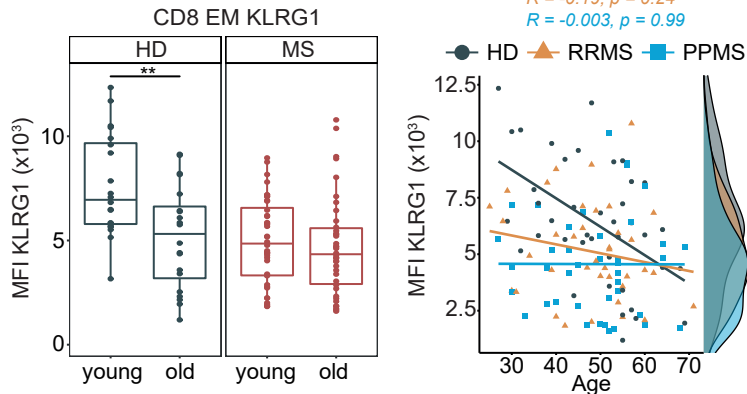
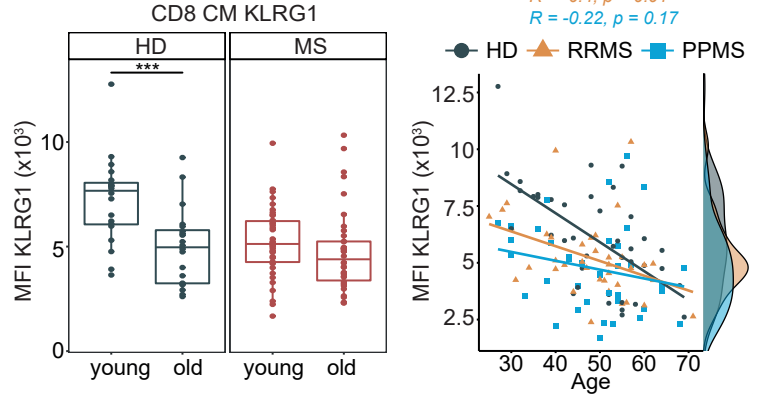
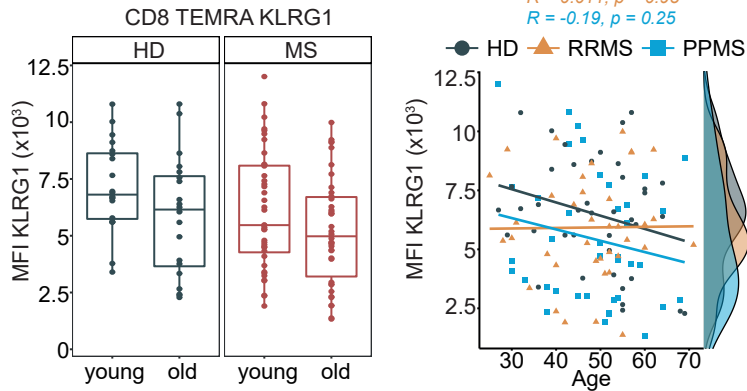
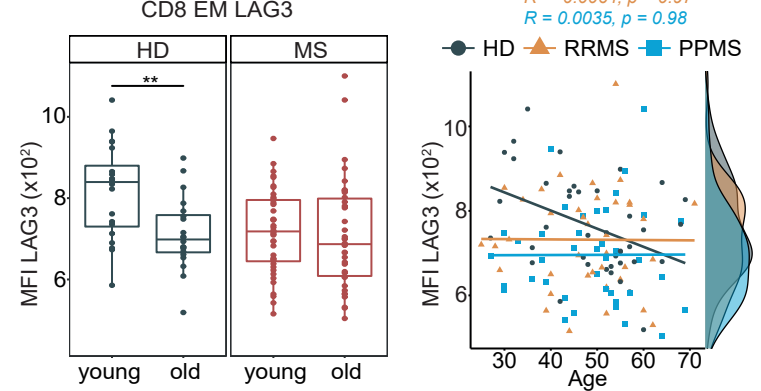
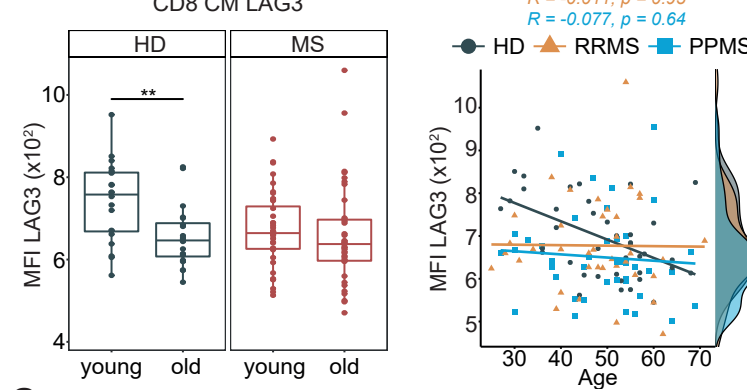
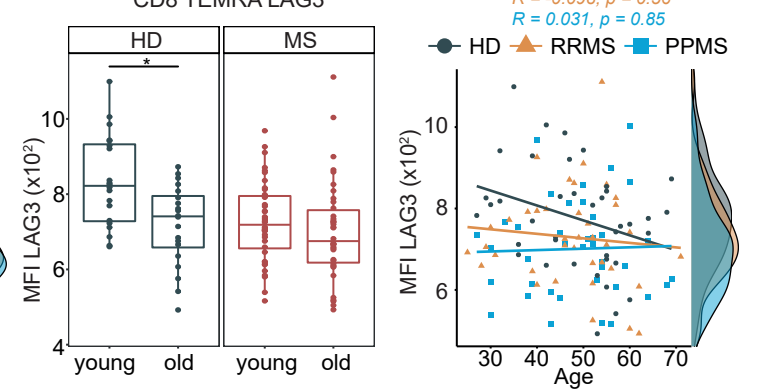
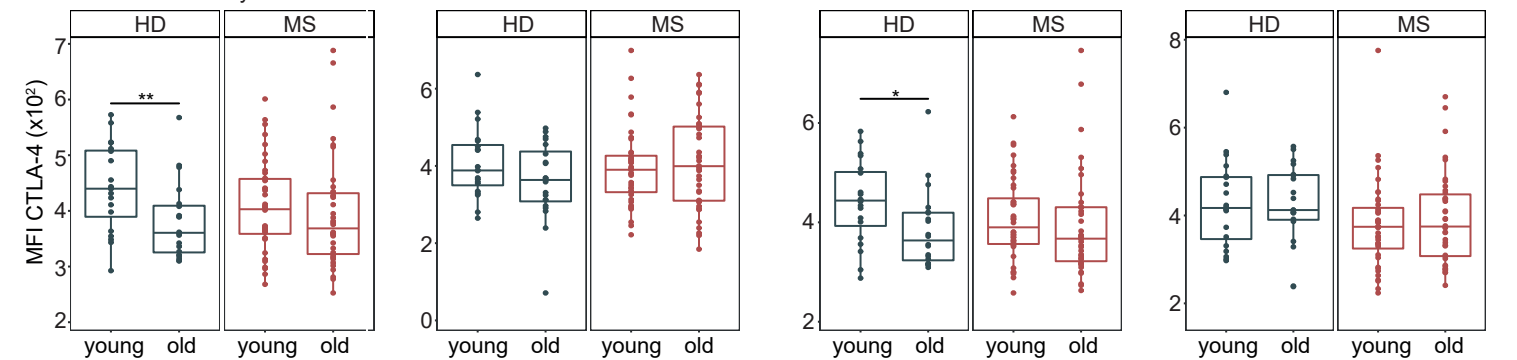
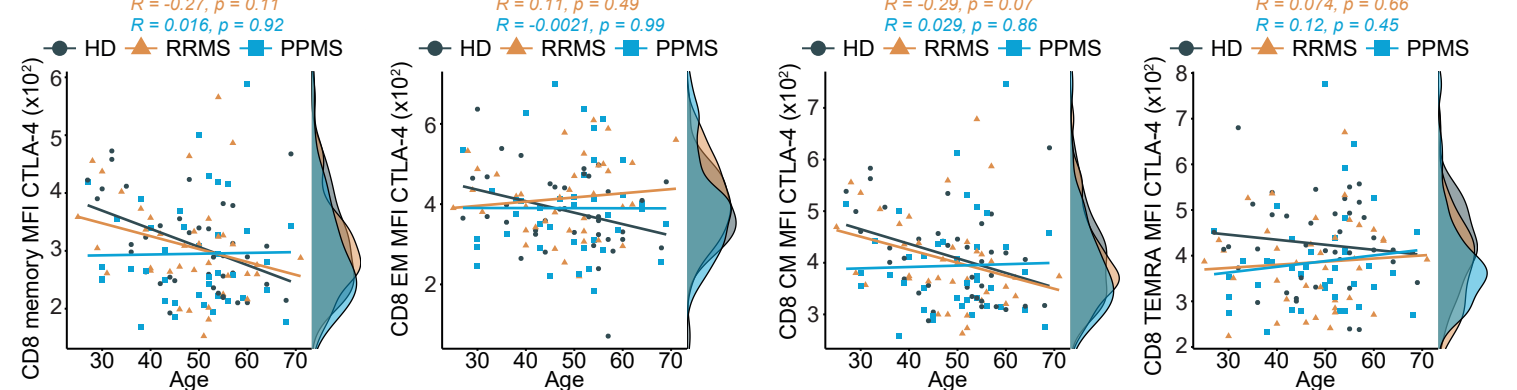


**A****B****C****D****E****F****G****H**

**eFigure 6 Expression of immunoregulatory markers in the CD8 memory compartment of young and old MS patients and HD.** Flow cytometric analysis of frozen PBMC from young ( $\leq 50$  years) and old ( $> 50$  years) patients with multiple sclerosis (MS) (MS: young:  $n=40$ ; old:  $n=38$ ; relapsing-remitting MS (RRMS): young:  $n=20$ , old:  $n=18$ ; primary progressive (PPMS): young:  $n=20$ , old:  $n=20$ ) and healthy donors (HD) (young  $n=20$ ; old:  $n=20$ ). Demographic data of study subjects are depicted in eTable 1. **(A-C)** Mean Fluorescence Intensity (MFI) of KLRG1 on effector memory (EM) **(A)**, central memory (CM) **(B)** and TEMRA (C) CD8 T cells of MS patients and HD (*left*). Correlation analysis of KLRG1 expression on EM **(A)**, CM **(B)** and TEMRA **(C)** CD8 T cells with age (*right*) of HD ( $n=40$ ), RRMS ( $n=38$ ) and PPMS ( $n=40$ ) patients. **(D-F)** MFI of LAG3 on EM **(D)**, CM **(E)** and TEMRA **(F)** CD8 T cells of MS patients and HD (*left*). Correlation analysis of LAG3 expression on EM **(D)**, CM **(E)** and TEMRA **(F)** CD8 T cells with age (*right*) of HD ( $n=40$ ), RRMS ( $n=38$ ) and PPMS ( $n=40$ ) patients. **(G)** MFI of CTLA-4 on memory, EM, CM and TEMRA CD8 T cells of HD and MS patients. **(H)** Correlation analysis of CTLA-4 expression on memory, EM, CM and TEMRA CD8 T cells with age of HD ( $n=40$ ), RRMS ( $n=38$ ) and PPMS ( $n=40$ ) patients. Data are displayed as boxplots of the median and the 25<sup>th</sup> and 75<sup>th</sup> percentile  $\pm$  IQR. Statistical analysis was conducted by two-tailed Mann-Whitney test. For correlation analysis, the Pearson product-moment correlation coefficients (Pearson's R) were computed. Differences were considered statistically significant with the following  $P$ -values:  $*P < 0.05$ ,  $**P < 0.01$ ,  $***P < 0.001$  and  $****P < 0.0001$