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Memory T Cell Populations in Human Leukemia

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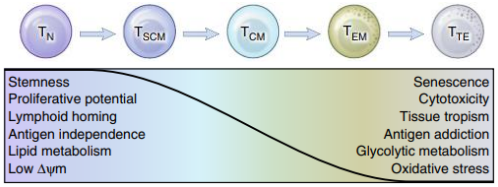
Background

- Knowledge about the nature of T cells in cancer, particularly memory T cells, is vital prior to potential incorporation into immunotherapies for leukemia such as:
  - Immune checkpoint inhibitors
  - Bispecific T-cell engagers
  - Chimeric antigen receptor (CAR) tumor-specific T cells
- T cells are made up of diverse subpopulations including **memory CD8+ T cells** which are further classified into **central memory T cells** (Tcm), **effector memory T cells** (Tem), and **T memory stem cells (Tscm)**.
- **Tscm**, the most recently characterized of these is of interest due to its:
  - Longevity
  - Self-renewal properties
  - Ability to create the full spectrum of memory CD8+ T cells
- **Objective:** To determine potential presence and frequency of memory T cell populations in human leukemia at diagnosis and after induction chemotherapy.

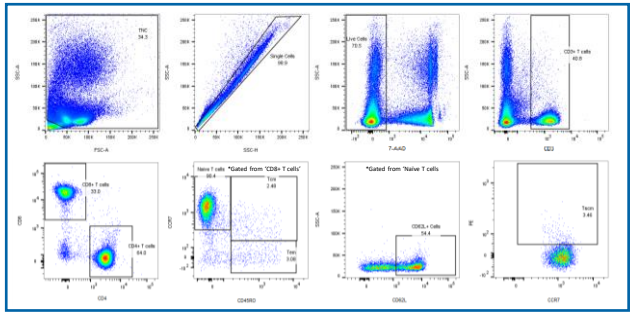


Gattinoni L, Speiser DE, Lichterfeld M, Bonini C. T memory stem cells in health and disease. *Nat Med*. 2017;23(1):18-27. doi:10.1038/nm.4241

Methods

- Children's Mercy Cancer Center Biorepository provided samples from 16 patients with **premature B cell acute lymphoblastic leukemia (pre-B ALL)** from peripheral blood (PB) and/or bone marrow (BM).
- 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.

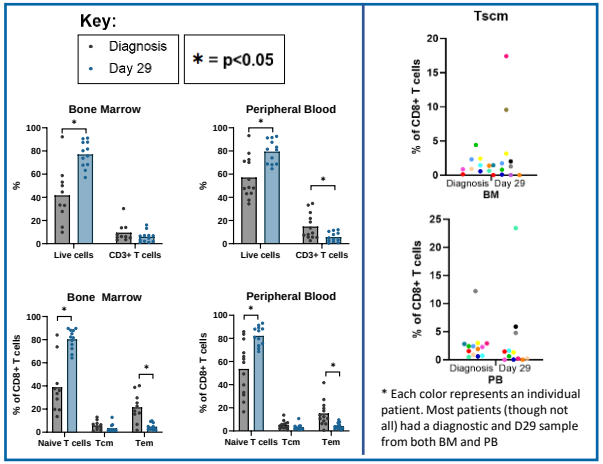
Gating Strategy



Results

- The absolute cell counts were not significantly different between diagnosis and D29.
- The live cell percent was lower at diagnosis than D29 (PB- 57.2% vs 79.4%, p=0.001; BM- 41.7% vs 77.0%, p<0.001).
- T cell frequencies were lower at D29 (PB- 14.8% vs 5.74%, p=0.014; BM- 9.5% vs 5.9%, p=0.217).
- $CD4^+$ T cells and $CD8^+$ T cells were not significantly different between diagnosis and D29.
- Among $CD8^+$ T cells, **naïve cells markedly increased from diagnosis to D29** (PB- 53.6% vs 82.2%, p<0.001; BM- 38.8% vs 80.3%, p<0.001) with a corresponding **significant decrease in Tem** (PB- 15.1% vs 4.2%, p=0.002; BM- 21.6% vs 4.7%, p<0.001).
- Tscm (reported as a percentage of $CD8^+$ T cells) were detected in all samples at diagnosis (PB range- 0.49-12.2%; BM range- 0.12-4.4%).
- After induction chemotherapy, two patients had no Tscm detected. The remainder demonstrated varying numbers of Tscm (PB range- 0.038-23.4%; BM range- 0.013-17.4%).
- Differences between diagnosis and D29 were not significant; however, **percentages of Tscm were lower in 9 of 12 patients after chemotherapy.**

Results (cont.)



* Each color represents an individual patient. Most patients (though not all) had a diagnostic and D29 sample from both BM and PB

Conclusions

- Induction chemotherapy led to decreased differentiated $CD8^+$ T cells with recovery of mostly naïve cells by D29.
- Furthermore, we established the presence of Tscm in most pediatric pre-B ALL samples.
- The decline of Tscm in most patients requires functional analyses to determine their role in leukemia and potential for use in immunotherapy.
- Studies are ongoing to detect differences in memory T cell populations based on response to induction chemotherapy.
- Further study is needed to investigate the potential impact of these changes on risk of relapse.
- References available upon request
- Acknowledgement: Funding for this project was provided by Big Slick.