

formation of bronchiole during development.

5-3.

Prostaglandin E2 induces dual-specificity phosphatase 1, thereby attenuating inflammatory genes expression in human synovial fibroblasts

(社会人大学院博士課程4年整形外科学分野)

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【Background】 Degeneration of cartilage and joint pain are characteristic features of osteoarthritis (OA). Matrix metalloproteinases (MMPs) play roles in joint destruction. Nociceptive and nerve growth factor (NGF)-associated pain are known to be involved in OA. Although nociceptive pain related to prostaglandin (PG) E2 is produced by cyclooxygenase (COX)-2, our previously study reported that inhibition of PGE2 by selective COX-2 inhibitors enhanced MMPs and NGF expressions, inversely, PGE2 suppressed these expressions.

【Purpose】 To investigate the mechanism by which PGE2 suppresses MMPs and NGF expressions by focusing on MAP kinases (p38, ERK and JNK) phosphorylation and their endogenous phosphatase, dual specificity phosphatase (DUSP) 1 in human synovial cells.

【Method】 Human synovial cells were stimulated with PGE2 and/or IL-1b. Phosphorylation of MAPK was evaluated by Western blotting. DUSP1 knock-down cells were prepared by transfecting DUSP1 siRNA and the levels of DUSP1, MMPs and NGF expressions were examined by real-time PCR.

【Result】 DUSP1 expression was significantly induced by PGE2 after 30 minutes with peaked at 1 hour, and then decreased over time. Induction of DUSP1 by IL-1b was transient with a peak of 1 hour and decreased to unstimulated levels within 3 hours. When the PGE2-pretreated cells were stimulated with IL-1b, DUSP1 expression was additively increased after 1 hour and decreased to unstimulated levels after 3 hours. IL-1b-

induced MAPK phosphorylation was enhanced in DUSP1 knockdown cells. IL-1b-induced MMPs and NGF expressions were significantly enhanced in DUSP1 knock down cells.

【Conclusion】 PGE2 was found to induce DUSP1, thereby attenuating the MMPs and NGF expressions following the suppression of MAPK. DUSP1 would be a novel target molecule for OA that attenuates MAPK and following MMPs and NGF expressions.

6-1.

Reliability Assessment of Variability of Distal Tibial Rotation References for Total Knee Arthroplasty

(社会人大学院博士課程4年整形外科学分野)

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【Purpose】 In TKA operation, rotational alignment of tibial component is one of the most important factors that leads to the good postoperative results. We examined the reliability of the distal tibial rotation references: anterior-posterior axis (distal AP axis): using 3DCTs of the knee osteoarthritis cases. We also examined whether the reference axis are affected by severity of OA.

【Method】 282 patients (301 knees) who were planned TKA for osteoarthritis took part in this study. We used their images of Full-length CT of the lower limbs. From these data, We reconstructed 3D images of the proximal tibial joint surface, ankle joint surface, and foot using Lightspeed VCT VISION (GE Healthcare) as an analysis software. Proximal tibial anterior-posterior axis (proximal AP axis: defined as the line connecting the medial edge of the tibial nodule and the center of the PCL attachment) and 3 distal AP axes (D1: anterior-posterior axis of the talus, D2: vertical line of the medial-lateral ankle axis, and D3: Second metatarsal axis) projected on the same plane. We measured three angles: $\angle D1$ (between Proximal AP axis and D1), $\angle D2$