Why is this rare blood disease so important to study?

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What is MDS/T-LGL?

- **T-LGL, T-cell large granular lymphocytic leukemia: Rare, chronic leukemia.**
  - **Arises from large granular lymphocytes (white blood cells) such as killer (CD8) T cells.**
  - **Can transform into aggressive disease.**
- **Causes: Autoimmune diseases, infections, mutations.**
- **Associated with autoimmune diseases.**
  - **Slow-growing, but can progress.**
- **Prognosis: Varies, complications affect course.**

- **MDS or myelodysplastic syndrome: Ineffective blood cell production.**
  - **Abnormal stem cells in marrow. Dysplastic cells die prematurely, cytopenias.**
- **Causes: Primary or therapy-related MDS.**
- **Risk factors: Age, genetics, chemicals.**
- **Categorized by IPSS scoring system.**
  - **Low-risk: Better prognosis, supportive care.**
  - **High-risk: Can progress to AML.**
- **Treatment: Chemotherapy or stem cell transplant.**

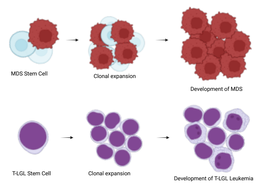


Figure 1. Expansion of "bad" cells from "bad" stem cells, showing how they can take advantage of your body and spread.

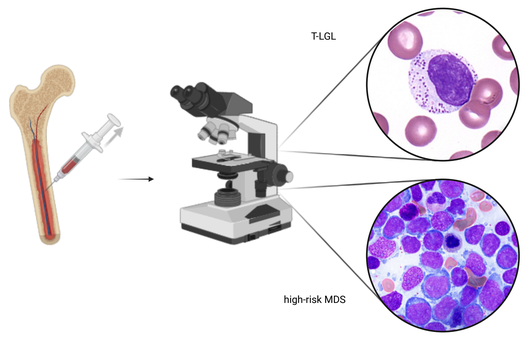


Figure 2. Bone marrow biopsy from patient. Diagnosis of both diseases calls for histological review. Both diseases will show up under the microscope looking much different than healthy bone marrow.

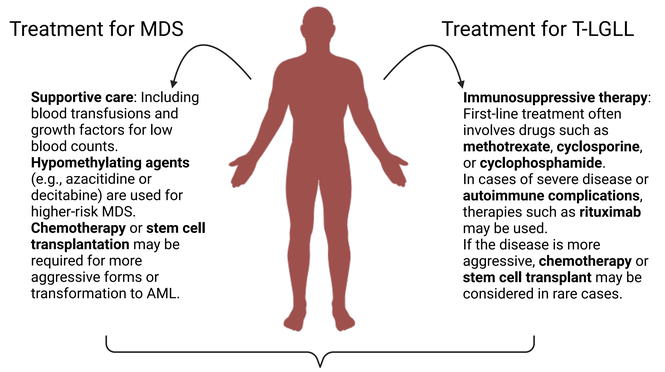
Why is it important to study?

0.2 cases of MDS/T-LGL out of

1,000,000

People in the United States

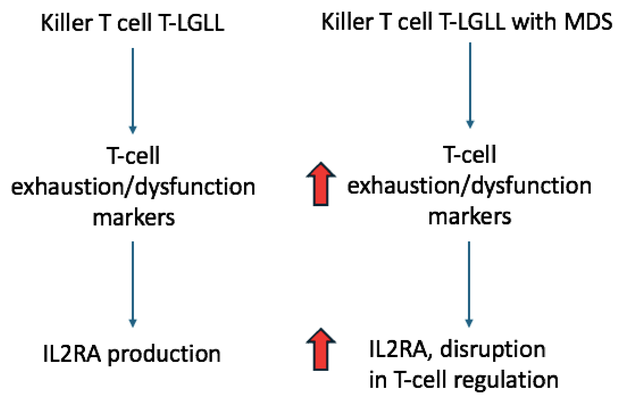
MDS combined with **T-LGL** is an **extremely rare disease combination**, meaning there is a **dire lack of research** and **funding** towards **improving life** and **prognosis** of these patients.



What do we think is going on?

- **T-cell exhaustion in MDS:** chronic immune activation
  - T-cells become less effective, contributing to the persistence of abnormal cells and progression of MDS.
- IL-2 is a protein responsible for telling T-cells what to do.
  - **IL-2RA** is a key receptor for IL-2 signaling, essential for T-cell activation, proliferation, and survival.
  - In **T-LGL leukemia**, IL-2RA expression is often **elevated** on malignant T-cells, contributing to their **expansion** and **chronic immune activation**.

There may be a mechanism between **IL-2RA in MDS and T-LGL** that could suggest **possible therapies**.



Our research so far

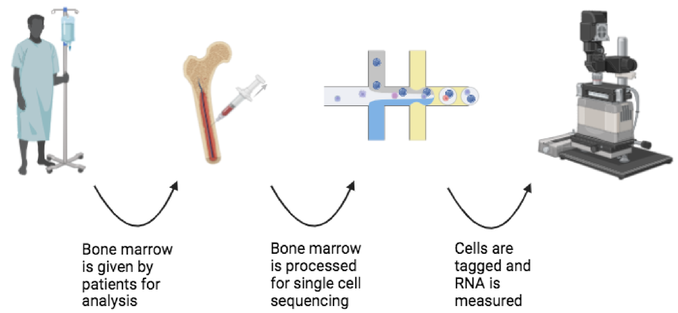


Figure 3. Process of acquiring bone marrow samples and analyzing these samples via single cell sequencing.

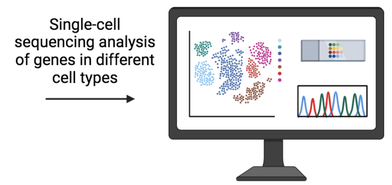


Figure 4. Schematic of single cell sequencing analysis. Each cell is analyzed for what genes are "on" and "off" in different types of cells.

Our findings so far:
- CD8+ (killer) T-cell Disruption:
  - Abnormal T-cell development in MDS/TLGL.
- Increased IL-2RA Expression in killer T cells
- T-cell Exhaustion Markers increased

Future directions:
- Analysis of the metabolism of these cells
- Measure IL-2RA in other blood tissues
- Analysis of the specific T cell markers in these patients

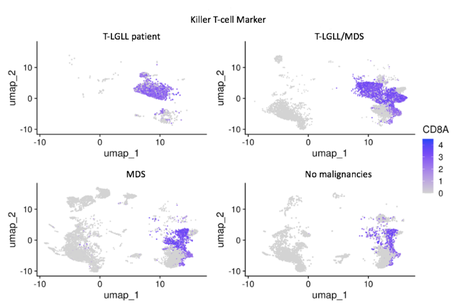


Figure 5. Plot derived from single cell sequencing showing the density and location of killer T cells in different patients.

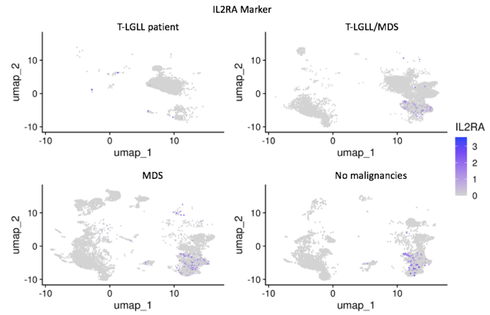


Figure 6. Plot derived from single cell sequencing, showing an overlap of IL-2RA expression in killer T cells, especially in the T-LGLL/MDS setting.

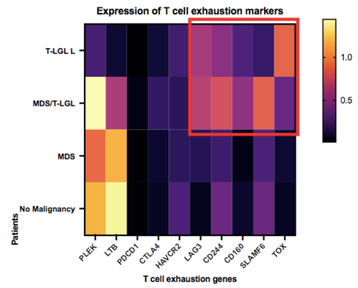


Figure 7. Heat-map showing the relative expression of T cell exhaustion genes. The lighter colors indicate a higher expression and the darker color indicates lower expression. The box indicates an emphasis on T cell exhaustion being upregulated especially in the T-LGLL and MDS/T-LGLL compartment.