Seminar のお知らせ

（アドバンス生命理学特論ではありません）

Non-coding RNAs involved in active chromatin domain formation in brest cancer

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場所：　理学部 A 館 2 階　A222 号室

A222 Room, 2nd Floor, Science A Building

In the nucleus, genomic DNA is intricately folded into several layers, which are critical for nuclear function and organization. Nuclear long non-coding RNAs (ncRNAs) are integrated in the chromatin regulation. Here we show that a cluster of ncRNAs which we termed as Eleanors (ESR1 locus enhancing and activating non-coding RNAs), is induced from a large chromatin domain during breast cancer recurrence, and activates genes within the domain.

Estrogen receptor alpha (ER)-positive breast cancer that undergoes endocrine therapy often acquires therapy-resistance, resulting in recurrence. To elucidate the underlying mechanism, we performed transcriptome analyses using human ER-positive breast cancer cell line, MCF7 and its derivative LTED (long-term estrogen deprivation), which recapitulates the endocrine therapy-resistance. We found that the gene for ER (ESR1) was up-regulated in LTED, accompanying emergence of ncRNAs, Eleanors, from approximately 0.7 Mb region including ESR1 and other three co-regulated genes. This “Eleanor chromatin domain” corresponded to topologically associating domain independently determined by HiC (chromosome conformation capture) technology. This domain is active A-compartment in breast cancer, while it is repressive B-compartment in non-mammary cells, suggesting that Eleanor transcription may be a driving force to activate the domain in cancer. In the nucleus, Eleanors were associated with the active ESR1 transcription site and formed distinct RNA foci both in LTED cells and patient tissues. Depletion of Eleanors resulted in repression of ESR1 mRNA and LTED cell proliferation.

Our results revealed a novel type of ncRNA-mediated chromatin domain formation, which could be a good diagnostic and therapeutic target for recurrent breast cancer.

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