p-296

Friday

Restoring Dysfunctional Regulatory T cells Through Ex Vivo Expansion in Frontotemporal Dementia

Abdulmunaim Eid, Maria Pascual, Joseph Masdeu, Stanely Appel, Alireza Faridar

State of the art
Inflammation is a significant component of frontotemporal dementia (FTD). Co-localization of neuroinflammation and brain protein aggregation has been previously documented in the clinical setting of FTD. However, the role of the adaptive immune system particularly regulatory T cells (Tregs) is unclear. We hypothesize that Tregs immunomodulatory mechanisms are compromised and shift the immune system towards a proinflammatory status which might contributes to disease progression.

Method
24 FTD individuals and 16 aged-matched controls were studied. Tregs were isolated from venous blood and co-cultured with corresponding Tresps and proliferation of Tresps was determined. Plasma assays of 48 cytokines were obtained through Olink® Target Cytokine panel. Tregs were expanded ex vivo in the presence of expander beads, interleukin-2 and rapamycin to promote their suppressive function.

Result
The suppressive function of Tregs on Tresps proliferation was significantly compromised in FTD individuals, compared to controls. The Olink analysis of pro-inflammatory mediators revealed increases in plasma levels of CXCL9, CXCL10, CXCL11, and TNFa in FTD individuals. Finally, Tregs were expanded ex vivo which substantially restored and enhanced their suppression of responder T cell proliferation and pro-inflammatory macrophage activation.

Conclusion
Tregs immunomodulatory function is compromised in patients with FTD, that is associated with upregulation of plasma inflammatory chemokines and cytokines. Combining these two key findings, we propose that pro-inflammatory peripheral immune cells contribute to neuroinflammation and disease progression in FTD. Restoration of Treg function could be explored as a means to modulate the inflammatory status of Alzheimer disease.

Conflicts of interest

N/A