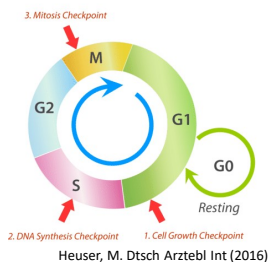
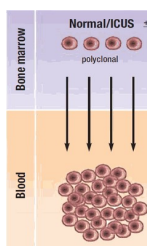


Clonal Hematopoiesis in Patients with Diamond Blackfan Anemia

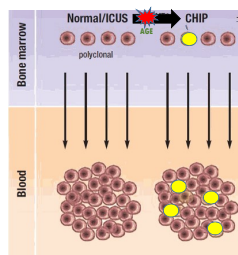
Michelle Nash, MD
 Fellow, Pediatric Hematology/Oncology
 Cohen Children's Medical Center



Polyclonal Hematopoiesis

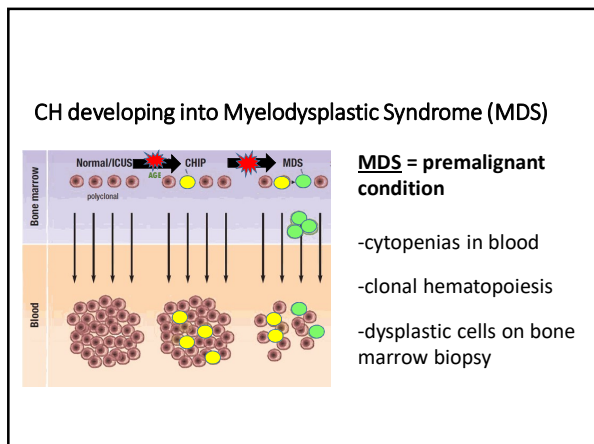


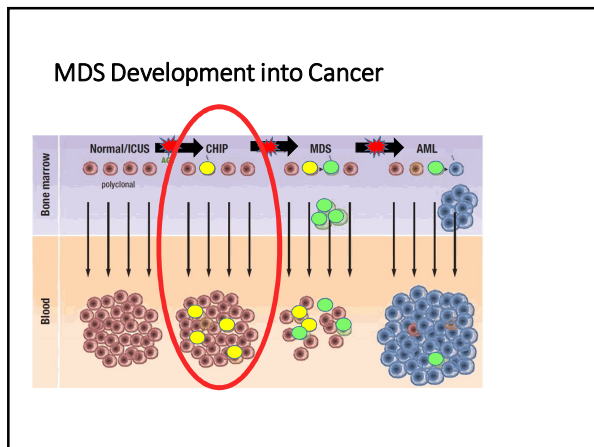
Clonal Hematopoiesis (CH)

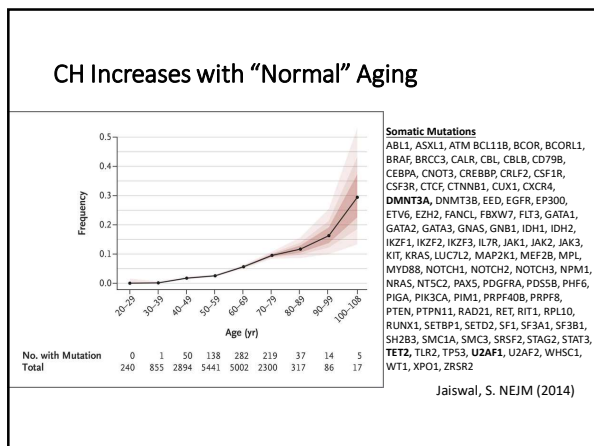


- Clonal Hematopoiesis of Indeterminate Potential (CHIP)
- Normal part of **aging**: 10% people older than 70 years of age carry somatic mutations

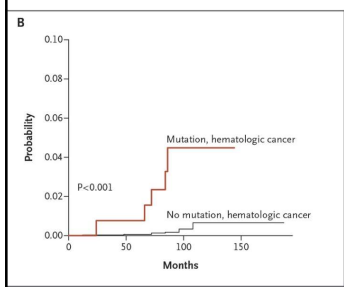
= Mutations







CH increases risk of Hematologic Cancer



- Hematologic cancers more common by factor 11.1%
- Absolute risk hematologic cancer approximately 0.5-1% per year
- Also increases risk of all cause mortality
- Increased risk cardiovascular disease

Jaiswal, S. NEJM (2014)

How does this relate to DBA?

- Patients with DBA have increased risk of **MDS and AML**

Diamond Blackfan Anemia Registry (DBAR): 702 patients

3 cases of Acute Myeloid Leukemia (AML)
-O/E Ratio: 28.8

8 cases of MDS
-O/E Ratio: **352.1**

Vlachos, A. Blood (2018)

MDS in DBA

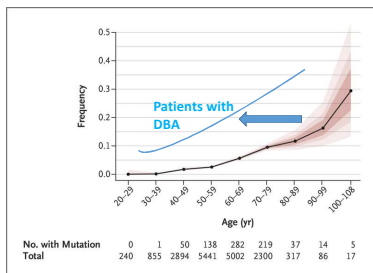
Median age at diagnosis of MDS in general population = 66-70 years old, less than 10% of the patients are younger than 50 years

Median age of patients with MDS in DBAR = **26 years old**

2 patients in DBAR with MDS were found to have CH



Our Hypothesis:



Patients with DBA have an accelerated rate of accumulation of somatic mutations (CH).

Research

- **Hypothesis:** Patients with DBA have an accelerated rate of accumulation of somatic mutations (CH).
- **Methods:**
 - whole exome sequencing to look for somatic mutations associated with CH
 - when available, samples stored in the biorepository will be evaluated to determine the rate of mutation acquisition
- **Requirement:** 5 mL of Peripheral Blood

How Can this Help Patients with DBA?

- Eventually this data can help us identify which patients **may be at risk for the development of blood cancer** and how closely they need to be monitored
- Early identification could lead to a greater chance of cure of blood cancers



To Participate

- If interested in signing up for the study please let Michelle Nash know and can coordinate blood draw here at camp
mnash2@northwell.edu
- At this time accepting patients > 18 years of age, and those who have not had a hematopoietic stem cell transplant



Mobilization of stem cells from patients with Diamond Blackfan anemia



Gene Therapy is Coming!

- All gene therapy requires stem cells to be used
- But can we get stem cells from patients with DBA?
 - At what age does it become more difficult to get cells?
 - Can patients with high iron burdens mobilize their stem cells?
 - Do the different types of mutations mobilize differently?



Upcoming Clinical Trial

- G-CSF (Neupogen) and Plerixafor used to stimulate your stem cells to come out into the blood in the periphery
- We would collect these cells and freeze them for future use
- Potentially looking at age 4 and above