Session 4: Genetic testing in the diagnosis of myeloid neoplasms (excluding acute leukemia)

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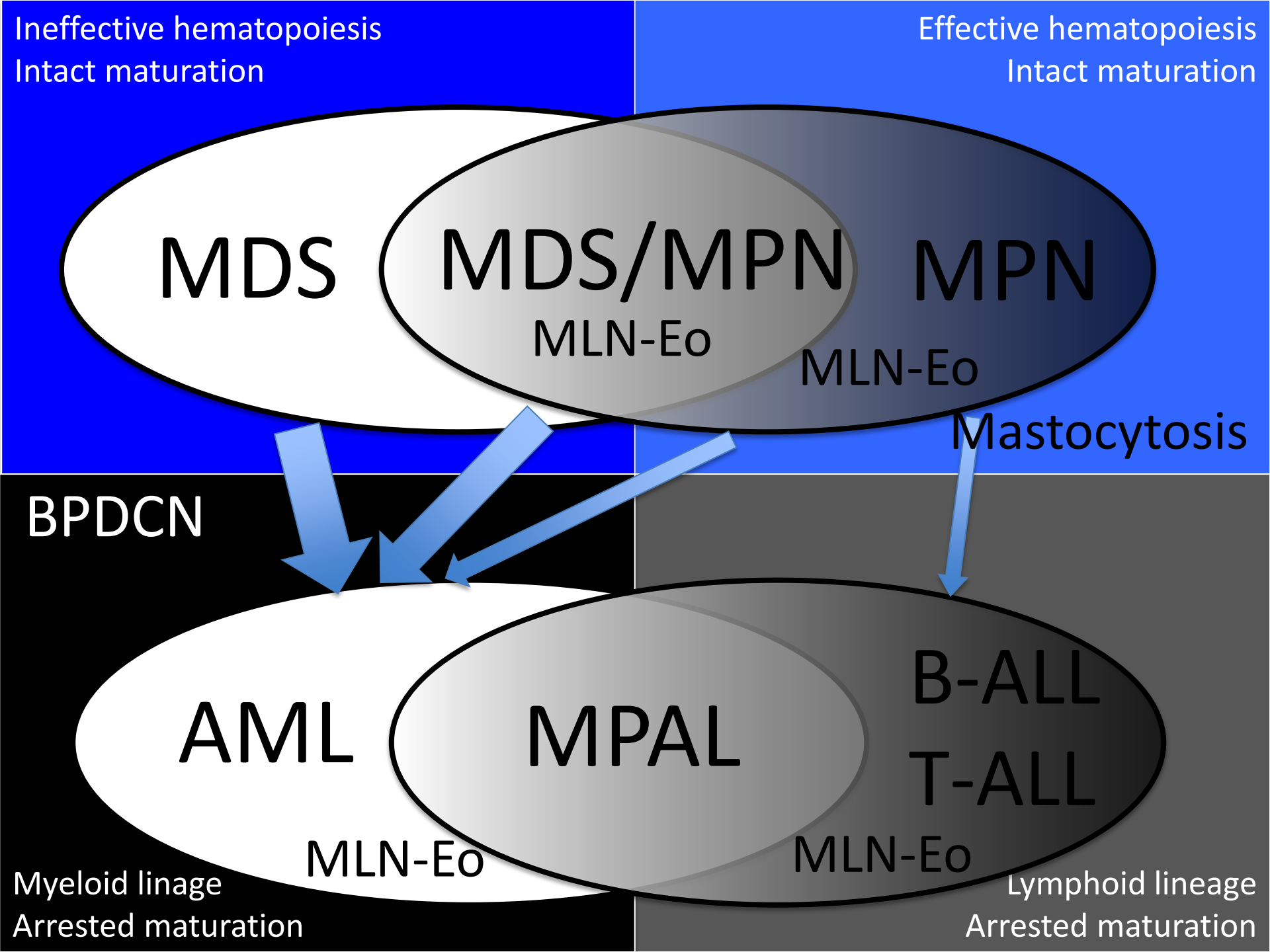
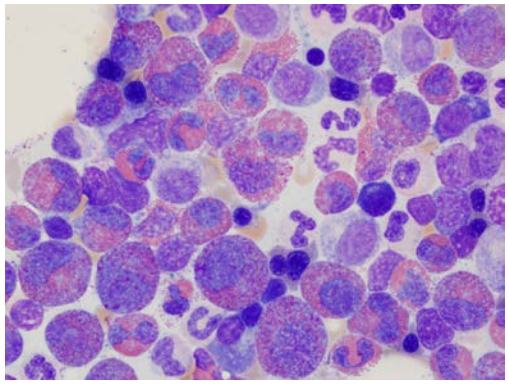
Disease categories discussed in Session 4

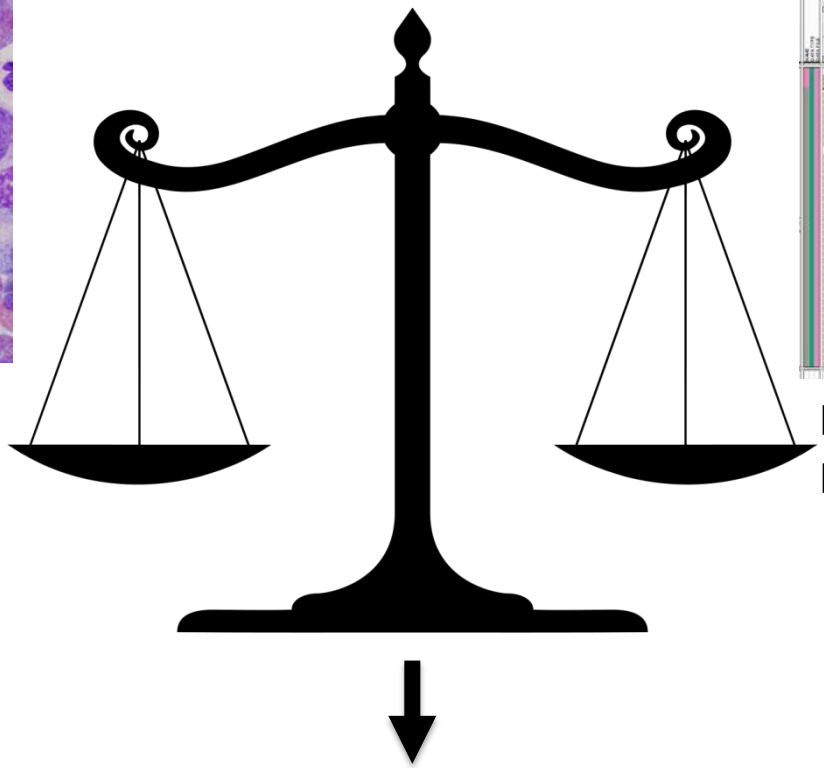
Myeloproliferative neoplasms (MPN)	Sessions 4 & 6
Mastocytosis	Sessions 4 & 6
Myeloid/lymphoid neoplasms with eosinophilia and gene rearrangement (*PDGFRA*, *PDGFRB*, *FGFR1* or *PCM1-JAK2)*	Sessions 4 & 6
Myelodysplastic/myeloproliferative neoplasms (MDS/MPN)	Sessions 4 & 6
Myelodysplastic syndromes (MDS)	Sessions 4 & 6
Blastic plasmacytoid dendritic cell neoplasm (BPDCN)	Sessions 4 & 6


Ineffective hematopoiesis
Intact maturation
Effective hematopoiesis
Intact maturation
MDS
MDS/MPN
MLN-Eo
MPN
MLN-Eo
Mastocytosis
BPDCN
AML
MLN-Eo
MPAL
B-ALL
T-ALL
MLN-Eo
Myeloid linage
Arrested maturation
Lymphoid lineage
Arrested maturation

Diagnostic hematopathology 2017



Dsyplasia
Cellularity
Differential counts
CBC
Clinical history
Immunophenotype



Diagnosis

Karyotype/FISH
NGS panels
- -mutation spectrum
- -variant frequencies
- -germline variants
- -VUSs
- -CHIP/CCUS
- -prognostic significance
- -targeted therapies

NGS panels: General trends in mutation patterns

- MDS – spliceosome genes (*SF3B1*, *SRSF2*), *ASXL1*, *RUNX1*, *EZH2*
- MPNs – *JAK2*, *CALR*, *MPL*, *CSF3R*
- MDS/MPN
  - Atypical CML- *ASXL1*, *TET2*, *SETBP1*
  - CMML – *SRSF2*, *TET2*, *CBL*, *ASXL1*
  - MDS with ring sideroblasts and thrombocytosis – *JAK2* + *SF3B1*
  - JMML – RAS pathway mutations (*PTPN11, KRAS/NRAS*)
- CHIP – *TET2*, *DNMT3A*, *ASXL1*

General issues addressed in this session

- Newly defined entities in the WHO Classification system
  - Myeloid neoplasm with *PCM1-JAK2*
- Are there any truly specific molecular genetic abnormalities?
  - Yes: ex. t(8;21);*RUNX1-RUNX1T1*
  - But not these: ex's. *CSF3R* p.T618I or *JAK2* p.V617F
  - And certainly not in these genes: *DNMT3A*, *TET2*
- How helpful are 'typical' mutation patterns in supporting a particular diagnosis?
  - "Oligomonocytic" chronic myelomonocytic leukemia
- What about 'atypical' patterns?
  - Atypical CML with mutated *CSF3R*

General issues addressed in this session

- Establishing clonality using NGS panels
  - Diagnosis of CEL, NOS with “molecular genetic” abnormalities
  - Beware of CHIP
- Variants of uncertain significance (VUSs)
  - Germline or somatic?
- Finding unexpected mutations that change the diagnosis
  - Detection of a *KIT* D816V mutation led to an unanticipated diagnosis (systemic mastocytosis)
- Synthesizing morphologic and molecular genetic findings

Oral presentation cases

- #124 – Dr John Goodlad: Atypical chronic myeloid leukemia
- #351 – Dr. Madhu Menon: Chronic myelomonocytic leukemia-0
- #156 – Dr. Jeffrey Craig: Systemic mastocytosis with associated hematologic neoplasm (CMML-0)
- #171 – Dr. Shunyou Gong: Juvenile myelomonocytic leukemia
- #376 – Dr. Magdalena Czader: Myeloid neoplasm with *PCM1-JAK2*
- #300 – Dr. Geetha Jagannathan: Chronic eosinophilic leukemia, NOS
- #314 – Dr. Habibe Kurt: Blastic plasmacytoid dendritic cell neoplasm


EXIT 5A
71 SOUTH
Reactive process
CLOSED
670 EAST
CHIP?
Left 2 Lanes
71 NORTH
MPN-U
1 1/4 MILES
EXITS 4A-
23
aCML vs
CNL
EXIT ONLY