Editorial Commentary

Post-traumatic osteoarthritis (PTOA) animal model to understand pathophysiology of osteoarthritis

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Osteoarthritis (OA) is one of the most prevalent chronic diseases in the world. Many researchers have attempted to determine the exact pathophysiology of OA. Although the biochemical changes that drive the disease remain poorly understood but the anatomical changes that occurs are well characterized. The hallmark changes that are seen in OA include joint space narrowing, subchondral cyst formation, subchondral sclerosis, and osteophyte formation. These pathological changes in the subchondral bone have been observed in human patients as well as in animal models of OA (1). The changes that are seen in OA are thought to result from "wear and tear". This is evidenced by the fact that damage is greatest in the regions of the joints that experience the most mechanical forces (1,2). Post-traumatic osteoarthritis (PTOA) is a subtype of OA that occurs after a traumatic injury. Current research states that the involved joint has a fivefold risk of OA over a lifetime (3). The increased risk of OA from PTOA has sparked the interest of researchers as to the correlation between insult and the development of OA. Animal models of OA have been used in many studies to characterize the macroscopic, metabolic, and molecular changes in joints affected by OA. The standard way to study PTOA has been the medial meniscus transection (MMT) mouse model or the anterior cruciate ligament transection (2).

To investigate the changes at the molecular level, there have been multiple studies using joint as a whole tissue using the PTOA mouse model. The studies prior to the regional gene expression analysis (4) only looked at global joint changes in relation to the contralateral joint (5-8). Previously, Chang *et al.* identified 1,446 genes that were differentially regulated in the PTOA model showing up-regulation of MMP3, FN, and COMP (7). They also identified several novel genes such as Suco, Sorcs2, and Medag. Sieker *et al.* also looked at molecular changes in the PTOA but in Porcine Model. They reported dysregulation of 1,275 genes and most significant changes observed in MMP1, COCH, POSTN, CYTL1 and PTGFR (6). The dysregulation of these factors are known to be associated with OA and other studies have shown similar outcomes.

The study of regional gene expression is of interest to the scientific community due to its novelty. The study by Salazar-Noratto *et al.* takes a slightly different approach and looks at specific changes that take place in distinct regions of the joint of a rat with MMT induced OA. Many of the studies that preceded this study have pooled samples taken from different parts of the joint and only compared entire joints to each other. Those studies identified genes that had a known association with OA and some novel genes. Salazar-Noratto *et al.* reported that there were changes seen in the distal medial synovial membrane, osteophyte tissue and the medial tibial plateau (4). Some of these changes are consistent across all regions of the joint. However, this study brings to light subtle differences in the way that different regions of the joint are affected. The data also shows that the changes that are seen in OA begin with changes in the chondrocytes which progress to changes in the extracellular matrix, which leads to the phenotypical

changes that are known to define OA (4). The changes that were seen in the medial tibial plateau were not originally seen in previous studies such as under expression of Frbz and Germ1 and their effect on the wnt pathway, which plays a role in differentiation of chondrocytes and has an effect to matrix production. The study also confirmed the results of previous published studies (5,6).

Salazar-Noratto *et al*. [2019] study is an innovative approach which provides a deeper and more detailed understanding of the pathophysiology of OA. The study provides some data that is very similar to previous studies that have established the foundation of our understanding of OA. One specific benefit of this study is that it provides a more detailed view of what is happening in different parts of the joint over time following a traumatic insult. Salazar-Noratto *et al.* [2019] performed MMT model of PTOA in male rats for their studies (4). It will be interesting to perform similar kind of study in female animal model. OA is known to affect women at a slightly higher rate than men (9,10).

In conclusion, this study presents some novel findings that characterize the effects of OA on specific regions of the knee joint. The studies strengths are that it pinpoints specific changes that were not previously observed and opens the door to understand OA pathogenesis research in new direction. The investigation of the specific regional changes across PTOA models is warranted and this study sets a solid ground work for future studies to improve our knowledge and potentially early treatment of PTOA.

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Footnote

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