

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), $\angle D2$

(between Proximal AP axis and D2), and $\angle D3$ (between Proximal AP axis and D3). All measurement was done as external rotation direction was +. We measured Kellgren-Lawrence classification and femorotibial angle (FTA), using full-length X-ray photograph of the lower limbs, to assess the stage of OA and coronal alignment of knees.

【Results】 $\angle D1$ was $-0.8 \pm 10.6^\circ$, $\angle D2$ was $-3.3 \pm 19.1^\circ$, and $\angle D3$ was $-0.6 \pm 11.4^\circ$. There were no significant correlation between angles and the severity of OA (grade1 were 3, grade2 were 19, grade3 were 83 and grade4 were 196 knees) or the changes of coronal alignment (average of FTA was 182.0 ± 5.1) caused by OA.

【Discussion and Conclusion】 The second metatarsal axis was considered to be highly reliable as the distal AP axis, but there was variation of accuracy among cases. We could not find out the correlation between the variation of the distal AP axis and the stage of OA or the changes of coronal alignment of the lower limbs. Therefore, we considered that the variation of distal tibial rotation references may depend on individual differences in the torsion of the lower leg. When we use the distal AP axis as tibial rotation reference, it is important to understand the difference between distal and proximal AP axis in each cases, to prevent installation errors of rotation position.

6-2.

Association of high sensitivity C-reactive protein to aneurysm sac shrinkage in patients with abdominal aortic aneurysms undergoing endovascular aneurysm repair

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【Background】 The factors associated with aneurysm shrinkage after endovascular aneurysm repair (EVAR) are not well established. Since inflammation is implicated in aneurysm pathophysiology, we

hypothesized that high sensitivity C-reactive protein (hsCRP) was associated with aneurysm shrinkage after EVAR and compared the preoperative hsCRP between patients with and without aneurysm shrinkage after EVAR.

【Methods】 From November 2013 to April 2019, 143 patients undergoing EVAR at our university hospital were included in this study. Aneurysm size was compared between that on preoperative computed tomography (CT) and that on postoperative CT. A change in aneurysm size ≥ 5 mm was considered to be significant, whether due to enlargement or shrinkage.

【Results】 Aneurysm size showed a significant decrease from 50.6 ± 9.8 mm to 47.1 ± 10.3 mm at 1 year. Aneurysm shrinkage was observed in 48 patients (34%), a stable aneurysm was noted in 93 patients (65%), and aneurysm enlargement was noted in 2 patients (1%). The mean preoperative hsCRP was 0.33 ± 0.54 mg / dL. Univariate analysis showed that preoperative hsCRP ($p = 0.029$) and renal cyst ($p = 0.002$) were associated with aneurysm shrinkage. Multivariable analysis showed that preoperative hsCRP (OR 0.22; 95% CI 0.05-0.96; $p = 0.042$) and renal cyst (OR 0.31; 95% CI 0.15-0.67; $p = 0.002$) were independent risk factors for aneurysm shrinkage.

【Conclusions】 Preoperative hsCRP was independently associated with aneurysm shrinkage after EVAR. This data suggests that hsCRP can be a negative predictor for aneurysm shrinkage after EVAR.

6-3.

Gross anatomical study on a vacant space of arteries in the transverse mesocolon

(医学部医学科4年)

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【Introduction】 Previous studies on the arterial distribution to the transverse colon have focused on only the bifurcation of arteries. Due to a lack of detailed studies on the positional relation between the transverse colon and the running course of the arteries, we