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POSTER ABSTRACTS

722.ALLOGENEIC TRANSPLANTATION: ACUTE AND CHRONIC GVHD, IMMUNE RECONSTITUTION

Double-Negative T Cells Attenuate Acute Graft-Versus-Host Disease By Modulating CD4 + T Cell Activation Post-Allo-HSCT

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Background: Acute graft-versus-host disease (aGVHD) is a major and life-threatening complication following allogeneic hematopoietic stem cell transplantation (allo-HSCT). Double-negative T cells (DNTs) have demonstrated potent cytotoxicity against various hematological tumors, and emerging evidence from animal experiments and clinical studies suggests their potential in predicting and treating aGVHD. Thus, DNTs may be a novel and versatile immunotherapy for aGVHD and relapse management post-allo-HSCT due to the function of harnessing the anti-leukemic effects and immune regulation. Nevertheless, the precise mechanisms underlying DNT-mediated aGVHD prevention remain unclear.
Results: In vitro, DNTs inhibited the proliferation of CD4 + T cells in a dose-dependent manner, and significantly inhibited the expression of CD25 on CD4 + T cells. CD4 + T cells inhibited by DNTs displayed decreased interleukin-2 secretion, reduced cell volume, nuclear condensation, and diminished mitochondrial number and volume. Transcriptome sequencing analysis verified significant downregulation of DNA replication, cell cycle, mitochondrial matrix metabolism, JAK-STAT, interleukin-17, and mitosis signaling pathways in CD4 + T cells co-cultured with DNTs. In addition, we found DNTs arrested CD4 + T cells at the G0/G1 phase, hindering their transition to the S phase, and inhibited CD4 + T cell proliferation by the CD25-JAK-STAT pathway. However, DNTs had no adverse effects on the activity and colony-forming capacity of allogeneic hematopoietic progenitor cells in vitro. Importantly, DNT infusion significantly improved the survival of mice in aGVHD model, reduced splenomegaly, downregulated CD25 expression on CD4 + T cells, and attenuated CD4 + T cell infiltration into host lungs, liver, and spleen, and effectively ameliorated organ damage (Figure 1).
Conclusion: Our findings suggest that DNTs attenuate acute aGVHD by affecting the proliferation and activation of CD4 +T cells via the CD25-JAK-STAT pathway, which is important to the prevention and management of aGVHD.

Disclosures No relevant conflicts of interest to declare.

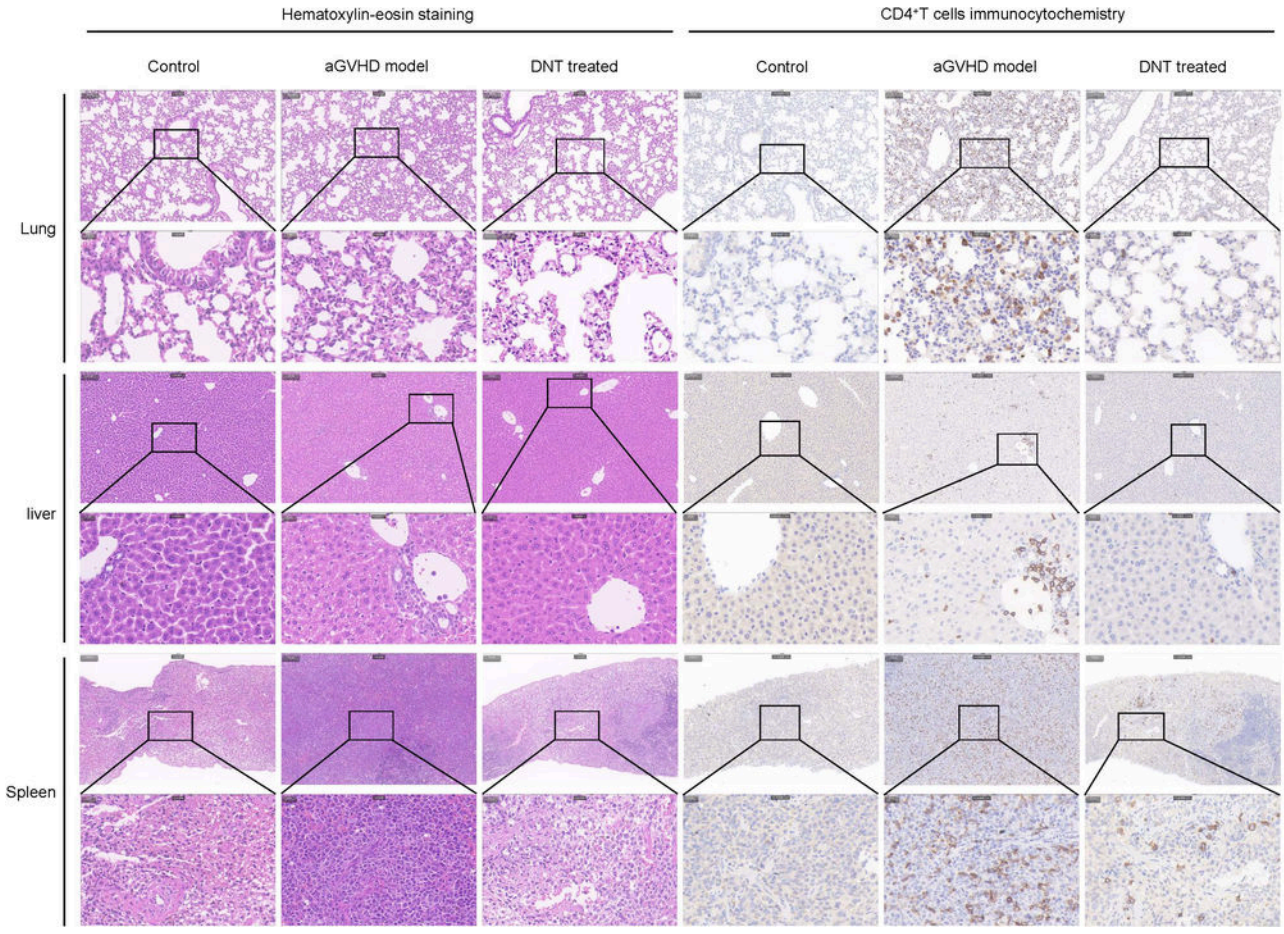

Figure 1

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