INTERPLAY OF TRANSFORMING GROWTH FACTOR BETA 1 AND ENDOTHELIN 1 SIGNALLING IN SUBCHONDRAL OSTEOBLAST DYSFUNCTION IN OSTEOARTHRITIS

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BACKGROUND: Osteoarthritis (OA) is a common degenerative disease among elderly with some cases associated with hypertension. Endothelin-1 (ET-1) is a hypertension agonist which has been shown to induce type I collagen secretion and inhibit mineralisation in osteoblasts. Upregulation of transforming growth factor beta 1 (TGFβ-1) is associated with the onset of OA. Crosstalks between TGFβ-1 and ET-1 may increase the OA severity.

METHODS: Nine advanced OA patients with total knee replacement were selected. Comparison of gene expression profile of osteoblasts between medial and lateral sides of tibial plateau were performed. Quantitative gene expression level of type I collagen (α1 and α2), endothelin A receptor (ETAR) and B receptor (ETBR), ET-1, and TGFβ-1 were detected in OA osteoblasts treated with or without TGFβ-1 and TGFβ-1 inhibitor.

RESULTS: Gene expression levels of ET-1, ETAR, and ETBR were correlated with changes of bone mineral density ($p<0.069$), trabecular bone number ($p<0.079$), and bone volume fraction ($p<0.051$) in medial side. Upregulation of ETAR (>2.4-fold), type I collagen (α1: >12.5-fold, α2: >1.3-fold), and endogenous TGFβ-1 (>4.5-fold) were detected in TGFβ-1–induced osteoblasts.

CONCLUSION: Differences in osteoblast-associated gene expression in medial and lateral tibial plateaux might be due to the severity of subchondral bone degeneration. The TGFβ-1 increased type I collagen and ETAR expression in osteoblasts harvested from medial compartment, which might be dependent on ET-1 signalling.