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Survival and homing of *ex vivo* expanded donor derived dendritic cells after allogeneic BMT

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Introduction

Little is known about survival and trafficking of *ex vivo* expanded dendritic cells (eDCs) after adoptive transfer in animals. We investigated the trafficking patterns of eDCs in mice that had received allogeneic BMT.

Methods

C57BL/6 ($H2^b$) BM was depleted of $B220^+$, $CD3^+$ and $GR1^+$ cells and was expanded for 7 days with GM-CSF, IL-4 and Flt3L. A retroviral vector encoding for luciferase (luc) and gfp was used for transduction. EDCs were analyzed by FACS and functionality was tested with MLR. EDCs from C57BL/6 donor mice were injected i.v. at 4×10^6 per animal into BALB/c recipients that had received either allogeneic myeloablative BMT (BALB/c-mbl) or non-myeloablative BMT (BALB/c-n/mbl) conditioning. Survival and *in vivo* trafficking of gfp/luc^+ eDCs were monitored by bioluminescent imaging (BLI). Tissues were examined for gfp^+ eDCs using immunofluorescence microscopy. Additional experiments were performed with eDCs generated from gfp-transgeneic animals (C57BL/6-TgN(ActbEGFP)1OSB, $H2^b$).

Results

Expansion of depleted BM with GM-CSF, IL4 and FLT3L induced a polyclonal population of $CD11c^+CD11b^+$ and $CD11c^-CD11b^+$ eDCs. Both populations expressed CD40, CD80, CD86 and MHC II. No $CD3^+$ or $NK1.1^+$ cells were found, the number of $CD19^+$ cells ranged from 0–2.5%. After transduction, gfp^+ cells represented up to 36% of viable cells. EDCs were functional in a MLR assay. After injection, transduced cells were monitored *in vivo* with BLI for up to 100 days. In BALB/c-mbl and BALB/c-n/mbl eDCs were initially detected in the area of the lungs and later in the area of the gut, spleen and thymus. Using immunofluorescence microscopy, gfp/luc^+ eDCs and gfp-transgenic eDCs were detected at different time points in the spleen, Peyers patches, thymus and lymph nodes. During the observation period no animal exhibited signs of GvHD.

Conclusion

Here, we show that donor-derived, *ex vivo* expanded DCs survive in hosts after allogeneic, MHC mismatched BMT for at least 6 weeks. EDCs migrate to lymphoid organs like spleen, Peyers patches, lymph nodes and thymus. Myeloablative or non-myeloablative conditioning does not significantly affect trafficking patterns. Mice that had received eDCs developed no clinical signs of GVHD. The ability to visualize DC survival and trafficking gives new insight into the biology of adoptively transferred DCs and will help to optimize DC based treatment strategies.