RIKEN BDR

Women and Future in Science Seminar

Transcriptional regulation by a nuclear domain

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Spatio-temporal remodeling of extracellular matrix orients epithelial sheet folding

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13:00-14:00 JST

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Transcriptional regulation by a nuclear domain

The nuclear space is compartmentalized by nuclear domains such as nucleolus, nuclear speckle, and PML body, allowing multiple biological reactions to proceed without confusion. However, the contribution of nuclear domains to genomic function is largely unknown. Promyelocytic leukemia (PML) nuclear bodies are spheres of 0.1–1.0 um in diameter found in the nucleus and involved in various biological processes, including senescence, tumor suppression, and antiviral responses. It has been reported that several chromatin regulators localized in PML bodies, implying the potential role for PML bodies in chromatin regulations. However, little is known about their role on gene expression due to technical limitation. Thus, we developed APEX-mediated chromatin labeling and purification (ALaP) to identify the genomic regions proximal to PML bodies. We found that PML bodies associate with active regulatory regions across the genome and with ~300 kb of the short arm of the Y chromosome (YS300) in mouse embryonic stem cells. The PML body association with YS300 is essential for the transcriptional activity of the neighboring Y-linked clustered genes. Mechanistically, PML bodies provide specific nuclear spaces that the de novo DNA methyltransferase DNMT3A cannot access, resulting in the steady maintenance of a hypo-methylated state at Y-linked gene promoters. In this seminar, I will discuss the transcriptional regulation by PML body.

Spatio-temporal remodeling of extracellular matrix orients epithelial sheet folding

Biological systems are inherently noisy; however, they produce highly stereotyped tissue morphology. Drosophila pupal wings show a highly stereotypic folding through uniform expansion and subsequent buckling of wing epithelium within a surrounding cuticle sac. The folding pattern produced by buckling is generally stochastic; it is thus unclear how buckling leads to stereotypic tissue folding of the wings. We found that the apical extracellular matrix (aECM) protein, Dumpy, guides the position and direction of buckling-induced folds. Dumpy anchors the wing epithelium to the overlying cuticle at specific tissue positions. Tissue-wide alterations of Dumpy deposition yielded different buckling patterns. We further found that Dumpy anchorage is maintained over 12hrs before folding, but it is removed by apically-localized extracellular proteases immediately after the initiation of folding. The depletion of the proteases also led to abnormal wing folding, suggesting that not only the patterned Dumpy deposition but also temporal regulation of its degradation is required for proper wing folding. In summary, we propose that spatio-temporal ECM remodeling shapes stereotyped tissue folding through dynamic interactions between the epithelium and its external structures.

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