

# 慶應医学会例会

下記により例会を開催いたしますので、多数ご来聴ください。

記

日時 2026年3月19日(木) 15:00

場所 ジェイキック会議室

演題 **Hoxa9 in B-to-Myeloid Lineage Switching**

Chen Zhao MD. PhD.

Department of Pathology, School of Medicine, Case Western Reserve University

Title: Hoxa9 in B-to-Myeloid Lineage Switching

Abstract: Leukemia and lymphoma cells frequently exhibit lineage plasticity as a survival mechanism under therapeutic pressure. This plasticity facilitates immune evasion, promotes more aggressive phenotypes, and contributes to drug resistance and treatment failure. B-cell plasticity has been recognized both clinically and experimentally for decades. Experimental studies have shown that CEBPa overexpression or PAX5 deletion can induce B-cell conversion into the myeloid lineage. However, whether these manipulations faithfully recapitulate pathological B-to-myeloid conversion remains unclear, and they do not result in transformation into myeloid leukemia.

Our recent findings demonstrate that co-activation of NF- $\kappa$ B and Notch signaling in committed B cells is sufficient to induce splenic marginal zone lymphoma, followed by transformation to diffuse large B-cell lymphoma. Intriguingly, NF- $\kappa$ B/Notch co-activation drives B-cell conversion into the myeloid lineage, ultimately leading to the development of acute myeloid leukemia (AML). Further analyses indicate that Notch signaling, via Rbpj, but not NF- $\kappa$ B signaling, accelerates B-to-myeloid conversion. (内線-63692)

担当 分子生物学教室 教室  
責任者 入江 奈緒子 教授  
担当者

以上

Using unbiased high-throughput approaches, we compared gene expression and DNA methylation profiles between pre-transplanted NF- $\kappa$ B/Notch co-activated B cells and converted AML cells. These studies identified Hoxa9 as a pivotal driver of B-cell-to-AML transformation. To further investigate its role, we generated Hoxa9 transgenic mice. Notably, Hoxa9-expressing B cells undergo conversion to myeloid cells and ultimately progress to AML. Together, our findings suggest that Notch activation facilitates the initiation of B-to-myeloid conversion, whereas Hoxa9 upregulation drives malignant progression.