



ABSTRACT FORM

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Specific T cell regulation of distinct T helper responses in different disease stages of human filariasis

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Background Chronic helminth infections induce T cell hyporesponsiveness, which may affect immune responses to other pathogens or vaccines. Filarial infections are potent in immune suppression which is associated with induced regulatory T (Treg) cells. This study investigates the Treg cell capacity to suppress filaria-specific immune responses during different stages of human filarial disease.

Methods Lymphedema (n=23), microfilaremic (MF) (n=23) and uninfected (n=23) individuals were selected in a filaria-endemic area in north Flores, Indonesia. In a field setting PBMC were isolated; CD4CD25^{hi} T cells were magnetically depleted and subsequently *in vitro* cytokine production in response to *Brugia malayi* antigen (BmA) was analyzed in total and Treg cell depleted PBMC.

Results In microfilaremic subjects BmA-specific IFN-gamma responses were lower, while higher IFN-gamma levels were observed in lymphedema patients compared to the endemic normal group. IL-17 secretion was lower in MF-positives compared to lymphedema cases and uninfected controls. In parallel, BmA-specific IL-10 production was enhanced in microfilaremics in contrast to both MF-negative groups. Depletion of Treg cells restored IFN-gamma production by microfilaremic individuals to levels observed in the uninfected group while IL-10 and IL-17 levels did not change. Th2 responses were not affected by presence of infection or by depletion of Treg cells.

Conclusion These data demonstrate that filaria-associated human Treg cells influence immune responses to specific antigens, dependent on disease stage. Presence of microfilaria suppresses specific inflammatory Th1 and Th17 responses, whereas patients with chronic disease seem to lack such regulatory responses to filarial antigens. These findings might be important when considering the targeted prevention of filaria-induced lymphedema and elephantiasis.

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