講演情報

一般演題口演セッション

[O-28] 一般演題口演セッション28　【英語】

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座長:長峯 隆(札幌医科大学医学部神経科学講座), 石浦 浩之(東京大学医学部附属病院脳神経内科)

[O-28-2] Cell-free DNA profiling reveals neutrophils as type1 interferon driver in neuromyelitis optica

○村田 尚[1], 木下 允[1], 安水 良明[1,2], 元岡 大祐[3], 別府 祥平[1], 白石 直之[1], 杉山 靖子[1], 木原 圭梧[1], 多田 智[1], 甲田 亨[1], 小中 八郎[4], 高松 漂太[4], 熊ノ郷 淳[4], 奥野 龍禎[1], 望月 秀樹[1]
(1.大阪大学医学系研究科 神経内科, 2.大阪大学免疫学フロンティア研究センター, 3.大阪大学微生物病研究所附属遺伝情報実験センター, 4.大阪大学医学系研究科 呼吸器・免疫内科学)

[Objectives]Recently accumulating evidence suggests the pivotal role of type 1 interferon (IFN-1) signature in the pathogenesis of neuromyelitis optica spectrum disorder (NMOSD). However, the mechanism of the initial trigger that augments IFN-1 signature in peripheral immune system of NMOSD remains to be elucidated. [Methods]Clinical samples were obtained from aquaporin-4 antibody-positive NMOSD patients. IFN-1 induction in peripheral blood mononuclear cells (PBMC) by serum-derived cell-free DNA (cfDNA) was assessed in combination with blockades of DNA sensors in vitro. The DNA methylation profile of cfDNA fractions was analyzed by bisulfite sequencing to elucidate the cellular origin of cfDNA. Furthermore, we analysed the induction of neutrophil extracellular trap (NET)-associated cell death (NETosis) in NMOSD and evaluated the efficacy of pharmacological intervention of NETosis. [Results]DNase treatment, cGAS-inhibitor and toll-like receptor 9 antagonist efficiently inhibited IFN-1 production. DNA methylation pattern of cfDNA in NMOSD patients demonstrated that the predominant cellular source was neutrophils. Whole blood transcriptome analysis also revealed neutrophil activation in NMOSD. In addition, enhanced NETosis induction was observed with NMOSD sera, and efficient pharmacological inhibiton of NETosis with dipyridamole was observed. [Conclusions]Our study highlights the previously unrevealed role of cfDNA predominantly released by neutrophil in the induction of IFN-1signature in NMOSD.