eFigures

**eFigure 1:** (A) Representative flow cytometry plots of the expression of int.α4 in memory CD4 T cells and the expression of int.β7 in int.α4+ memory CD4 T cells (gray filled histogram). The black thick line histogram represents the int.β7 expression on cells pre-incubated for one hour at 37 degrees with an anti-int.β7 (FIB504) unlabeled antibody. (B) Overlay showing the expression of int.β1 in int.α4+int.β7- and int.α4+int.β7+ memory CD4 T cells pre-incubated (black thick line) or not (gray filled) for 1 hour at 37 degrees with an anti-int.β1 (P5D2) unlabeled antibody. The gray thin line histograms represent the FMO (Fluorescence Minus One) control for int.β1 staining. (C) Representative flow cytometry plots of CXCR3 and CCR6 expression on CXCR5- int.β7- and CXCR5- int.β7+ memory CD4 T cells.
**eFigure 2:** Percentages of integrin $\beta^7$- and integrin $\beta^7+$ memory CD4 T cells expressing TNF$\alpha$, GM-CSF, IL-17A, IL-17F, IL-13, IL-2, IL-4 and IL-5 in healthy donors after PMA and Ionomycin stimulation. Paired Student $t$ test.
Figure 3: (A) Representative plots of integrin $\alpha 4$ versus integrin $\beta 1$ (top row) and integrin $\alpha 4$ versus integrin $\beta 7$ (bottom row) expression for a healthy donor, a RRMS NTZ- and a RRMS NTZ+ patient. Gated on memory CD4 T cells. (B-C) Median of fluorescence intensity of int.$\alpha 4$ expression on memory CD4 T cells (B) and of int.$\beta 7$ expression on int.$\beta 7^+$ memory CD4 T cells (C) in healthy donors (n=61), RRMS NTZ- (n=19-24) and RRMS NTZ+ (n=29-32) groups. (D) Overlay of the expression of int.$\beta 7$ in memory CD4 T cells from a healthy donor (gray line), a patient RRMS NTZ- (blue line) and a patient RRMS NTZ+ (orange line) on the left. Percentages of int.$\beta 7^+$ cells in memory CD4 T cells in healthy donors (n=61), RRMS NTZ- (n=24) and RRMS NTZ+ (n=32) patients on the right. (E) Absolute numbers per $\mu$l of blood CD4 T cells and memory CD4 T cells in healthy individuals (n=57) and patients with RRMS not treated (NTZ-, n=32) or treated (NTZ+, n=34) with natalizumab. One-way ANOVA followed by Tukey’s multiple comparison test.
**eFigure 4:** (A) Overlays of int.α4 and int.β1 expression on memory CD4 T cells, int.β7- and int.β7+ memory CD4 T cells of a healthy individual (gray line), a patient with RRMS NTZ- (blue line) and a patient with RRMS NTZ+ (orange line). Light gray filled histograms represent cells unstained for the marker of interest (FMO control). (B) Median of fluorescence intensity of int.α4 and int.β1 expressed by int.β7- memory CD4 T cells in healthy donors (n=61), RRMS NTZ- (n=19) and RRMS NTZ+ (n=29) groups.
**eFigure 5**: EDSS, duration of the disease and total number of relapses of patients with RRMS NTZ- and NTZ+ included in the study. Unpaired Student t test.
eFigure 6: Correlations in patients with RRMS between the percentages of CXCR3+CCR6+ (Th17/Th1) cells among int.β7+ memory CD4 T cells and the EDSS score, the duration of the disease and the number of past relapses. Each dot represents a sample from an individual subject (RRMS NTZ-: blue symbols, RRMS NTZ+: orange symbols). Linear regression are indicated by black solid lines.
eFigure 7: (A) Percentages of integrin β7- and integrin β7+ memory CD4 T cells expressing IFNγ, IL-10, IL-4, IL-5, IL-13, TNFα and MIP-1β in healthy donors, RRMS NTZ- and RRMS NTZ+ groups. One-way ANOVA followed by Tukey’s multiple comparison test. (B) Representative flow cytometry plot of the expression of IFNγ and IL-17A (top row) and of GM-CSF and IL-17A (bottom row) by int.β7+ memory CD4 T cells in a healthy donor, a patient RRMS NTZ- and a patient RRMS NTZ+. 
**Figure 8:** (A-B) Correlations between the percentages of IFNγ+IL-17A+ (A) and GM-CSF+IL-17A+ (B) cells contained in integrin β7+ memory CD4 T and clinical parameters: EDSS score, duration of the disease and number of past relapses. Each dot represents a sample from an individual subject (blue symbols for RR MS NTZ- patients, orange symbols for RRMS NTZ+ patients). Linear regression are indicated by black solid lines. (C-D) Comparison of the percentages of IFNγ+IL-17A+ (C) and GM-CSF+IL-17A+ (D) cells in integrin β7+ memory CD4 T cells in NTZ- (blue) and NTZ+ (orange) RRMS patients with similar EDSS values or range of disease duration.