

Pathogenesis of CLL and biomarkers

Pathogenetic moments

1 Antigenic stimulation of lymphocytes with specific BCR

2 Continuous Ag stimulation
Antigen driven oligoclonal expansion

3 Genetic features

4 Clinical phenotype

Prognostic markers

Specific BCR subsets
e.g. stereotyped (VH3-21, others)

Activation markers/microenvironment
e.g. CD38, CD49d, ZAP70, TCL1, LPL

Genetic instability
Telomere shortening
11q-, 17p-, *IGHV* unmutated
Complex karyotype
TP53, *BIRC3*, *SF3B1*, *Notch1*

Tumor load and host characteristics
Stage, $\beta 2$ micro, sCD23, sTK
Age, gender, performance status,
Comorbidities