東北大学グローバルCOE

Network Medicine 創生拠点

NM高等教育セミナー

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Histone demethylase JMJD2B/KDM4B functions as a co-factor of estrogen receptor

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Estrogen plays a pivotal role in the development and progression of breast cancer. Estrogen receptor (ER)-positive cancer is the most common subtype of breast cancer. Patient prognosis has been greatly improved by the use of selective ER modulators (SERMs) such as tamoxifen. However, a critical remaining problem is the eventual emergence of therapeutic resistance to SERMs. Thus, determining the molecular basis of the ER signaling pathway will be crucial for understanding the biology of breast cancer, overcoming SERM resistance, and identifying novel therapeutic targets to enhance efficacy in cancer treatment.

We have identified that JMJD2B (also known as KDM4B) constitutes a key component of the estrogen signaling pathway. JMJD2B is expressed in a high proportion of human breast tumors, and that expression levels significantly correlate with ER positivity. In addition, 17-beta-estradiol (E2) induces JMJD2B expression in an ERα dependent manner. JMJD2B is recruited to ERα target sites, demethylates H3K9me3 and facilitates transcription of ER responsive genes including MYB, MYC and CCND1. As a consequence, knockdown of JMJD2B severely impairs estrogen-induced cell proliferation and the tumor formation capacity of breast cancer cells. In addition, Jmjd2b-deletion in mammary epithelial cells exhibits delayed mammary gland development in female mice.

Taken together, these findings suggest an essential role for JMJD2B in the estrogen signaling. Further studies in the ER-JMJD2B signaling pathway will advance our knowledge of the oncogenic signaling networks and perhaps reveal novel therapeutic approaches to combat breast cancer.

本セミナーは医学履修課程特別セミナー等を兼ねています。受講学生は履修簿を持参し、セミナー修了後にサインを受けること。聴講は自由大歓迎です。学部生の皆さんもぜひどうぞ。

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