

P-27-070**Interplay of FAK, BMP, and mTOR signaling pathways regulates heparan sulfate glycosaminoglycan homeodynamics in mesenchymal stem cells**P. Chung^I, F. Lin^I, W. HuangFu^{II}, I. Liu^I^INational Taiwan University, Taipei, Taiwan, ^{II}College of Medical Science and Technology, Taipei Medical University, Taipei, Taiwan

Heparan sulfate glycosaminoglycans (HS-GAGs) are polysaccharides that are present in a wide range of physiological and pathological processes. The aim of this study was to examine the regulation of HS-GAG biosynthesis in bone marrow-derived mesenchymal stem cells (BM-MSCs) and the mechanisms involved. Through quantitative analysis, it was determined that HS-GAG biosynthesis follows a specific kinetic model, with levels reaching a plateau after approximately 48 hours. When treated with heparinase III (HepIII), the homeostatic regulation of HS-GAGs was disrupted, leading to a linear increase in their levels. The presence of intact HS-GAGs played a role in facilitating the assembly of the matrix (fibronectin, collagen I) and the dynamics of cell adhesion during the early stages (1–8 h), which were negatively affected by HepIII treatment. Transcriptomic analysis did not reveal any differentially expressed genes, suggesting that the regulatory mechanism is non-transcriptional. The saturation pattern of HS-GAG levels was found to correlate with the focal adhesion kinase (FAK), bone morphogenetic protein (BMP), and mammalian target of rapamycin (mTOR) signaling pathways. Inhibition of these pathways resulted in a decrease in HS-GAG biosynthesis, indicating cross-talk between them. FAK inhibition downregulated the BMP and mTOR pathways, while BMP inhibition affected the BMP and mTOR pathways. mTOR inhibition disrupted HS-GAG biosynthesis and also impacted the BMP and FAK pathways. Notably, the stimulation of HS-GAG biosynthesis by BMP2 was mediated through the mTOR pathway, and could be negated by mTOR inhibition. These findings provide insight into the tightly regulated homeodynamic mechanism for HS-GAG biosynthesis in BM-MSCs, which is governed by the interplay between the FAK, BMP, and mTOR signaling pathways, ultimately impacting matrix assembly and cell adhesion processes.

P-27-071**CCL8 and IL-8 mediate the crosstalk between endothelial cells and triple-negative breast cancer (TNBC) cells, resulting in the aggravation of TNBC**E.S. Kim^I, S. Nam^I, H.K. Lim^I, S. Lee^I, K. Kim^I, H.K. Song^{II}, H. Lee^I, K. Kang^I, Y. Kwon^{III}, Y. Chun^{III}, S.Y. Park^{IV}, J. Jung^I, A. Moon^I^IDuksung Innovative Drug Center, College of Pharmacy, Duksung Women's University, Seoul, South Korea, ^{II}College of Chemistry, Duksung Women's University, Seoul, South Korea, ^{III}College of Pharmacy, Chung-Ang University, Seoul, South Korea, ^{IV}Department of Pathology, Seoul National University College of Medicine, Seoul National University Bundang Hospital, Seongnam, South Korea

Triple-negative breast cancer (TNBC) is an aggressive type of breast cancer with a poor prognosis for which no effective therapeutic measures are currently available. The present study aimed to investigate whether interactions with endothelial colony-forming cells (ECFCs) promote aggressiveness of TNBC. We showed that co-culture increased the invasive and migratory phenotypes of both MDA-MB-231 and ECFCs. Through a cytokine antibody array and RT-PCR, we revealed that co-culture induced secretion of the CCL8 from ECFCs and that of IL-8 from MDA-MB-231 cells. CCL8 was crucial for ECFC-induced IL-8 secretion and invasion of MDA-MB-231 cells as well as for MDA-MB-231-enhanced MMP-2 secretion and angiogenesis of ECFCs. We suggest c-Jun as a transcription factor for CCL8-induced IL-8 expression in MDA-MB-231 cells. IL-8 was important for co-culture-induced CCL8/MMP-2 upregulation and invasion of ECFCs. Notably, our findings reveal a positive feedback loop between CCL8 and IL-8, which contributes to the aggressive phenotypes of both ECFCs and TNBC cells. Using an MDA-MB-231 cell-based xenograft model, we show that tumor growth and metastasis are increased by co-injected ECFCs. Increased IL-8 was observed in tissues with bone metastases in mice injected with conditioned media from co-cultured cells. High IL-8 levels are correlated with poor recurrence-free survival in TNBC patients. Together, these results suggest that CCL8 and IL-8 mediate the crosstalk between ECFCs and TNBC, leading to aggravation of tumorigenicity in TNBC.

P-27-072**Research on deriving the key molecules of gender-specific cancer malignancy mechanism**

S.Y. Kim, J. Kim

Department of Chemistry, College of Science and Technology, Duksung Women's University, Seoul, South Korea

Gender differences in cancer can be expressed as gender differences for extrinsic or intrinsic factors, such as exposure to cancer-causing external environments, cancer-related gene expression and regulatory mechanisms under the influence of sex chromosomes or sex hormones, and biological responses induced by stress in cells and tissues. Therefore, it is essential to consider gender specificity in the diagnostic procedures for cancer and the evaluation of cancer treatment. In this study, 314 genes showing statistically significant differences in expression depending on sex hormone estrogen treatment were identified by comparative analysis of the MCF7 cell line, a female-derived cell line, using total