EXPRESSION PATTERNS OF REGULATORY T-CELL MARKERS IN ACCEPTED AND REJECTED NON-HUMAN PRIMATE KIDNEY ALLOGRAFTS

Krista G.Haanstra, Jacqueline A.M. Wubben, Ivanela Kondova, **Margreet Jonker**

Biomedical Primate Research Centre, PO box 3306, 2280GH Rijswijk, The Netherlands

The identification of FOXP3 expressing cells in recipients of an allograft, in particular inside the graft itself, may help to define criteria for immunosuppressive drug withdrawal. We therefore examined expression patterns of several regulatory T-cell (Treg) markers in kidney biopsies and kidney tissues taken at the time of graft rejection from monkeys treated with αCD40, αCD86, CsA, a combination of these, or after drug withdrawal.

Tissue biopsies were taken at several time intervals after MHC mismatched kidney transplantation. Formalin fixed material was scored according to the Banff97 criteria. Frozen sections were stained using peroxidase and alkaline phosphatase techniques using a set of antibodies reactive with T cells (CD3, CD4, CD8), B cells (CD20), macrophages (CD68) and DC (CD83). In addition the following Treg cell markers were used: CD25, CTLA4 and FOXP3.

In advanced stages of rejection, organized multifocal nodular infiltrates, with mature CD83+DCs, T-cells and B-cells could be found. In contrast, interstitial infiltrates contain more macrophages, less T-cells and few B-cells.
Tissue samples were subdivided in tissues with 1) no or borderline rejection with a sub group of 4 animals that were long term off immunosuppression, 2) subclinical rejection (Banff 1A or higher without serum creatinine rise) and 3) clinical rejection (Banff 1A or higher with serum creatinine rise). Expression of FOXP3, CD25 and CTLA-4 was mainly found in nodular infiltrates of tissue samples with subclinical and clinical ejection. A significant correlation was found between the percentage $FOXP3^+$ cells and markers for rejection, i.e. creatinine levels and Banff interstitial and tubular infiltrate scores. Thus no rejection had the least cells with Treg cell markers, subclinical rejection more and clinical rejection the most. The type of immunosuppression did not influence the expression of Treg markers. Four animals with prolonged drug-free survival showed the lowest FOXP3 expression. In contrast, latent TGF-β1 was found in biopsies of these animals while much less in animals with rejection.

We conclude that intragraft expression of FOXP3 and other Treg markers in NHP kidney allografts is not confined to tolerated grafts but should be considered as part of the normal immune response during rejection.