大学院特別講義

（医歯学先端研究特論）（生命理工学先端研究特論）
（医歯理工学先端研究特論）

下記により大学院特別講義を行いますので、多数ご来聴下さい。

記

1．講　師

College of Pharmacy, Kyungpook National University
Director, Vessel-Organ Interaction Research Center, VOICE (MRC)
President, Korean Society of Vascular Biology and Medicine

Prof. You Mie Lee

2．演　題　**A gatekeeper function of Runx3 in cancer and endothelial cell-driven liver fibrosis**

3．日　時　２０２５年１０月３１日（金）１７：００～１９：００

4．場　所　M&D タワー11 階　大学院講義室３

5．要　旨

Inactivation of the tumor suppressor Runt-related transcription factor 3 (RUNX3) plays an important role in early tumorigenesis. We have previously demonstrated that RUNX3 is silenced by epigenetic modifications and protein methylation under hypoxic conditions, a key feature of the tumor microenvironment. Furthermore, we found that RUNX3 is essential for HIF-1α degradation, establishing its role as a sentinel in the early stages of cancer development. Building on these findings and recognizing that the vascular endothelium is a crucial gatekeeper of tissue homeostasis and adaptation to pathological challenges, we hypothesized that RUNX3 is also responsible for this gatekeeping function in endothelial cells. To test this, we created mice with endothelial-specific deletion of Runx3 and assessed the resulting phenotypic changes in liver pathogenesis. Mice with endothelial Runx3 deficiency developed gradual and spontaneous liver fibrosis due to the loss of LSEC (liver sinusoidal endothelial cells) characteristics. Single-cell RNA sequencing and quantitative RT-PCR revealed that leucine-rich alpha-2-glycoprotein 1 (LRG1) was highly expressed in RUNX3-deficient LSECs and activated hepatic stellate cells in a paracrine manner. We also found that circulating LRG1 levels were elevated in mouse models of liver fibrosis and in patients with fatty liver and cirrhosis, suggesting its potential as a biomarker. Additionally, single-cell RNA sequencing analysis demonstrated a change in a subset of the CD8+ T cell population suggesting that T cell differentiation may contribute to the fibrotic process in mice with endothelial-specific Runx3 deletion. In conclusion, our research reveals that RUNX3 is a crucial gatekeeper in ECs as well as in cancer development. Understanding this crucial communication between the endothelium and the tissue microenvironment in the absence of Runx3 can provide valuable insights for targeted therapeutics in liver fibrosis as well as cancer.

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