



# Session 8

## Genetics Revealing the Biology of Lymphoid Neoplasms

**Nathanael Bailey MD**  
University of Pittsburgh

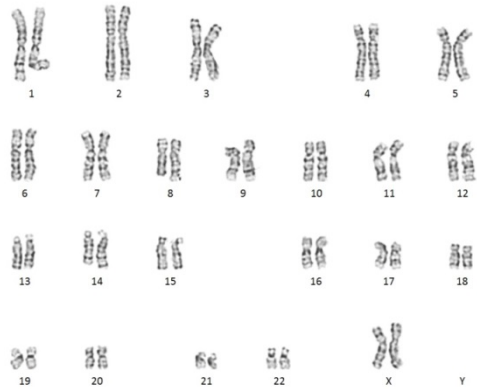
**Megan S. Lim, MD PhD**  
University of Pennsylvania

11:05 – 11:15 Introduction

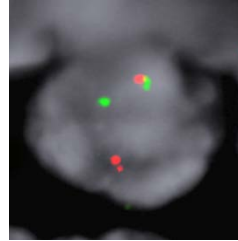
11:15 – 12:30 Case Presentations

12:30 – 12:50 Summary

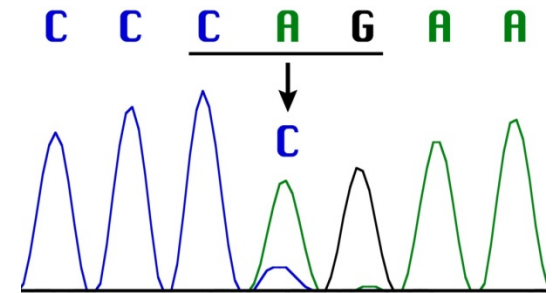
# Evolution of Genetic Testing in Lymphoma



Metaphase karyotyping

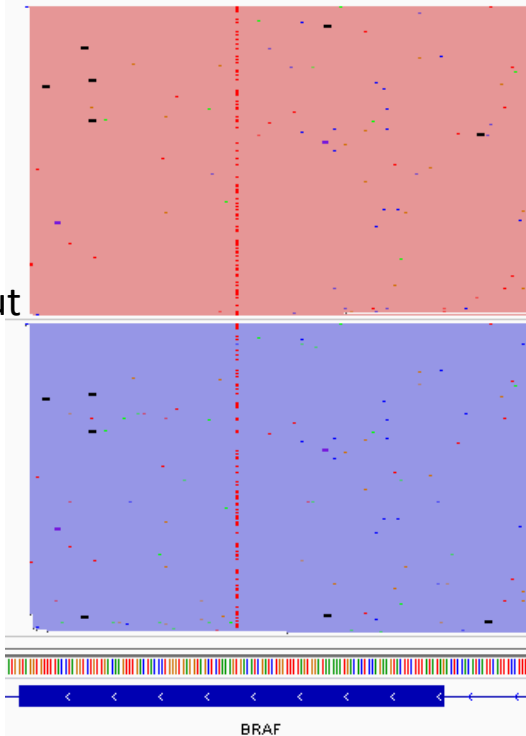


Fluorescence *in situ* hybridization

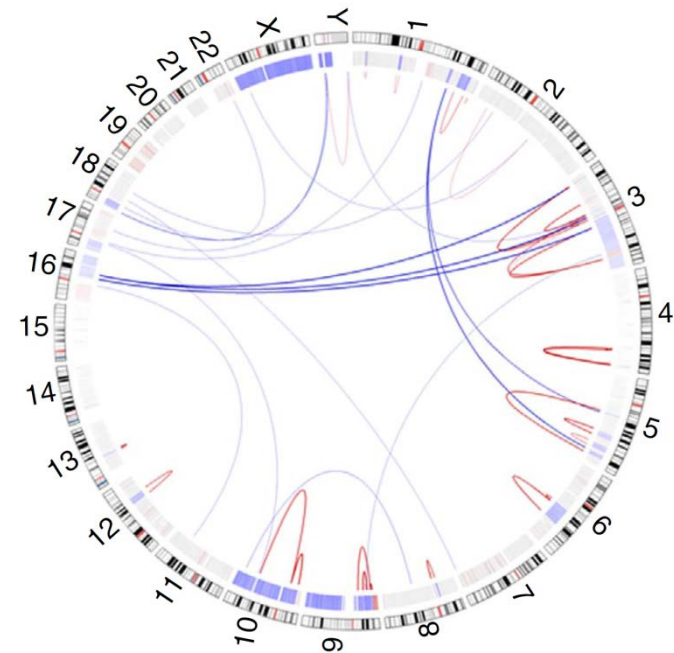


Single-gene sequencing

High-throughput sequencing

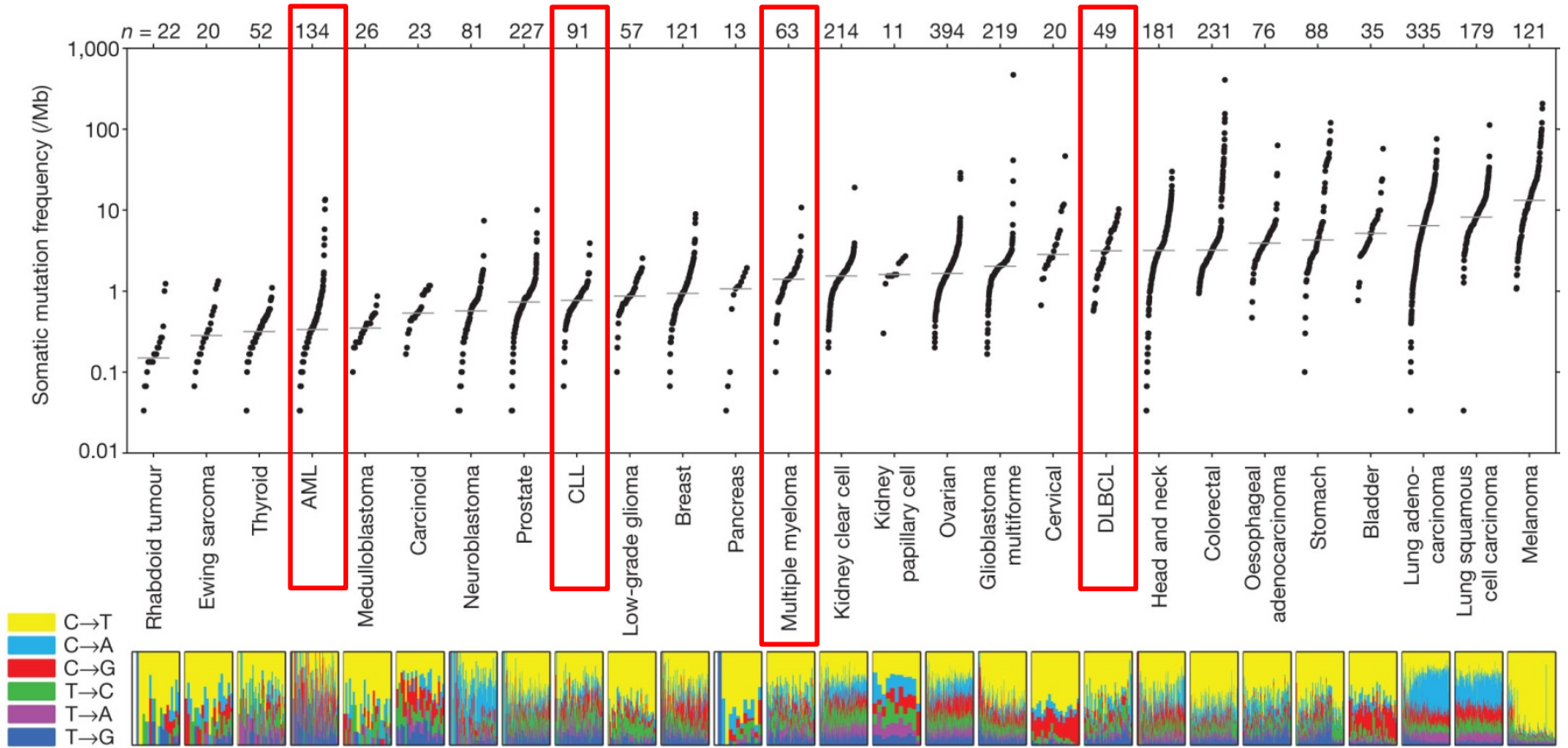


BRAF

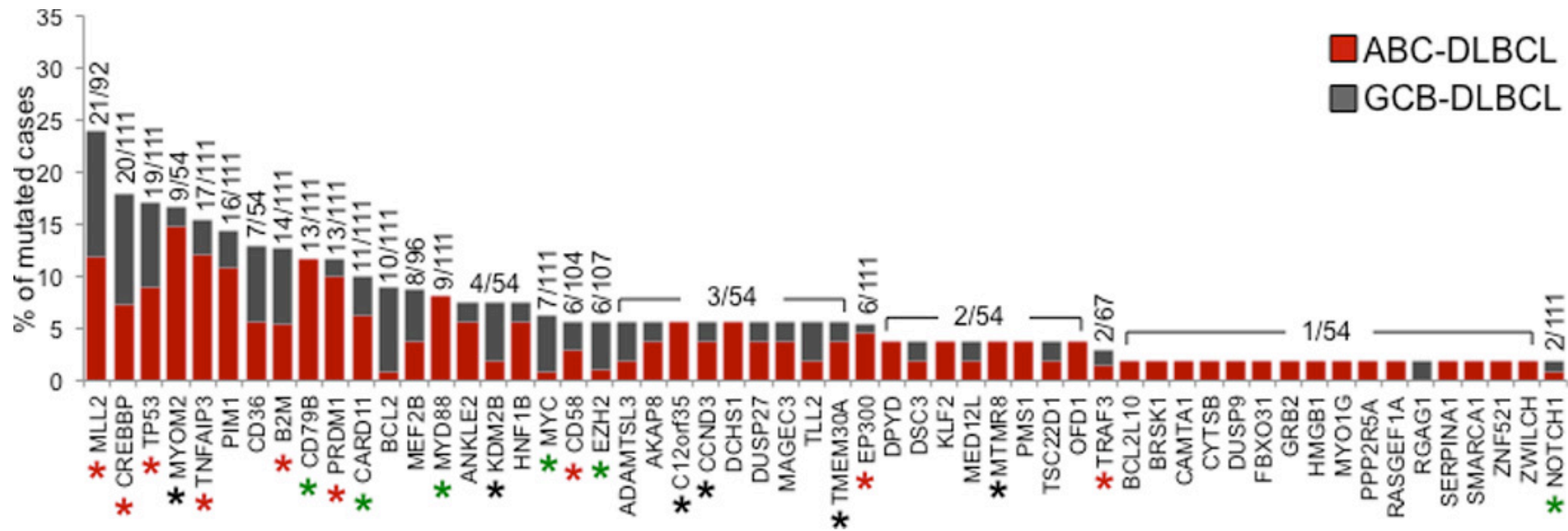


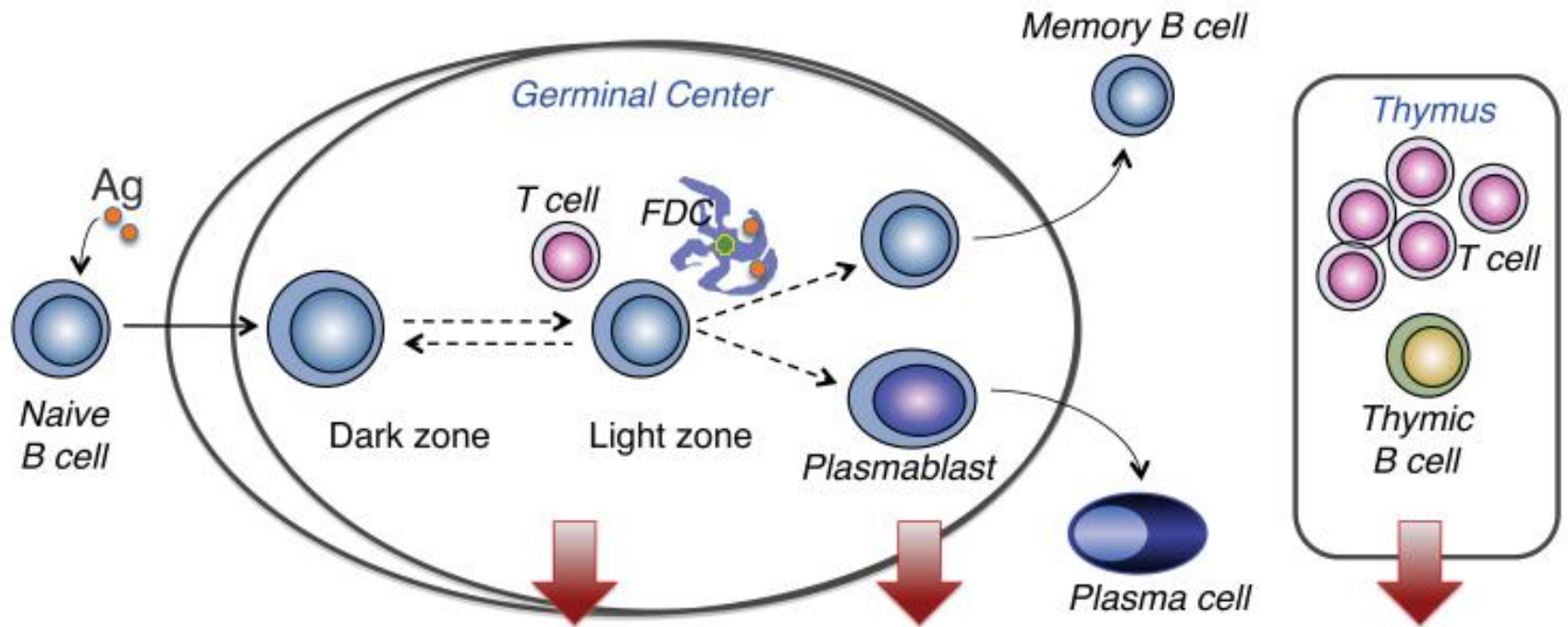
Integrated genomic analysis

# Lymphoid neoplasms are mutationally complex tumors



# Mutational heterogeneity of lymphoma





### GCB- and ABC-DLBCL

Gene	%
BCL6 Tx	20-40
MLL2/MLL3 M	32-38
CREBBP/EP300 M/D	32
B2M/CD58 M/D	21-29
TP53 M	20
MEF2B M	11
FOXO1 M	8

### GCB-DLBCL

Gene	%
BCL2 Tx/M	34
GNA13 M	25
EZH2 M	22
BCL6 BSE1 M	15
MYC Tx	10
miR17-92 G	6-12
PTEN D	6-11

### ABC-DLBCL

Gene	%
TNFAIP3 M/D	30
MYD88 M	30
CDKN2A/B D	30
BCL2 Amp	24-30
PRDM1 M/D	25
CD79A/B M	20
CARD11 M	9

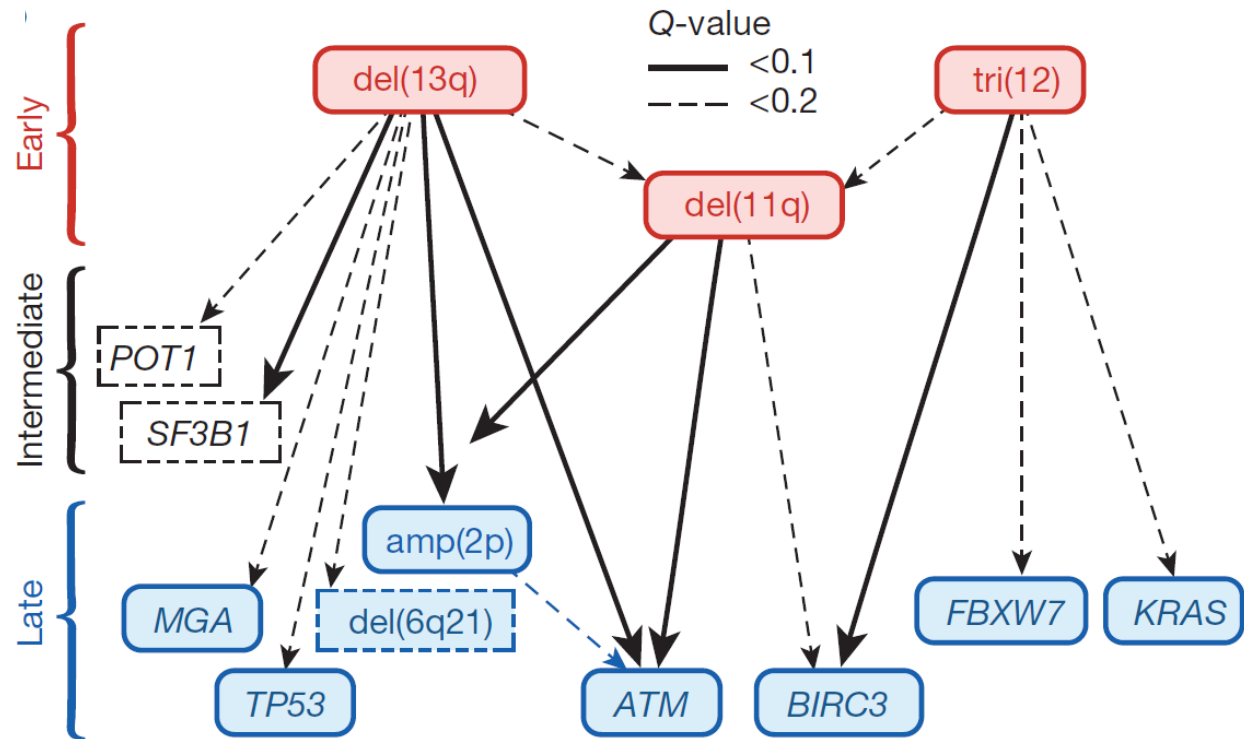
### PMBCL

Gene	%
PDL1/2 Amp/Tx	49
SOCS1 M	45
CIITA Tx	38
STAT6 M	36
TNFAIP3 M	36
JAK2 Amp	30
TP53 M	20
PTPN1 M	20

■ epigenetic modification   ■ proliferation   ■ BCL6 deregulation   ■ NF-κB/BCR signaling   ■ DNA damage response  
 ■ immune escape   ■ apoptosis   ■ terminal differentiation   ■ JAK/STAT signaling   ■ cell cycle   ■ other

# NGS allows assessment of within-tumor clonal heterogeneity in lymphomas

NGS allows identification of subclonal mutational events, increasing our understanding of the temporal acquisition of mutations during disease progression



# Session 8 Themes

- New genetic/genomic techniques allow novel insights into lymphoid biology
- These techniques have moved from the research setting and are being ever more commonly utilized in clinical practice
- The cases that will be presented illustrate both the opportunities and challenges of incorporation of genetic information in routine clinical practice

# Session 8 Themes

- Cases in this session illustrate several themes of molecular testing in lymphoid neoplasia:
  - Assessment of transformation and transdifferentiation events
    - as a result of novel therapies (CAR-T)
    - clonal evolution as part of the disease progression
  - Exploration of the clonal relationship of different tumors
    - Evaluate for shared IG/TCR rearrangements
    - Shared somatic mutations



# Session 8 Themes

- Cases in this session illustrate several themes of molecular testing in lymphoid neoplasia:
  - Identification of “aggressive” molecular genetics in morphologically or clinically indolent lymphomas
  - Identification of “discordant” or unusual mutations and implications for lymphoma classification
  - Molecular results that assist classification/diagnosis of lymphoma, and cautionary examples where molecular testing was misleading or unhelpful

<b>Case Number</b>	<b>Presenter</b>	<b>Institution</b>	<b>Time</b>
<b>SH2017-0086</b>	<b>Leticia Quintanilla-Fend</b>	Institute of Pathology, Tuebingen	11:15
<b>SH2017-0327</b>	<b>Rohit Gulati</b> Magdalena Czader Christin Tsao	Indiana University	11:27
<b>SH2017-0338</b>	<b>Andrew Evans</b> Yi Ding, Todd Laughlin, Paul Rothberg, Carla Casulo, and Richard Burack	University of Rochester	11:39
<b>SH2017-0359</b>	<b>Shiraz Fidai</b> Sandeep Gurbuxani, Megan M.McNerney, Gordana Raca, Madina Sukhanova, Michael Thirman, John Anastasi, Elizabeth Hyjek	University of Chicago	11:51
<b>SH2017-0210</b>	<b>Jonathon Gralewski</b> Ginell R. Post MD, PhD and Youzhong Yuan MD	University of Arkansas	12:03
<b>SH2017-0035</b>	<b>Mariusz Wasik</b> Q Zhang, HY Wang, A Bogusz, P Zhang, E Orlando, X Liu, S Brooks, E Tomczak, C Watt, J Morissette, SJ Schuster	University of Pennsylvania	12:15