



第 338 回 つくば分子生命科学セミナー

TSUKUBA MOLECULAR LIFE SCIENCE SEMINAR

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

演者 : Dr. Hitoshi Okada

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日時 : 2011 年 12 月 26 日 (月) 17:00-18:30

会場 : 医学学系棟 4 階 482 室

要旨 :

Estrogen is a key regulator of normal function of female reproductive system and plays a pivotal role in the development and progression of breast cancer. Estrogen receptor (ER)-positive breast 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 ER α dependent manner. JMJD2B interacts with ER α and components of the SWI/SNF-B chromatin remodeling complex. JMJD2B is recruited to ER α 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. Interestingly, genome-wide approaches have identified focal gene amplification of JMJD2B in human brain tumors. These findings highlight the clinical relevance of JMJD2B's functions in the growth of ER-positive breast cancer as well as its potential oncogenic function. Furthermore, 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 further our knowledge of the mechanisms of nuclear and oncogenic signaling pathways and perhaps reveal novel therapeutic approaches to combat breast cancer.

岡田先生の研究室はポスドクを募集中です！ポスドク希望者は是非参加して下さい。

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