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The Pig as an Osteoarthritis Translational Research Model

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Translational Research Model

Among degenerative and chronic diseases, osteoarthritis (OA) occupies a relevant place affecting millions of people worldwide. Ten years ago (2005), just in the United States, the Centres for Disease Control and Prevention (CDC,USA) estimated that 27 million adults were affected by OA. OA accounts for 47.4% of all arthritis-related hospitalizations, meaning over three million hospitalizations for OA as principal diagnosis in 2011 [1]. OA commonly affects the middle-aged and elderly, although injuries due to the practice of high impact exercise have increased the ailment in younger people. OA remains an important public health issue, not only because it decreases the patient's quality of life but also because of the financial burden incurred when treating the disease, especially when it develops at early age. Total (direct and indirect) annual costs of OA per patient may reach $5700 (US dollars FY2000) [2]. In addition, OA was ranked as the 11th highest contributor to global disability and 38th highest in DALYs, meaning up to $3.4 to $13.2 billion per year of job-related OA costs [3]. With the extended life expectancy and increase in obesity of the world's population, the real burden of OA surely has been underestimated and it is expected a large increase in the frequency of the disease in the near future, which will demand health services to treat it. By 2030, the number of adults affected with doctor-diagnosed arthritis is projected to reach 67 million, or 25% of the adult population in the US [1].

In spite of its importance and the relevant studies made in the last 10 years, OA is a disease whose cause is not completely understood. There are also several areas where information is still lacking; these include: epidemiology, pathophysiology, environmental risk factors, genetic predisposition and lifestyle factors [4,5]. Currently, there is no cure for OA, and the most common treatments only ease the symptoms. Therefore, prevention is the only sensible alternative for the moment, while the cause of the disease is elucidated and effective biomarkers; early diagnostic tools and imaging technology are available.

In biomedical research, experimentation is essential for identifying the mechanisms and basis of diseases. However, many scientific studies cannot be performed directly in humans, because of ethical and logistic reasons; therefore, animal models are required. Animal models play a major role in helping to understand the mechanisms of diseases, developing methods for diagnosis, and identifying targets for treatment [6-8].

In fact, there are many animal models used to elucidate the basic biology of OA and to characterize candidate biomarkers for OA diagnosis and treatment [6-8]. Small animals are inexpensive and easy to handle, but the information obtained may be less applicable to humans. Therefore, in order to facilitate the translation of results from animals to humans, larger and more similar animal models are needed. The joints in large animals (dogs, goats, sheep, pigs, and horses) are anatomically and biomechanically similar to human joints [8]. In addition, arthroscopic procedures can be performed on larger animals and the data can be analysed using diagnostic imaging [8]. Moreover, comprehensive studies that involve synovial tissue and fluid are more likely to be carried out in large specimens. Finally, large animal models might provide clinically relevant information required for the FDA approval of diagnostics and biologics [8]. Among large animals, pigs are ideal because of their anatomical, physiological and genetic similarities to humans [9-12]. Pigs have been used as models for several human diseases. They are most similar to humans in terms of their anatomy, neurobiology, cardiac vasculature, gastrointestinal tract, and genome [9-12]. In addition, technological advances in cloning and transgenics have permitted the application of genetically modified and cloned pigs in translational research [8-12]; thus, pigs have become the non-rodent biomedical model of choice [13]. Moreover, the litter size of pigs allows a researcher to obtain several similar test subjects for experiments and their fast maturation permits the set up and completion of experiments in a relatively short period of time.

In rheumatology and orthopaedics, pigs have been used as animal model [14] and source of articular chondrocytes to study the physiopathology of OA [15,16]. Notably, pigs are useful models for studying the repair and regeneration of focal cartilage defects [14,18]. Furthermore, the porcine joint size, weight-bearing requirements, and cartilage thickness mimic human characteristics better than those of small animal models [19,20].

In this paper [21], juvenile pigs developed fibrillation, fissures, chondrocyte cluster formation, decrease in proteoglycan content and up regulation of the OA-associated proteins MMP-3, MMP-13, procaspase-3 and IL-1, in their articular cartilage, after partial menisectomy and exercise, all of these features resembling early human OA. Moreover, histological analysis of the synovial membrane revealed mild synovitis, characterized by hyperplasia, cell infiltration and neoangiogenesis. These results show the suitability of using pigs to study the physiopathology of OA. Pigs can also be useful for identifying new candidate biomarkers and test novel treatments in preclinical studies.

In a time when new early diagnostic tools, novel therapeutic measures, and a full understanding of the pathology of OA are needed, the pig, as an experimental translational model, may contribute decisively to speed up these studies.

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