ポスター

[1P]F. 神経系の疾患 2

2022年6月30日(木) 13:00 ～ 14:00 ポスター会場2 (宜野湾市民体育館)

[1P-102]ニーマンピック病 C型における免疫系による神経変性制御

*安田 徹[1]、内山 徹[1]、望月 秀樹[2]、小野寺 雅史[1] (1. 国立成育医療研究センター、2. 大阪大学大学院医学系研究科神経内科学)

キーワード：Lysosome storage disrder, Niemann-Pick disease type C, Purkinje cell, immune system

Niemann-Pick disease type C (NPC) is an autosomal-recessively inherited lysosomal storage disorder affecting an estimated 1 in 120,000 live births worldwide. Mutations in NPC1 or NPC2 gene represent approximately 95% or 5% of total patients with NPC, respectively. Their gene products, NPC1 and NPC2 proteins, function cooperatively in late endosomes and lysosomes to transport unesterifed cholesterol to the plasma membranes and the other organelles in the cell. Typical clinical feature of the disease is neurovisceral accumulation of unesterified cholesterol and several forms of glycosphingolipids. NPC can present with a broad range of clinical manifestation from a neonatal acute fatality to an adult-onset chronic disease associated with neurodegeneration. The development of neurological symptoms, including cerebellar ataxia, laughter-induced cataplexy, dystonia, and progressive dementia, affects quality of life of the patients drastically. Hence, it is essential to explore the pathogenic events that trigger and/or promote the neurodegenerative process for future clinical interventions. In this study, we addressed an involvement of immune system in neuropathogenic process using a murine model of NPC. Breaching of blood-brain barrier and infiltration of monocyte-derived macrophages correlated spatially and temporally with the loss of cerebellar Purkinje cells, which is a hallmark of neurodegeneration in NPC. Reduction of microglial cells and circulating monocytes ameliorated Purkinje cell degeneration. On the other hand, lack of acquired immune system enhanced cerebellar ataxic phenotype and Purkinje cell loss, suggesting that lymphoid cells may have therapeutic effect in NPC. We found that peripheral injection of CD4/CD25-double-positive regulatory T cells ameliorated cerebellar ataxia and Purkinje cell loss. Our results disclose a previously unrecognized neuropathogenicity of immune system in NPC and would benefit future remedies for devastating neurological diseases.