### Poster presentation

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# PI6-55 LB. The role of CD4+ CD25+ regulatory T cells in the control of IL-10 mediated T cell impairment in chronic HIV Infection

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#### Background

T cell dysfunction in the presence of ongoing antigen exposure is a cardinal feature of chronic viral infections, including HIV. IL-10 has been implicated as an important mediator of this T cell exhaustion. The regulation of IL-10 production, however, remains poorly understood.

#### Methods

HIV-specific proliferative CD4+ T cell responses were assessed by CFSE assays performed after stimulation with recombinant HIV p24 in the presence of a blocking anti-IL10R antibody or an isotype control, with or without depletion of CD25+ cells. IL-10 production was measured in cell subsets by ICS or by luminex of culture supernatants from PBMCs depleted of CD14+, CD19+ or CD25+ cells. Finally, monocytes and regulatory T cells were sorted and cultured alone or together in transwell plates and secreted IL-10 was measured.

#### Results

Performing either blockade of IL-10R or depletion of CD25+ cells augmented HIV-specific CD4+ T cell proliferation in viremic patients, but not individuals with controlled viral load. Importantly, depletion of CD25+ cells significantly decreased the responsiveness to IL-10R blockade. ICS showed that CD14+ monocytes were the cellular subset which consistently produced the greatest amount of IL-10. When CD25+ T cells were depleted from PBMCs, however, the amount of IL-10 produced by monocytes was decreased. Consistent with this, purified monocytes that were cultured with regulatory T cells showed increased levels of IL-10 production relative to monocytes cultured alone. Disruption of cell-cell contact between Tregs and monocytes partially abrogated IL-10 induction.

#### Conclusion

These results indicate that IL-10-mediated inhibition of HIV-specific CD4+ T cell function critically depends on the interplay between regulatory T cells and monocytes. The data demonstrate that monocytes are the primary producers of IL-10 in PBMCs of chronically HIV infected individuals, and regulatory T cells are key inducers of monocyte IL-10 production. This inductive effect appears to be mediated via both diffusible factors and direct cell contact.