ポスター

[1P]F. 神経系の疾患 2

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[1P-241]神経炎症がパーキンソン病モデルマウスのα-シヌクレイン病理を増強する。

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キーワード：Parkinson's disease, α-synuclein, Neuroinflammation

Objective: α-synuclein (α syn) is a major component of Lewy bodies, a pathological hallmark of Parkinson's disease (PD), and its genetic mutations cause familial PD. In neurodegenerative diseases such as PD and Alzheimer's disease, the presence of Tumor necrosis factor-α and Interleukin (IL)-1-positive microglia involved in neuroinflammation has long been recognized as important, but the exact role of the immune response in disease progression is not clear. Although the relationship between α syn and microglia has been discussed from the perspective of neurodegeneration and neuronal damage, the propagation and aggregation of α syn have not been clearly demonstrated. In this study, we analyzed the molecular mechanisms of neuroinflammation and α syn propagation and aggregation induced by activated microglia using α syn fibril-injected mice. Methods: α syn fibrils were injected into the substantia nigra of both wild-type and ASC (apoptosis-associated speck-like protein containing caspase recruitment domain) KO mice. ASC forms a complex called the NLRP3 inflammasome, which induces the maturation and production of the pro-inflammatory cytokines IL-1β and IL-18 via the protease Caspase-1 (Misawa T, et al. Nat Immunol. 2013). Therefore, in ASC KO mice, microglial activation and induction of inflammatory cytokine production are suppressed. We analyzed the pathology of nigral dopaminergic neuronal loss, α syn aggregate formation, and microglial status and distribution in the brains of α syn fibril-injected wild-type and ASC KO mice.
Result: ASC KO mice showed reduced phosphorylated-α syn aggregate formation and dopamine cell loss in the substantia nigra compared to wild-type mice, but no significant difference in the propagation of α syn to the cortex or striatum. Conclusion: These results suggest that neuroinflammation is involved in the formation of α syn aggregates and the loss of dopaminergic neurons, and hence plays an important role in the progression of synucleinopathy.