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# Alteration of CD8<sup>+</sup>CD45RC<sup>int/neg</sup> regulatory T cells functions in Multiple Sclerosis and correlates with disease severity

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## BACKGROUND

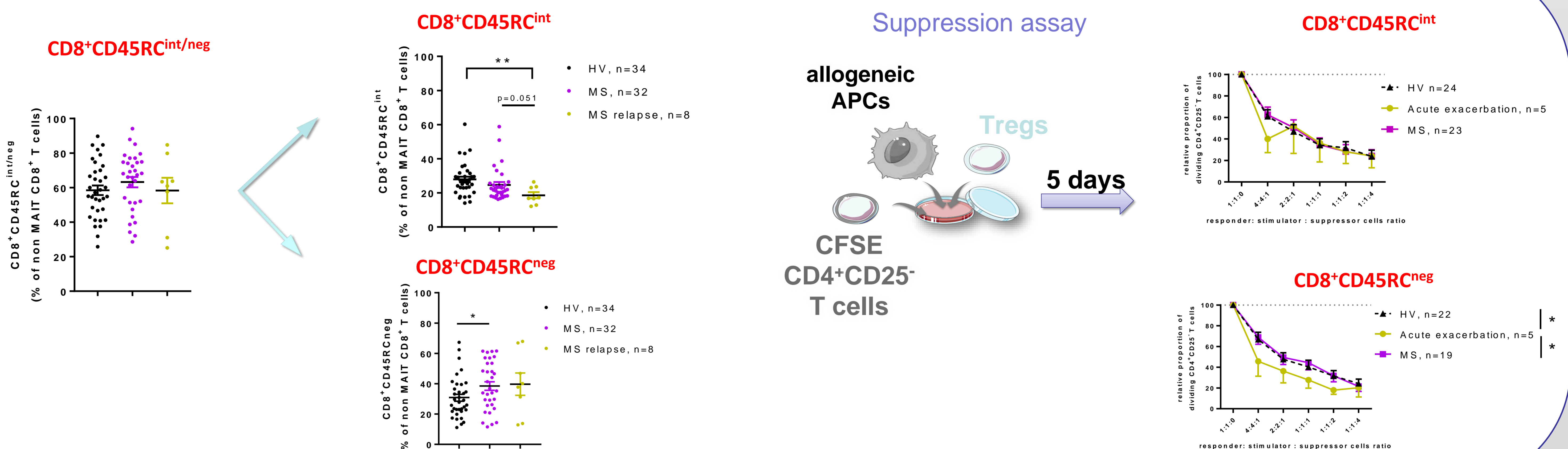
Autoimmune diseases can develop following pathological activation of autoreactive effector cells and/or, alternatively, after weakening of self-protective regulatory mechanisms. Most of the studies have focused on CD4<sup>+</sup> Tregs and the **role of CD8<sup>+</sup> Tregs in Multiple Sclerosis (MS) remains largely unexplored**. We previously reported the suppressive properties of rat and human CD8<sup>+</sup>CD45RC<sup>int/neg</sup> Treg cells, expressing Foxp3 and acting through IFN $\gamma$ , TGF $\beta$  and IL34 cytokines (Guillonau, JCI, 2007; Bézie, JCI, 2015, Bézie, Front. Immunol., 2018). Thus, their **potency of suppression** make them strong candidates of disruptive immune tolerance, especially in MS where CD8<sup>+</sup> T cells play a major role. **Thus, the overarching goal of this study is to define the role of CD8<sup>+</sup> regulatory T cell in MS pathogenesis**

## MATERIAL & METHODS

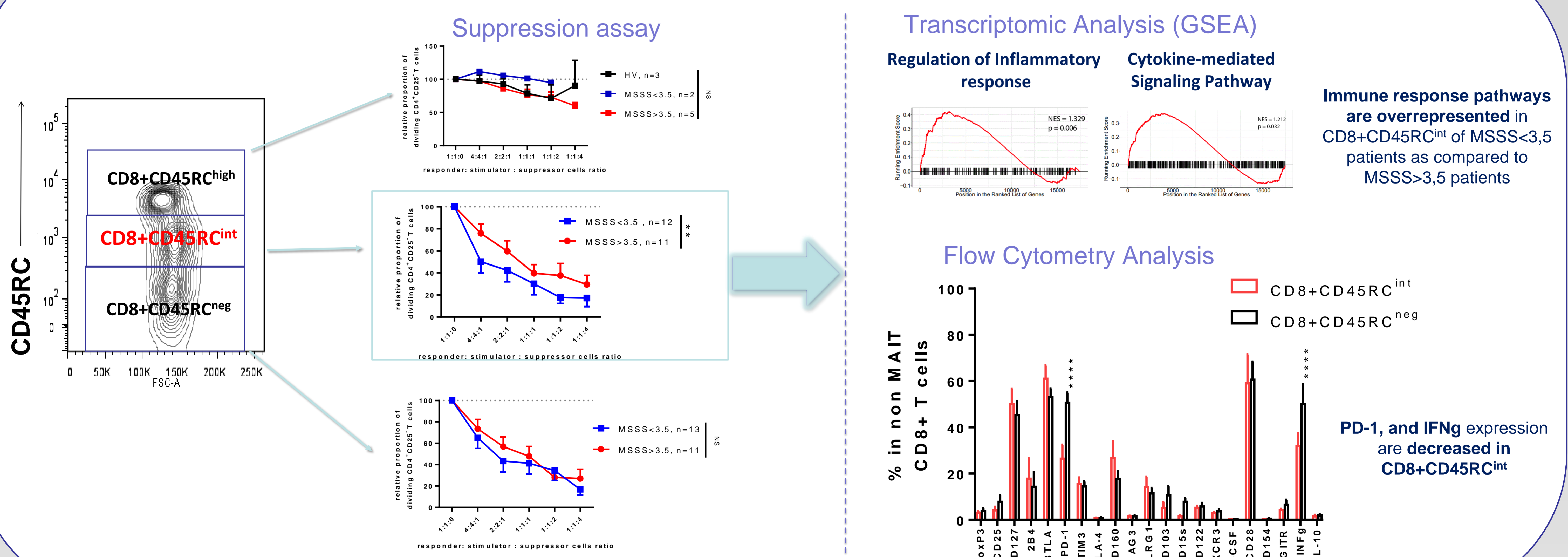
**56 untreated relapsing-remitting MS patients and 52 age- and gender-matched healthy volunteers (HV) were recruited.**

- **Tregs** were defined as CD3<sup>+</sup>CD8<sup>+</sup> (or CD4<sup>-</sup>) CD161<sup>low</sup>V $\alpha$ 7-CD45RC<sup>int/neg</sup> T cells. MAIT cells were excluded from all analysis.
- **Staining:** T cells were stimulated or not 5h with PMA+ionomycin including 4h with BFA before FACS depending on the marker investigated.
- **Transcriptomic analysis:** 3'-Digital Gene Expression Sequencing was performed on unstimulated cells. Analysis was performed using R packages and KEGG, Reactome and Gene Ontology databases for Gene Set Enrichment Analysis (GSEA).

## CD8<sup>+</sup>CD45RC<sup>int</sup> TREGS FREQUENCY IN BLOOD IS REDUCED DURING EXACERBATION WHEREAS CD8<sup>+</sup>CD45RC<sup>neg</sup> TREGS ARE MORE FREQUENT WITH ENHANCED SUPPRESSIVE FUNCTIONS



## IN SEVERE PATIENTS WITH A HIGHER MULTIPLE SCLEROSIS SEVERITY SCORE, CD8<sup>+</sup>CD45RC<sup>int</sup> TREGS FUNCTION IS IMPAIRED



## CONCLUSION

For the first time, we demonstrate an **impairment of CD8<sup>+</sup>CD45RC<sup>int</sup> Tregs in MS**.

We propose to define two populations of CD8<sup>+</sup>CD45RC Tregs:

- **CD8<sup>+</sup>CD45RC<sup>int</sup> are dysfunctional in severe MS patients and less frequent during exacerbations**
- **CD8<sup>+</sup>CD45RC<sup>neg</sup> Tregs react properly to inflammation with enhanced regulatory functions during exacerbations**

**We suggest CD8<sup>+</sup>CD45RC<sup>int/neg</sup> T cells and subsets may be potential therapeutic targets and prognostic tools in MS**

Authors have no financial disclosures that would be a potential conflict of interest with this presentation