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B cell differentiation is defective in Multiple Sclerosis patients

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Introduction
Clinical trials on the efficacy of B-cell depleting therapies in relapsing multiple sclerosis (MS) have suggested that B cells may contribute to MS pathogenesis, potentially through antibody independent mechanisms. Meningeal lymphoid follicle-like structures have been found in some progressive MS patients and meningeal inflammation seem to be observed in all forms of MS. Even if there have been many progresses in the understanding of B cell roles in MS, the exact implication and roles of plasma cells remain badly known.

Objective
• Characterization of the B cell differentiation profile of MS patients compared to healthy controls (HC)
• Characterization of the frequencies of the different TFH subsets in the blood and the cerebrospinal fluid (CSF)

Methods
• A two-step model of peripheral B cell differentiation

Characterization of a defective B cell differentiation profile in MS patients

Conclusion
For the first time, we show that MS patients present a defect in their B cell differentiation. We hypothesize that these plasmablasts are more pro-inflammatory in MS patients, and that the apoptotic cells are probably regulatory plasma cells. To explore this hypothesis, we plan now to perform cytokine analysis (Cytometry and LumineX), transcriptomic analysis, but also to test the supernatant’s cytotoxic effects on oligodendrocytes cultures.
We also show that MS patients present an altered TFH phenotype in periphery, and for the first time we highlight that TFH cells infiltrate the CSF of MS patients with an activated profile. We plan to investigate by immunohistochemistry wether TFH cells infiltrate the central nervous system of MS patients. To better understand the involvement of TFH cells in the pathophysiology of MS, we also prospect to assess the abilities of TFH cells to differentiate B cells by co-culture of autologous TFH cells with B cells.

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