The **COLL2-1 Peptide of Collagen Type II** : A New Actor of Synovitis in Osteoarthritis

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**Purpose**: Osteoarthritis (OA) is characterized by degradation of the extracellular matrix associated with inadequate repair responses including pro-inflammatory pathways of non-specific natural immune response. We evaluated the inflammatory effect of Coll2-1 peptide in osteoarthritic synoviocytes and rats by comparing peptide-induced inflammatory reaction with the one induced by bovine type II collagen or streptococcal cell wall.

**Methods**: Human synoviocytes from knee OA patients (n=10) were pre-treated with AS0619 or CIA-095 (500µM, 1 and 2.5µM) before a 24 hours treatment with Coll2-1 peptide ([HRGYPGLDGG])2-4.5µM or 4.5nmol). Expression of Interleukin (IL)-8, Vascular Endothelium Growth Factor (VEGF) and phosphorylation of the IκBα and p65 were evaluated. Either Coll2-1 peptide, bovine type II collagen (CIA), streptococcal cell wall (SCW) or saline solution (100µl SC or 50µl IA) were injected into Lewis rats (n = 108). The Coll2-1 peptide was subcutaneously injected (SC, 20 and 20µg/100µl/animal) or intra-articular (IA; 0.5 and 5µg/50µl/animal). The bovine type II collagen was SC injected (200µg/100µl/animal), the streptococcal cell wall in IA (5µg/50µl/animal). The animals were injected on day 10 and monitored for 21 or 28 days. Visual evaluation of the severity of arthritis and histological lesions were performed.

**Results**: Coll2-1 peptide increases IL-8 and VEGF expression by OA synovial fibroblast cells. Results are expressed as mean ± SEM (n=10). *P<0.05 and **P<0.01.

AS0619, a specific Coll2-1 IgG reverses the effect of Coll2-1 peptide on IL-8 expression. Results are expressed as mean ± SEM (n=10).

*P<0.05.

Coll2-1 peptide activates the nuclear factor NF-κB. The protein extracts are probed for phospho-NF-κB p65, phospho-IκBα and HSC70 (control) by Western blot analysis using specific antibodies. t: apocynine (0.2mM) and diphenyleneiodonium (6.35 10⁻³Mm).

Coll2-1 peptide acts through TLR-4 receptors. Results are expressed as mean ± SEM (n=4). *P<0.05.

**Conclusions**: Coll2-1 peptide is able to induce an inflammatory reaction and structural changes in articular cartilage and subchondral bone comparable but in a lesser extent than those induced by SCW and bovine type II collagen. Coll2-1 may initiate non-specific natural immunity and therefore is a therapeutic target for biotherapy.