Poster

# [P26-9] P26-9: Oncologic drugs (5): Pharmacokinetics, TDM practice

Chair: Kiyoshi Mihara, Japan

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## [P26-9-9] Tumor suppressor CYLD as a novel prognostic biomarker in primary breast cancer

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### Background

Cylindromatosis (CYLD) acts as a tumor suppressor by regulating various cell signaling pathways, such as nuclear factor-κB (NF-κB) signaling pathway. Although recent studies have shown that loss of functional CYLD is potentially-correlated with tumor progression, the clinical significance of CYLD expression in various types of malignancies, including breast cancer, remains to be elucidated. The aim of this study was to clarify the clinical significance of CYLD in breast cancer and its roles in tumor progression.

### Methods

CYLD mRNA expression in matched normal breast tissue samples and tumor breast tissue samples from 26 patients with breast cancer were evaluated. By means of immunohistochemistry, we also investigated CYLD protein expression and its clinical significance in 244 breast cancer cases. In addition, we determined the effects of CYLD expression on cell viability, cell migration, and NF-κB activity in breast cancer cells (MDA-MB-231 cells).

### Results

Compared with normal breast tissues, breast cancer tissues exhibited significant reduction of CYLD mRNA expression. Downregulation of CYLD promoted cell survival and migratory activities through NF-κB activation in MDA-MB-231 cells. Interestingly, CYLD overexpression clearly suppressed receptor activator of NF-κB ligand (RANKL)-induced NF-κB activation, suggesting that CYLD downregulation may promote breast cancer metastasis via NF-κB activation, including RANKL signaling. In addition, our immunohistochemical analysis revealed that reduced CYLD protein expression was significantly correlated with estrogen receptor negativity, high Ki-67 index, high nuclear grade, decreased disease-free survival, and reduced breast cancer-specific survival in primary breast cancer. Furthermore, our clinical analysis also indicated that the reduced CYLD expression was an independent factor for poor prognosis in breast cancer.

### Conclusions

CYLD downregulation may contribute to breast cancer metastasis through activation of NF-κB including RANKL signaling and serve as a novel prognostic biomarker in primary breast cancer.