

Targeting signalling pathways in hematological malignancies: Are we close to the end of histopathological classification and the chemotherapy era?

Is a purely biological classification of lymphoma possible?

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NO DISCLOSURES

What is a purely biological classification of lymphoma?

Genetic translocations?

Mutated genes (exome/genome sequencing?)

Status of important kinases?

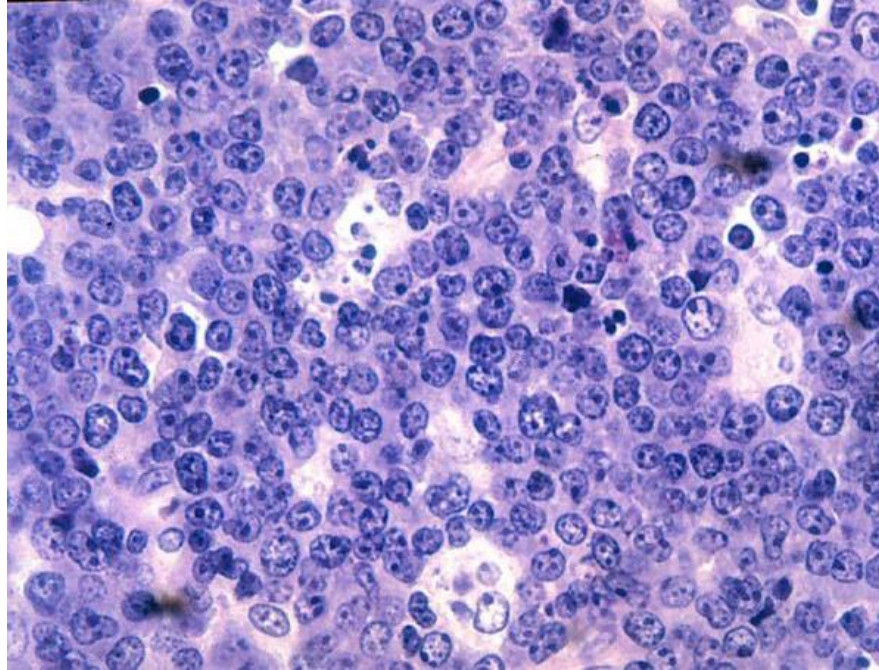
Epigenetic/methylation profile?

Proteome?

Pathway? How to measure activation/inactivation?

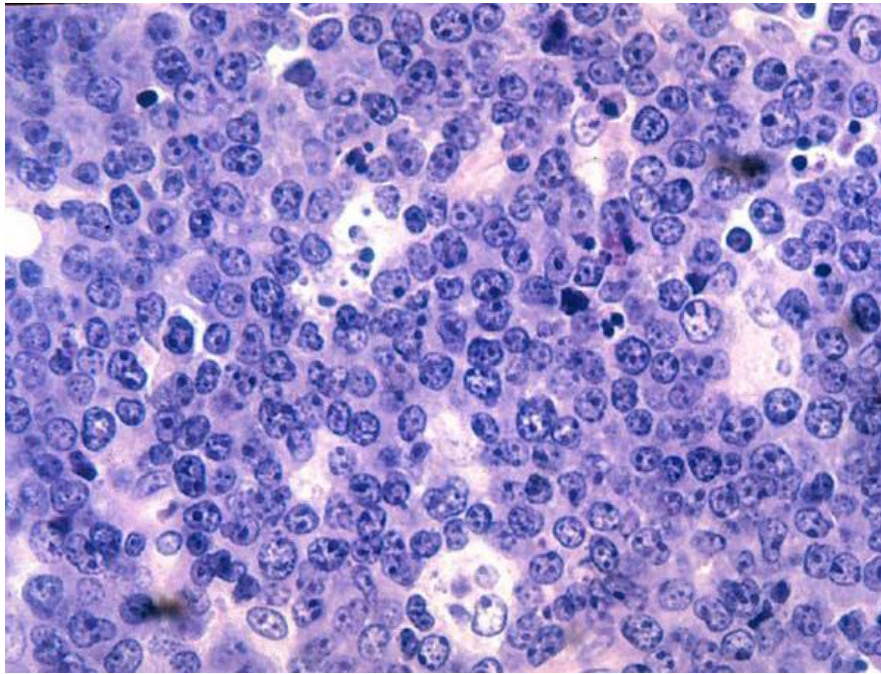
Is histopathology/immunohistochemistry no biology?

Burkitt Lymphoma

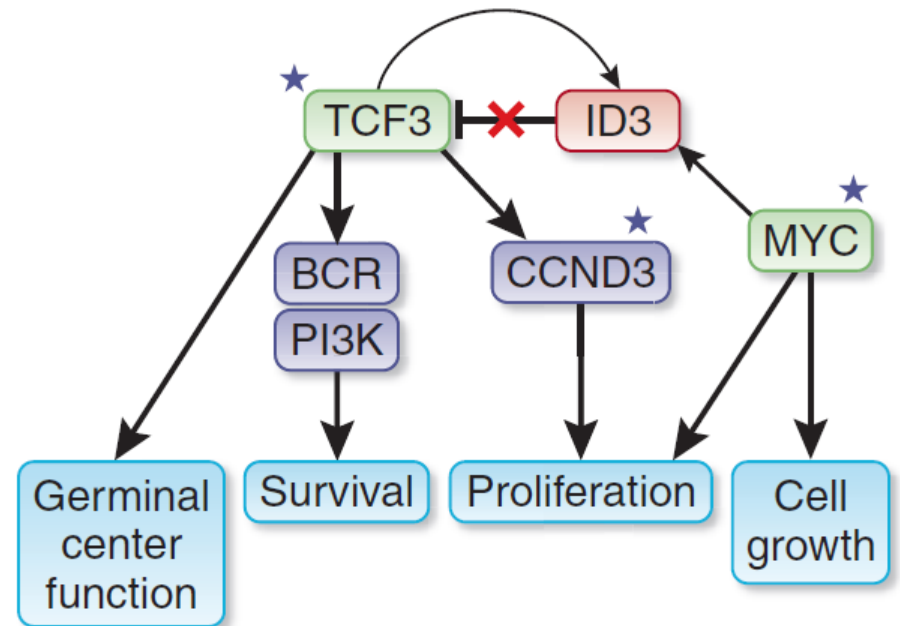


Morphology = Biology!

Burkitt Lymphoma

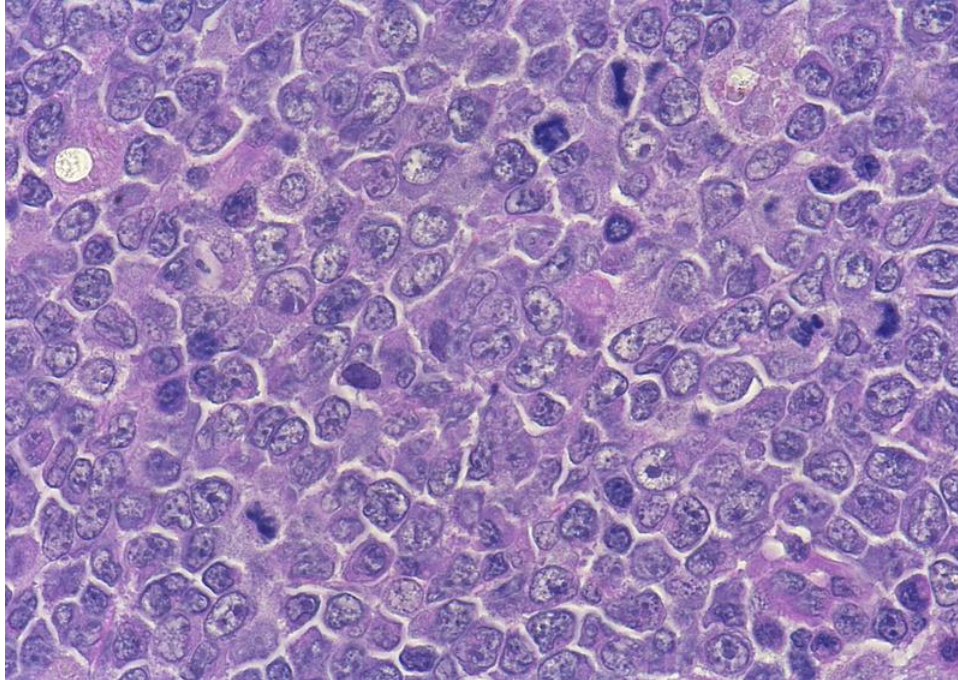


CD20+, CD10+, BCL2-, Ki-67 100%



Morphology = Biology!

Diffuse large B cell lymphoma



Morphology \neq Biology!

Diffuse large B cell lymphoma

- DLBCL has clinico-pathologic subtypes
- DLBCL NOS is clinically, morphologically and genetically heterogeneous
- Translocations (BCL2, BCL6, MYC) are important pathogenetic mechanisms
- Genetics/Pathways in DLBCL
 - p53, NFkB, B-cell receptor signalling,
 - Toll-like/interleukin receptor signalling, histone modifications,
 - FOXO1 pathway, metabolic ('ox/phos') signature
- Distinction between GCB/ABC DLBCL remains important
- DLBCL with MYC/BCL2 (double hit) translocations have poor outcome
- DLBCL with high MYC/BCL2 expression (IHC) have inferior outcome

Consequences for therapeutic approaches?