Osteoarthritis (OA) is a chronic-degenerative and incapacitating disease, characterized by deterioration of the articular cartilage, synovitis, and alteration in the peri-articular and subchondral bone [1]. Rodent animal models have contributed to the understanding of the basic biology of the OA and have helped to describe new candidate biomarkers for diagnosis and treatment [2]. However, rodents and humans are different in many aspects, including physiological traits and gene expression. Thus, rodent models cannot sufficiently mimic human diseases in some cases and large animal models remain needed. Pigs have been used as models for human diseases because they are similar to humans in terms of anatomy, neurobiology, cardiac vasculature, gastrointestinal tract, and genome [3]. Therefore, we analyzed the articular cartilage pathology in pigs with induced joint instability to determine if this model could be useful for the study of OA pathogenesis.

Based on our rat OA model [4], joint pathology was induced in Vietnamese pigs (Sus scrofa domestica) by unilateral knee meniscectomy and post-surgery exercise for 20 days; sham-operated pigs were used as controls. Cartilage sections were fixed with 4% paraformaldehyde in PBS and stained with safranin O-fast green to assess proteoglycan content. Immunohistochemistry was performed to determine the expression of IL-1β and MMP-3 proteins.

Histological analysis of cartilage slices from meniscectomized pigs produced pathologic characteristics similar to OA such as: chondrocytes cluster formation, fibrillation and depletion of proteoglycan content, mainly in the superficial zone of cartilage (Figure 1). Metalloproteinases are enzymes involved in the degradation the cartilage extracellular matrix; therefore, we analyzed the expression of MMP-3. Immunohistochemistry studies showed an increase in MMP-3 expression in meniscectomized pigs when compared to sham operated controls (not shown). Since MMP-3 expression is induced by pro-inflammatory cytokines, such as IL-1β, we investigated the expression of such cytokine in cartilage slices. IL-1β immunostaining increased strongly in cartilage from menisectomized pigs when compared with sham operated controls (Figure 2). Taken together, our results suggest that minipigs developed OA pathology as consequence of meniscectomy and exercise and therefore could be a useful model to study the physiopathology of OA disease. However, further studies are required to validate such OA model.

References

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Fig. 1: Proteoglycan content in porcine articular cartilage. Proteoglycan content was assessed by the safranin O-fast green staining in cartilage slices from sham operated pigs (left) and menisectomized pigs (right). In menisectomized animals is evident the chondrocytes cluster formation (arrow) and fibrillation (arrowhead). Scale bar: 50 µm.

Fig. 2: Expression of IL-1β in porcine articular cartilage. IL-1β expression was determined by immunohistochemistry in cartilage slices from sham operated pigs (left) and menisectomized pigs (right). Scale bar: 50 µm.