Interleukin 33

Interleukin 33 (IL-33) is a protein that is involved in the immune system's response to infection and inflammation. It belongs to the family of cytokines, which are signaling molecules that are produced by cells and play important roles in cell-to-cell communication.

IL-33 is produced by a variety of cells, including epithelial cells, endothelial cells, and immune cells. It acts as an alarm signal to alert the immune system of tissue damage or infection. IL-33 binds to its receptor, ST2, which is expressed on immune cells such as T cells, mast cells, and eosinophils, among others. This binding activates the immune cells and triggers an immune response.

IL-33 is involved in a variety of immune-related processes, including the development of Th2 cells, which produce cytokines that are important in the immune response to parasites and allergies. IL-33 has also been implicated in asthma, autoimmune diseases, and cancer.

Overall, IL-33 plays an important role in the regulation of the immune system and the response to infection and inflammation.

The lymphatic drainage system of the brain, composed of the glymphatic system and meningeal lymphatic vessels (MLVs), plays an essential role in the clearance of toxic waste after brain injury. The neuroprotective effect of interleukin 33 (IL-33) in TBI mice has been demonstrated; however, its impact on the brain lymphatic drainage is unclear. Liu et al. established a fluid percussion injury model to examine the IL-33 administration effects on neurological function and lymphatic drainage in the acute brain of TBI mice. They verified that exogenous IL-33 could improve the motor and memory skills of TBI mice and demonstrated that in the acute phase, it increased the exchange of cerebrospinal and interstitial fluid, reversed the dysregulation and depolarization of aquaporin 4 in the cortex and hippocampus, improved the drainage of MLVs to deep cervical lymph nodes, and reduced tau accumulation and glial activation. Liu et al. speculated that the protective effect of exogenous IL-33 on TBI mice's motor and cognitive functions is related to the enhancement of brain lymphatic drainage and toxic metabolite clearance from the cortex and hippocampus in the acute stage. These data further support the notion that IL-33 therapy may be an effective treatment strategy for alleviating acute brain injury after TBI. [1)]

A study assessed the expression and prognostic significance of IL-33 in human astroglial brain tumors. Protein levels of IL-33 were determined by immunohistochemistry using a tissue microarray containing 95 human gliomas. mRNA expression data of IL-33, as well as of its receptors, IL-1 receptor-like 1 protein, and IL-1 receptor accessory protein (IL1RAcP), were obtained from The Cancer Genome Atlas database. IL-33 protein was expressed heterogeneously in tumor tissue but was not detected in normal brain tissue. There was no differential IL-33 protein expression by tumor grade, while IL-33 protein expression was associated with inferior survival in patients with recurrent glioblastomas. Interrogations of the TCGA database indicated that mRNA expression of IL-33 and IL-33 receptors was heterogeneous, and IL-33 and IL1RAcP mRNA levels correlated with the tumor grade. Elevated IL-33 mRNA levels were associated with the inferior survival of glioblastoma patients. Therefore, IL-33 may play an important role in the pathogenesis and prognosis of human gliomas [2)].

1)

Liu M, Huang J, Liu T, Yuan J, Lv C, Sha Z, Wu C, Jiang W, Liu X, Nie M, Chen Y, Dong S, Qian Y, Gao C, Fan Y, Wu D, Jiang R. Exogenous interleukin 33 enhances the brain's lymphatic drainage and toxic protein clearance in acute traumatic brain injury mice. Acta Neuropathol Commun. 2023 Apr 7;11(1):61. doi: 10.1186/s40478-023-01555-4. PMID: 37024941.

2)

Gramatzki D, Frei K, Cathomas G, Moch H, Weller M, Mertz KD. Interleukin-33 in human gliomas: Expression and prognostic significance. Oncol Lett. 2016 Jul;12(1):445-452. Epub 2016 May 25. PubMed PMID: 27347163.