GMSI 2019

WINNER

Dr Laure Michel

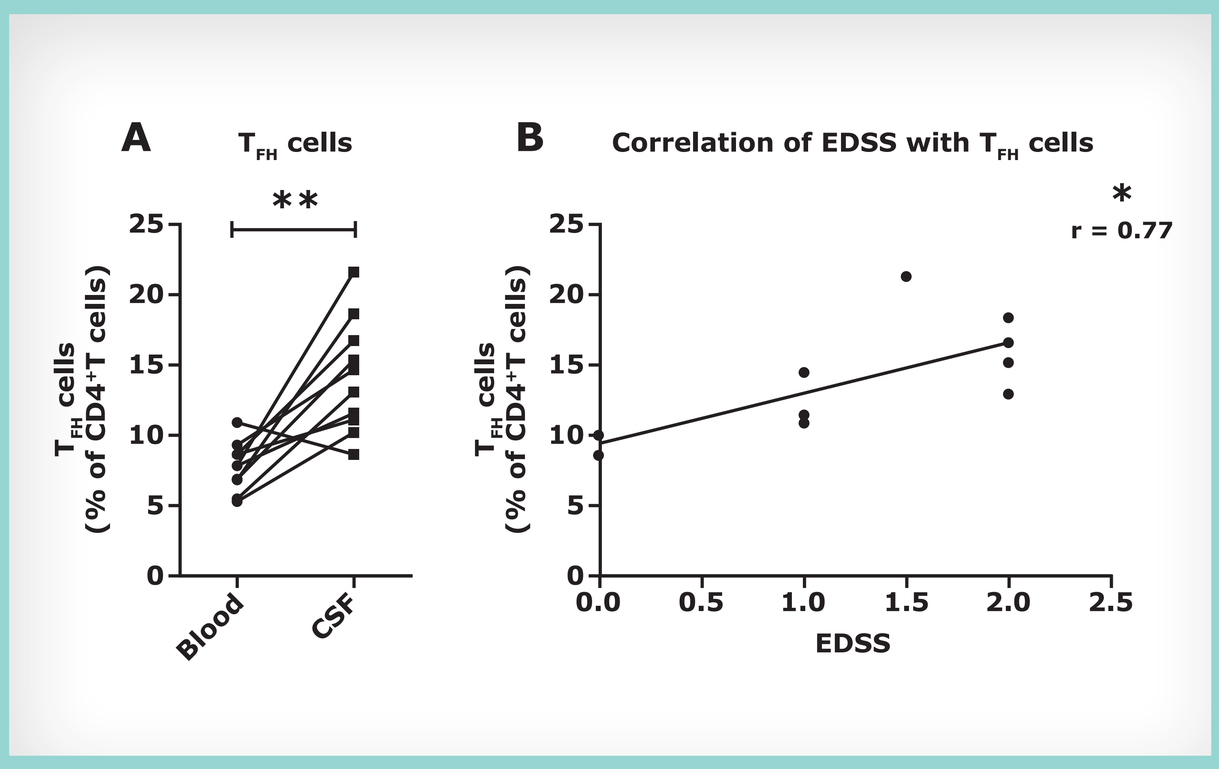
Unité Mixte de Recherche (UMR) S1236, INSERM, Université de Rennes, Etablissement Français du Sang, Rennes, France

Suivi Immunologique des Thérapeutiques Innovantes, Centre Hospitalier Université de Rennes, Etablissement Français du Sang, Rennes, France

T-cell/B-cell collaboration in multiple sclerosis: exploring an intimate relationship

Background

- Previous research has identified a proinflammatory profile of peripheral blood B cells in patients with MS, with a higher secretion of IL-6, LTa and GM-CSF
- However, little is known about the differentiation of B cells in patients with MS and the potential inflammatory (or regulatory) contribution of plasma cells in MS pathophysiology
- T_{FH} cells, which express CXCR5, are crucial for supporting B-cell differentiation by guiding their migration into B-cell follicles



Analysis of the frequency of T_{FH} cells in paired blood/CSF of patients with RRMS.
(A) Frequency of T_{FH} cells within CD4 T cells from patients with RRMS (n=10) in CSF and paired blood; (B) Correlation between the frequency of CSF-infiltrating T_{FH} cells and EDSS score. Spearman's correlation coefficient was used to analyse the relationship between variables

CSF, cerebrospinal fluid; CXCR5, C-X-C motif chemokine receptor 5; EDSS, Expanded Disability Status Scale; GM-CSF, granulocyte–macrophage colony-stimulating factor; LTa, lymphotoxin alpha; RRMS, relapsing–remitting MS; T_{FH}, follicular helper T

Hypothesis

- Our hypothesis is that some T_{FH} subsets are directly involved in autoreactive B-cell peripheral activation/differentiation at the early stage of MS (relapsing phase), and that these cells are able to migrate inside the CNS to contribute to the formation of tertiary lymphoid structures, which are directly associated with disease progression

Project synopsis

- The overall goal of this project is to fully elucidate where and how T_{FH} cells interact with B cells at different stages of MS disease and in different compartments
- To address our hypothesis:
  - We will perform a transcriptomic analysis (RNA sequencing) of CSF-infiltrating T_{FH} in MS
  - We aim to characterize B-cell differentiation abilities of circulating T_{FH} cells by performing co-cultures using memory/naive B cells from patients with MS and controls
  - We will perform migration assays of circulating T_{FH} cells subsets across human endothelial cells to assess the migration capacities of these cells
- These results will address the contribution of T_{FH}/B-cell crosstalk in MS and identify biological targets to normalize T_{FH}/B compartment homeostasis in order to inhibit inflammation and, ultimately, progression in MS

Merck KGaA,
Darmstadt, Germany

GBPMLR/NONNI/0719/0049d | August 2019

US/NPR/0119/0006(1)