Analysis of T cell specific predictive biomarkers of graft-vs-host disease and relapse following post transplant cyclophosphamide prophylaxis

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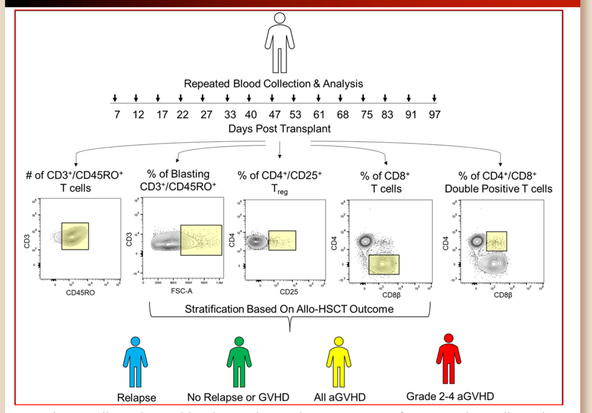
BACKGROUND

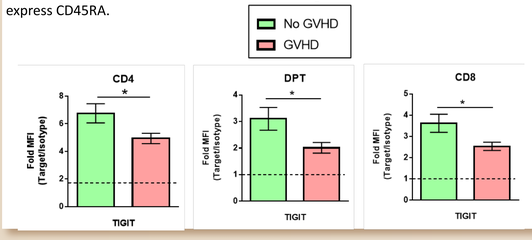
- Allogeneic hematopoietic stem cell transplantations (allo-HSCT) is a potentially curative treatment for patients with hematological malignancies
- Two common complications with allo-HSCT are high relapse rates and the development of acute graft-vs-host disease (aGVHD)
- Clinicians are currently unable to predict which patients will relapse or develop aGVHD after treatment
- This study sought to identify T cell specific metrics predictive of these negative outcomes

METHODS



In total we collected 417 blood samples with an average of 12 samples collected per patient. To ensure sample collection was equally distributed, 16 collection intervals were created ranging between 5-7 days in length with the goal of collecting one patient sample per collection interval.

Half a mL of blood was processed by RBC lysis and flow cytometry staining. T cells were distinguished by gating on live cells, HLA-class-I and CD3 expression. Importantly, for our analysis we only included T cells expressing CD45RO, which is an isoform of CD45 expressed by antigen-experienced T cells. While this population includes both effector and memory T cells, gating on CD45RO+ T cells allow us to exclude non-reactive naïve T cells clones coming from the donor as well as de-novo generated naïve T cells which would both express CD45RA.

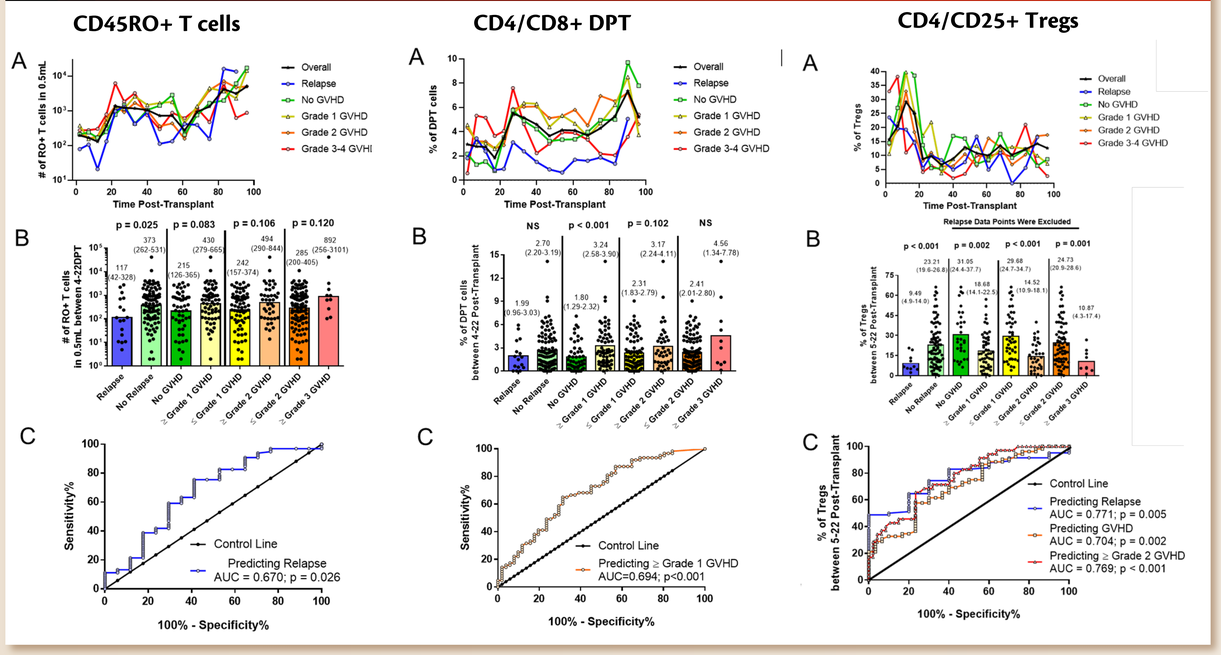


In conclusion, this study directly investigated metrics of T cell biology following adult allo-transplant w/PTCy using **417** blood samples collected from 35 patients across the first 100 days after transplant.

The early analysis of T cell metrics between days 5-22 is especially interesting, yielding **two** biomarkers predictive of relapse, **four** predictive of GVHD of any grade and **two** predicting > grade 2 acute GVHD. Additionally, we identified several biomarkers capable of predicting patient outcomes several weeks prior to their GVHD diagnosis.

In our analysis of the inhibitory and co-stimulatory molecules expressed after transplant, six were differentially expressed across the T cell subsets while only **TIGIT** was differentially expressed between GVHD and non GVHD patients.

RESULTS



CONCLUSIONS

- This study identified three key T cell population metrics that are predictive of either relapse or aGVHD development (# of CD45RO$^+$ T cells, % of DPT and % of T_{reg})
- Each metrics feasibility to predict negative outcomes is time-dependent
- Individual T cell populations express a unique repertoire of activation and inhibitory markers and may respond differently to immunotherapies
- This is the first study to identify a T cell specific predictive metric of allo-HSCT negative outcomes and will be further validated in a blinded prospective trial in the future.

ADDITIONAL KEY INFORMATION

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