Session 6

Genetics Revealing the Biology of Myeloid Neoplasms, Excluding Acute Leukemias

Session Chairs

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Session 4: Genetic Testing in the Diagnosis of Myeloid Neoplasms (Excluding Acute Leukemias)

Chairs: Robert Hasserjian and Todd Kelley

Session 6: Genetics Revealing the Biology of Myeloid Neoplasms (Excluding Acute Leukemias)

Chairs: Falko Fend and Elizabeth Morgan

Session 3: Genetic Testing in Diagnosis of Acute Leukemias

Chairs: Daniel Arber and Marian Harris

Session 7: Genetics Revealing the Biology of Acute Leukemias

Chairs: Magdalena Czader and David Czuchlewski

Session 2: Genetic Testing in the Diagnosis of Lymphoid Neoplasms

Chairs: Miguel Piris and Rebecca King

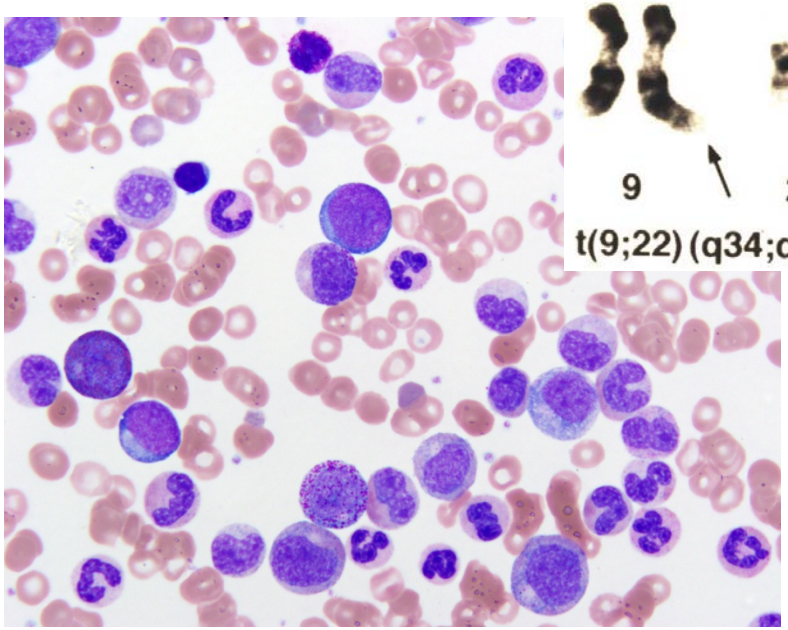
Session 8: Genetics Revealing the Biology of Lymphoid Neoplasms

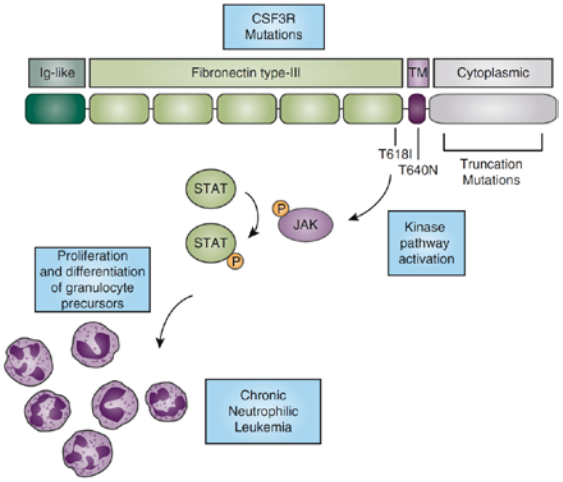
Chairs: Megan Lim and Nate Bailey

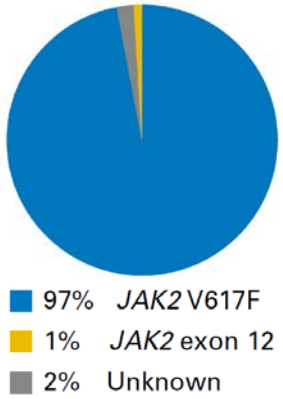
Table 1. WHO classification of myeloid neoplasms and acute leukemia

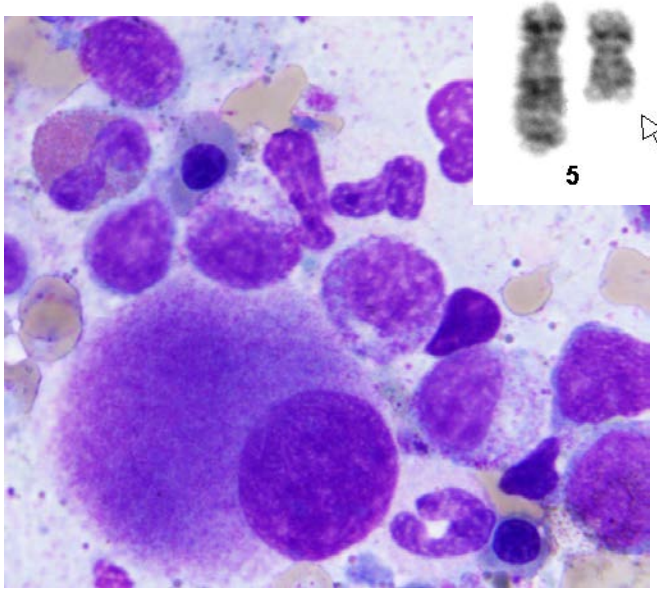
WHO myeloid neoplasm and acute leukemia classification
Myeloproliferative neoplasms (MPN)
Chronic myeloid leukemia (CML), *BCR-ABL1*$^{+}$
Chronic neutrophilic leukemia (CNL)
Polycythemia vera (PV)
Primary myelofibrosis (PMF)
PMF, prefibrotic/early stage
PMF, overt fibrotic stage
Essential thrombocythemia (ET)
Chronic eosinophilic leukemia, not otherwise specified (NOS)
MPN, unclassifiable
Mastocytosis
Myeloid/lymphoid neoplasms with eosinophilia and rearrangement of *PDGFRA*, *PDGFRB*, or *FGFR1*, or with *PCM1-JAK2*
Myeloid/lymphoid neoplasms with *PDGFRA* rearrangement
Myeloid/lymphoid neoplasms with *PDGFRB* rearrangement
Myeloid/lymphoid neoplasms with *FGFR1* rearrangement
Provisional entity: Myeloid/lymphoid neoplasms with PCM1-JAK2
Blastic plasmacytoid dendritic cell neoplasm
Myelodysplastic/myeloproliferative neoplasms (MDS/MPN)
Chronic myelomonocytic leukemia (CMML)
Atypical chronic myeloid leukemia (aCML), *BCR-ABL1*$^{-}$
Juvenile myelomonocytic leukemia (JMML)
MDS/MPN with ring sideroblasts and thrombocytosis (MDS/MPN-RS-T)
MDS/MPN, unclassifiable
Myelodysplastic syndromes (MDS)
MDS with single lineage dysplasia
MDS with ring sideroblasts (MDS-RS)
MDS-RS and single lineage dysplasia
MDS-RS and multilineage dysplasia
MDS with multilineage dysplasia
MDS with excess blasts
MDS with isolated del(5q)
MDS, unclassifiable
Provisional entity: Refractory cytopenia of childhood
Myeloid neoplasms with germ line predisposition

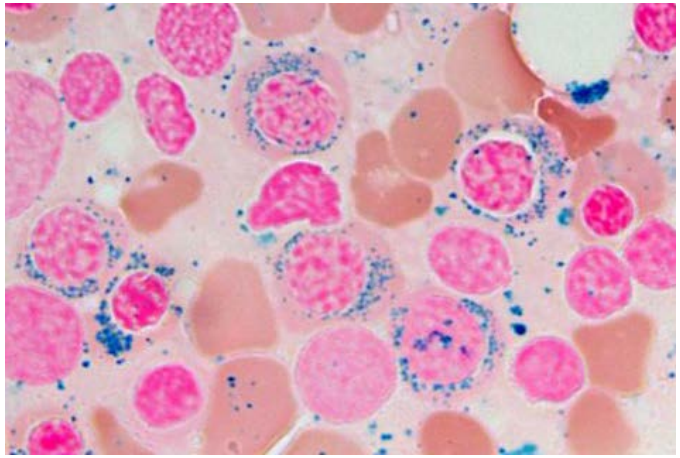
Polycythemia Vera

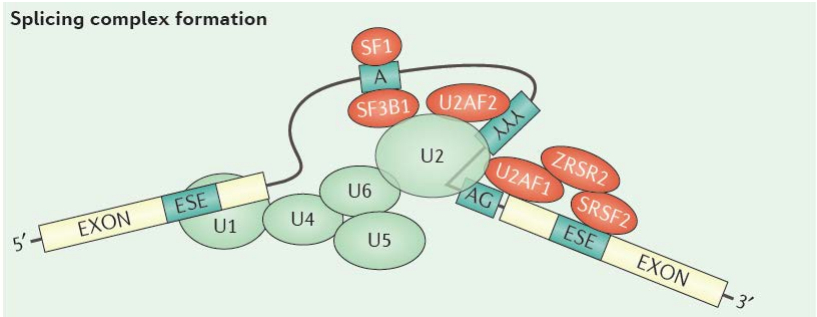












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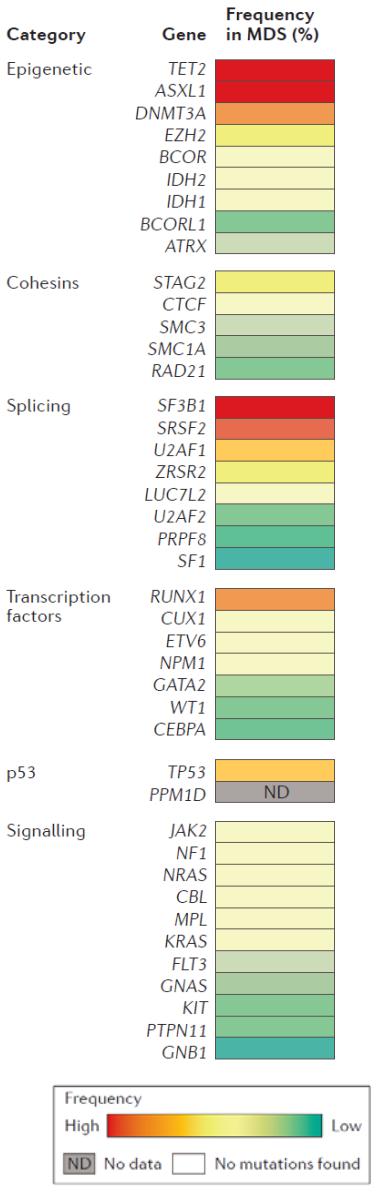
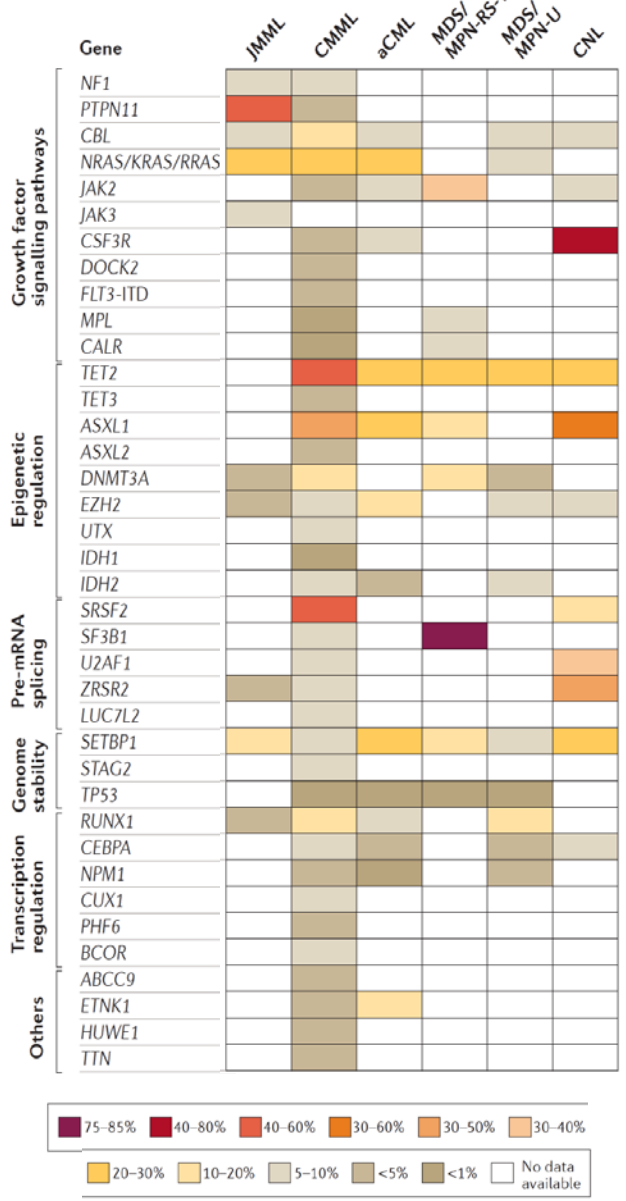
- High throughput genetic analysis has identified a large number of recurrent alterations in myeloid neoplasms with chronic evolution
  - diagnosis
  - prognosis
  - therapeutic decisions

- ***Challenges***
  - genetic complexity
  - many alterations are not disease-specific
  - serial acquisition or loss of mutations
  - co-mutation patterns
  - pre-malignant states

MDS



MDS/MPN



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Topics of Session 6: Genetics Revealing the Biology of Myeloid Neoplasms

- Chronic myeloid leukemia (CML):
  - Atypical genetic/phenotypic features of blast crisis (7 cases)
  - CML with other myeloproliferative or lymphoid neoplasm (4 cases)
- Ph-negative myeloproliferative neoplasms (MPN)
  - MPN with multiple or unusual/non-canonical driver mutations (7 cases)
  - MPN with atypical progression or transformation (3 cases)
- Myelodysplastic syndromes (MDS)
  - Atypical clinical presentation or disease association (3 cases)
  - Atypical mutations, e.g. 5q- with *JAK2* or *MPL* mutations (7 cases)
- MDS/MPN and other myeloid neoplasms
  - Atypical mutations or associated mastocytosis (7 cases)
- Myeloid/lymphoid neoplasm with *PDGFRA* rearrangement (1 case)

Questions Arising from Session 6

- The role and clinical impact of (extensive) genetic testing in unusual presentations or disease progression in “chronic” myeloid neoplasms
- The interpretation of typical driver mutations in atypical clinical and morphologic settings: classification issues
  - *JAK2* or *MPL* in MDS
  - *SF3B1* in MPN
  - *NPM1* in chronic myeloid neoplasms (CMML, aCML)
- Recognition and classification of unusual types of disease progression
- Interpretation of non-canonical variants in typical driver genes

6 Oral Presentations

- *Genetics revealing unusual disease progression*
  - #68: Dr. Al-Ghamdi
- *Shared genetic origin*
  - #244: Dr. Mroz
- *Typical driver mutation in atypical setting*
  - #267: Dr. Liontos
- *Myeloproliferative neoplasm with alteration of morphology/presentation reflecting underlying genetics*
  - #207: Dr. Nam
  - #238: Dr. Boiocchi
- *Overlapping genetic and molecular features*
  - #159: Dr. Lewis

Summary of 33 Additional Submitted Cases