

The 3-years survival rate was 82.0% in group A, and 63.7% in group B. Group B was significantly worse for over-all (OS) survival than group A. Multivariate Cox regression analysis showed that the patients who had RMML over 4.38 ($p=0.015$; HR 2.033; HR 95% CI 1.018-5.924), T2/3 were associated with worse OS.

【Conclusion】 This study found correlation between the loss of muscle after esophagectomy to discharge and worse OS in esophageal cancer.

5-1.

活性イオウ分子種の破骨細胞分化における作用機序の解明

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【目的】 近年、強い抗酸化能を持つ活性イオウ分子種 (RSS) が細胞内で生じることが明らかとなり (Proc Natl Acad Sci USA 111: 7606-11, 2014)、その主要な産生酵素としてシステイン-tRNA 合成酵素/システインパルスルフィド合成酵素 (CARS2/CPERS) が同定された (Nat Commun 8: 1177, 2017)。我々は、骨代謝で RSS が果たす役割を解明する目的で、今回、骨吸収を担う破骨細胞 (OC) の分化における RSS の機能を解析した。

【方法】 野生型および CARS2/CPERS+/-マウスの骨髄マクロファージ (MΦ) を OC 分化誘導因子 (RANKL) 存在下に 3 日間培養した。RANKL 依存的 OC 分化に対する NaHS および Na₂S_n (n: 2-4) の効果を OC 分化マーカーの発現で評価した。

【結果】 NaHS は OC 分化に影響しなかったが、Na₂S_n は OC 分化を促進し、その活性は n が大きい順に強かった。Na₂S₄ は破骨細胞分化のマスター転写因子である NFATc1 の発現と核移行を促進し、その上流シグナルであるカルシウム・カルシニューリン経路を活性化した。CARS2/CPERS+/-マウス MΦ の OC 分化は野生型 MΦ に比べ抑制されていたが、Na₂S₄ の添加で回復した。

【結論】 RSS は、カルシウム・カルシニューリン経路を活性化することで、破骨細胞分化を促進した。

5-2.

Expression of calcitonin gene-related peptide in the pulmonary neuroendocrine cells of mouse lung from embryonic to postnatal stages

(社会人大学院博士課程 3 年人体構造学分野)

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【Background】 Pulmonary neuroendocrine cells (PNECs) are proposed to be the first specialized cell type to appear in the developing lung. These cells exist in clusters that distribute throughout the bronchial epithelium (Ouadah et al., 2019). The proliferation of PNECs is related to the calcitonin gene-related peptide (CGRP) to promote epithelial repair after injured (Song et al., 2012). However, there is little information in relation to the CGRP and PNECs during development of lung.

【Objective】 We sought to determine whether CGRP and other related markers mRNAs makers are expressed in mouse lung during development from embryonic 12.5 days to postnatal 5 days.

【Methods】 Samples were collected on embryonic day 12.5 (E12.5), 14.5, 17.5 and postnatal day 0 (P0), 1, P (each stage n=4). The sections were observed by means of immunohistochemistry and *in situ* hybridization. The levels of CGRP and vascular endothelial growth factor (VEGF-A) mRNAs in the lungs were determined by the reverse transcriptional-polymerase chain reaction.

【Results】 CGRP-immunoreactive and CGRP mRNA-positive cell were increased from E14.5 to E17.5. The clusters of CGRP mRNA and anti-CGRP positive cells were clearly found on E17.5. The expression of CGRP and VEGF-A mRNA gradually increased from E12.5 to P1, and then attenuated from P1.

【Conclusions】 During the development of lung, CGRP may be related to the appearance of the PNECs formation from E14.5 to E17.5. Moreover, CGRP expression in bronchial epithelium might play an important role in the

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

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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), $\angle D2$