**Supplementary materials and methods**

*Antibodies, flow cytometry and ELISA*

The following anti-human antibodies were used for cell staining: CD3-FITC or -PECy7, CD4-FITC or -PE, CD8-FITC or -PE, CD34-FITC or -PE, and CD33-APC or –PECy5 were purchased from BioLegend. Data acquisitions were performed using either BD Accuri C6 Flow cytometry (BD Bioscience) or LSRII (BD Biosciences) Flow cytometers and data were analyzed using FlowJo software (Tree Star, Inc.).

*Cell lines*

Cell lines, AML3/OCI, MV4-11, Jurkat, Daudi, H460, and A549 were obtained from ATCC KG1a, EBV-LCL was obtained from The Center for Applied Genomics at The Hospital for Sick Children. AML3/OCI were cultured in alpha-MEM supplemented with 10% fetal bovine serum (FBS), EBV-LCL, Jurkat and Daudi were cultured in RPMI-1640 supplemented with 10% FBS, MV4–11 was cultured in IMDM supplemented with 10% FBS, H460 and A549 were maintained in DMEM/F12 supplemented with 10% FBS. All cell lines were incubated at 37 °C in 5% CO2

*Intracellular staining of CTLA-4*

*Ex vivo* expanded DNTs surfaced stained with anti-human CD3, CD4, and CD8 antibodies, and fixed and permeabilized using intracellular fixation and permeabilization kit (eBioscience). Permeabilized cells were stained with anti-CTLA-4 antibody (Clone L3D10) for 30 mins at 4 °C. After washing, cells were analyzed by flow cytometry.

*GvHD-model tissue damage scoring*

Mice treated with PBS, DNT, or PBMC were sacrificed and liver and lung tissues harvested, fixed in 10% formalin, and H&E stained. Liver and lung histology slides were blindly scored by a pathologist following the scoring charts below:

Liver GVHD scoring

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | 0 | 1 | 2 | 3 |
| Portal inflammation  | Absent | **Mild**Present in fewer than 30% of portal tracts | **Moderate**Present in more 30%-50% of portal tracts | **Severe**Present in majority (more than 50%) of portal tracts |
| Lobular Inflammation | Absent | **Mild**With little hepatocytes necrosis or apoptosis | **Moderate**With focal necrosis causing confluence and/or several apoptoses  | **Severe**With bridging/severe parenchymal necrosis |
| Bile duct injury | Absent | **Mild**Slight duct epithelium disorder with cytoplasmic eosinophilia | **Moderate**Duct epithelial disorganization with partial necrosis of affected ducts | **Severe**Extensive duct epithelial disorganization with complete necrosis of affected ducts  |
| Bile duct loss | Absent | **Mild**Affecting 30% or less | **Moderate**Affecting 30-60% | **Severe**Affecting more than 60%  |
| Cholestasis | Absent | **Mild**Visible only at 20X or higher magnification | **Moderate**Visible at 5-10x magnification but not easily | **Severe**Visible easily at 5x magnification |
| Total Score (/15) |  |  |  |  |

Lung GVHD Scoring

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | 0 | 1 | 2 | 3 |
| inflammation  | Absent | **Mild**Present around vessels without endotheliitis | **Moderate**Present with endotheliitis +-/ septal expansion+/- mild alveolar extension | **Severe**Present with extensive septal expansion, heavy intra-alveolar inflammation +/- hemorrhages +/- alveolar involvement |
| Bronchial/bronchiolar Epithelial injury | Absent | **Mild**Subepithelial inflammation with no intra-epithelial inflammation | **Moderate**Subepithelial inflammation with intra-epithelial inflammation but no epithelial necrosis and/or apoptoses | **Severe**Subepithelial inflammation with intra-epithelial inflammation and necrosis |
| Total Score (/6) |  |  |  |  |