**PURPOSE.** Osteoarthritis (OA) is characterized by degradation of the extracellular matrix associated with inadequate repair responses including pro-inflammatory pathways of nonspecific natural immune response. In this context, we evaluated the effect of type II collagen peptide (Coll2-1) and its nitrated form (Coll2-1NO) on oxidative stress and on the production of mediators of inflammation and angiogenesis by OA synoviocytes.

**METHODS.** Human synoviocytes from patients with knee OA (n=10) were treated for 24 hours in the presence or absence of Coll2-1 [10^6 HRGYPGLDG; 0.45 and 4.5 nmol] or Coll2-1NO [10^6 HRGYNIO]PGLDG; 4 and 40 pmol] peptides. For competitive inhibitions, the peptides were pre-incubated overnight at 4°C on shaker in the presence of A50619 and D37, 2 specific antisera respectively of Coll2-1 and Coll2-1NO. For the inhibition of TLR-4 receptor, synoviocytes are pre-treated 1 hour with CLI-095 (500 nM, 1 and 2.5 µM) before a 24 hours treatment with Coll2-1 at 4.5 nmol. Intracellular production of H2O2, GSH and NO was measured using fluorescent probes. The expression of Interleukins (IL)-6, -8, Vascular Endothelium Growth Factor (VEGF) and Thrombopondin-1 (TSP-1) was evaluated by quantitative real-time PCR. The phosphorylation of the IκB-α and p65, two key proteins in the NF-κB pathway were evaluated by Western blot in the presence or absence of oxidative stress inhibitors (apocynin; 0.2 mM and diphenyleneiodonium; 6.35 x 10^-7 M).

**RESULTS.**

![Figure 1](image1.png) Intracellular production of H2O2 by osteoarthritic synoviocytes in the presence of Coll2-1 (A) and Coll2-1NO (B). N=10 patients, * P<0.05 and ** P<0.01

![Figure 2](image2.png) Intracellular production of GSH by osteoarthritic synoviocytes in the presence of Coll2-1 (A) and Coll2-1NO (B). N=10 patients, ** P<0.01 and *** P<0.001

![Figure 3](image3.png) IL-8 (A) and TSP1 (B) expression by osteoarthritic synoviocytes in the presence of Coll2-1 and Coll2-1NO. N= 5-10 patients, * P<0.05 and ** P<0.01

![Figure 4](image4.png) Effect of Coll2-1, in the presence or absence of oxidative stress inhibitors (I), on the phosphorylation of p65 and IκB-α.

![Figure 5](image5.png) Effect of A50619 (A) and D37 (B) on the IL-8 and VEGF expression by osteoarthritic synoviocytes in the presence of Coll2-1 (A) and Coll2-1NO (B). * P<0.05

![Figure 6](image6.png) Effect of CLI-095 on the IL-8 expression by osteoarthritic synoviocytes in the presence of Coll2-1.

**CONCLUSION.** For the first time, we have shown that type II collagen peptides have pro-inflammatory, pro-angiogenic and immunomodulatory properties directly related with OA. These findings indicate that Coll2-1, a marker of cartilage degradation, could be a target for immunotherapy.