Role of IL-33 Mediated Chromatin Organization in Glial Cell Proliferation and Differentiation

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Abstract

Interleukin-33 (IL-33) was first found at a high level in the nucleus of endothelial cells, thereby referred as a nuclear protein. Yet, the molecule is considered as an alarmin to act as a classic cytokine through enzymatic cleavage upon tissue damage. The IL-33 precursor protein (about 31 kDa) consists of N-terminal homeodomain-like helix-turn-helix and IL-1-like cytokine domain. The N-terminal contains a chromatin-binding motif and nuclear localization sequence (NLS) that mediates nuclear translocation and association with histones in heterochromatin. The previous study from my laboratory has also shown that IL-33 could act as the cytokine via the interaction with ST2 to promote glioma tumorigenicity and microglia invasion by the regulation of chemokine (C-C motif) ligand 7 (CCL7) expression. Our recent study has also indicated that IL-33 expression was detected in the nuclei of oligodendrocyte precursor cells (OPCs) in postnatal rat corpus callosum, as well as in myelin-producing glia in the central nervous system (CNS), oligodendorcytes (OLs), in adult mice and rats. In addition, maturation of OLs was suppressed by the downregulation of IL-33 expression in OPCs using lentivirus-mediated shRNA delivery. Nevertheless, it remains to be uncovered how nuclear IL-33 regulates the differentiation of OPCs and mediates the proliferation of glioma cells. Through a chromatin fiber analysis, we have observed that nuclear IL-33 molecules were associated with chromatins in C6 glioma cells. The distribution of the chromatin granules in wildtype (WT) and IL-33 gene deficient OPCs is under investigation through transmission electron microscopy. Thus, we attempt to further determine the structure of chromatin and chromosome in OPCs and human glioma cell line through Soft X-Ray Tomography.

Keywords – Chromatin, interleukin-33, histone, cell differentiation, oligodendrocyte

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