Regulatory T cells modulate dendritic cell maturation and function

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Introduction

Graft versus host disease (GVHD) is a major and potentially life threatening complication associated with haematopoietic stem cell transplant.

Regulatory T cells (Treg) have shown to ameliorate GVHD whilst still maintain an adequate immune response against pathogens (1). However the clinical trials have not fully elucidated the mechanisms of Tregs action. One mechanism in which Tregs exert their effect is by modulating dendritic cells (DCs).

Aim

To examine how dendritic cell function is modulated by ex vivo expanded Treg.

Methods

Immuno-magnetic isolated monocytes were cultured in GM-CSF & IL-4 for 7 days

Treg added on day 3

LPS added on day 6

Tregs depleted

Cells harvested

Phenotype Flow cytometry

Morphology Cytospin

Phagocytosis FITC dextran uptake

T cell proliferation CFSE

Cytokine production CBA

Treg characteristics

Treg in PBMC Isolated Treg Expanded Treg Expanded Treg

Thymidine suppression assay

Expanded Treg exhibited high levels of CD25&Foxp3 and a dose dependent suppression of alloreactive CD8+ T cell proliferation.

Treg treated DCs had lower cytokine production

IL-6

IL-10

IL-12p70

Conclusions

- Treg treatment prevented maturation of monocyte derived DCs phenotypically and morphologically
- Treg treatment significantly reduced DC secretion of IL-6, IL-12 and IL-10
- The phagocytic ability of Treg treated DCs was similar to that of Mature DC
- Treg treated DCs appeared to be less potent in stimulating alloreactive T cell proliferation although not statistically significant
- Further studies are required to dissect whether Treg could exert their immune modulation via altering DC properties only rather than locking DC-T cell interaction

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References