Impaired regulatory T cell function in Waldenström's Macroglobulinemia.

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Rationale: Since IL-6 and Mastocytes, both typically associated to Waldenström Macroglobulinemia (WM), can modulate regulatory T cell (Treg) development and function in various ways, we postulated that the Treg subset might be modified in these patients.

Methods: We compared naïve (rTreg) and activated regulatory T cell (aTreg) counts in WM, healthy controls and CLL patients used here as a disease control group. All samples were analysed less than 2 hours after phlebotomy, in order to avoid cryopreservation bias. For functional analysis, aTregs and rTregs were then FACS-sorted from peripheral blood, and bone marrow in one case.

Results: We found that circulating proportions of aTregs and rTregs among CD4 T cells were not drastically different in WM (n=27) from those found in healthy, age-matched, individuals. However, CD4+CD25+foxp3+ WM Tregs were found dramatically impaired, when tested functionally. In a criss-cross test performed in two patients, WM Tregs did not inhibit autologous T cell proliferation, while control Tregs could inhibit WM naïve T cell proliferation.

Conclusion: We conclude that Treg function is frequently impaired in WM.

Discussion: These results strengthen the hypothesis that immune regulation defects might account for the transition from Monoclonal Gammopathy of Undetermined Significance (MGUS) to WM or Multiple Myeloma (MM). WM B-cells could escape immune control by modulating Treg function. More generally, we propose that regulatory control could represent an important check-point during B cell development.