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## Introduction

Filarial disease is an immunologically complex disease with various aspects in different disease stages. A hallmark of helminth infections is modulation of the host immune system, inducing T cell hypo-responsiveness. It has been shown that Treg cells are associated with suppression of T cell responses in human helminth infection. Unravelling Treg kinetics and mechanisms may provide novel pathways to eliminate this major burden of neglected communicable diseases. This study investigates Treg phenotype and function in microfilaremic individuals, lymphedema patients and endemic controls.



**Aim** To demonstrate the role of Tregs in immune hypo-responsiveness in human filariasis

## Methods

### Study population

From a filaria-endemic area in Flores, 23 MF-positives, 23 non-microfilaremic lymphedema patients and 23 uninfected healthy controls were included in Treg cell experiments.

### Treg depletion assay

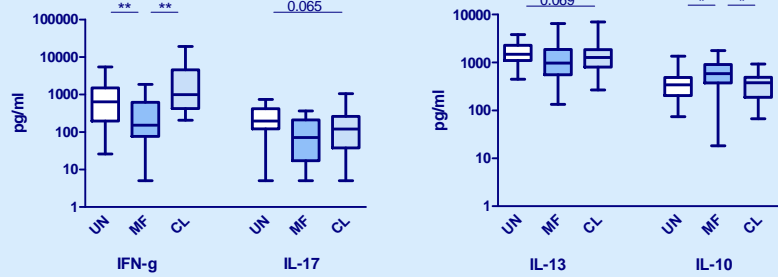
Donor PBMC were magnetically depleted of CD4<sup>+</sup>CD25<sup>hi</sup> cells and compared to mock-depleted total PBMC. Cells were stimulated for 4 days with *Brugia malayi* antigen (BmA). Culture supernatants were included in Luminex assays to determine Th1, Th2, Th17 and regulatory cytokines. Proliferation was assessed by flowcytometric detection of CFSE and cells with diminished CFSE fluorescence were determined as percentage divided cells.

### Analysis

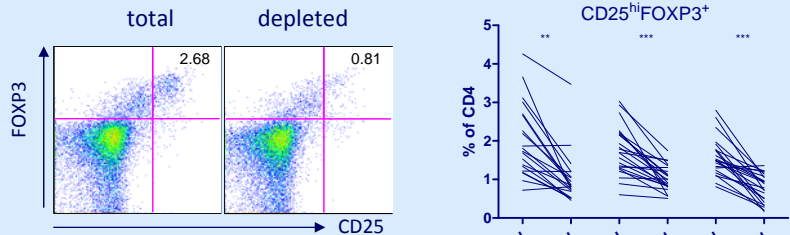
Non-parametric statistics were performed in SPSS, with rank tests for paired data.

## Results

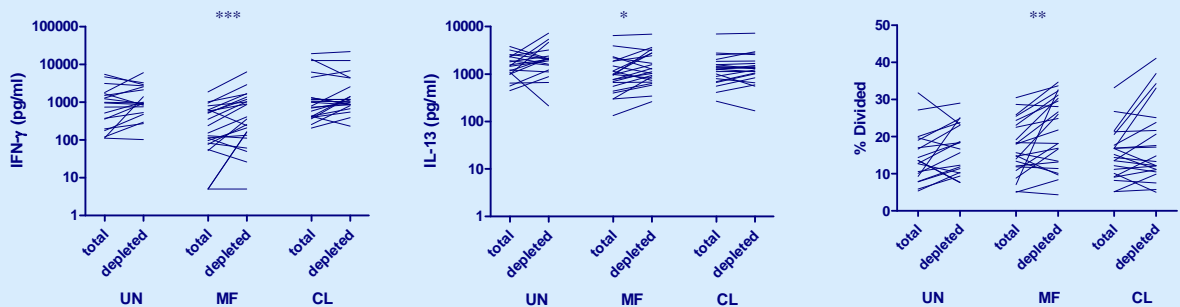
**Figure 1** Th1, Th17 and Th2 responses are suppressed in microfilaremic subjects



**Figure 2** Efficient depletion of CD25<sup>hi</sup>FOXP3<sup>+</sup> Tregs in all groups



**Figure 3** Th1, Th2 & T cell proliferation responses are increased after Treg depletion in MF only



\* p<0.05  
\*\* p<0.01  
\*\*\* p<0.001

## Conclusions

During microfilaremia, differential T cell responses are suppressed while IL-10 production is higher compared to MF-negative individuals  
In vitro Treg depletion is similarly effective in different infection groups  
Th1 and Th2 responses are restored to levels observed in MF-negatives after removal of Treg cells, Th17 and IL-10 are not affected  
T cell proliferation is increased after Treg cell depletion as well in microfilaremic subjects only

## Impact

These findings could be translated to novel options for treatment of filariasis and other helminth infections