Characterization of Osteoarthritic Synovium and Synovial-Derived Fibroblasts In Relation To Obesity

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INTRODUCTION:

Obesity contributed to the development of knee osteoarthritis(OA). Limited studies looking at well-characterized clinical samples to investigate the cellular and molecular effects of chronic inflammation and obesity on OA. Focusing specific sites on OA synovium membrane(SM) may provide ideas to possible pathophysiological processes that can be targeted for therapeutic purposes. This study was thus conducted to: (i)characterize histopathological changes of OA SM and (ii)determine the cellular and molecular changes in OA SM derived fibroblast(SDF), demonstrate changes in patients who are obese(BMI>27.5kg/m^2)[1] compared to non-obese.

MATERIALS & METHODS:

SMs were collected from subjects who underwent arthroplasty and arthroscopy procedures(MREC reference no: 20164-2398). Groups include non-OA and non-obese(G1,n=3), non-OA and obese(G2,n=3), OA and non-obese(G3,n=3) and; OA and obese(G4,n=3). SMs underwent histopathology analysis and primary SDF culture. The changes in the OA SMs were scored using the Krenn synovitis score[2] and morphological differences in primary SDF were recorded. Total RNA extracted from SDF were used for microarray gene expression profile analysis.

RESULTS:

Blinded histopathologic evaluation showed apparent changes in G1 to G4. Synovial hyperplasia and inflammatory cells infiltration were observed in G2, G3 and G4. Lymphocytes were observed in G3 and the existence of macrophages was more apparent in G4. Synovitis grade increased from G1 to G4. SDF global gene expression profiles analysis showed upregulation of VEGFA-VEGFR2 signaling pathway and focal adhesion-PI3K-AKT-mTOR-signaling pathways.

Table 1 Top most upregulated genes in respective groups.

Groups	**Genes**	**Fold changes**	***p*-value**
G4vsG3	FBLN1	337.95	0.0008
G4vsG2	FBLN1	700.11	0.0024
G4vsG1	PLA2G2A	133.25	0.0226
G3vsG2	HAS1	169.31	3.23E-07
G3vsG1	HAS1	161.01	1.62E-07
G2vsG1	DDX3Y	101.18	0.0326

DISCUSSIONS:

FBLN1 shown to be upregulated in G4vsG3 and G4vsG2, may contribute to the fibrosis process of the SM in the G4. PLA2G2A was upregulated in G4 and this signifies an important role of macrophage infiltration of the OA SM.

CONCLUSION:

Obesity shown to be associated with synovial inflammation. Molecular pathways in SDF associated with OA pathogenesis were identified.

REFERENCES:

1. Zainudin et al. 2014. *Journal of the ASEAN Federation of Endocrine Societies* 26(2): 101.
2. Krenn, et al. 2006. *Histopathology* 49(4): 358–364.