DANDRITE
Danish Research Institute of Translational Neuroscience
Nordic EMBL Partnership for Molecular Medicine

AARHUS UNIVERSITY

Virtual DANDRITE Lecture

Thursday 29 April 2021

12.00 – 13.00

Online via Zoom

Please find Zoom link via the Outlook calendar invitation. If you have not received this, please write an e-mail to Kathrine: kh@dandrite.au.dk

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Microglia dysfunction and new therapeutic approach in primary microgliopathy

Microglia originating from yolk sac exert various functions to maintain the homeostasis in the brain, and their functional breakdown appears to be involved in the pathophysiology of various neurological diseases. In this seminar, loss of homeostatic microglia and new therapeutic approaches for primary microgliopathy will be discussed. ASLP (adult-onset leukoencephalopathy with axonal spheroids and pigmented glia) known as a primary microgliopathy is an adult-onset leukoencephalopathy caused by CSF1R mutation. CSF1 receptor encoded plays an important role in the function of microglia. In brain of ALSP patients, homeostatic microglia are significantly reduced. Bi-allelic CSF1R mutations cause childhood-onset severe phenotype and elimination of microglia from the brain parenchyma. Since microglia also almost disappear in CSF1R-deficient mice and rats, CSF1R deficiency and loss of microglia appear to be tightly associated across species. Based on the underlying mechanism of homeostatic microglia loss, novel approaches using cell transplantation of normal microglia-like cells have been attempted. Transplantation of wild-type bone marrow cells into Csf1r-/- mice results in replacement by donor-derived microglial-like cells in the recipient's brain. The concept of "microglial niche" may explain the rationale behind the microglial cell transplantation in disease condition(s). Hematopoietic stem cell transplantation (HSCT) has been attempted in 4 patients with ALSP. Beneficial effects by showing stabilization of the disease course have been observed. Although the effectiveness of HSCT for ALSP patients warrants further investigation, the approach of cell transplantation that replaces ruptured homeostatic microglia with normal microglia-like cells seems to be promising.