The 33rd Global and Local Infectious Diseases Research Seminar

RCGLID
OITA UNIVERSITY

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16:30-17:30

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Presenter : Lecturer Benjawan Saechue

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Venue: OITA Univ. RCGLID Meeting Room & Zoom

PRC2 in myeloid cells in the context of fibrosis and cancer

Ezh2, a crucial subunit of the polycomb repressive complex 2 (PRC2), is essential for epigenetic regulation through histone methylation. Although its function in various cell types is well documented, the specific role of Ezh2 in myeloid cells and its contribution to disease processes, such as hepatocellular carcinoma (HCC) and fibrosis, particularly scleroderma, remain largely unexplored. This study investigates the effects of myeloid-specific Ezh2 deficiency on tumorigenesis and fibrotic skin disease using mouse models.

A myeloid-specific Ezh2 knockout (Ezh2 KO) model was used to perform two parallel studies: (1) HCC progression, assessed using orthotopic transplantation of Dt81-Hepa1-6 liver tumor cells, and (2) fibrosis development, induced by bleomycin. In the HCC model, Ezh2 KO mice exhibited significantly more liver tumor foci than wild-type controls, along with elevated expression of tumor markers EpCam and Afp. Notably, TNF-α, a key pro-inflammatory cytokine, was markedly upregulated in the liver tissues of Ezh2 KO mice, indicating a heightened inflammatory response. This suggests that Ezh2 deficiency fosters a pro-inflammatory, pro-tumoral microenvironment, likely by altering macrophage polarization and increasing TNF-α production. In the fibrosis model, Ezh2 deficiency resulted in a reduction of fibrotic and inflammatory responses. Although both wild-type and Ezh2 KO mice developed skin fibrosis after bleomycin treatment, collagen accumulation and the expression of fibrosis markers such as TGF-β and IL-6 were lower in the Ezh2 KO group. The reduced expression of EZH2 in these mice appeared to directly attenuate the fibrotic response. Although statistical significance was not achieved, the data indicated a trend toward diminished fibrosis severity in the Ezh2-deficient mice.

These findings reveal that myeloid-specific Ezh2 deficiency promotes tumorigenesis by creating a pro-inflammatory, TNF-α driven environment in HCC, while it mitigates fibrosis by reducing collagen deposition and inflammatory responses, partly due to the lower expression of EZH2 in fibrotic tissue. The dual role of Ezh2 in disease pathogenesis highlights its potential as a therapeutic target in both cancer and fibrotic conditions.

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