

Artificial antigen presenting cells for tolerance induction in BMT

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GvHD in BMT can be reduced using recipient-derived immature or costimulation reduced dendritic cells (DC) and donor derived T cells. Regulatory T cells produced by this method prevent GvHD, while still preserving GvL reactions. However, this setting bears the risk of recipient-derived dendritic cells presenting leukemic antigen in a tolerogenic setting and thereby tolerizing the donor T cells to these antigens. Therefore, we used an alternative strategy by creating artificial antigen presenting cells (aAPC). In our system, we generated aAPCs by inducing expression from the MHCII locus. This was achieved by transfecting CIITA into fibroblasts using the C3H derived L929 cell line as a model. Coculture of this aAPC with allogenic Balb/C T cells lead to reduced T cell proliferation after second encounter with C3H cells (compared to T cells cultured on DC). We could also show the generation of CD25+ CTLA4 expressing T cells, which are assumed to be of a regulatory phenotype. Taken together, we conclude that using aAPC will be a safe method to generate regulatory T cells for prevention of GvHD while preserving GvL.