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T Cell Populations And Response To Chemotherapy In Human Leukemia

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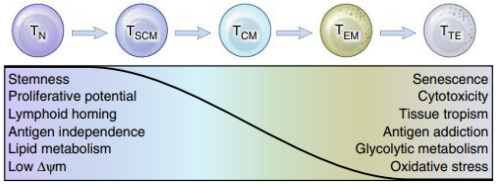
Background

- One important prognostic indicator in pediatric leukemia is **minimal residual disease (MRD)** detected at the end of induction chemotherapy.
- Compared to having no MRD detected (MRD-), detecting any level of MRD in the bone marrow (BM) at the end of induction (MRD+) is associated with:
  - Increased risk of relapse
  - Poorer overall survival
- Discovering differences between these patients, specifically in T cell subsets such as **memory CD8⁺ T cells** and **T memory stem cells (Tscm)** could lead to new targets for cancer therapy and improvement in treatment for higher risk disease.
- **Objective:** To determine differences in T cell populations in human leukemia in patients with MRD+ vs MRD- disease after induction chemotherapy.

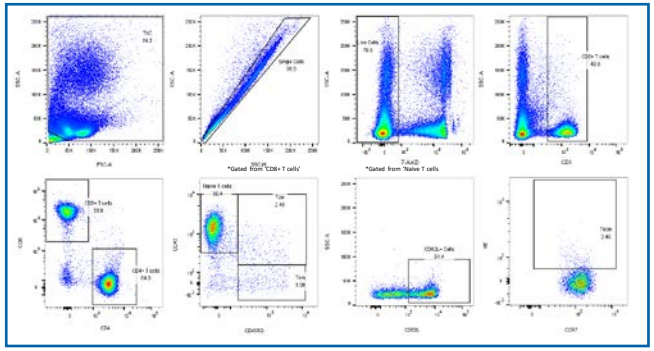


Gattinoni L, Speiser DE, Lichterfeld M, Bonini C. T memory stem cells in health and disease. *Nat Med*. 2017;23(1):18-27. doi:10.1038/nm.4241

Methods

- Samples were from 8 pediatric patients with **premature B cell acute lymphoblastic leukemia (pre-B ALL)** from BM.
- 4 patients were MRD+ after induction and 4 patients were MRD-.
- Timepoints were at diagnosis and day 29 (D29) of induction chemotherapy.
- Flow cytometric analysis of cytotoxic memory T cell populations was performed and analyzed using descriptive statistics and the t-test.

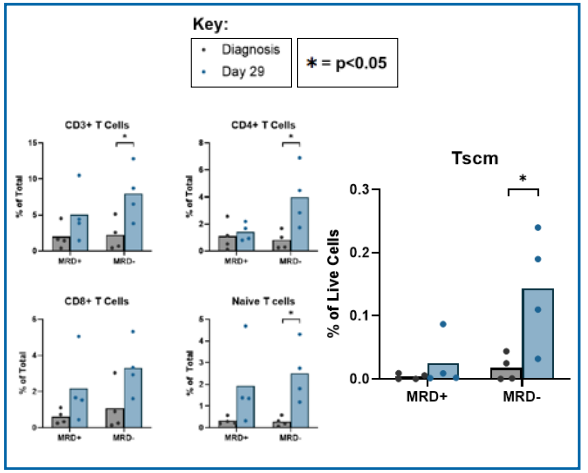
Gating Strategy



Results

- For all patients, both MRD+ and MRD-, the mean live cell percentages were not different between diagnosis and D29 (76.9% vs 85.1%, p=0.111).
- CD3⁺, CD4⁺, and CD8⁺ T cells were all higher at D29 (CD3⁺ - 2.1% vs 6.5%, p=0.011; CD4⁺ - 1.0% vs 2.7%, p=0.044; CD8⁺ -0.8% vs 2.7%, p=0.018).
- Naïve T cells increased from diagnosis to D29 (0.4% vs 3.4%, p=0.009).
- Tscm were also elevated at D29 (0.01% vs 0.08%, p=0.042).
- When the patients were **sub-grouped based on MRD status**, similar differences were seen in the MRD- group between diagnosis and D29 (CD3⁺ - 2.2% vs 7.8%, p=0.039; CD4⁺ - 0.8% vs 4.0%, p=0.035; CD8⁺ - 1.1% vs 3.3%, p=0.073; Naïve- 0.4% vs 3.8%, p=0.039; Tscm- 0.02% vs 0.1%, p=0.037).
- In the **MRD+ subgroup, none of the previously described differences were detected** (CD3⁺ - 2.0% vs 5.1%, p=0.197; CD4⁺ - 1.1% vs 1.4%, p=0.644; CD8⁺ - 0.6% vs 2.17%, p=0.175; Naïve- 0.5% vs 2.95%, p=0.173; Tscm- .004% vs 0.02%, p=0.355).

Results (cont.)



Conclusions

- Recovery of immune function is anticipated after induction chemotherapy for pre-B ALL.
- Our data demonstrate the expected increase in T cell subsets in patients with MRD- BM at D29 but not in patients with MRD+ BM.
- The discovery of **poorer immunological recovery in MRD+ patients** requires additional study to determine what makes MRD+ disease different.
- This could introduce new immunotherapy targets in human leukemia.
- References available upon request
- Acknowledgement: Funding for this project was provided by Big Slick.