including chondrocytes (2). However; its role in OA has not been studied. To address this issue; we investigated whether PACAP expression is affected in OA cartilage obtained from experimentally-induced OA rat models; and then studied the effects of PACAP in isolated chondrocytes exposed to IL-1β *in vitro* to mimic the inflammatory milieu of OA cartilage. OA induction was established by histomorphometric and histochemical analyses. Changes in PACAP distribution in cartilage or its concentration in synovial fluid (SF) were assessed by immunohistochemistry and ELISA. Results showed that PACAP abundance in cartilage tissue and SF was high in healthy controls. OA induction decreased PACAP levels both in affected cartilage and SF. *In vitro*; PACAP prevented IL-1β-induced chondrocyte apoptosis; as determined by MTT assay; Hoechst staining and western blots of apoptotic-related proteins. These changes were also accompanied by decreased i-NOS and COX-2 levels; suggesting an anti-inflammatory effect. Altogether, these findings support a potential role for PACAP as a chondroprotective agent for the treatment of OA.

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References:

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Keywords

PACAP; Osteoarthritis; ACLT; Immunohistochemistry; Bcl-2; BAX; Caspase-3.