Optimal Response to Dimethyl Fumarate is Mediated by a Reduction of Th17.1 cells after 3 Months of Treatment

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Objective:
Since a percentage of relapsing-remitting multiple sclerosis (RRMS) patients do not exhibit an optimal response to dimethyl fumarate (DMF), the objective of this study was to identify early biomarkers of treatment response by analysing changes in peripheral leukocyte subpopulations directly in whole blood samples.

Background:
DMF is one of the most promising therapies for RRMS patients since it exerts immunomodulatory and neuroprotective effects. However, not all the patients remained with no evidence of disease activity following 12 months treatment. The identification of early biomarkers of treatment response could be useful for the selection of the most appropriated treatment for each patient.

Design/Methods:
Longitudinal and prospective study analysing peripheral blood leukocyte subpopulations in 22 RRMS patients before initiating DMF treatment (baseline) and following 1, 3, 6 and 12 months of follow-up. Patients were classified as NEDA (no evidence of disease activity) or ODA (ongoing disease activity) based on clinical and radiological data obtained during the follow-up, and differences between groups of patients were analyzed.

Results:
The beneficial effect of DMF was associated with a specific depletion of memory CD4+ and CD8+ T lymphocytes and B cells. Importantly, only NEDA patients showed: i) a shift from a pro- to an anti-inflammatory profile, with an increase of Th2 cells and a decrease of Th17.1 lymphocytes; ii) an induction of transitional B cells; and iii) an increase of regulatory CD56bright NK cells.

Conclusions:
The optimal response to DMF is mediated by a shift to anti-inflammatory and immunoregulatory profile, showing Th17.1 lymphocytes as a potential early biomarker of treatment response.