

# BIO MED 2024

LES JOURNÉES POUR L'AVENIR DE LA BIOLOGIE MÉDICALE

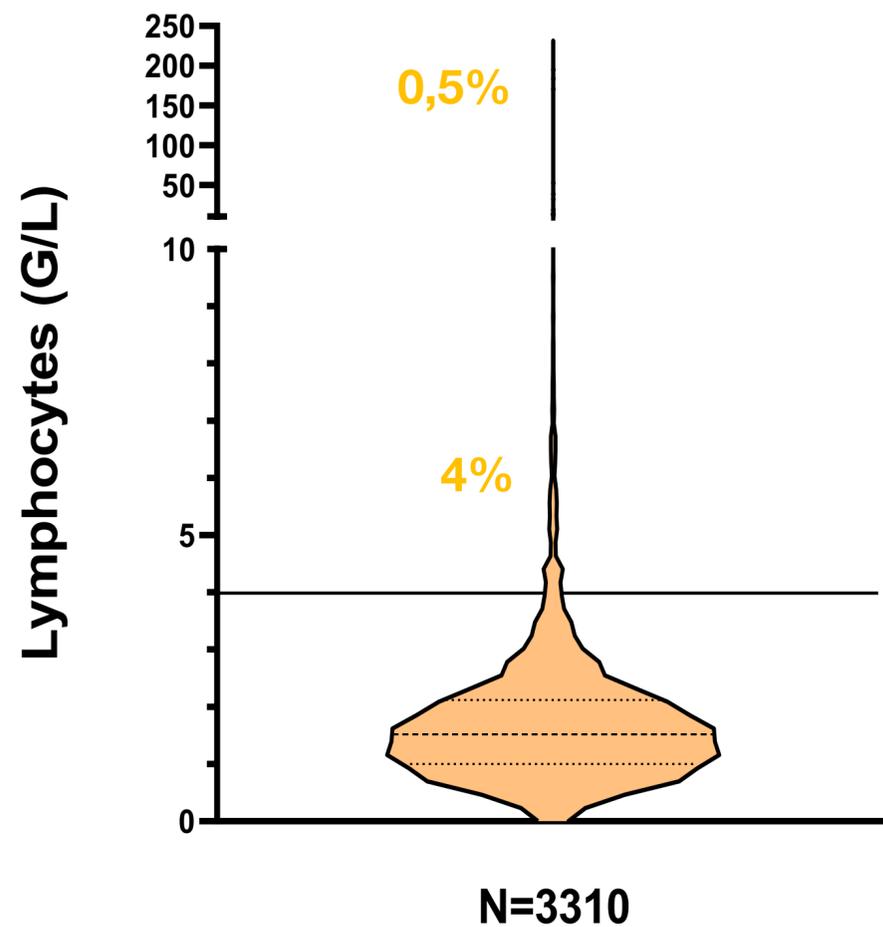
JEUDI 23 &  
VENDREDI 24  
MAI 2024

Orientation diagnostique sur les hyperlymphocytoses  
Explorations moléculaires dans le diagnostic des  
hémopathies lymphoïdes

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Laboratoire d'Hématologie  
CHU RENNES

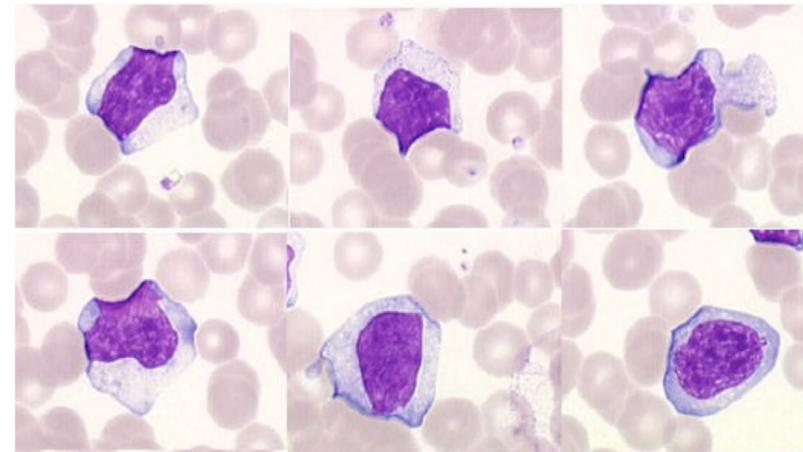
# Hyperlymphocytose

- Lymphocytes supérieurs à 4G/L chez l'adulte
- Situation fréquente



Début Mai 2024, CHU Rennes

## Lymphocytoses polymorphes transitoires



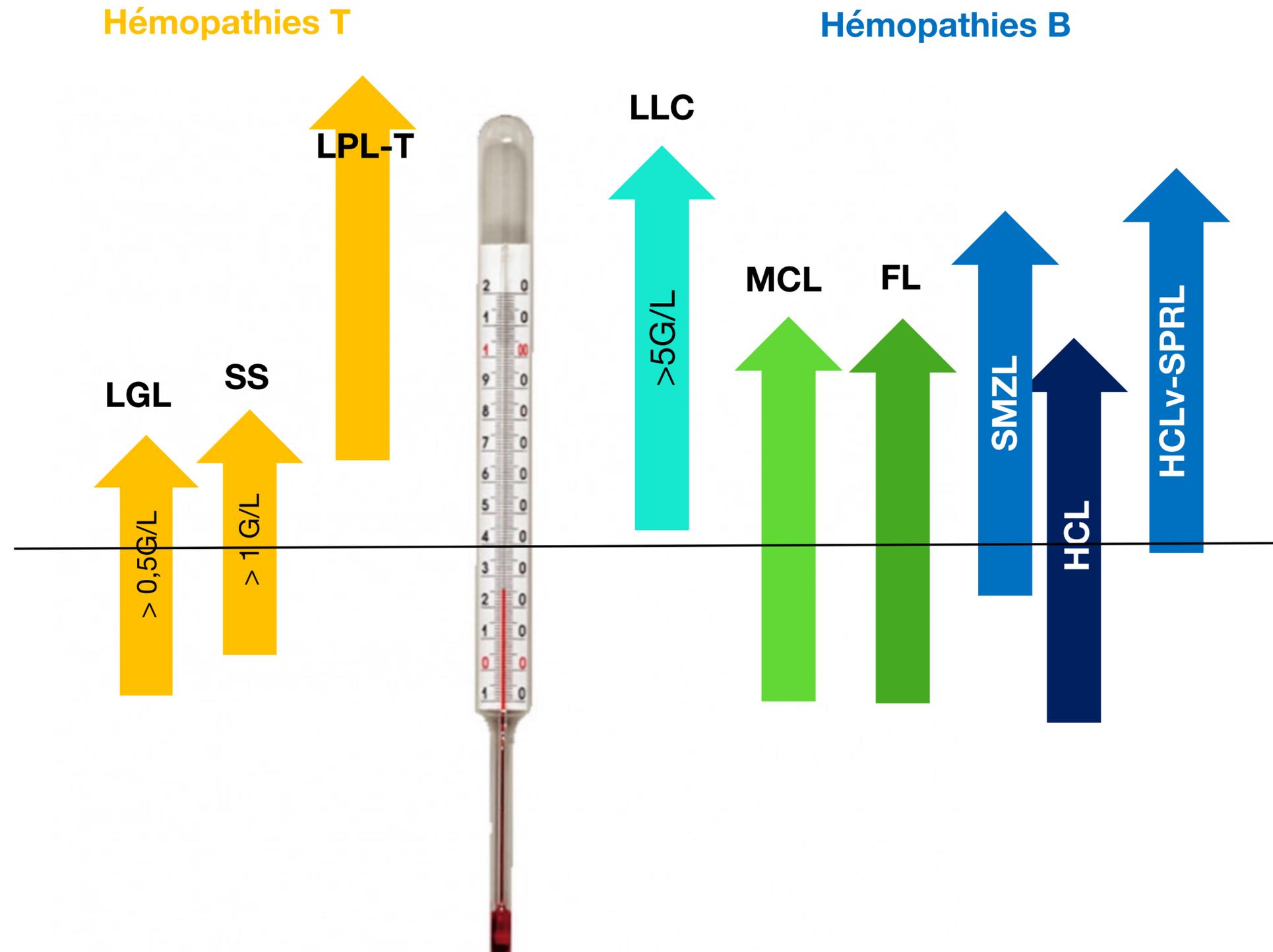
Syndrome mononucléosique

## Lymphocytoses monomorphes Chroniques Cellules anormales Contexte clinique évocateur d'hémopathie

↓

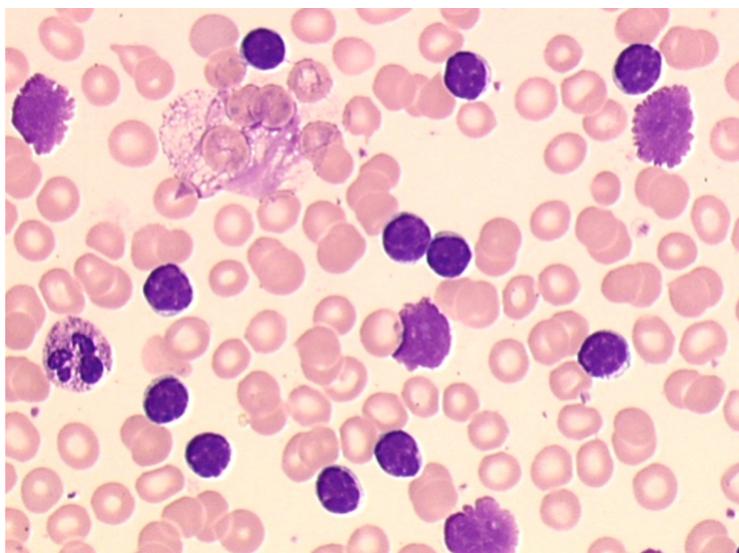
Cytométrie  
Biologie moléculaire?

# Hyperlymphocytose



# Leucémie lymphoïde chronique

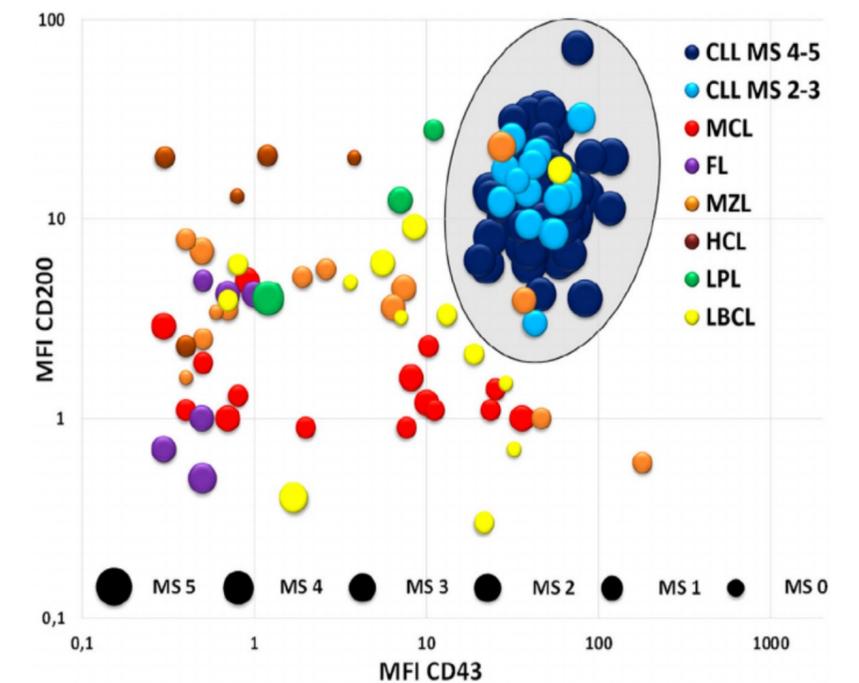
- 1<sup>ère</sup> cause de lymphocytose maligne chez l'adulte
- > 5G/L de lymphocytes B clonaux
- Aucun impact diagnostique de la biologie moléculaire



Lymphocytose monomorphe  
Ombre de Gümprrecht

Marker	Score points	
	1	0
Smlg	Weak	Strong
CD5	Positive	Negative
CD23	Positive	Negative
FMC7	Negative	Positive
CD22 or CD79b	Weak	Strong

Score Matutes  $\geq 4$

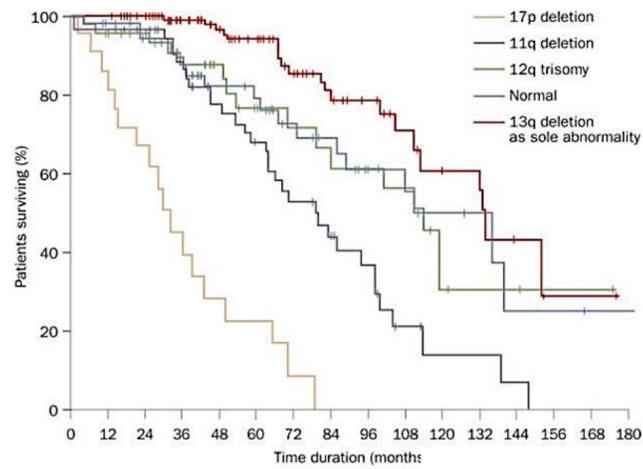


CD200 et CD43 fort

# Leucémie lymphoïde chronique

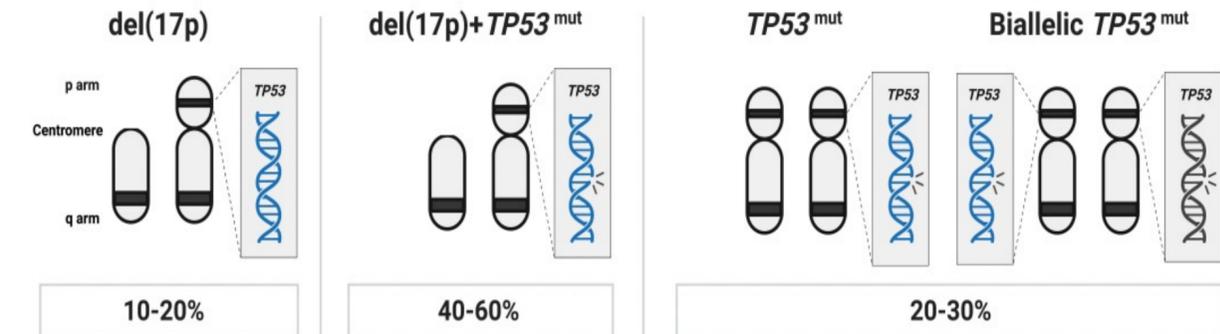
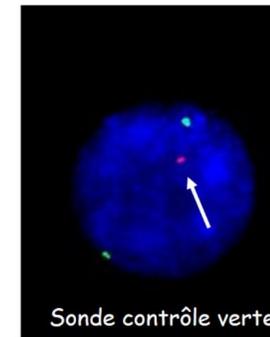
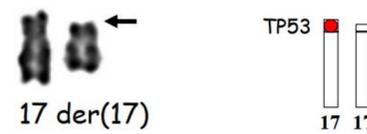
- Impact pronostique et thérapeutique des altérations du gène TP53

## del17p



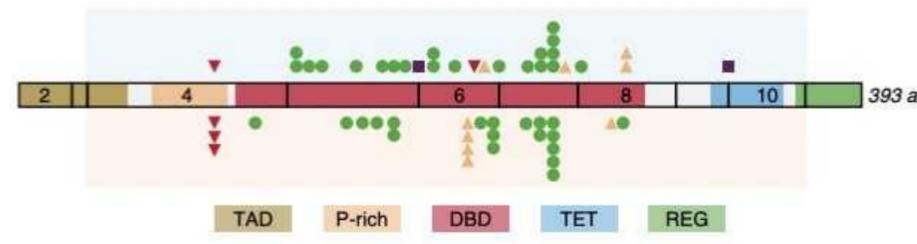
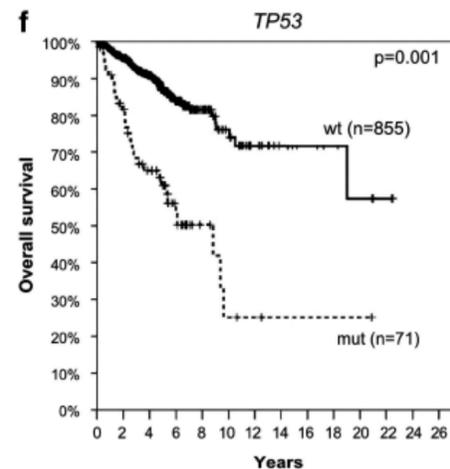
Donner, NEJM 2000

### Délétion (17p) (TP53)



Mollstedt. Front Oncol. 2023

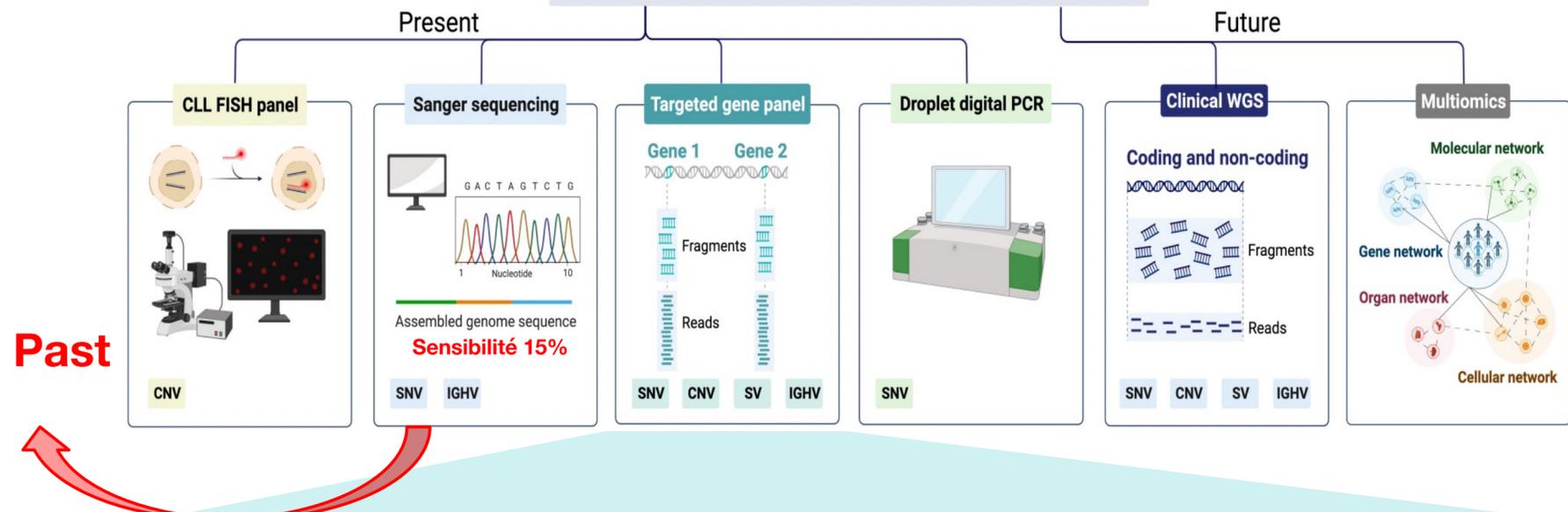
## Mutations TP53



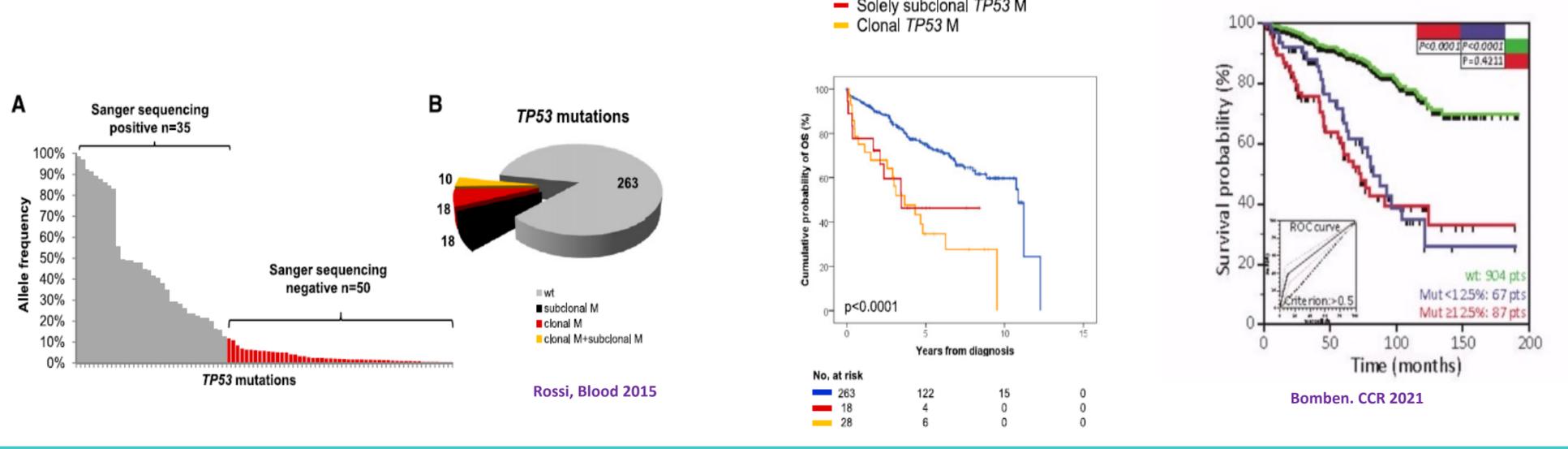
Nadeu. Blood 2016

# Leucémie lymphoïde chronique

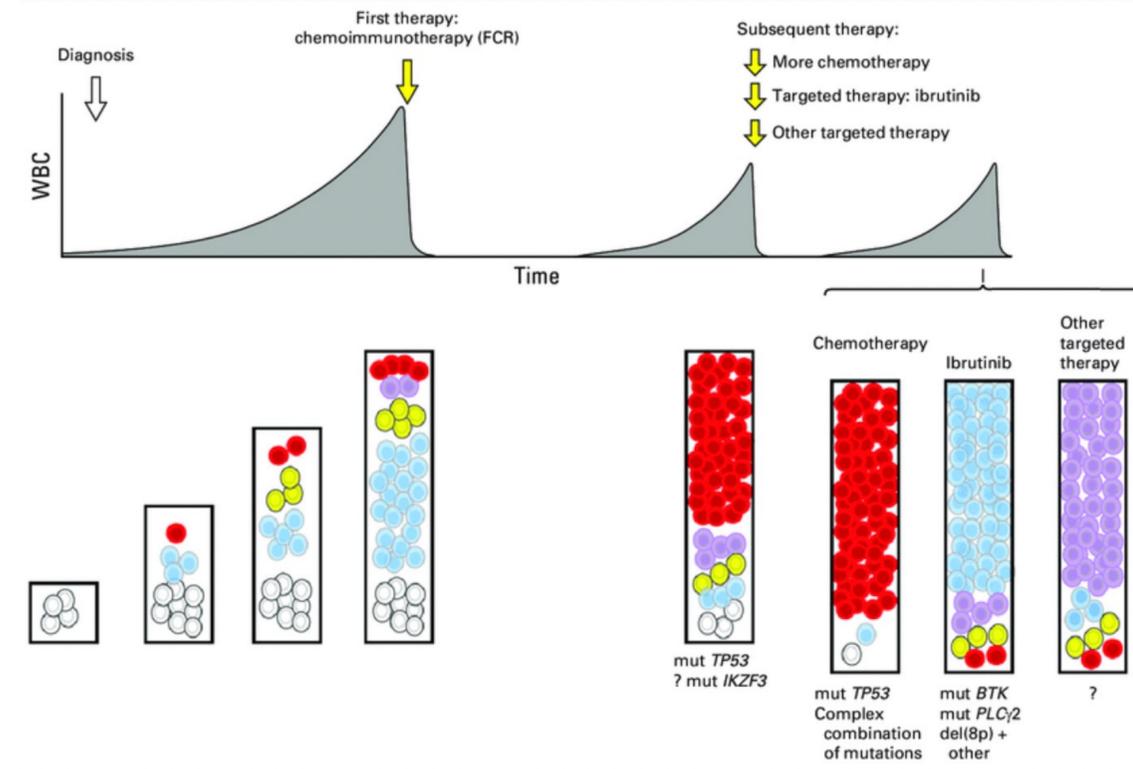
## Precision diagnostics in chronic lymphocytic leukemia



### Impact des altération sous clonale de TP53



Mollstedt. Front Oncol. 2023

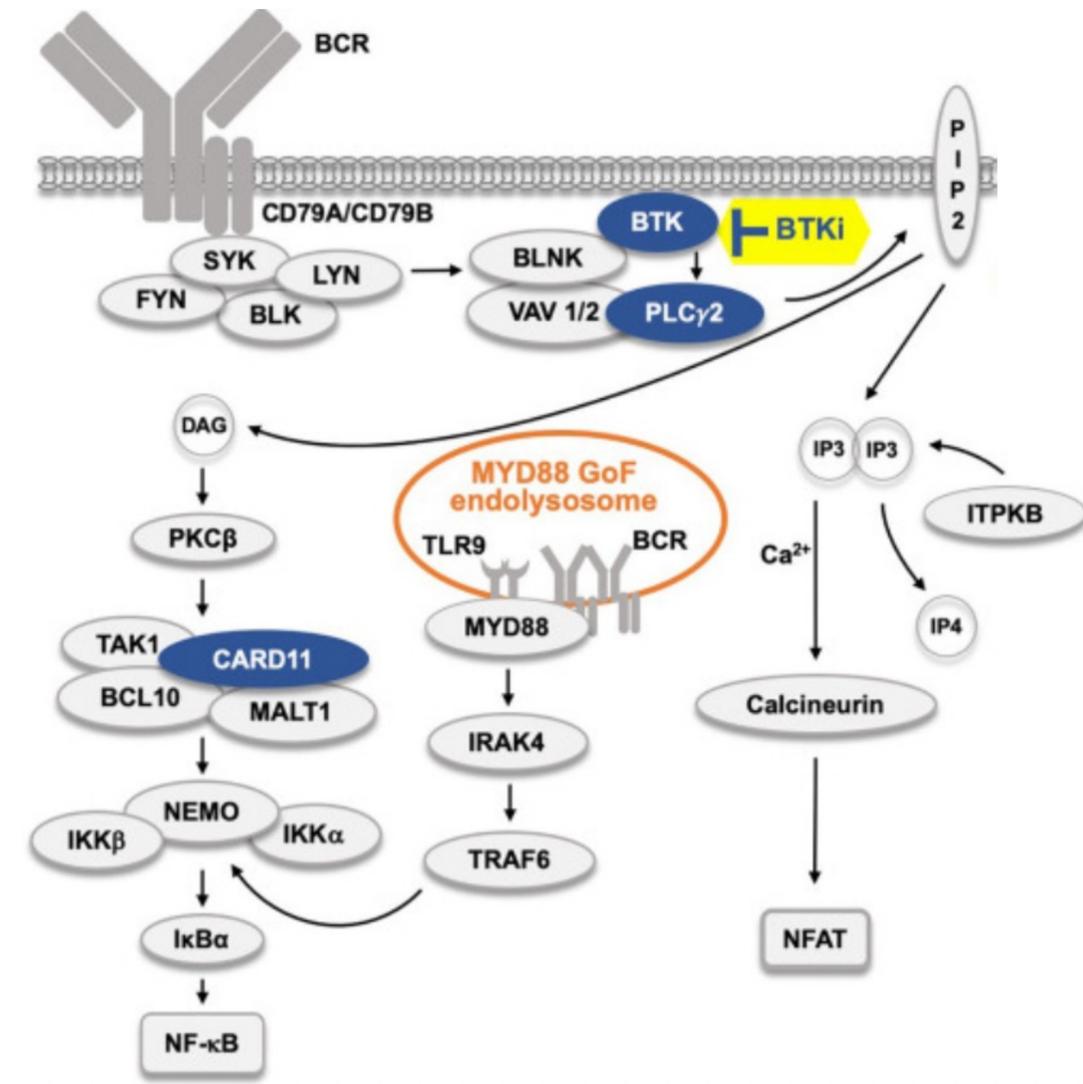
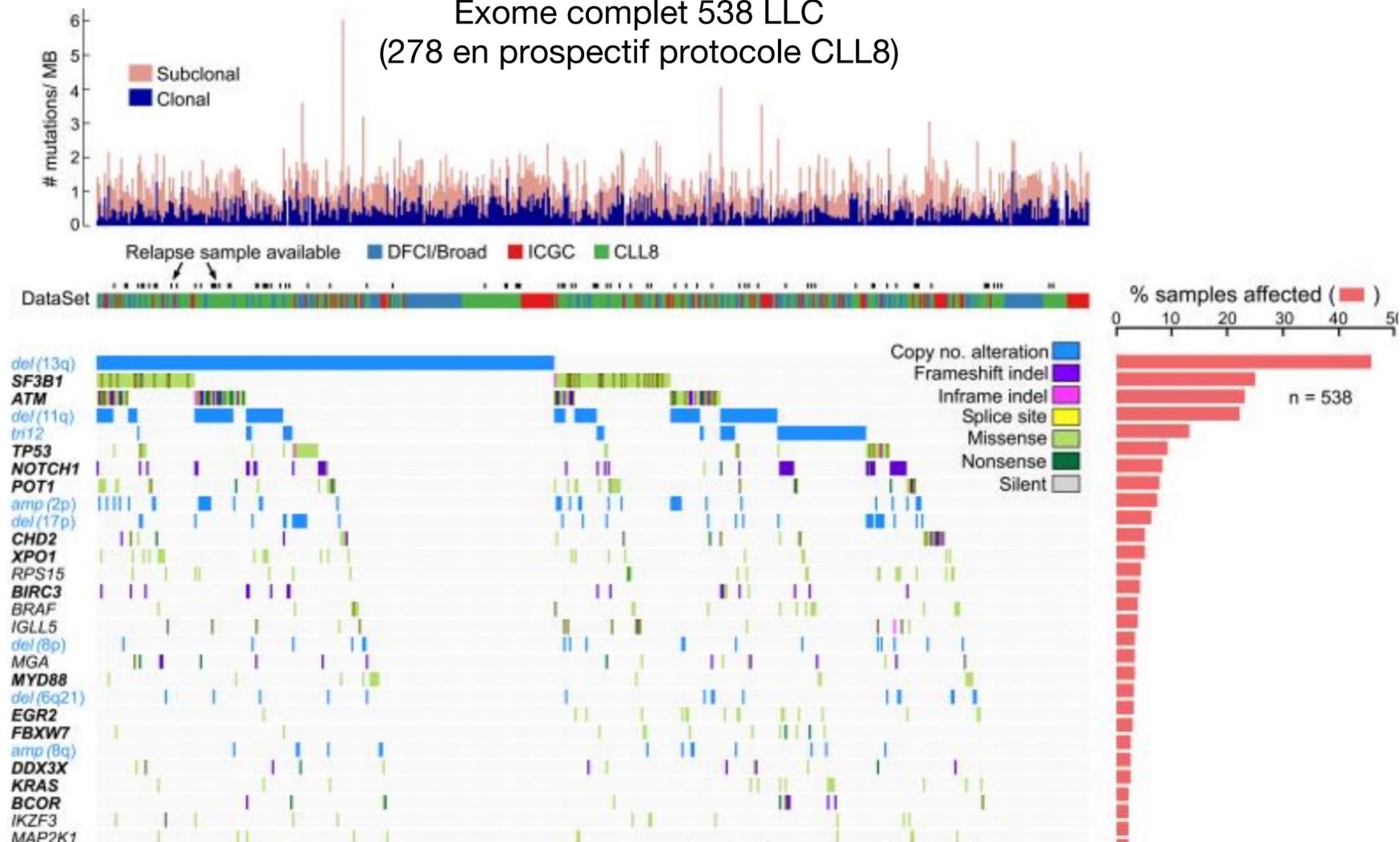


Landau, Nature 2015

# Leucémie lymphoïde chronique

- Aucun impact en routine des autres mutations...
- Hormis les mutations de résistances aux iBTK

Exome complet 538 LLC  
(278 en prospectif protocole CLL8)



# Leucémie lymphoïde chronique

## Inhibiteurs covalents

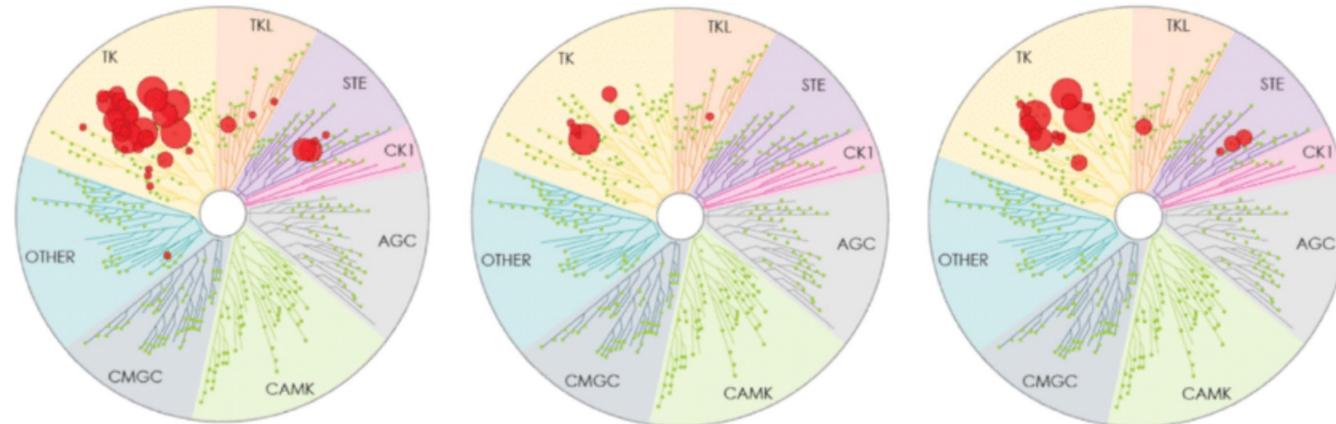
## Inhibiteurs non-covalents

Ibrutinib

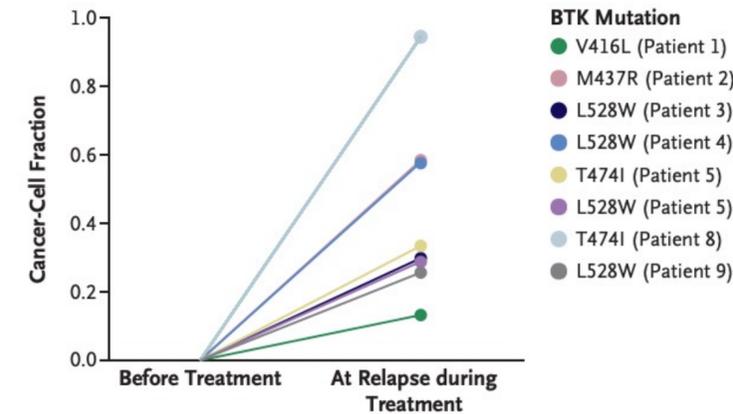
Acalabrutinib

Zanubrutinib

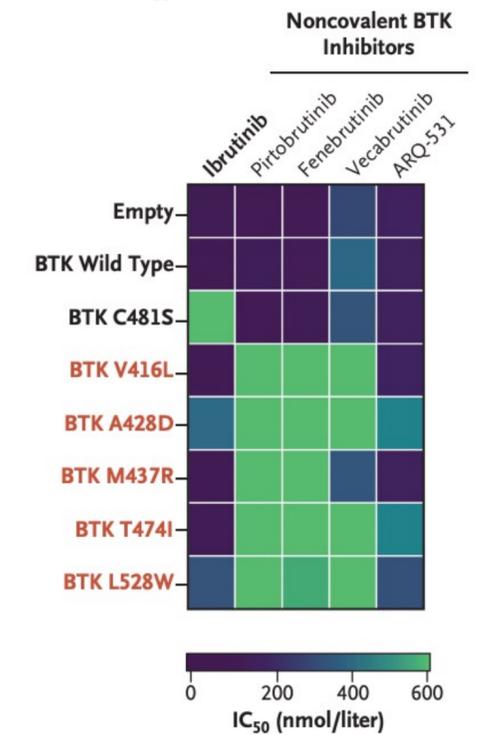
Pirtobrutinib



A Cancer-Cell Fraction of Non-C481 BTK Mutations

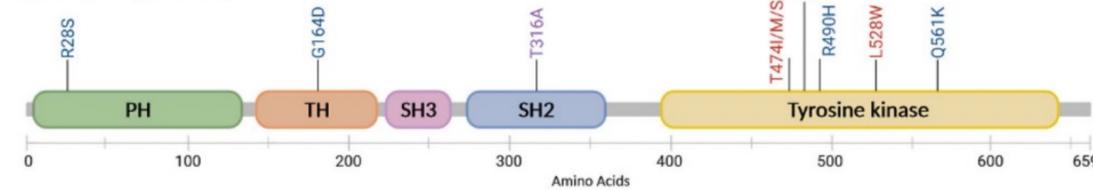


Heat Map of IC<sub>50</sub> Values

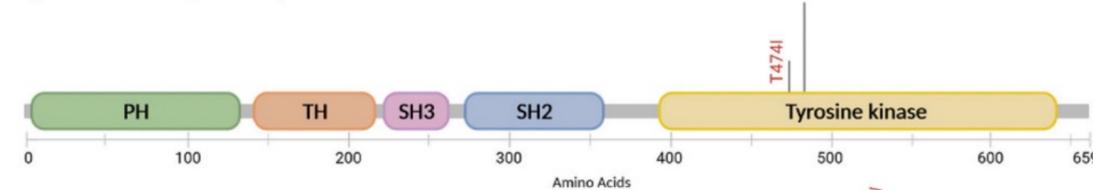


BTK (Xq22.1)

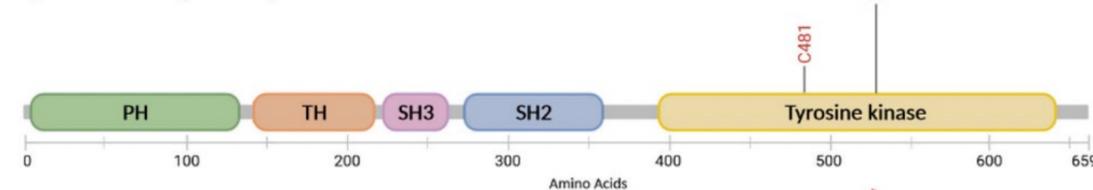
a) Ibrutinib (covalent)



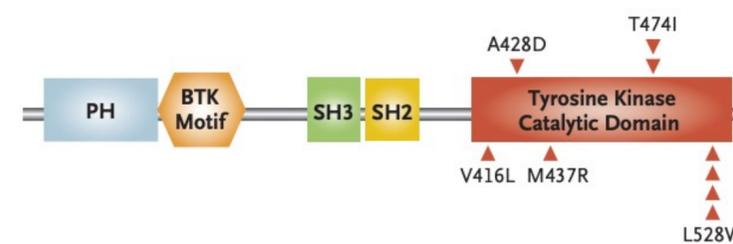
b) Acalabrutinib (covalent)



c) Zanubrutinib (covalent)



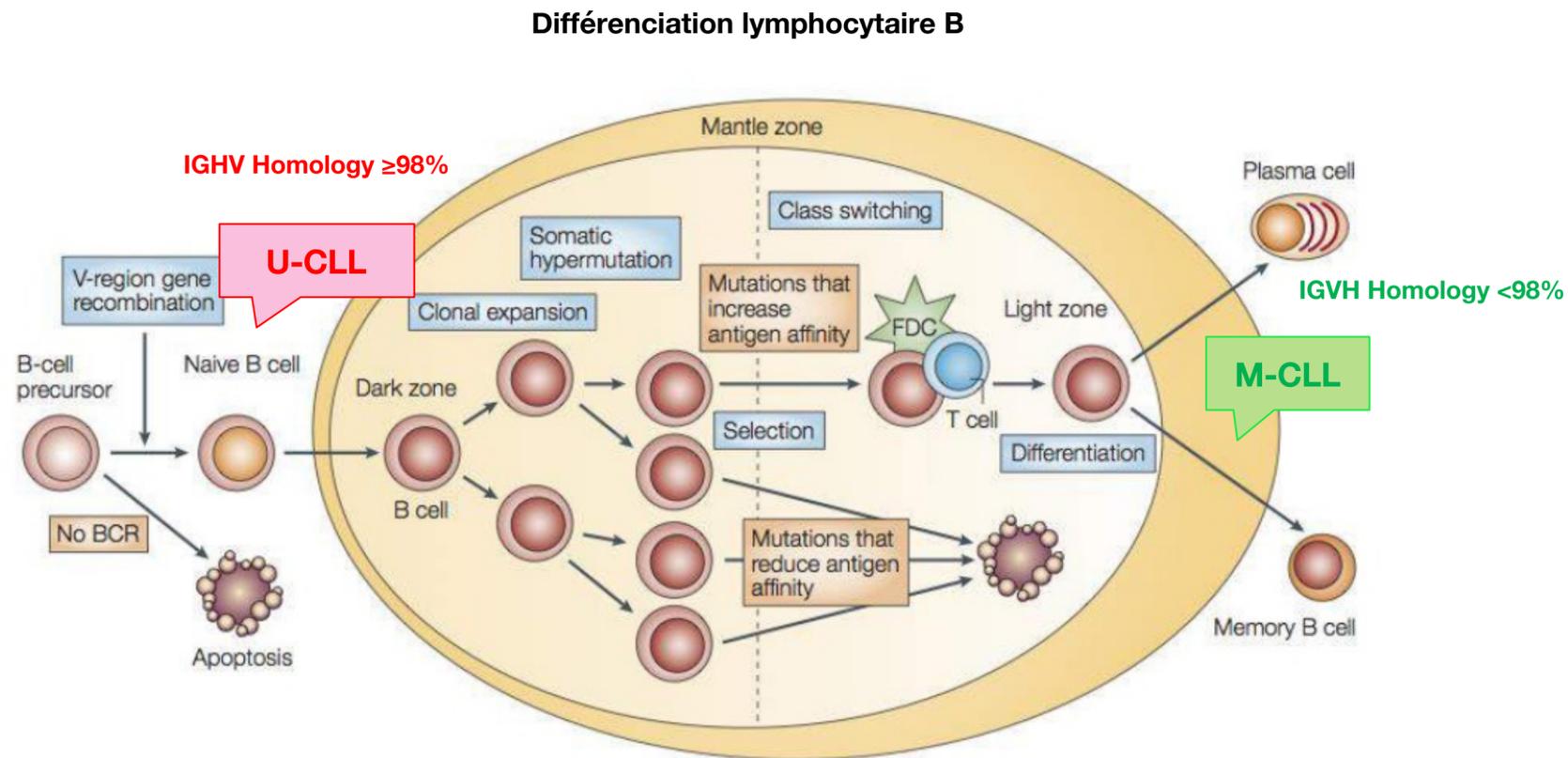
B Locations of BTK Mutations



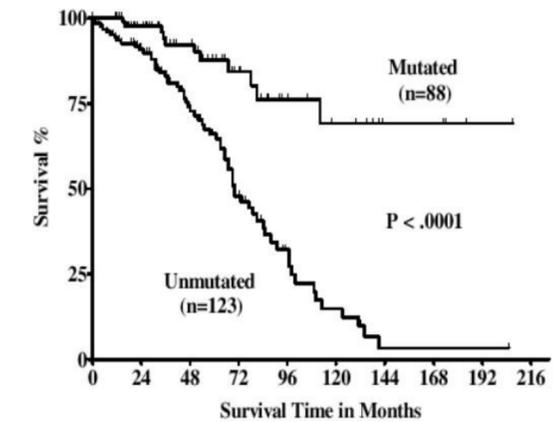
Wang et al, NEJM. 2022

# Leucémie lymphoïde chronique

- Statut mutationnel IGHV

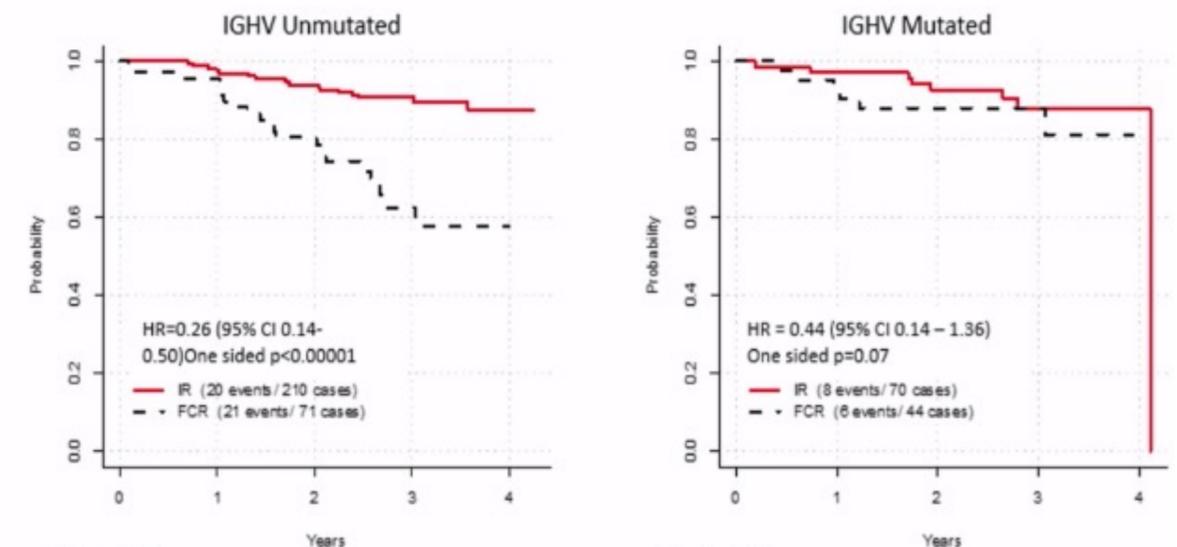


## Impact pronostique

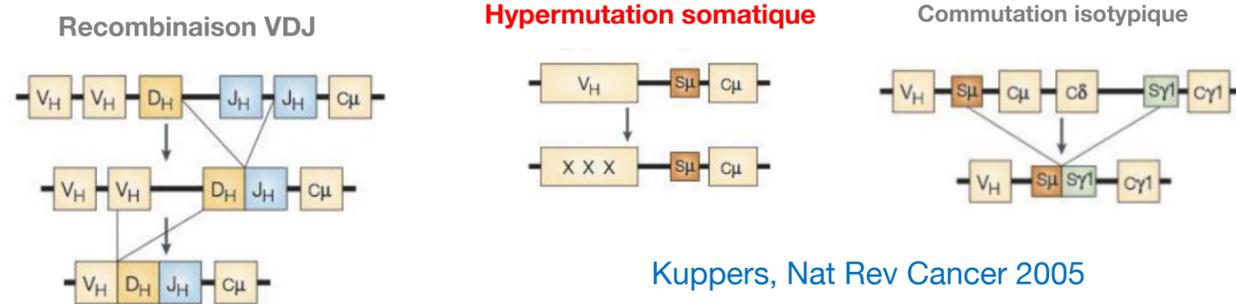


Hamblin, Blood 1999

## Intérêt des thérapies ciblées chez les patients IGHV non muté



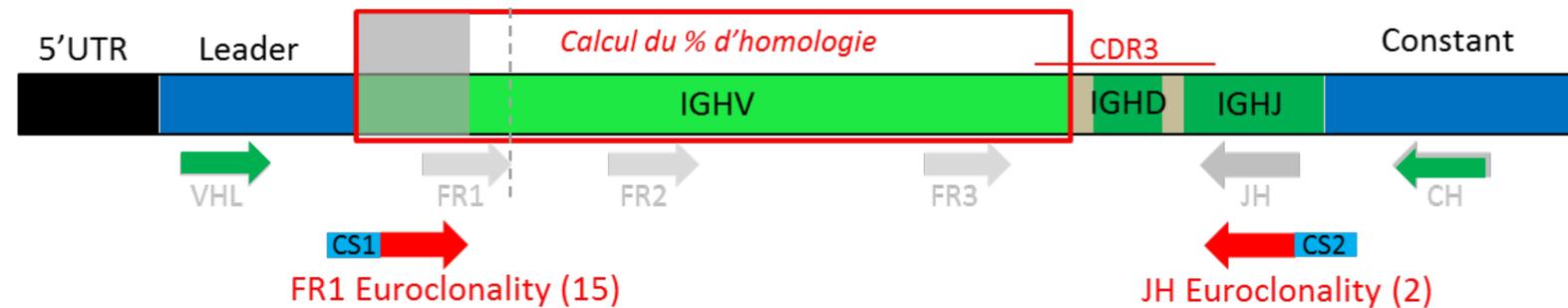
Shanafelt, NEJM 2019



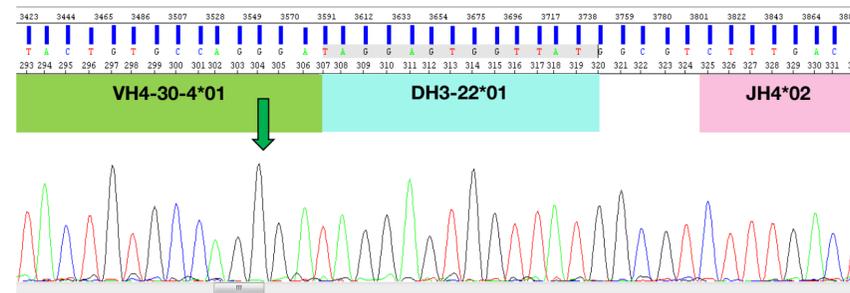
Kuppers, Nat Rev Cancer 2005

# Leucémie lymphoïde chronique

- Statut mutationnel IGHV



Séquençage Sanger



Sequence: 1 VHL

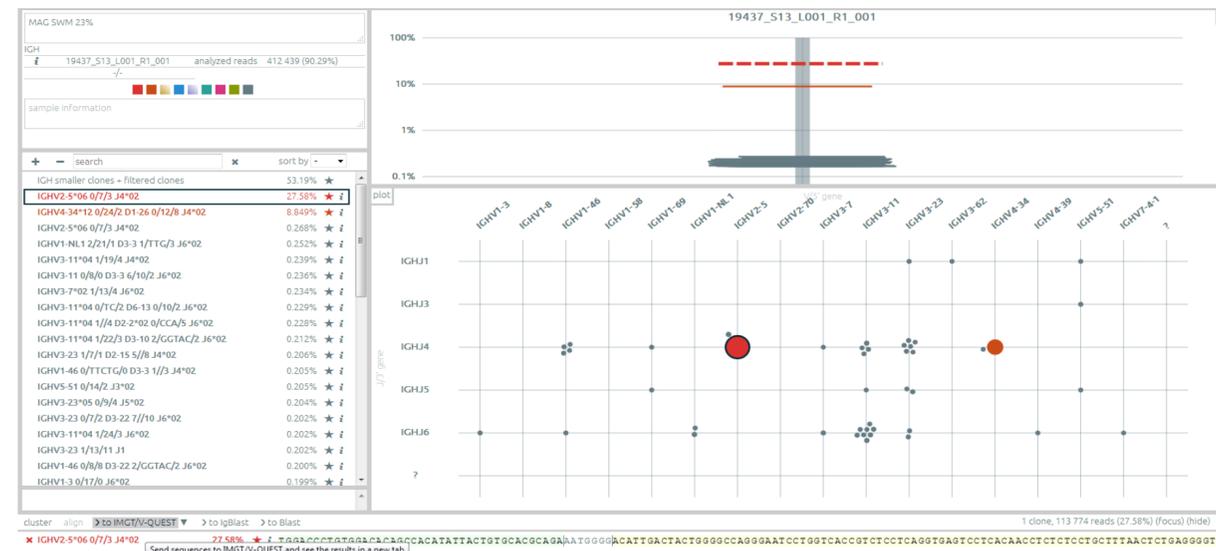
Sequence compared with the *Homo sapiens* (human) IG set from the IMGT reference directory

```
>VHL
actggtgaagccttcacagaccctgtccctcaactgcaactgtctctggtgactccatcac
cagtgatggtttctactggaattggtatccgcagcccccaaggaaggcctggagtgtat
tggttacatctatcacactggggcaactaogacaacccctccctcaggagtcagattac
catttcagtagacaggtcccaagaaacattccctcgaactgaactctgactgcccgc
agacacggcctgtattactgtgccaggataggagtggttatggcctcttctgactactc
gggcacgggaacccctgtcaactcctccatcaggatgcatccgcccccaacctttccc
cctcgtctcctgtgagaattccctcctcggatcagagcagcagctggccttggctgcctgc
acaggacttccctccgactccatcactttctcct
```



Result summary:	Productive IGH rearranged sequence: (no stop codon and in-frame junction)		
V-GENE and allele	Homsap IGHV4-30-4*01.F	score = 1143	identity = 93.13% (244/262 nt)
J-GENE and allele	Homsap IGHJ4*02.F	score = 213	identity = 93.75% (45/48 nt)
D-GENE and allele by IMGT/JunctionAnalysis	Homsap IGHD3-22*01.F	D-REGION is in reading frame 2	
FR-IMGT lengths, CDR-IMGT lengths and AA JUNCTION	[15.17.38.11]	[10.7.12]	CARDRSYGVFDYIW

NGS



Sanger

Séquences plus longues (VHL-CH)  
Recommandation ERIC  
Sur ARN  
Difficulté si multiples clones  
Laborieux

NGS

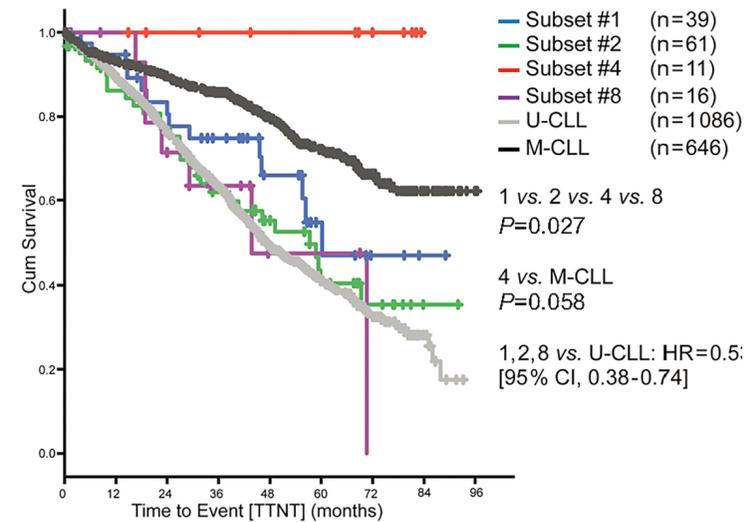
Plus rapide  
Sur ADN (facilité préanalytique)  
Analyse de tous les clonotypes (y compris sous clonaux)  
Taux d'échec moindre

# Leucémie lymphoïde chronique

- Statut mutationnel IGHV

Analyse de la séquence aa du CDR3 → Définition de subset

#	cases	mutational status	CDR3 len	V gene	J gene	sequence logo	clinical	cytogenomic
#2	212	mixed	9	IGHV3-21	IGH5		<ul style="list-style-type: none"> <li>aggressive</li> <li>1.9 (0-7.9)</li> <li>na</li> </ul>	<ul style="list-style-type: none"> <li>SF3B1 mut: 36-45%</li> <li>ATM mut: 26% (21/81 cases)</li> <li>TP53 aberrations: TP53 mut: 0-5%, del(17p): 0-4%</li> </ul>
#1	183	unmutated	13	IGHV1-3	IGH4		<ul style="list-style-type: none"> <li>aggressive</li> <li>1.6 (0-8)</li> <li>higher risk of immune thrombocytopenia</li> </ul>	<ul style="list-style-type: none"> <li>TP53 mut: 16% (21/135 cases)</li> <li>NFKB1 mut: 15% (17/112 cases)</li> <li>NOTCH1 mut: 19-27%</li> <li>del(13q): 20% (18/89 cases)</li> </ul>
#4	74	mutated	20	IGHV4-34	IGH5		<ul style="list-style-type: none"> <li>younger patients</li> <li>very indolent</li> <li>11.0 (0.9-13.5)</li> <li>na</li> </ul>	
#6	68	unmutated	21	IGHV1-69	IGH3		<ul style="list-style-type: none"> <li>aggressive</li> <li>1.6 (0-5.8)</li> <li>na</li> </ul>	<ul style="list-style-type: none"> <li>NOTCH1 mut: 22% (10/45 cases)</li> </ul>
#8	35	unmutated	19	IGHV4-39	IGH5		<ul style="list-style-type: none"> <li>aggressive</li> <li>1.5 (0-8.1)</li> <li>highest risk of Richter's transformation among all CLL subgroups</li> </ul>	<ul style="list-style-type: none"> <li>trisomy 12: 60% (15/25 cases)</li> <li>NOTCH1 mut: 30% (13/43 cases)</li> </ul>



## Interprétation

60%

Non muté % homologie >98%  
Mauvais pronostic (TFS et OS)  
LLC plus agressive

Préférer thérapie ciblée

CLL #2

Borderline 97-98%  
de signification clinique  
indéterminée

Muté <98%

35%

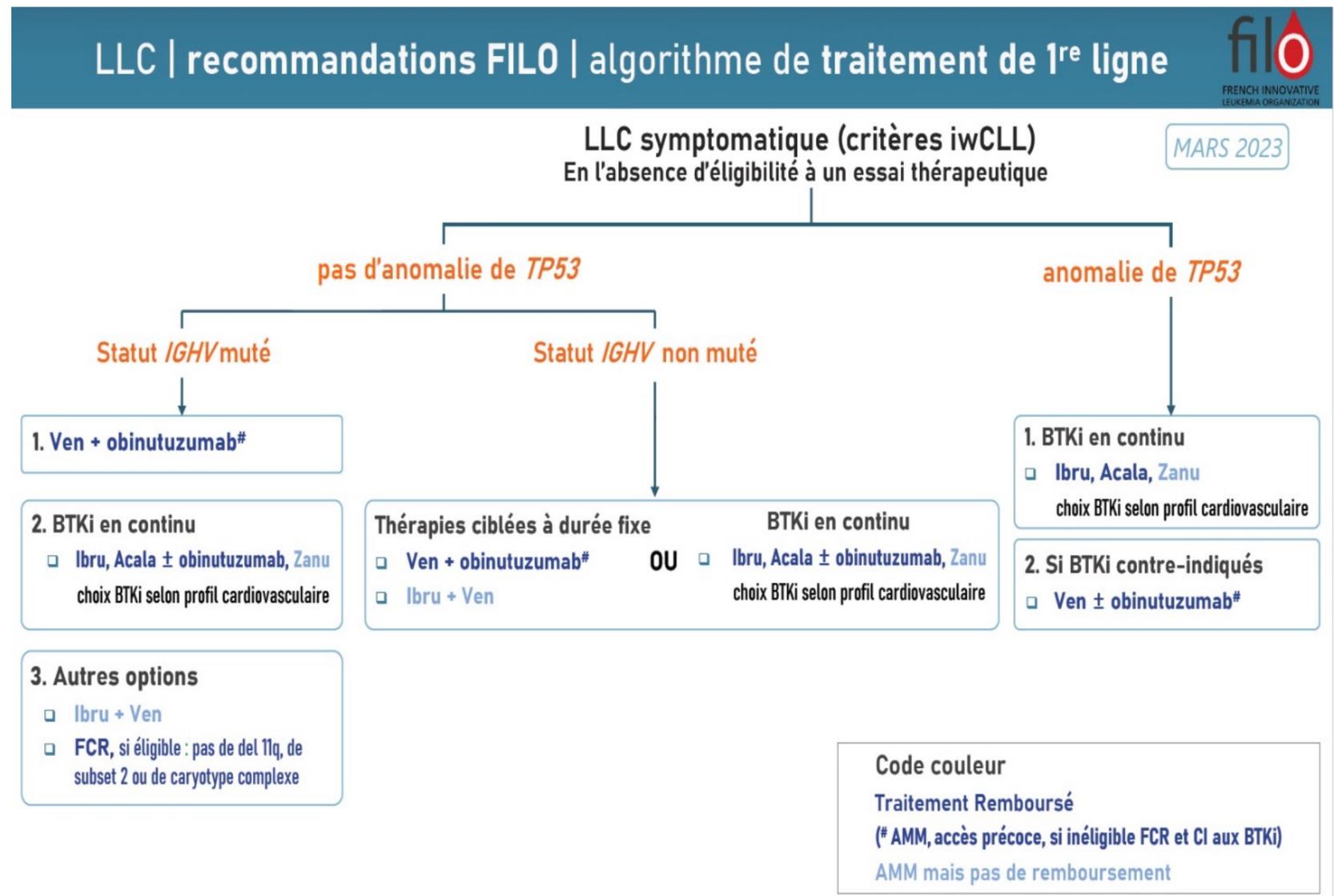
RFC???

Non interprétables  
Echec de PCR, réarrangements non  
productifs ou multiples clones de statut  
discordant

<5%

# LLC : synthèse

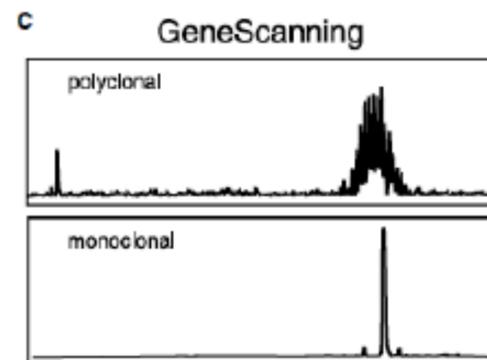
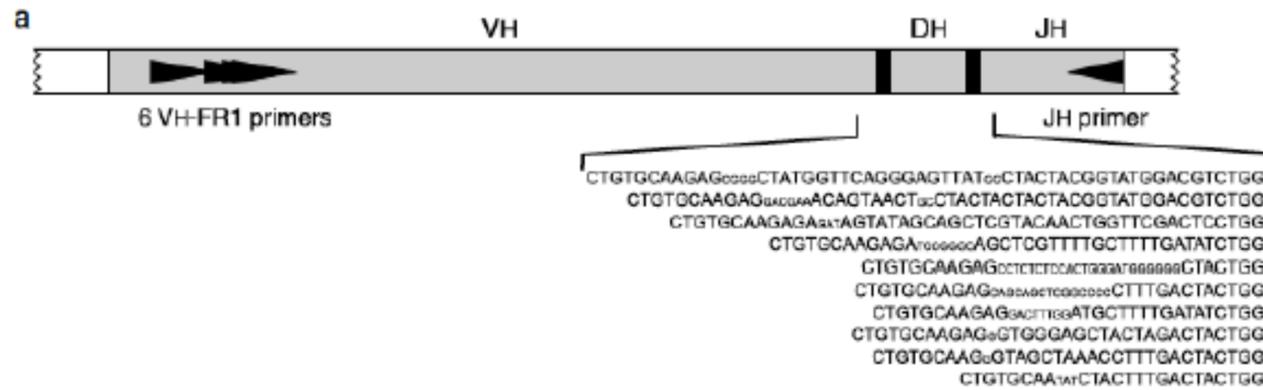
- Au diagnostic
  - Aucun examen systématique en l'absence de critère de traitement
- Avant première ligne
  - TP53 (FISH + NGS)
  - Statut IGHV
- A la rechute
  - TP53, mutations de résistance
  - Ne pas répéter le statut IGHV



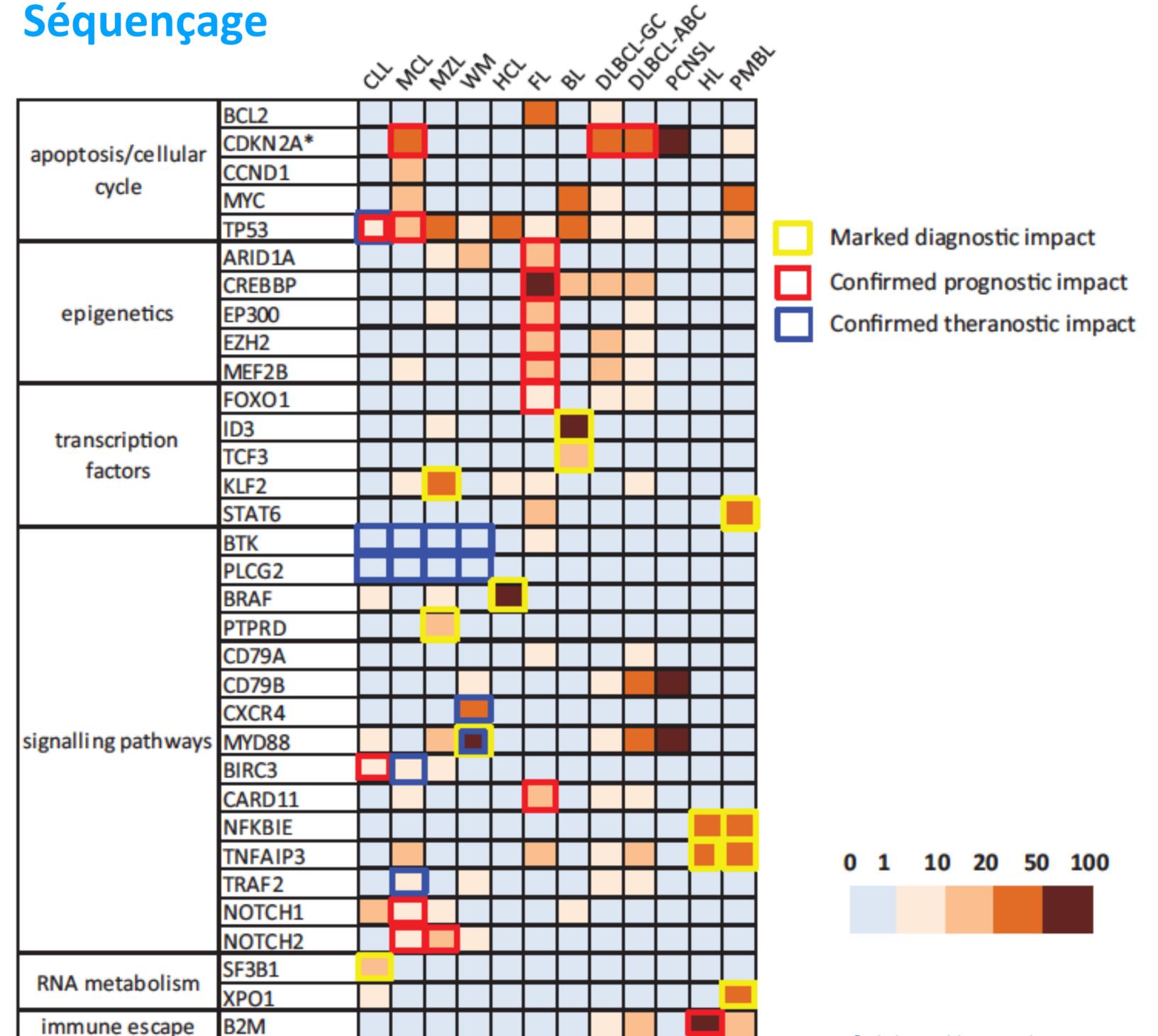
# Lymphome B de bas grade

## Clonalité Lymphoïde B

Recherche réarrangement clonal des gène des Immunoglobulines: *IGH* + *IGK*  
PCR analyse de fragment

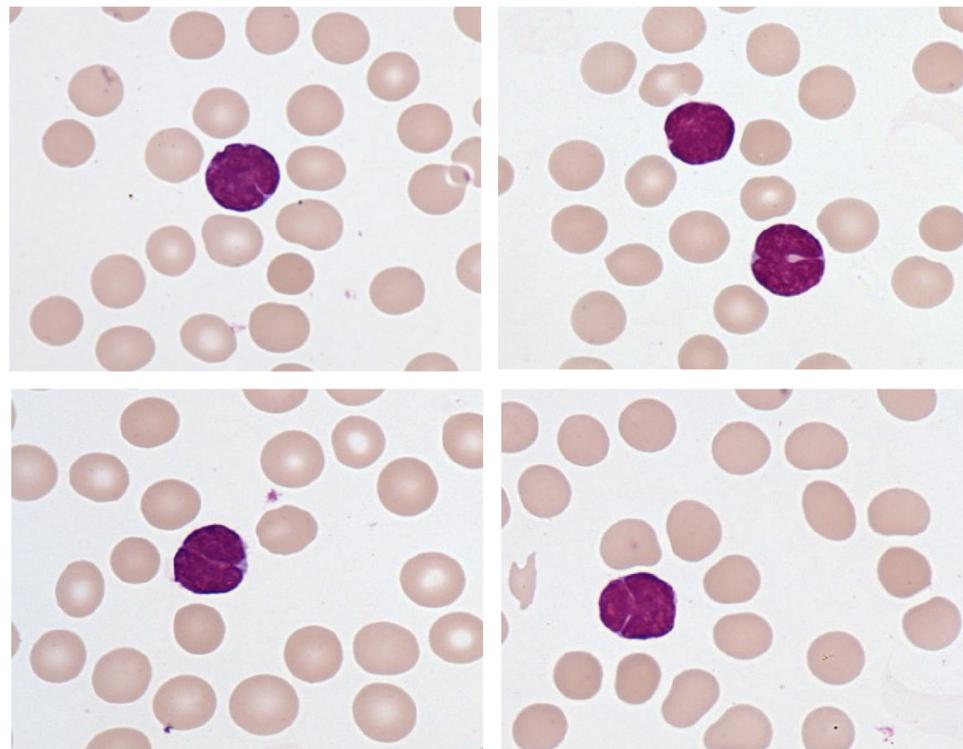


## Séquençage

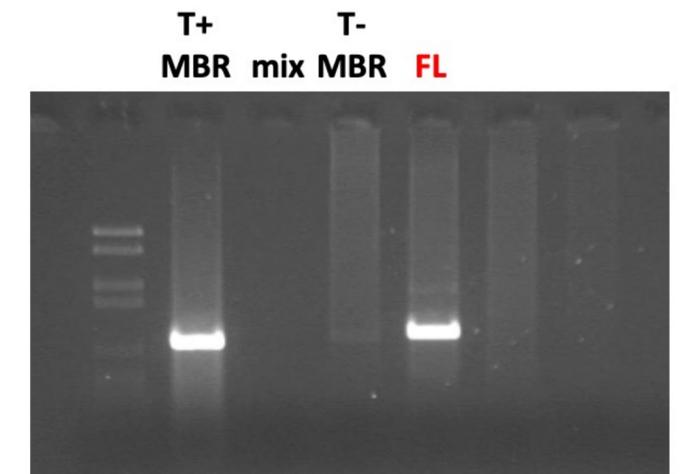
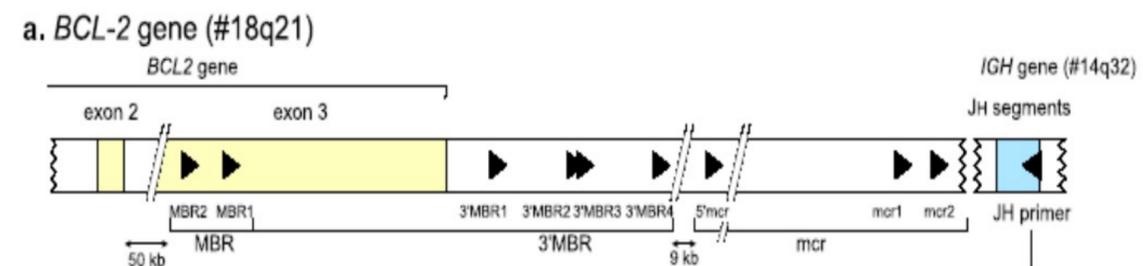


# Lymphome folliculaire

- Lymphome de bas grade le plus fréquent de l'adulte
  - Forme leucémique dans seulement 15% des cas
  - Diagnostic HISTOLOGIQUE+++
  - t(14;18) → BCL2-JH (hyperexpression de BCL2)



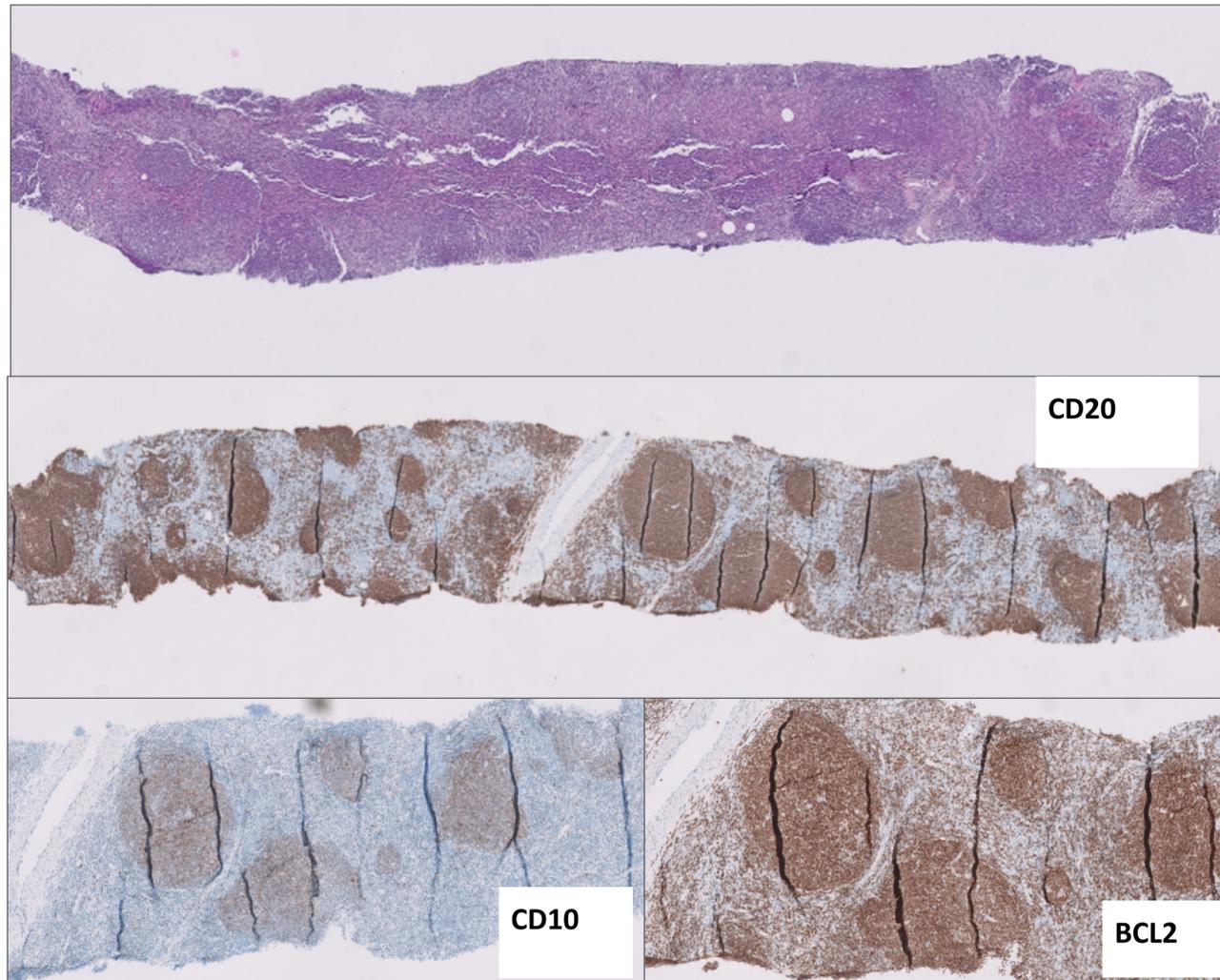
## Réarrangement BCL2-JH (PCR)



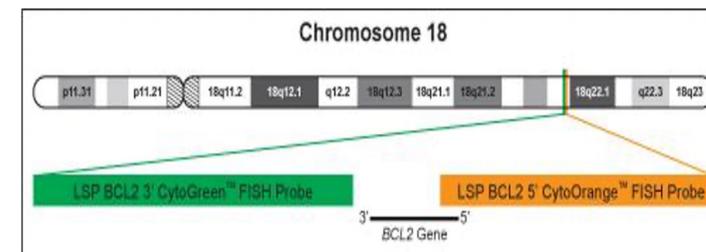
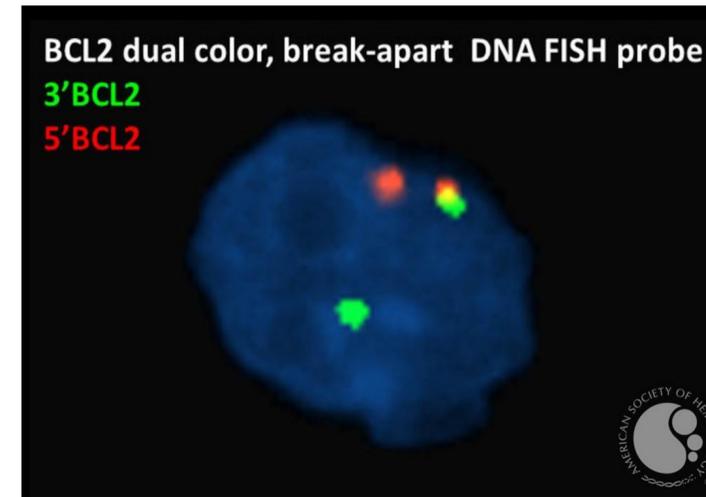
Si difficulté diagnostique  
Sensibilité 60% des FL liée au point de cassure

# Lymphome folliculaire

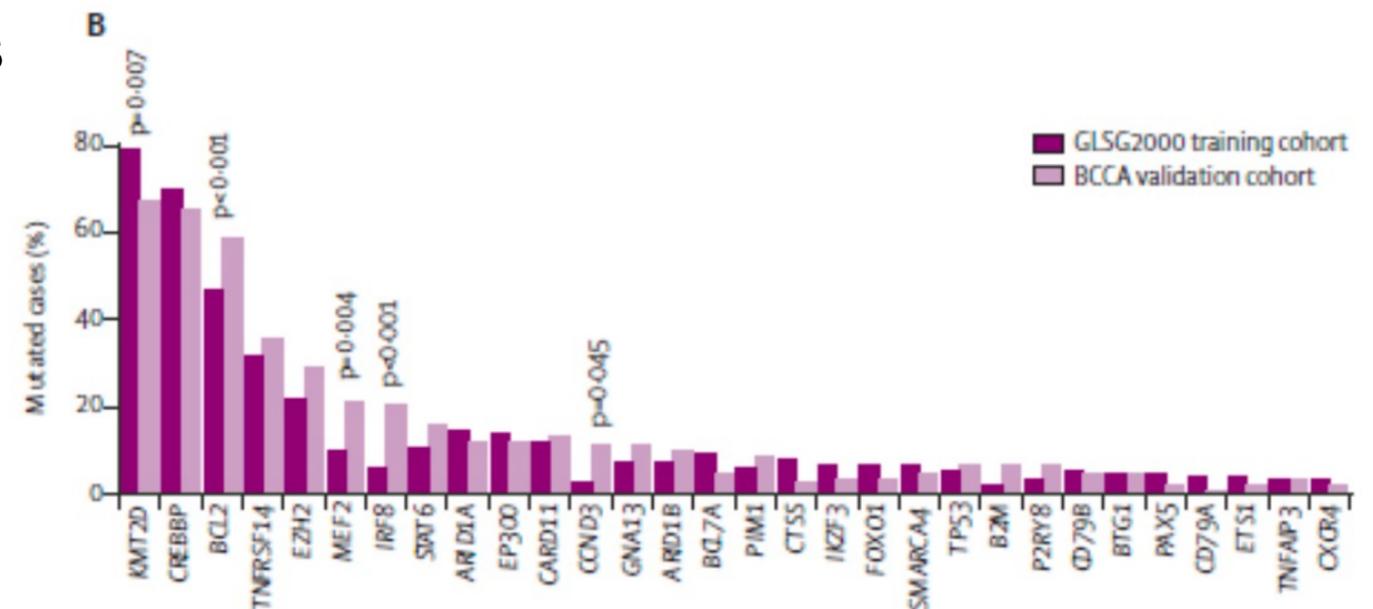
## Anatomopathologie



FISH si difficulté diagnostique



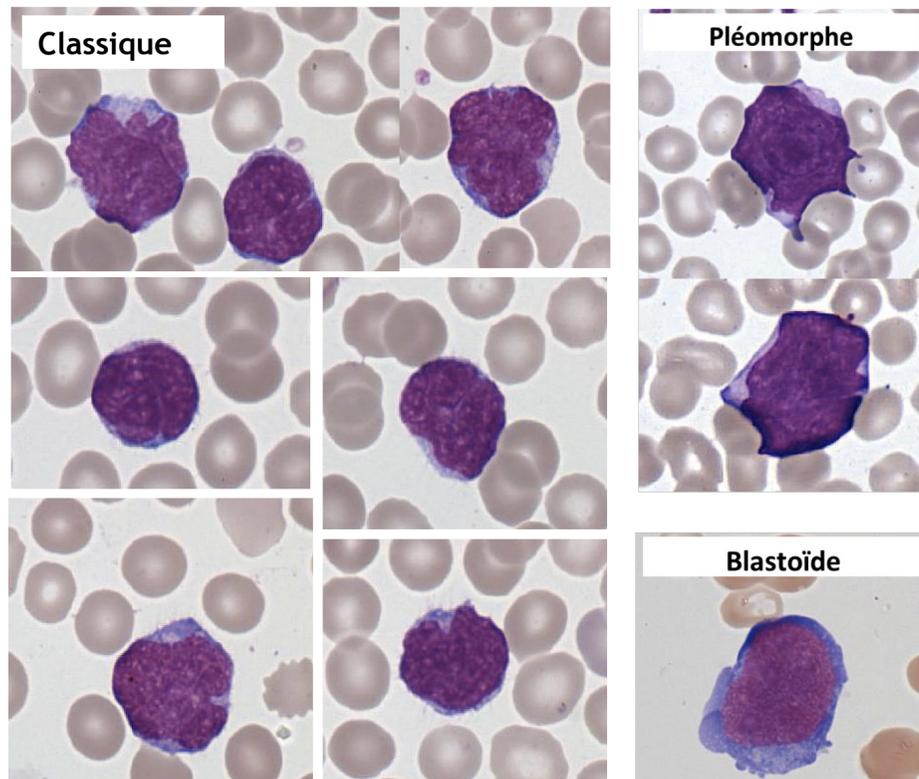
NGS



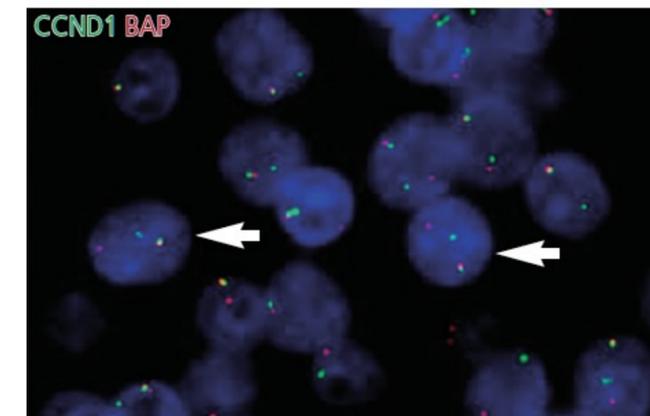
Pastore, Lancet Oncol 2015

# Lymphome du manteau

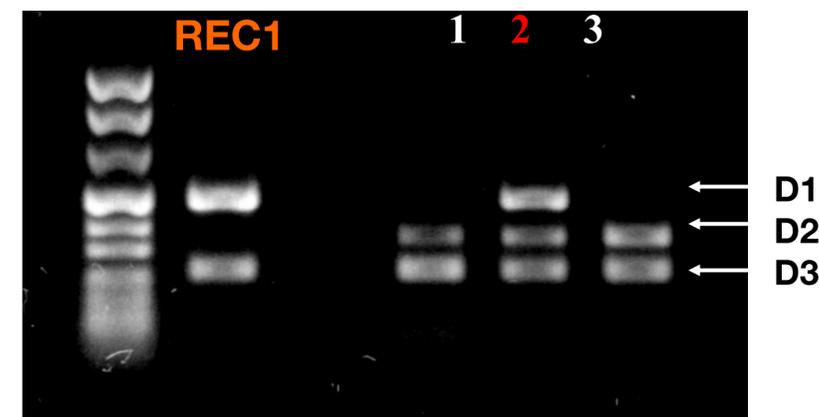
- Diagnostic cytologique parfois difficile
- Cytométrie : Matutes <4, souvent 1-2, CD200 négatif
- Intérêt diagnostique de l'hyperexpression de cycline D1



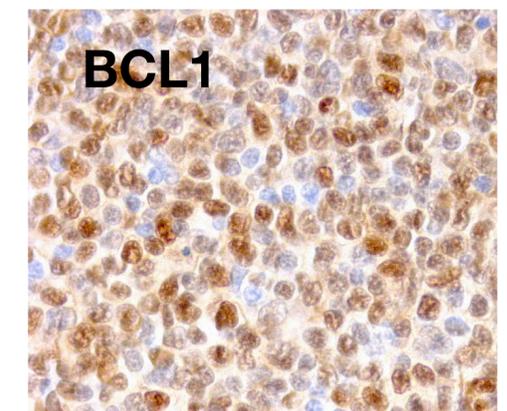
Translocation t(11;14)  
→ hyperexpression de CCND1/ BCL1



RT-PCR compétitive  
Amplification des cyclines D1, D2 et D3

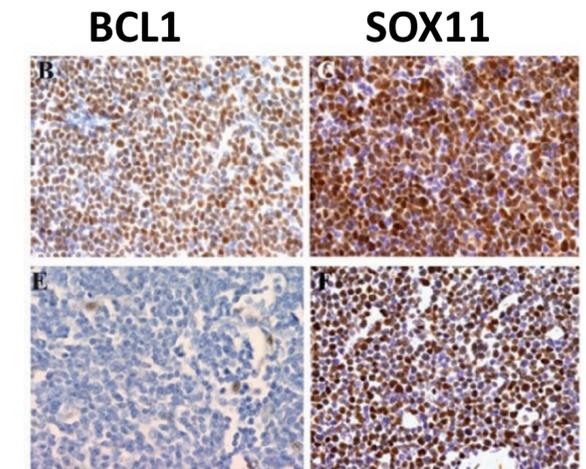
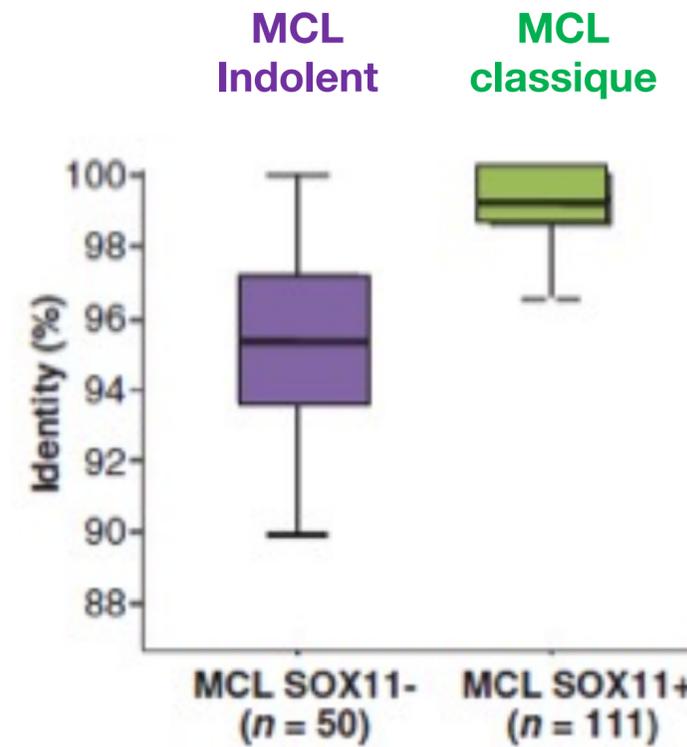
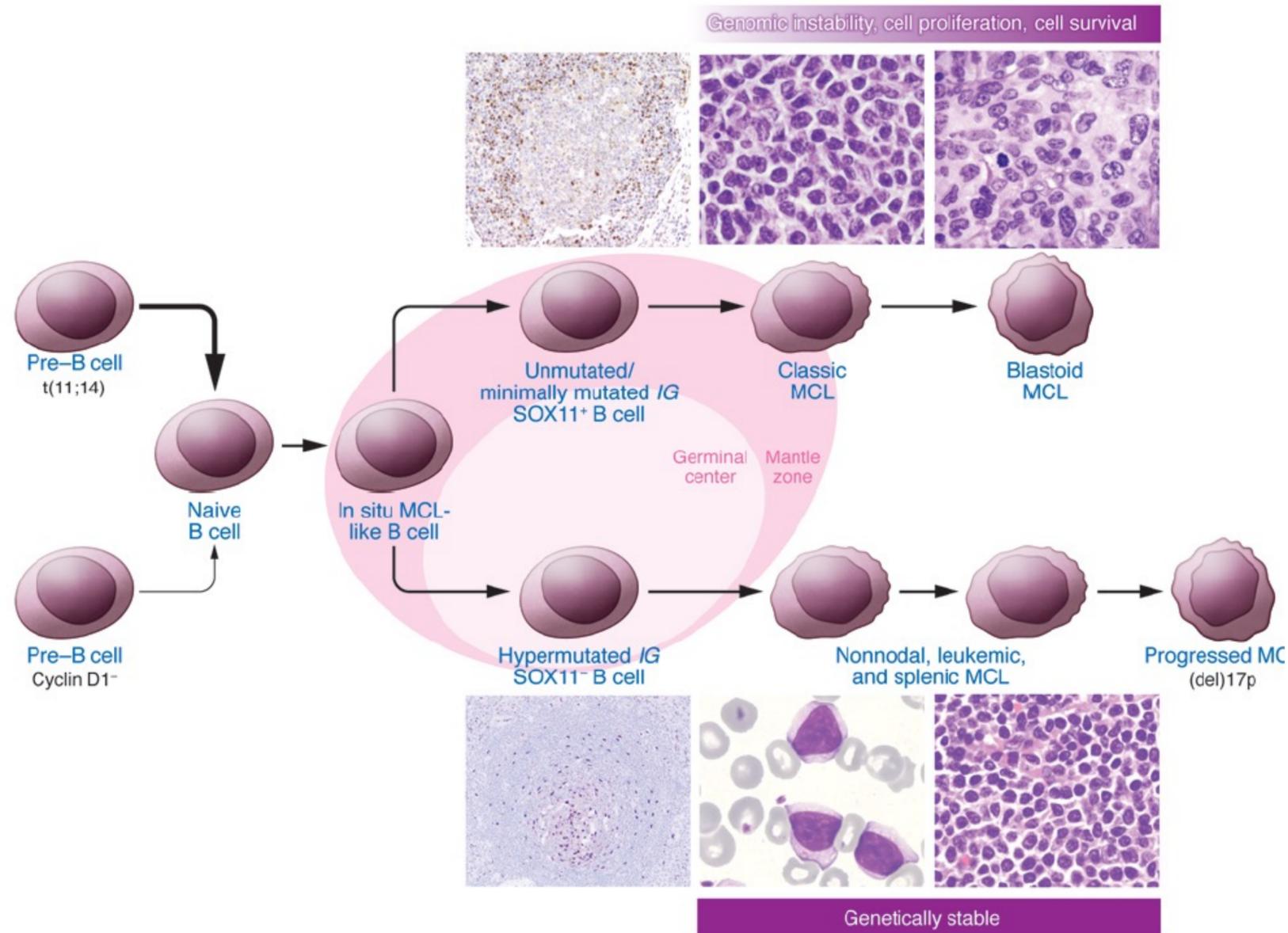


Immunohistochimie



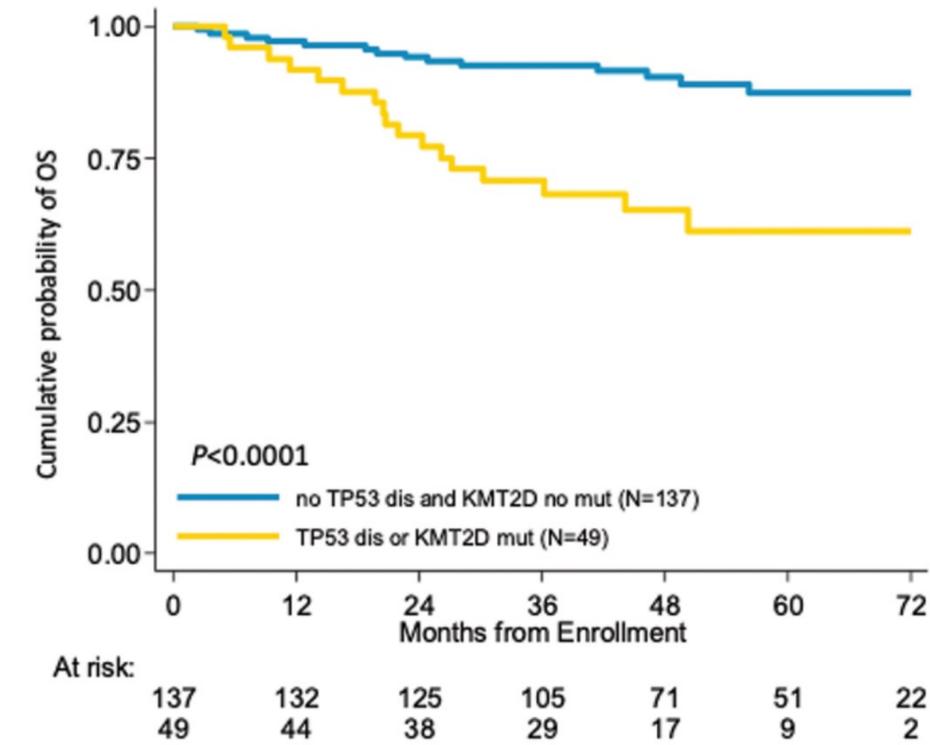
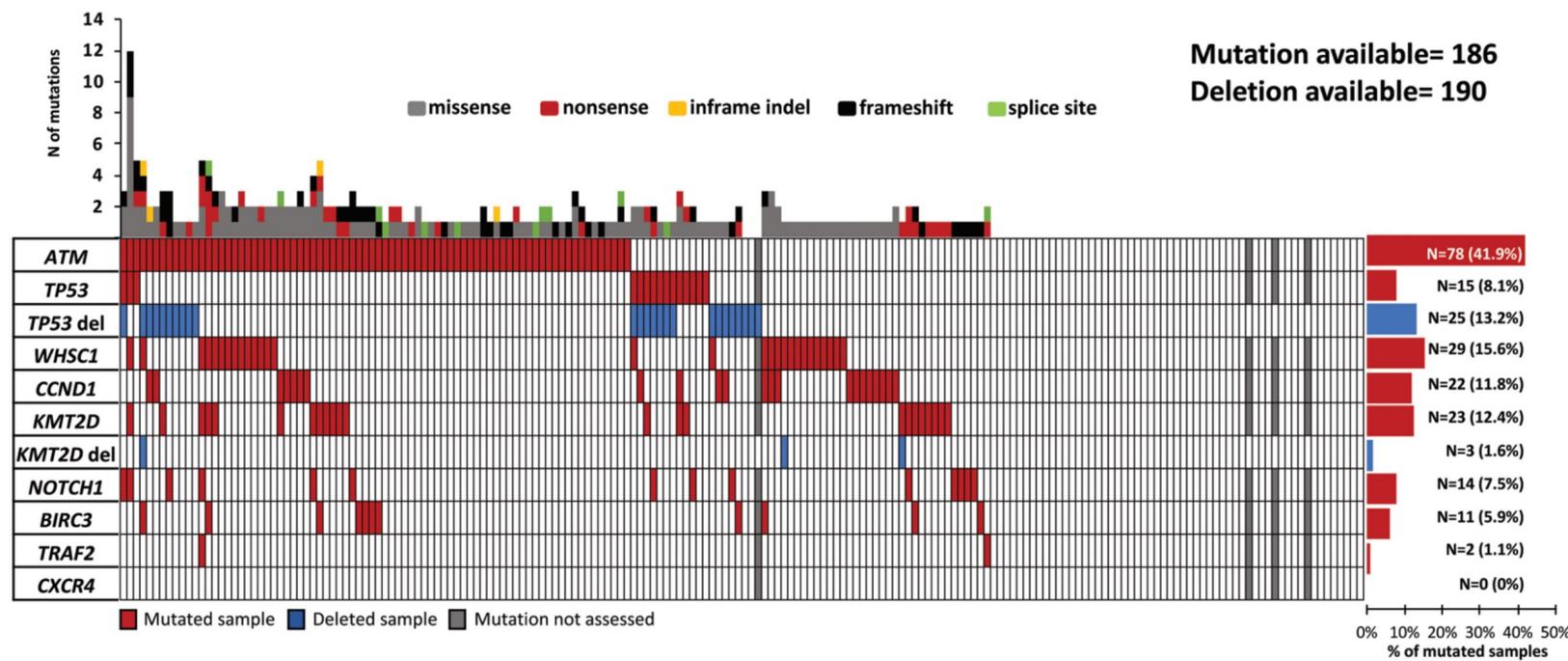
# Lymphome du manteau

- Physiopathologie et nouvelle classification

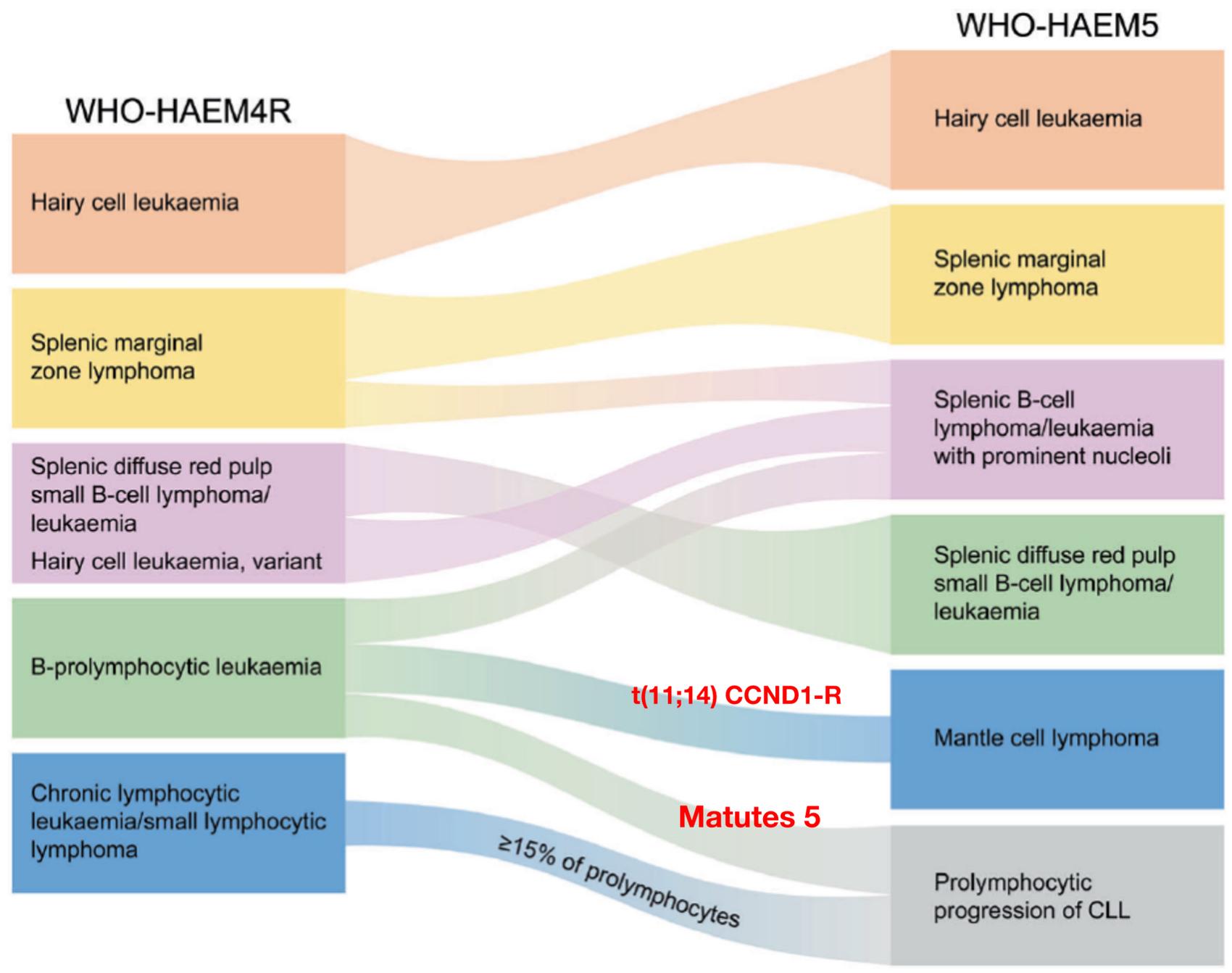


# Lymphome du manteau

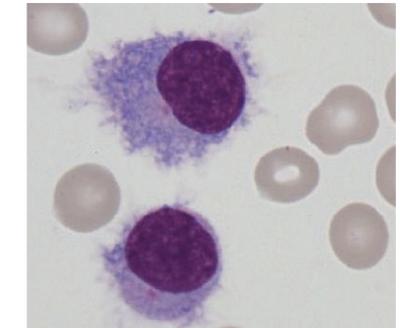
- Intérêt du séquençage NGS
  - Classification pronostique (TP53, ATM, KMT2D)
  - Intérêt thérapeutique
    - iBTK si TP53 muté? Mutation de résistance?



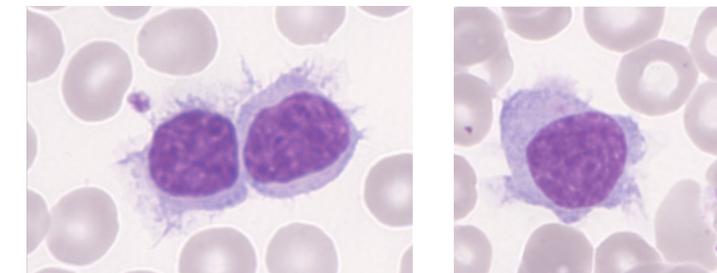
# Lymphocytes chevelus



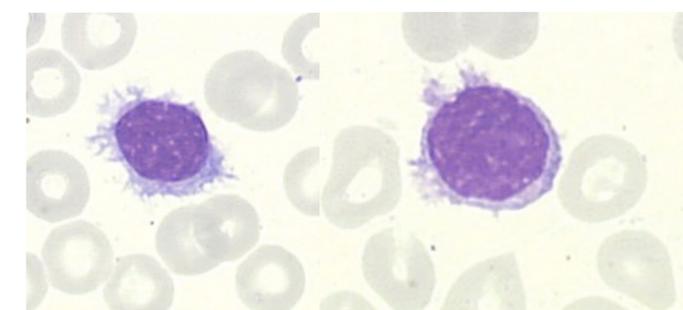
Tricholeucocytes



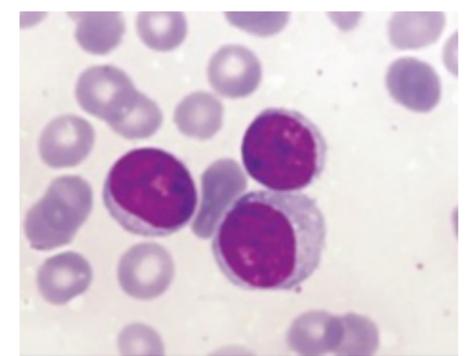
Tricholeucocytes variants



Lymphocytes vilieux

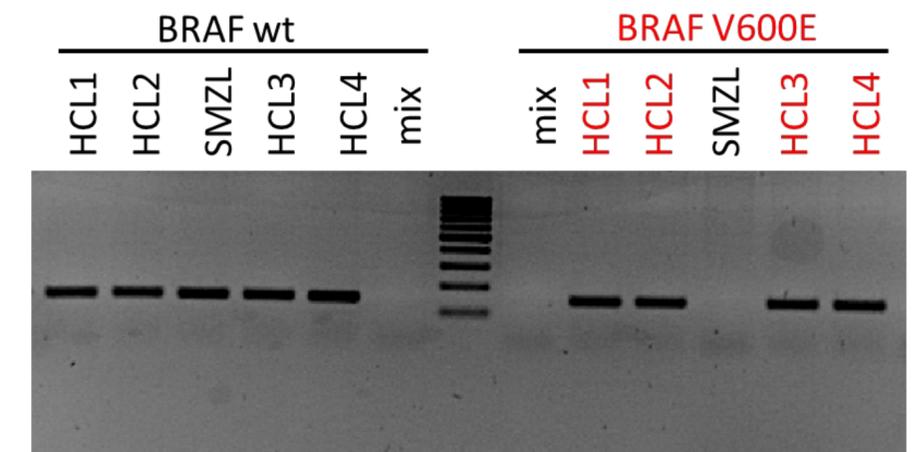
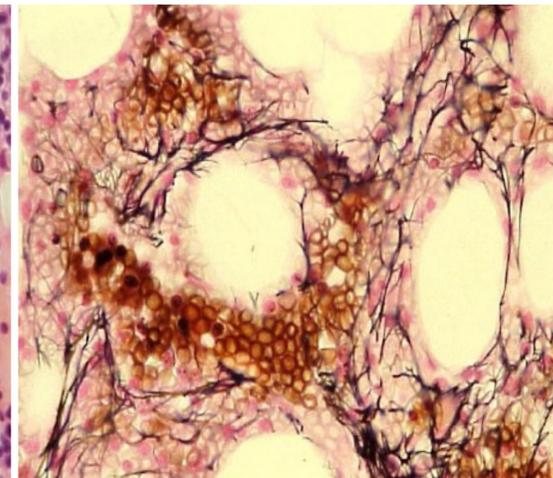
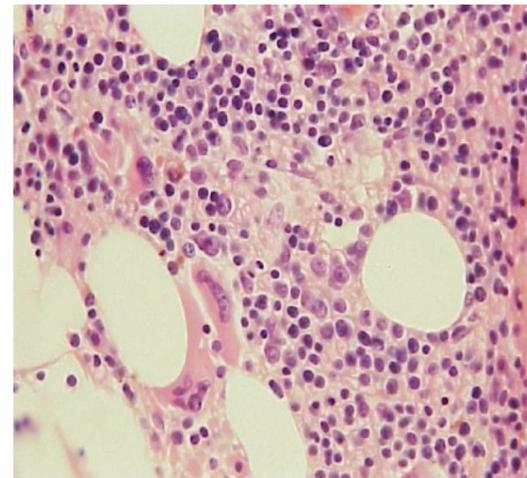
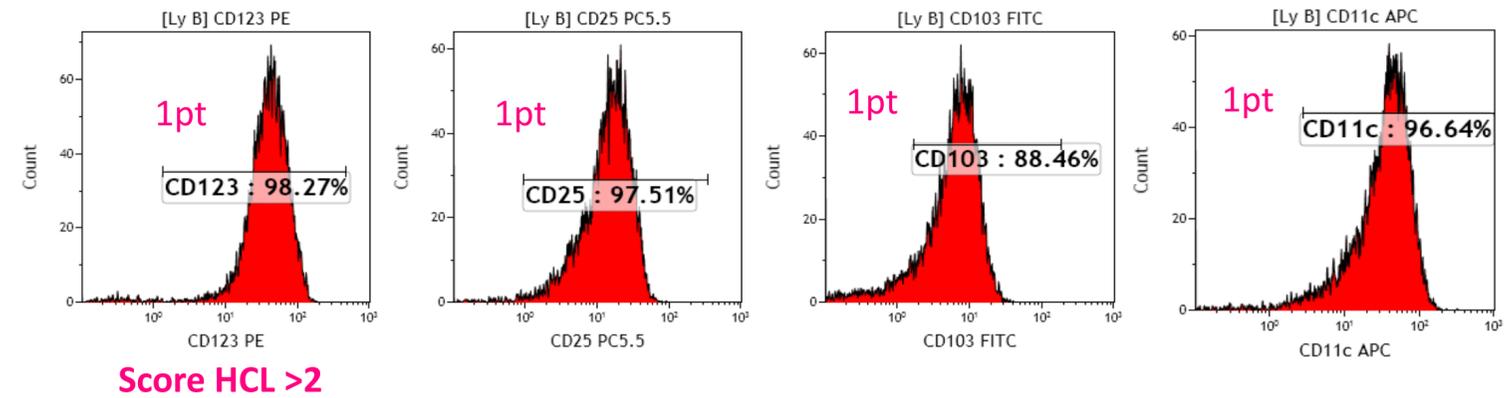
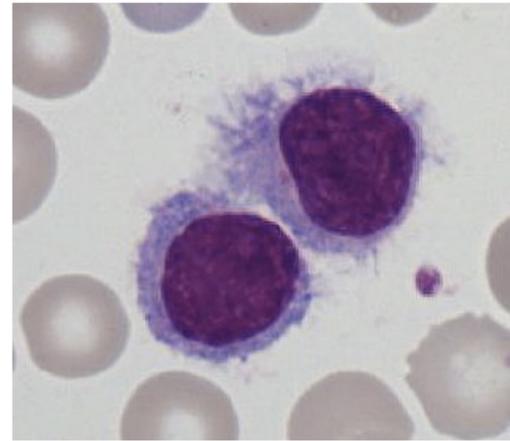


Prolymphocytes



# Leucémie à tricholeucocytes

- Rare 2% des leucémies
- Age médian 55 ans
- Pancytopénie (monocytopénie)
- Splénomégalie
- Myélofibrose
- **Mutation BRAF V600E (95%)**
- Sensibilité analogue des purines
- Bon pronostic



# Leucémie/Lymphome splénique B avec nucléole proéminent

- Anciennement: Leucémie prolymphocytaire B (non LLC, non manteau), HCL variant
- 0,5% des SLP

## Clinique

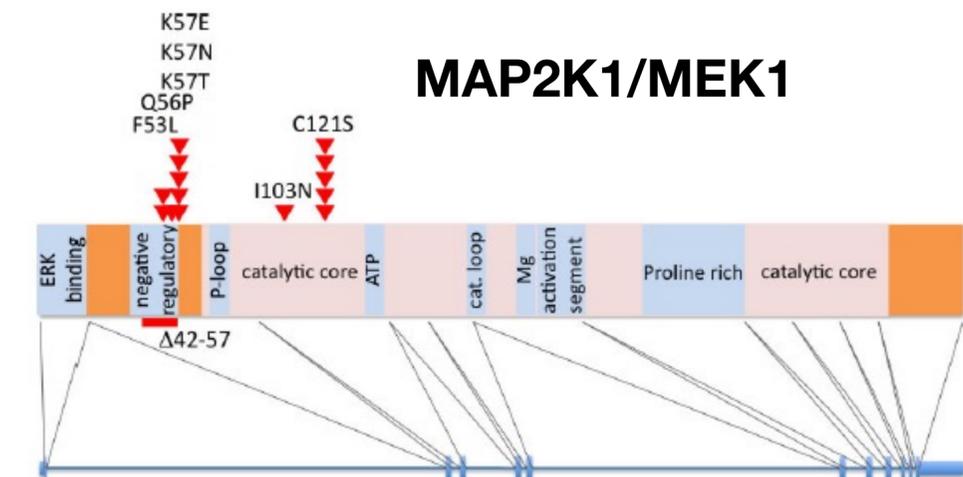
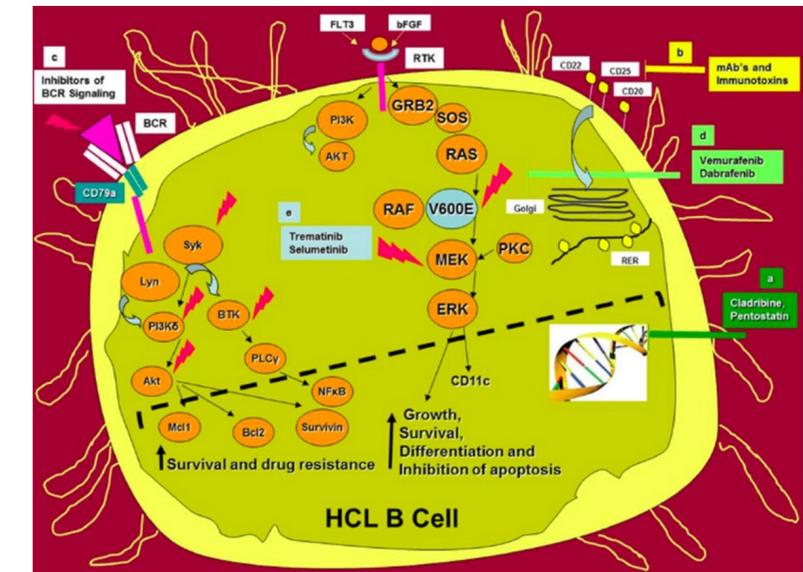
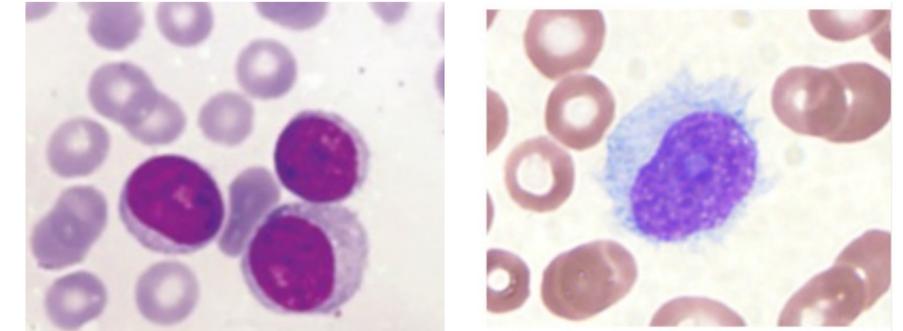
- Sujet âgé (médiane 71ans)
- Splénomégalie, lymphocytose élevée ly nucléés, cytopénies

## Histologie

- Localisation SPLENIQUE, médullaire, hépatique 1/3
- Infiltrat monomorphe diffus homogène de la pulpe rouge et sinus
- Atrophie de la pulpe blanche
- CD20, CD19+, CD11c+, CD103 et FMC7
- Négatif pour CD25, CD123, AnnexinA1

## Biologie moléculaire

- Absence BRAF V600E
- IGHV muté avec surreprésentation **VH4-34**
- **MAP2K1 mutation → Inhibiteurs de MEK**



# Lymphome splénique B diffus à petites cellules de la pulpe rouge

- Clinique

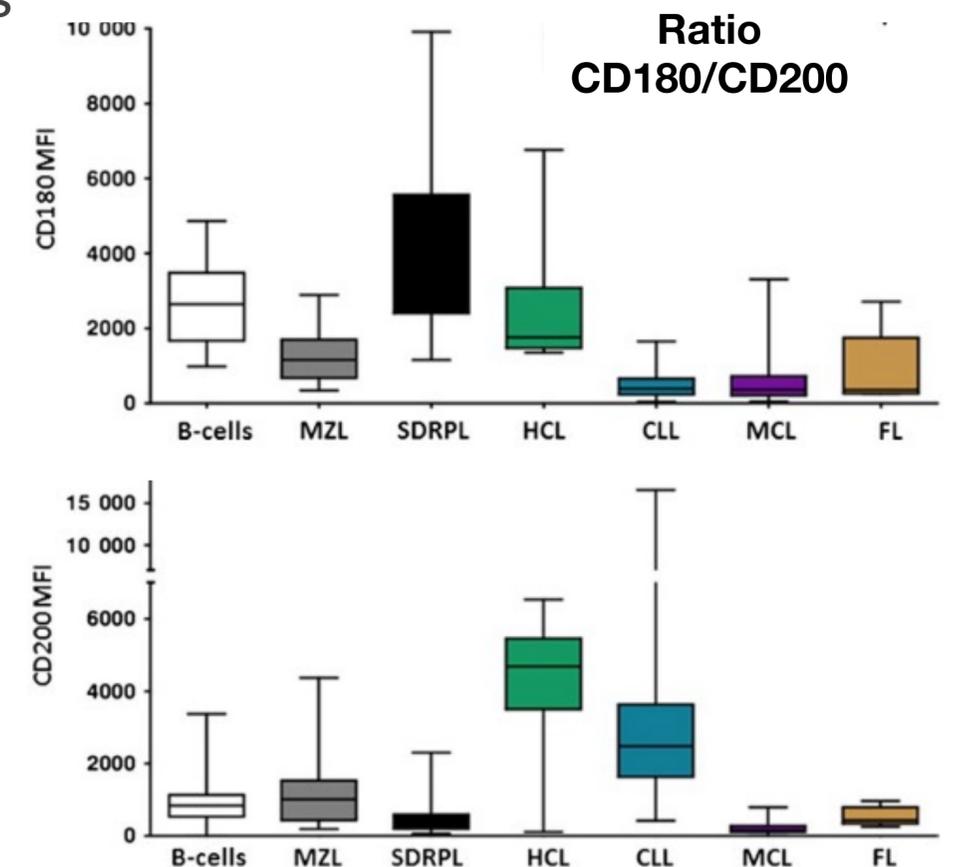
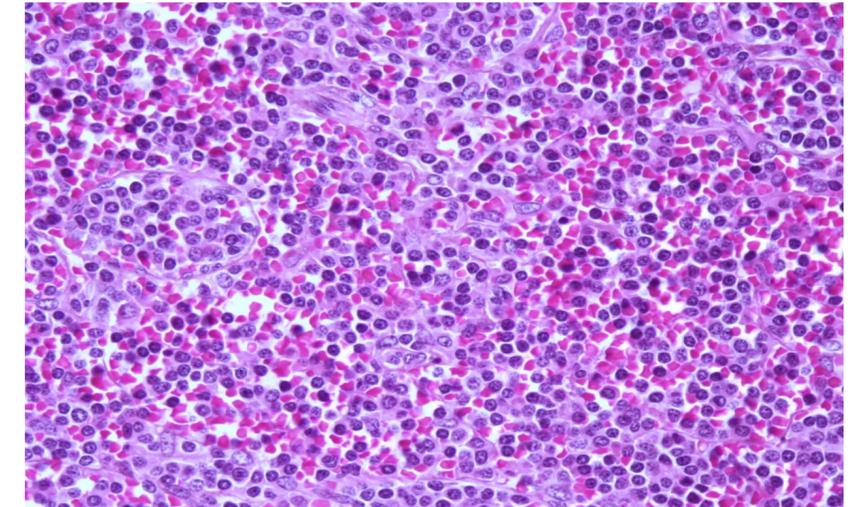
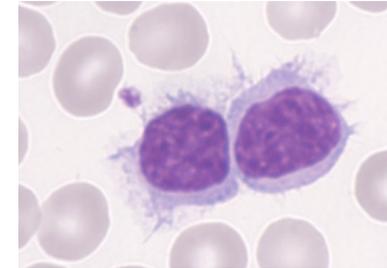
- Splénomégalie, lymphocytose **ly villeux**, peu de symptôme B

- Histologie

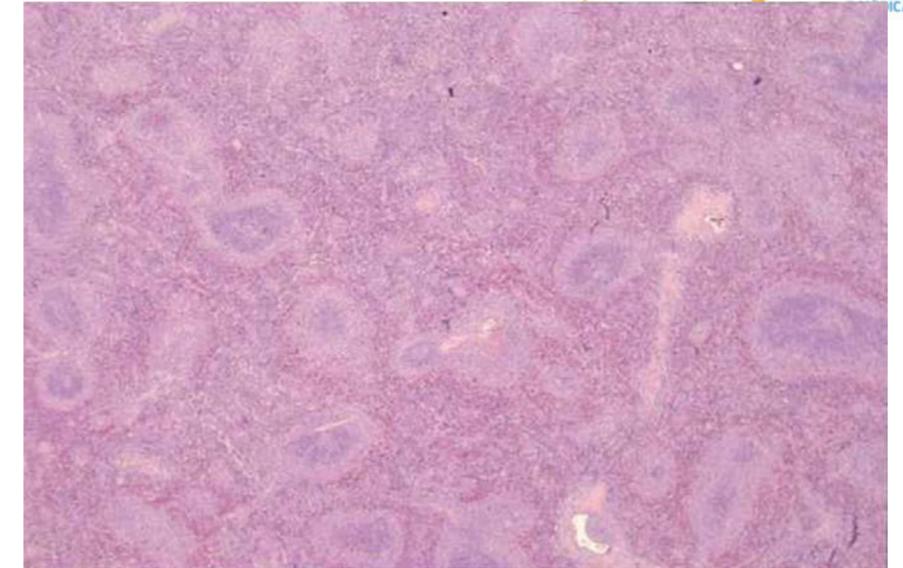
- Localisation SPLENIQUE isolée ++ (rarement ADP, foie)
- **Infiltrat monomorphe diffus homogène de la pulpe rouge et sinus**
- Destruction de l'architecture de la rate, aspect pseudosinusal, plaques hémorragiques
- Atrophie de la pulpe blanche
- **CD20, CD19+, DBA44 et IgG, CCND3 (70%)**
- Négatif pour CD5, CD10, CD23, CD43, BCL1, CD38

- Biologie moléculaire

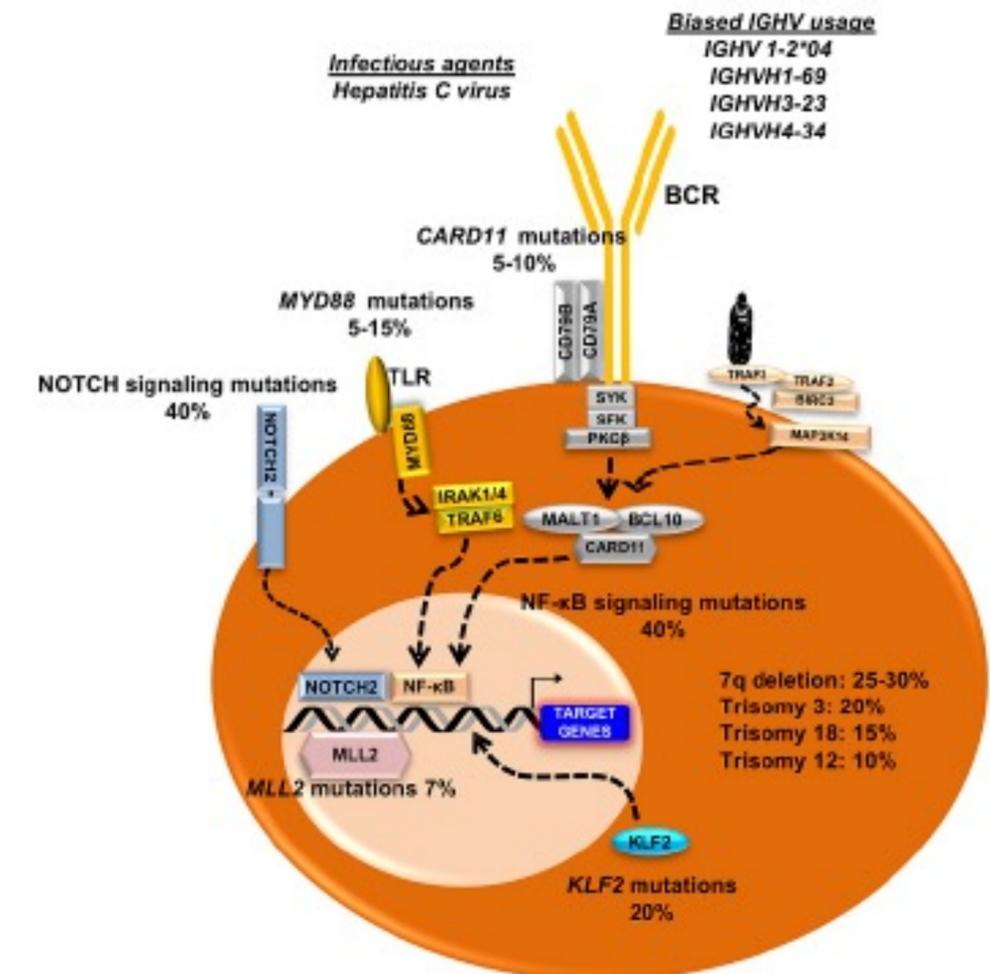
- Absence BRAF V600E
- IGHV muté avec surreprésentation VH4-34 et VH3-23
- **BCOR, CCND3 mutations**



# Lymphome splénique de la zone marginale

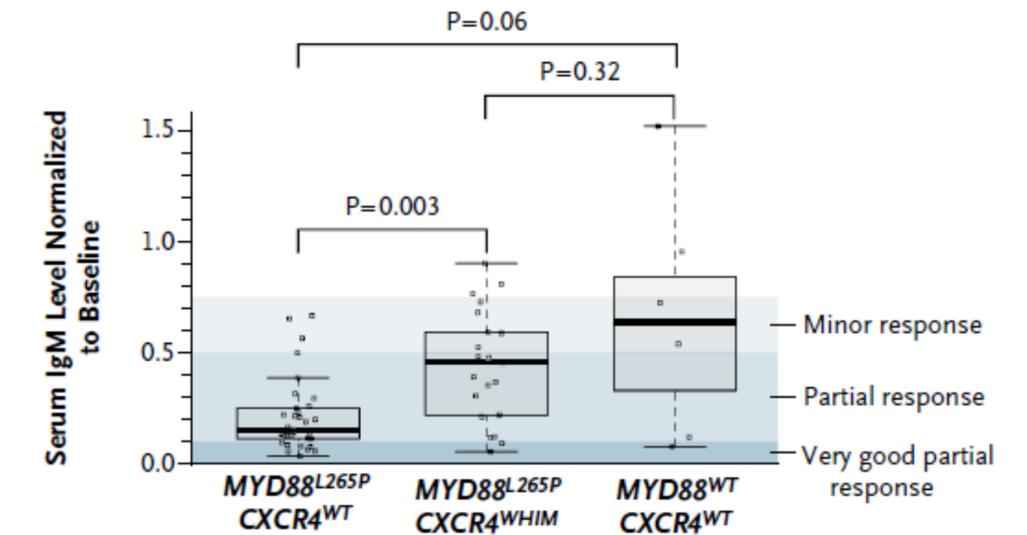


- Clinique
  - Age : 60-70ans
  - **Splénomégalie** >90%, peu de symptôme B
  - Manifestation auto-immunes (PTI, AHAI), cryoglobulinémie
  - Association hépatite C
- Hyperlymphocytose
  - **ly villeux, monocytoides, parfois lymphoplasmocytaires**
  - CD19+ CD20+, CD180+, CD11c+
- Histologie
  - **Infiltrat de la pulpe blanche, aspect en cocarde**
- Biologie moléculaire
  - Absence BRAF V600E
  - **KLF2, NOTCH2, MYD88, TNFAIP3**

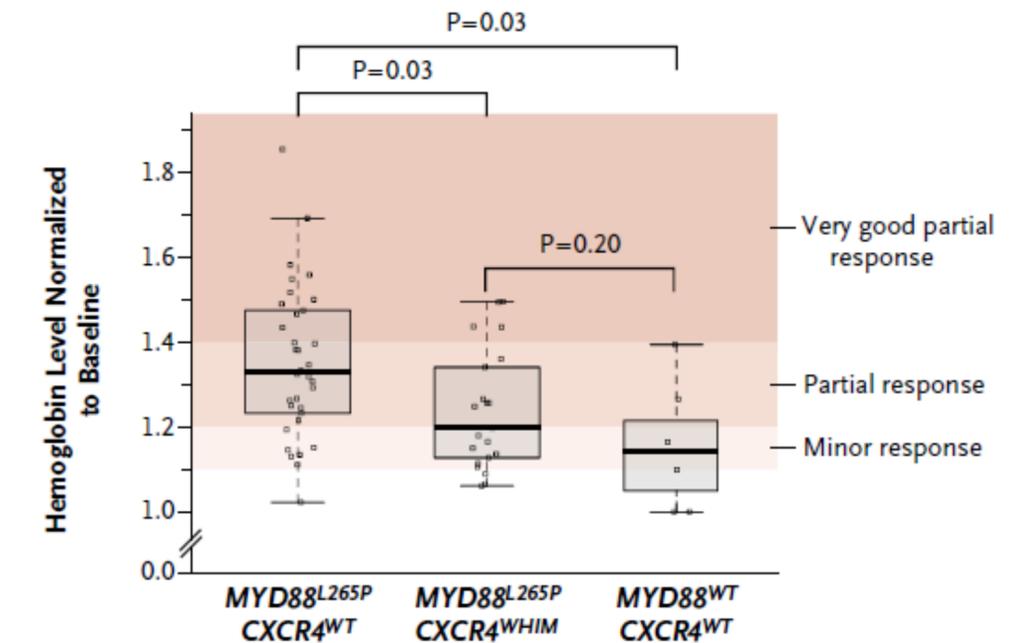


# Maladie de Waldenström

- Lymphocytose rare
  - Diagnostic différentiel des lymphomes splénique de la zone marginale
- Gammapathie monoclonale
  - Pic IgM
  - Infiltration médullaire par lymphoplasmocytes
  - Cytopénies
  - Manifestation cliniques liées à l'IgM  
Neuropathie, amylose, agglutines froides, cryoglobulinémie
- Biologie moléculaire
  - **MYD88 L265P (>90%)**
  - CXCR4
  - TP53 +/- BTK

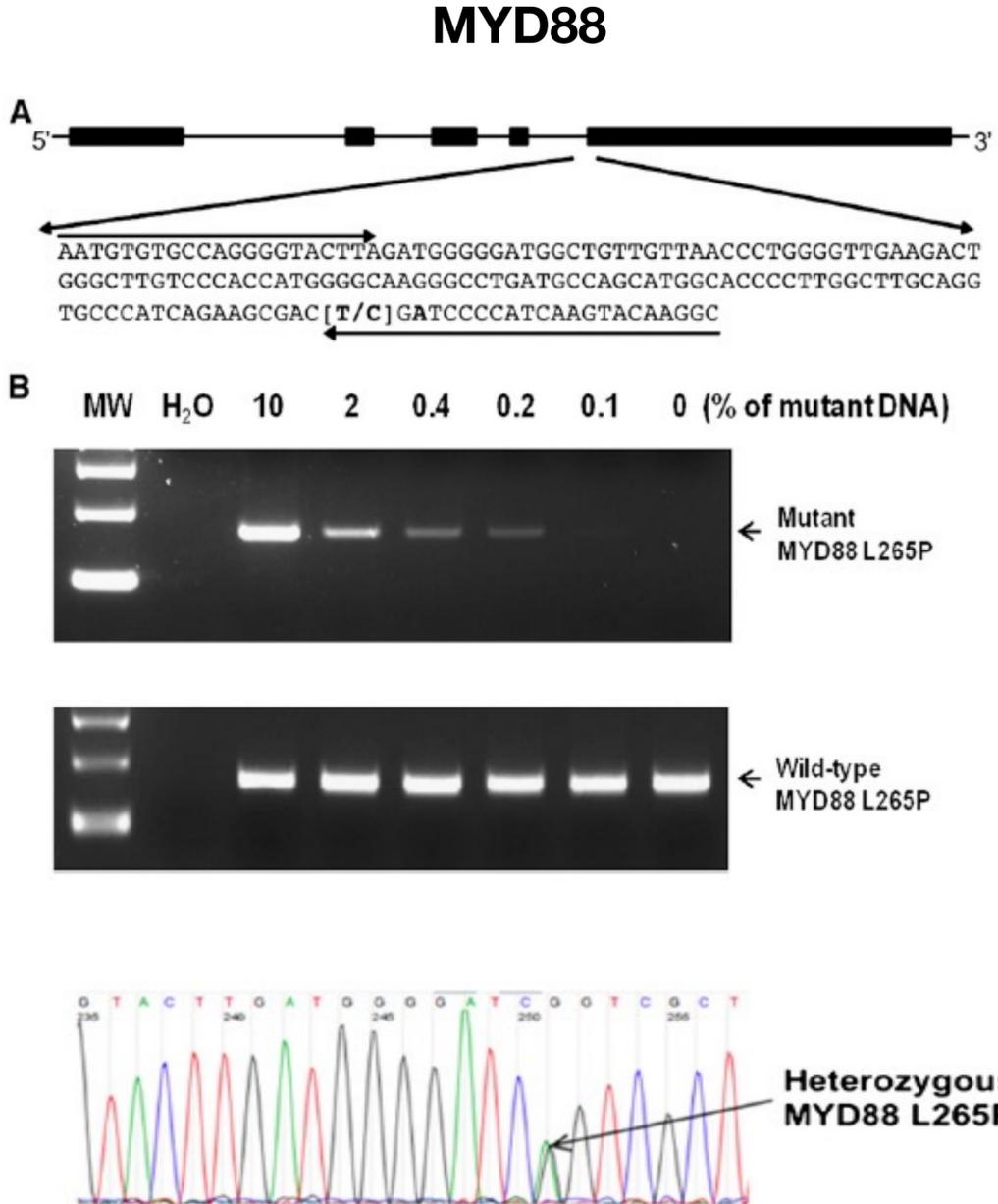


B

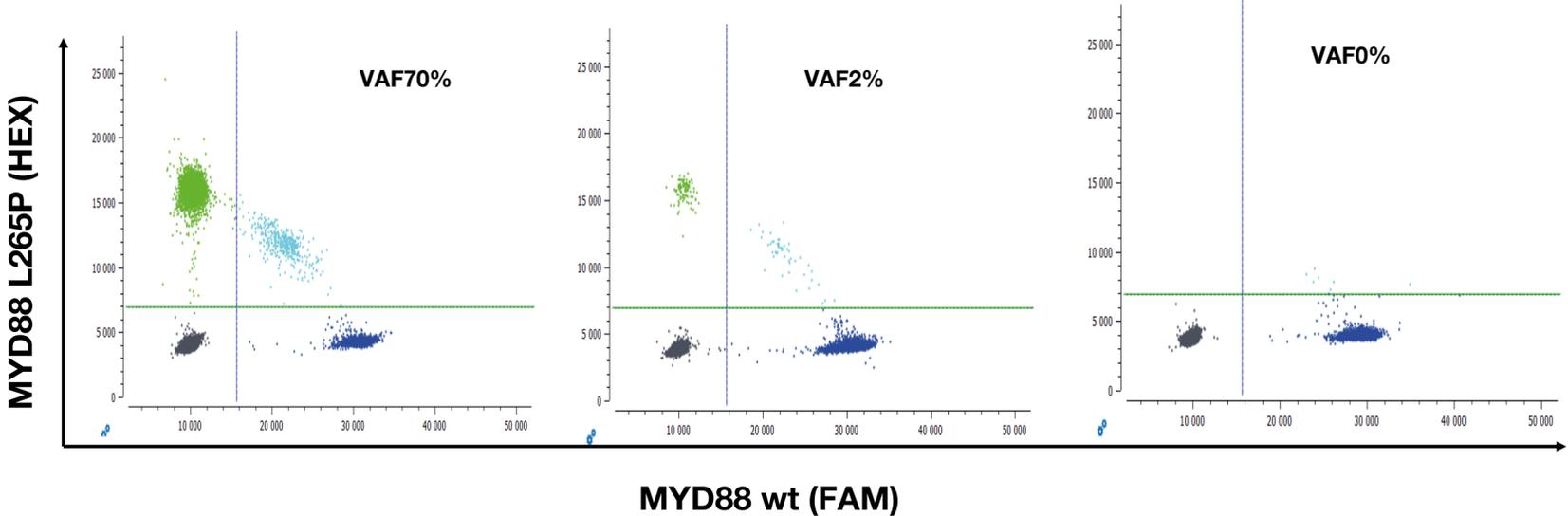
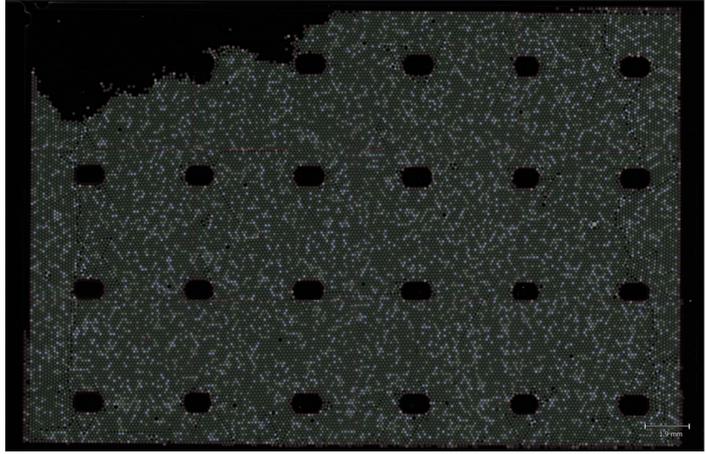
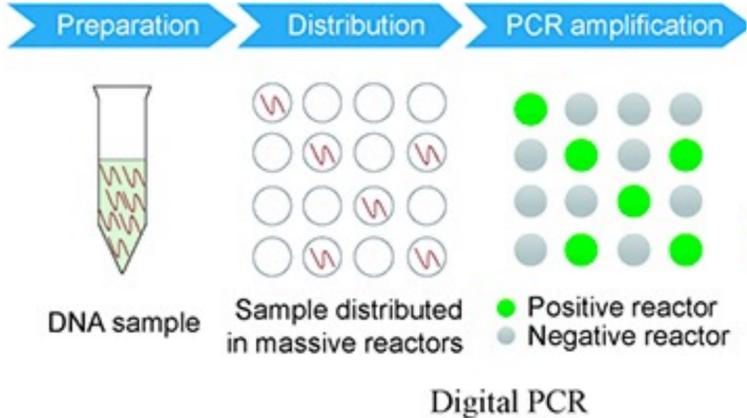


# Maladie de Waldenström

- PCR digitale



- Technique quantitative, sensible (0.3%)
- Utilisable sur sang, moelle, LCR (Bing-Neel)



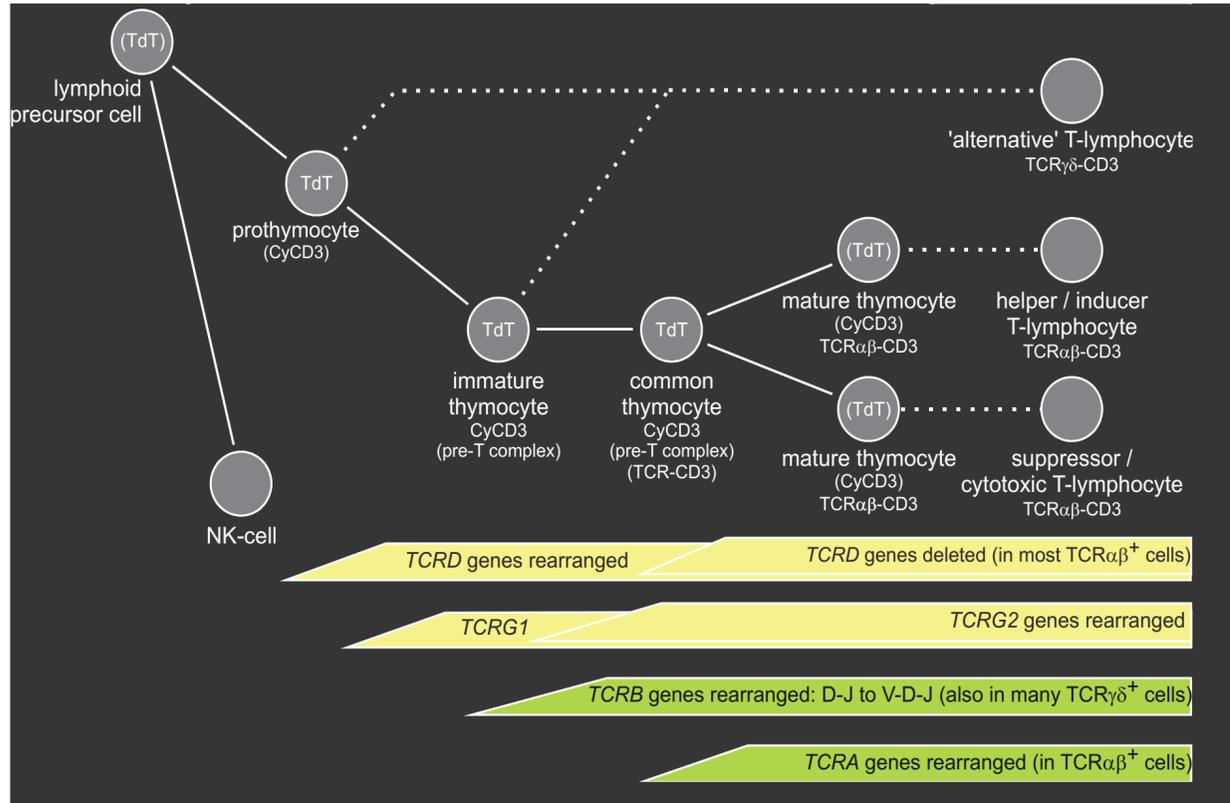
Feature	SDRPL	SMZL	SBPLN	HCL
<b>Histopathology</b>				
<b>Spleen pattern</b>	diffuse	Predominantly macronodular or less frequent	diffuse	diffuse
<b>Morphology</b>	monomorphous	small cells, marginal-zone cells, isolated large cells	Monomorphous with visible nucleoli	monomorphous
<b>Peripheral blood cytology</b>				
<b>cytology</b>	Monomorphous : <b>villous lymphocytes</b> (round and regular nucleus, clumped chromatin, small or not visible nucleolus basophilic cytoplasm with polar well-visible projections)	Polymorphous : small lymphocytes (round nucleus, condensed in small irregular clumps chromatin) admixed with lymphoplasmocytic cells	Monomorphous : intermediate between prolymphocytes and hairy cells, and distinct to villous lymphocytes by <b>prominent nucleolus</b>	<b>Monomorphous : hairy cells</b> (oval and indented nucleus, dispersed chromatin, abundant and pale cytoplasm with circumference projections)
<b>Immunophenotype by Immunohistochemistry</b>				
Cyclin D1	-	-	-	+
Cyclin D3	+	-	-	-
Annexin A1	-	-	-	+
<b>Immunophenotype by flow cytometry</b>				
CD11c	bright in ~67% of cases	moderate in ~70% of cases	bright in ~25% of cases	bright in 100% of cases
CD180	Strong in 100% of cases	Moderate in 93% of cases	nd	Strong in 100% of cases
CD200	Dim in 40% of cases	Moderate 93% of cases	nd	Strong in 100% of cases
CD103	positive in ~20% of cases	negative	positive in 65-100% of cases	bright in 100% of cases
CD123	positive in 3% of cases	negative	positive in 9% of cases	Bright positive in 100%
<b>Molecular profile</b>				
IGHV1-2*04 gene usage	<5%	~30%	unknown	unknown
IGHV4-34 gene usage	22%	8%	50%	unknown
del(7q)	~25%	~40%	~20%	~20%
NOTCH2 mutations	<2%	15-20%	0%	0%
KLF2 mutations (MYD88 + TNFAIP3)	<2%	~20%	0%	15%
CCND3 mutations	~25%	0%	unknown	0%
BCOR alterations (mutations and/or CNVs)	24%	<10%	unknown	0%
BRAF p.V600E	<1%	<1%	<10%	≥95%
MAP2K1 mutations	<10%	<1%	50%	<1%

# Lymphomes B : synthèse

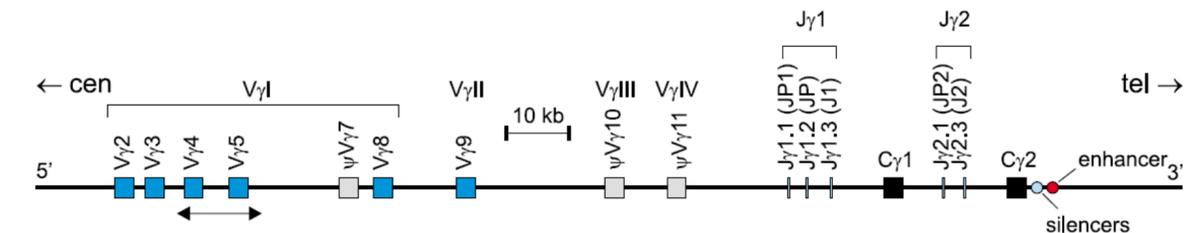
- Peu d'intérêt de la clonalité IGH en cas d'hyperlymphocytose
- Marqueurs diagnostiques
  - Folliculaire : BCL2-JH
  - Manteau (Cycline D1)
  - Leucémie à Tricholeucocytes BRAF V600E
  - Maladie de Waldenström MYD88 L265P
- NGS à discuter en fonction du contexte clinique et de la question thérapeutique

# Leucémies/lymphomes T matures

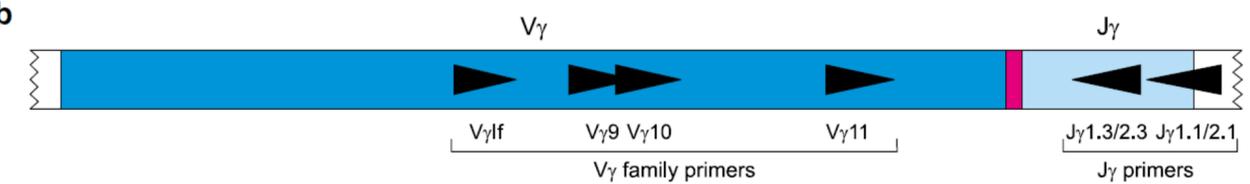
## Différenciation lymphoïde T



a. TCRG gene complex (#7p14)



b



TCRG tube A

Vγ1f (-178) 5' GGAAGGCCCCACAGCRTCTT 3'  
Vγ10 (-126) AGCATGGGTAAGACAAGCAA

TCRG tube B

Vγ9 (-141) CGGCACTGTCAGAAAGGAATC  
Vγ11 (-58) CTTCCACTTCCACTTTGAAA

TCRG tubes A and B

3' CGAGTATCATTGAAGCGGACCATT 5' (+64) Jγ1.1/2.1 (JP1/2)  
GAGAAACCGTCACCTTGTTGTG (+38) Jγ1.3/2.3 (J1/2)

```
CTGTGCAAGAGAGATAGTATAGCAGCTCGTACAACCTGGTTCGACTCCTGG
CTGTGCAAGAGATCCGGGcAGCTCGTTTTGCTTTTGATATCTGG
CTGTGCAAGAGcCTCTCTCCACTGGGATGGGGGCTACTGG
CTGTGCAAGAGcAGCAGCTCGGCCcCTTTGACTACTGG
CTGTGCAAGAGgACTTTGGATGCTTTTGATATCTGG
CTGTGCAAGAGeGTGGGAGCTACTAGACTACTGG
CTGTGCAAGeGTAGCTAAACCTTTGACTACTGG
CTGTGCAATATCTACTTTGACTACTGG
```

## → Etude du TCRG en première intension

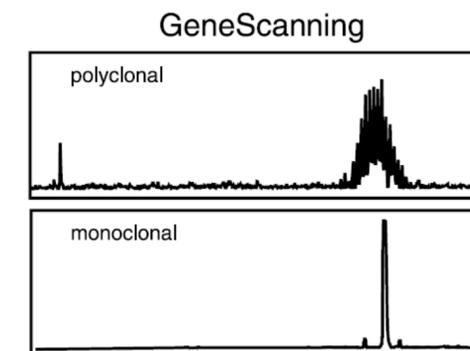
**Sensibilité : 98% pour les lymphomes T**

- Proliférations Tαβ ou Tγδ
- Lymphomes T matures ou lymphoblastiques T

→ TCRB si discordance clinique ou histologique

→ TCRD uniquement pour les proliférations Tγδ

## Discrimination par la taille



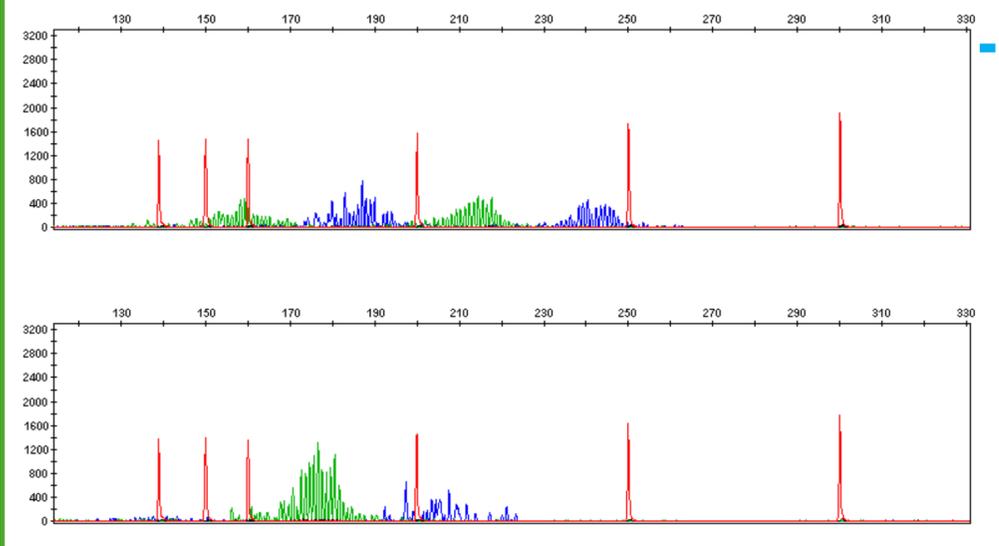
## Discrimination par la séquence

NGS



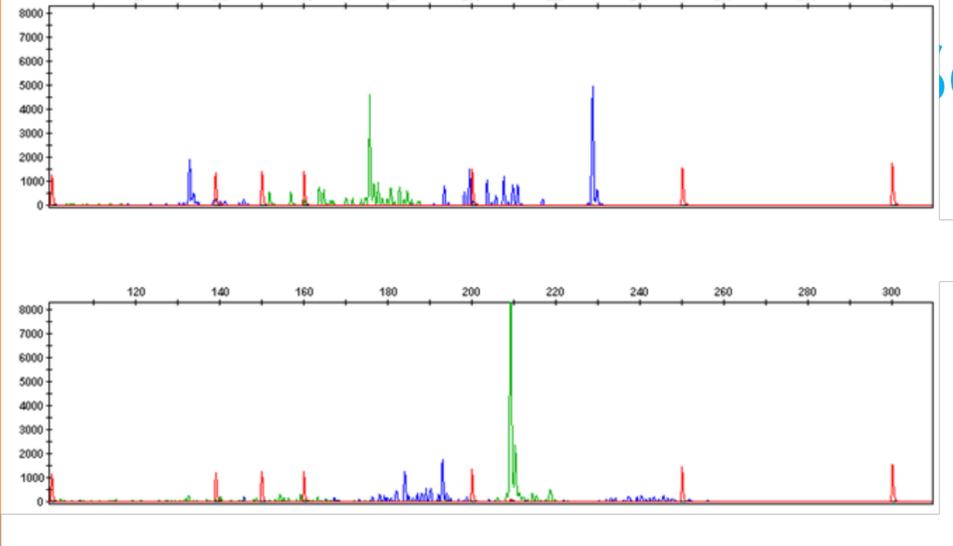
# Clonalité *TCRG*

## Polyclonal



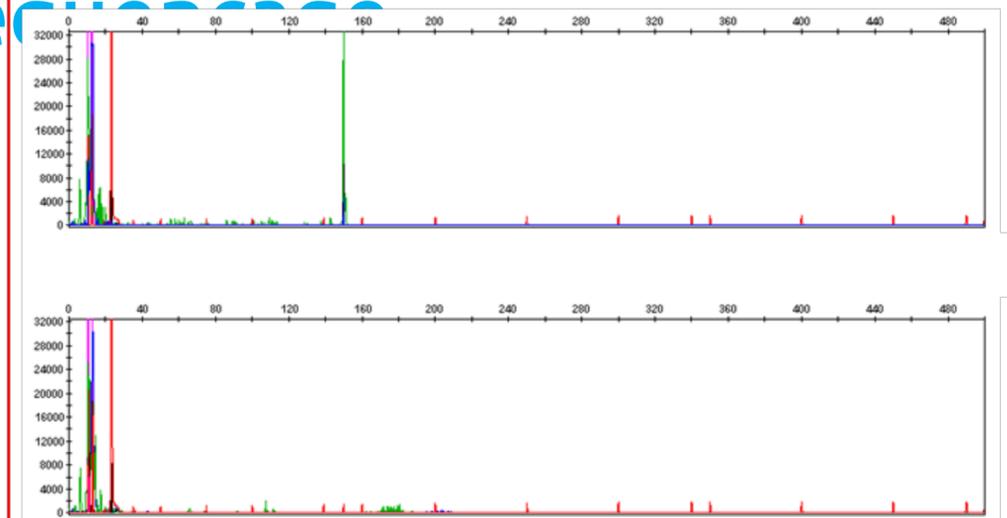
Absence d'argument moléculaire pour un lymphome

## Oligoclonal ( $\geq 3$ pics)

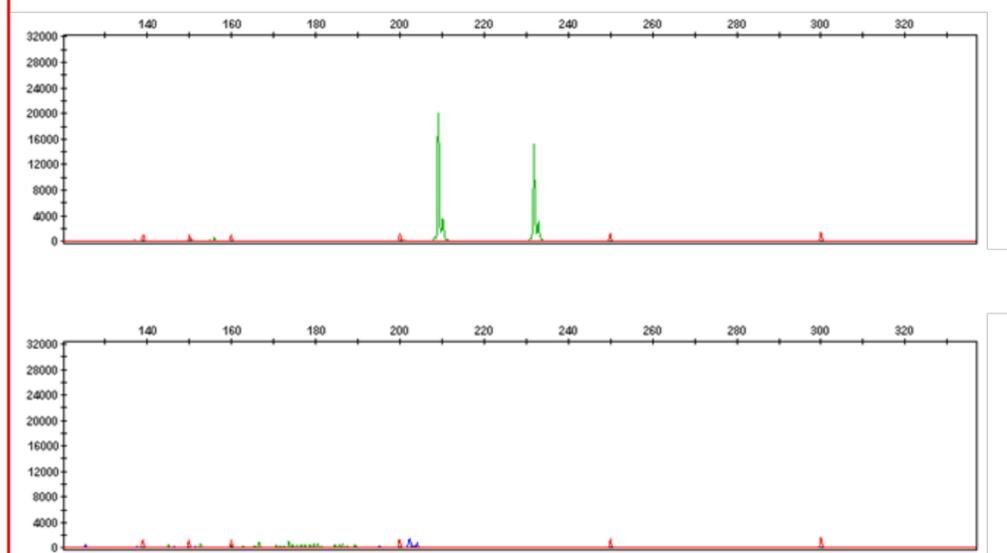


Expansion T réactionnelle (infection virale, auto-immunité, cancer)  
Répertoire T restreint (lymphopénie, âge)  
« vraie » prolifération lymphomateuse

## Monoclonal (1 pic)



## Monoclonal (2 pics)

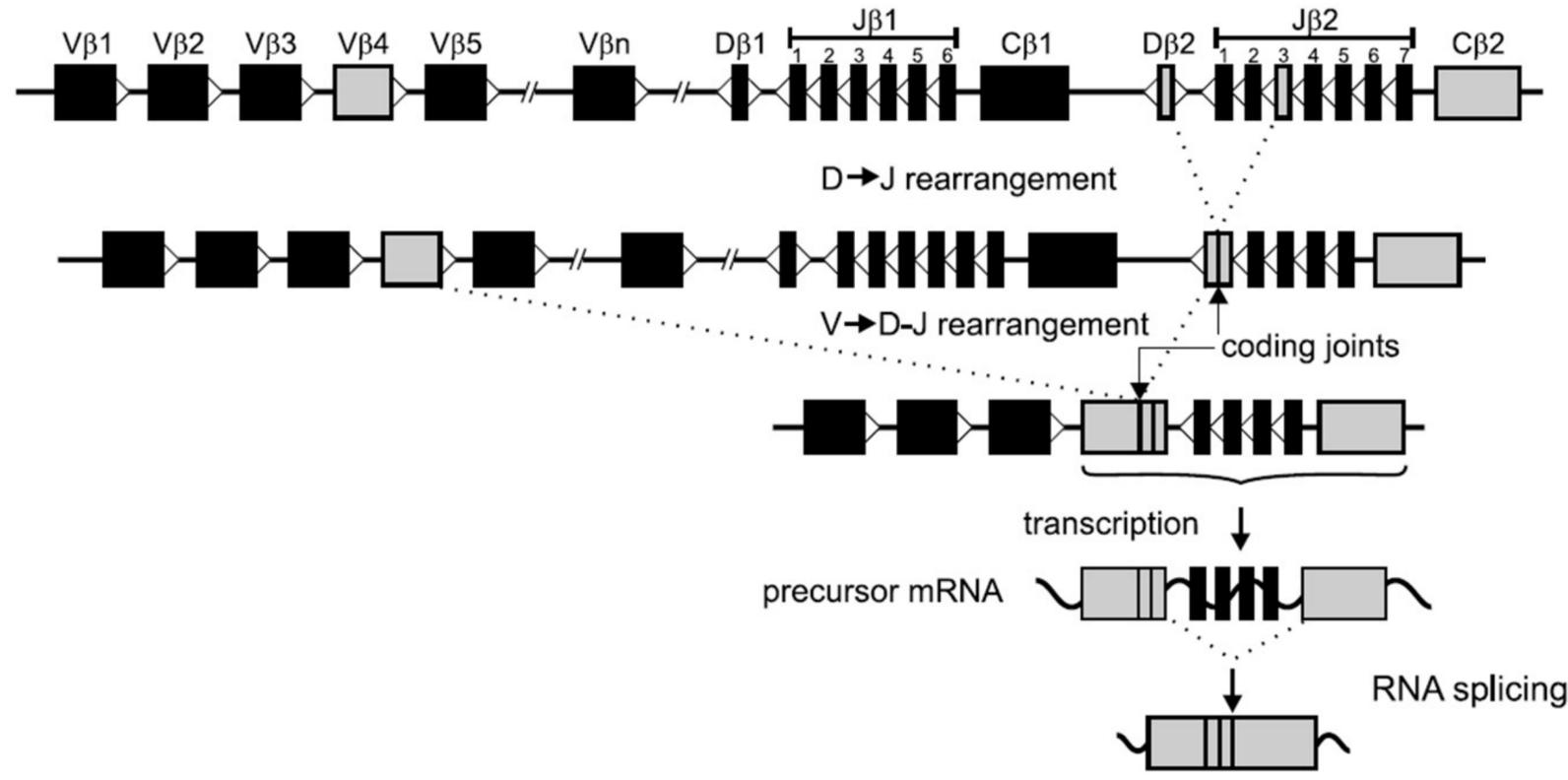


Prélèvement clonal  
Probable lymphome

**Confrontation nécessaire à la clinique et au reste du bilan**

# Clonalité *TCRB*

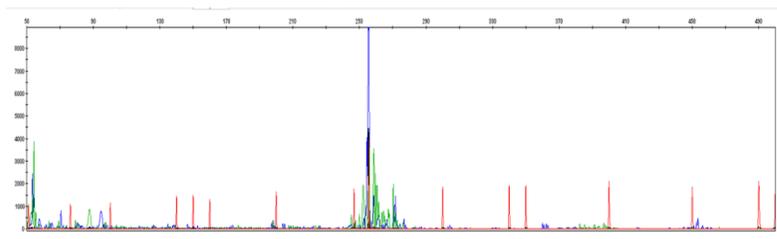
## Gène *TRB*



## BIOLOGIE MOLECULAIRE



## PCR analyse de fragment

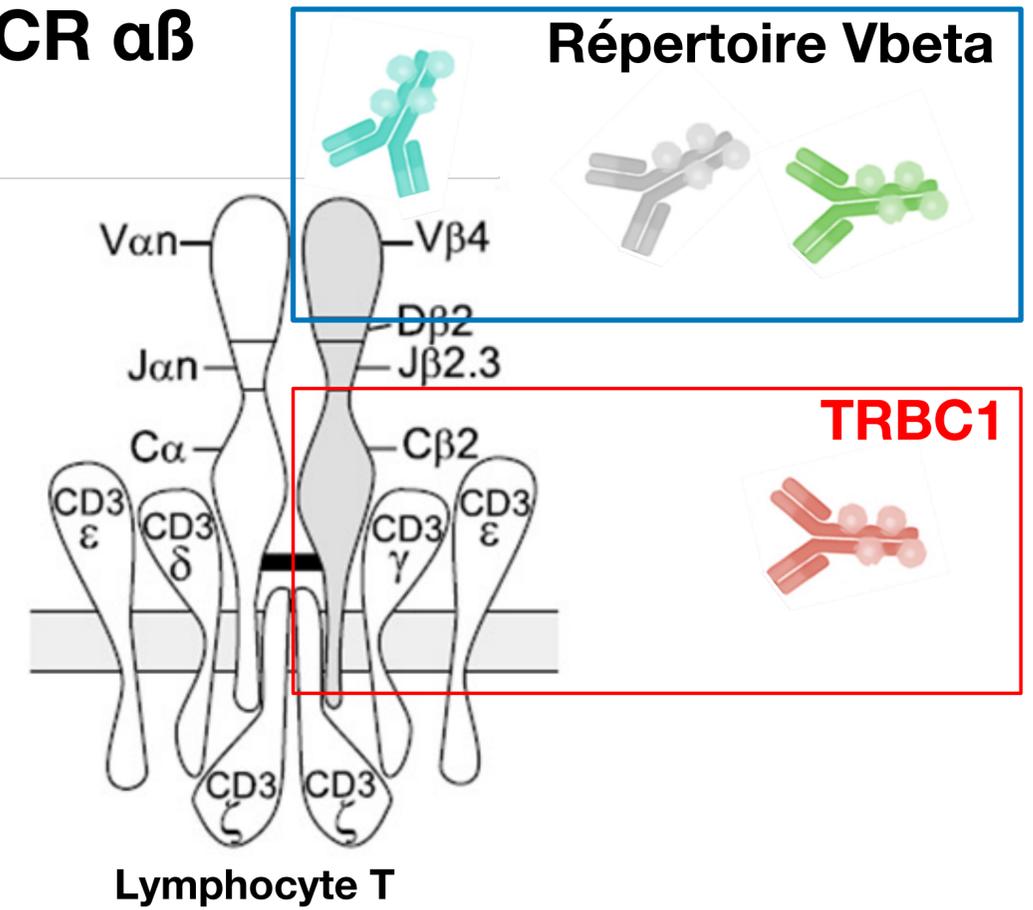


## NGS



Van Dongen, Leukemia 2003

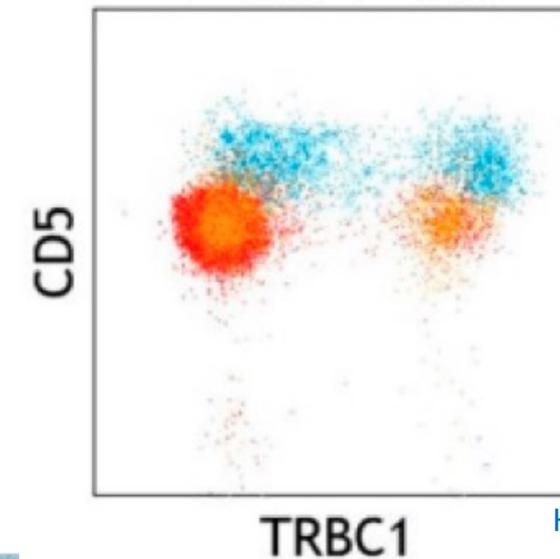
## TCR αβ



CYTOMETRIE

Lymphocyte T

## TCRαβ T-cells



Horna J Invest Dermatol 2021

# Syndrome de Sézary

- Erythrodermie
- $>1G/L$  de cellules de Sézary



## Blood

### B0 : Mycosis Fongoïde Erythrodermique

- Cellules de Sézary  $\leq 5\%$
- $CD4+CD7^-$  et  $CD4+CD26^- < 250 \mu L^{-1}$

### B1 : Pré-Sézary

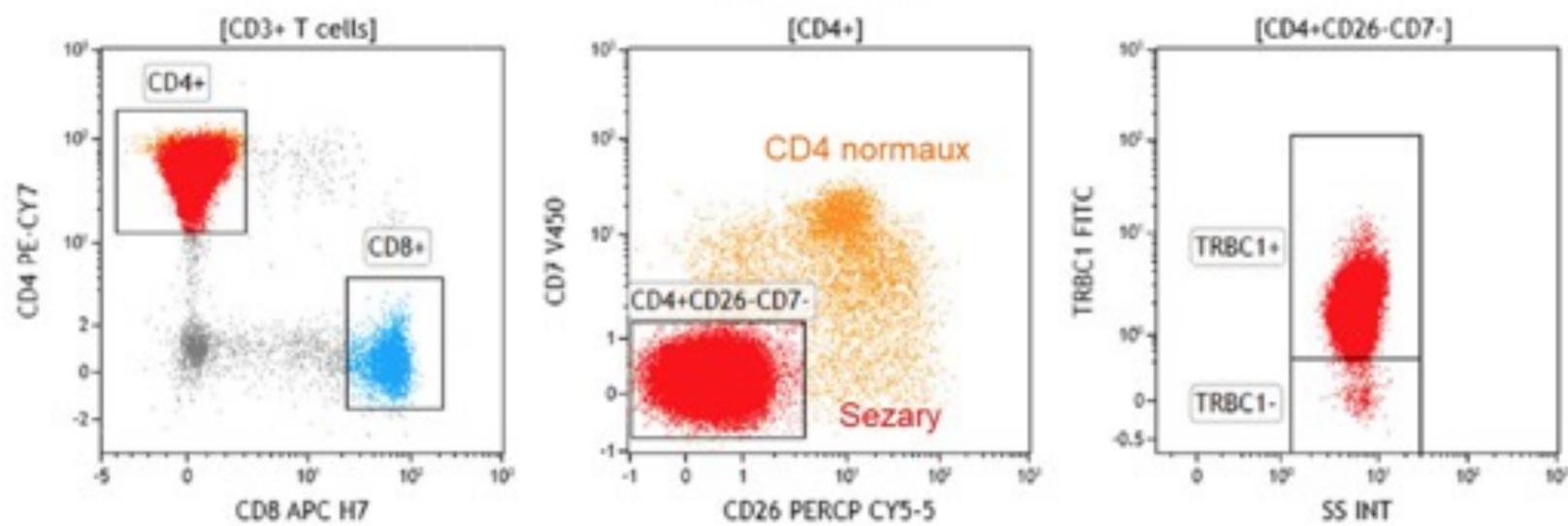
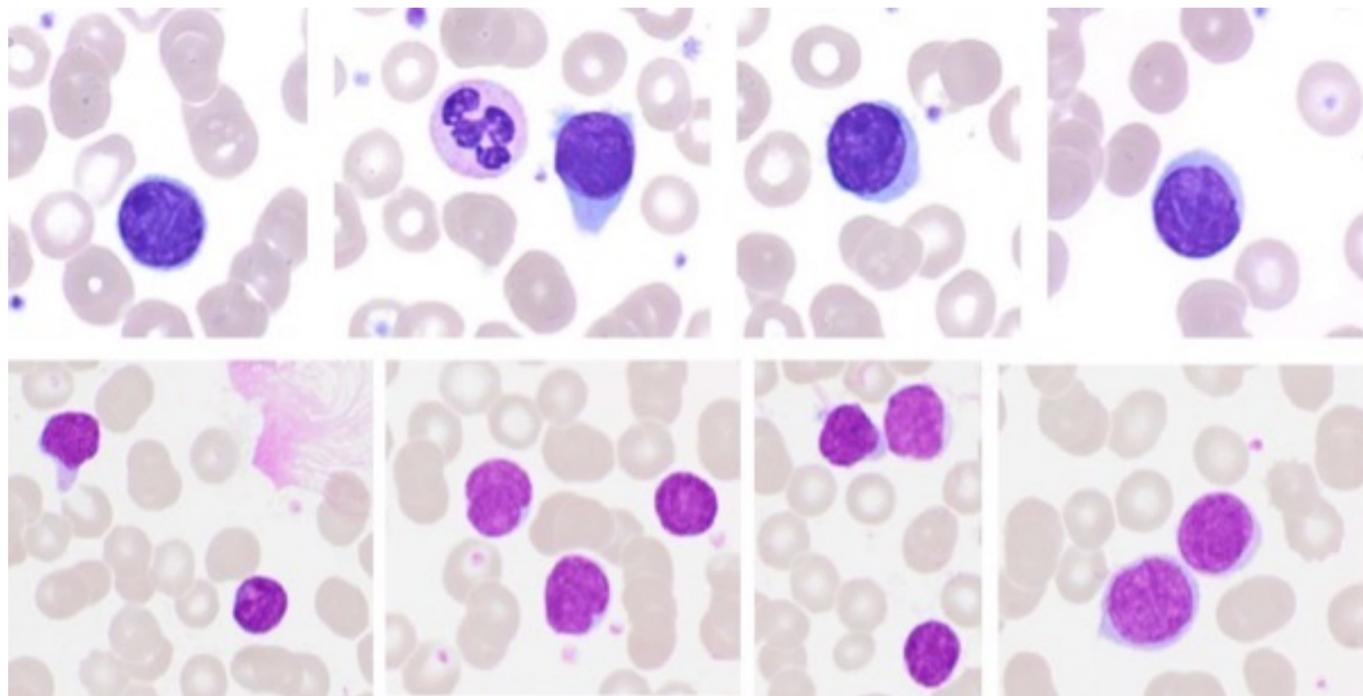
- Cellules de Sézary  $> 5\%$  mais  $< 1000 \mu L^{-1}$
- $CD4+CD7^-$  ou  $CD4+CD26^- \geq 250 \mu L^{-1}$  mais  $< 1000 \mu L^{-1}$

### B2 : Syndrome de Sézary

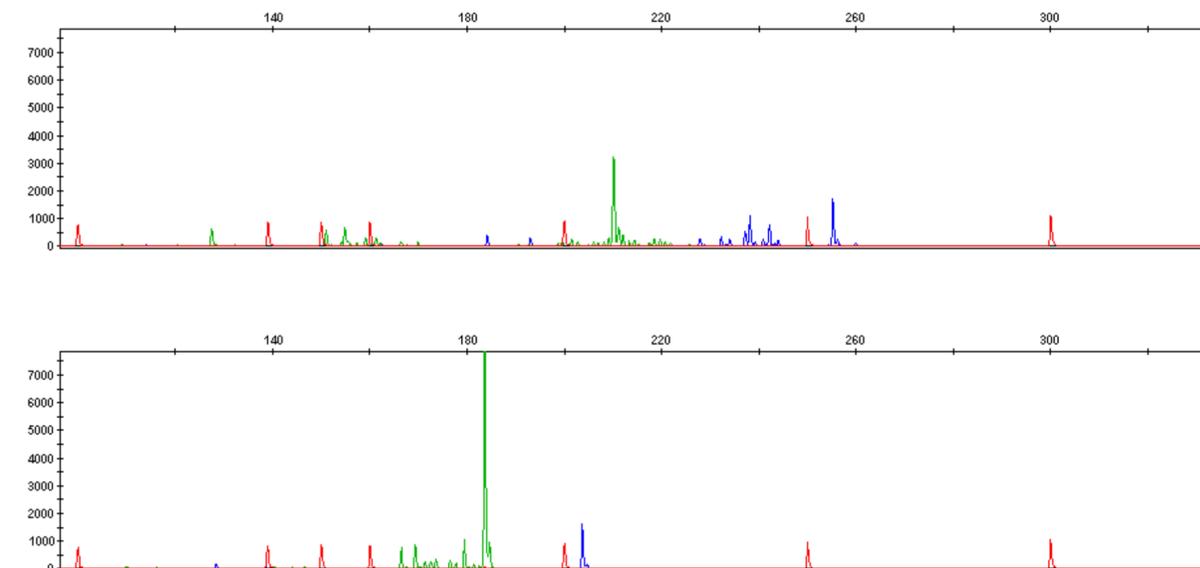
- Cellules de Sézary  $\geq 1000 \mu L^{-1}$
- Augmentation de la population TCD4 avec ratio T CD4/CD8  $\geq 10$
- Augmentation des TCD4 avec un phénotype anormal
  - $CD4+CD7^- \geq 40\%$
  - $CD4+CD7^- \geq 1000 \mu L^{-1}$
  - $CD4+CD26^- \geq 30\%$
  - $CD4+CD26^- \geq 1000 \mu L^{-1}$

**Même clone T dans la peau et le sang en biologie moléculaire**

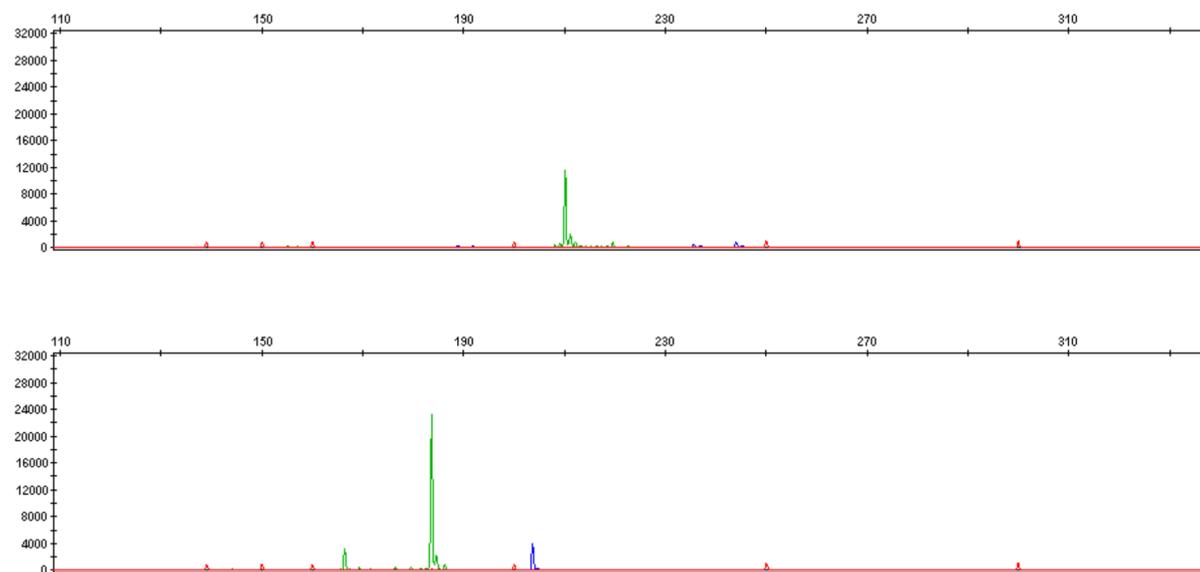
# Syndrome de Sézary



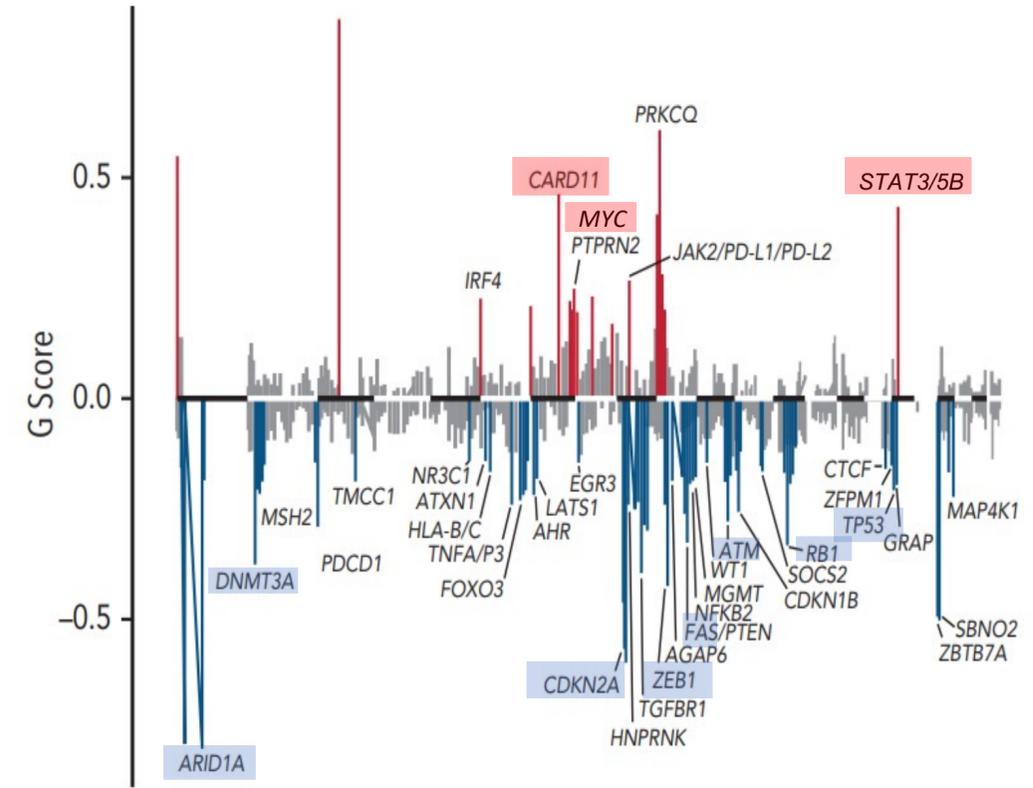
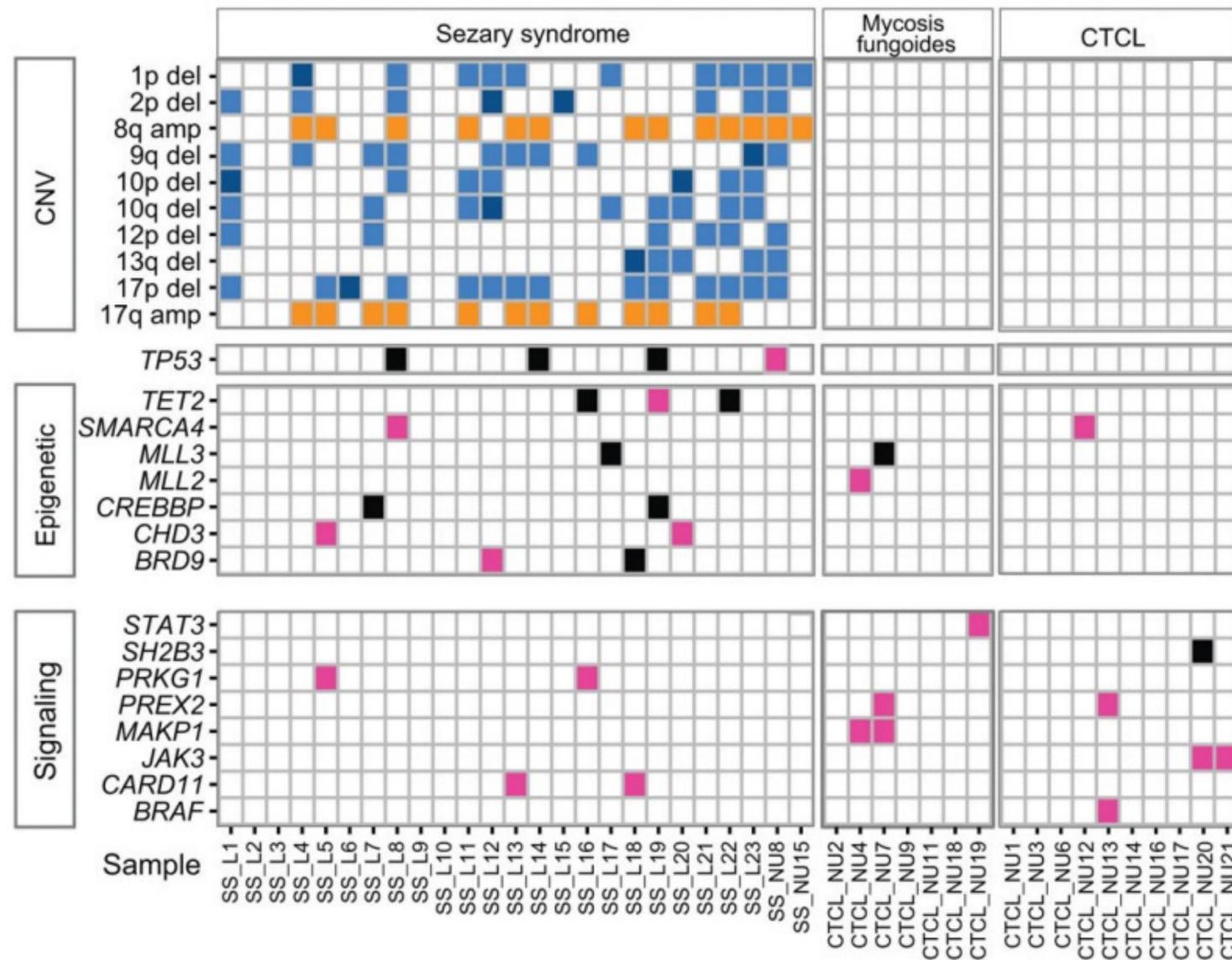
Sang



Peau



# Syndrome de Sézary

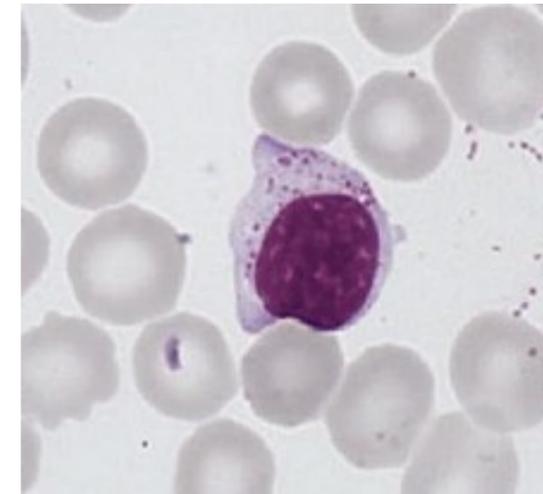


Aucun impact dans la prise en charge des patients

■ Homozygous deletion     ■ Missense mutation  
■ Heterozygous deletion   ■ Truncating mutation  
■ Amplification

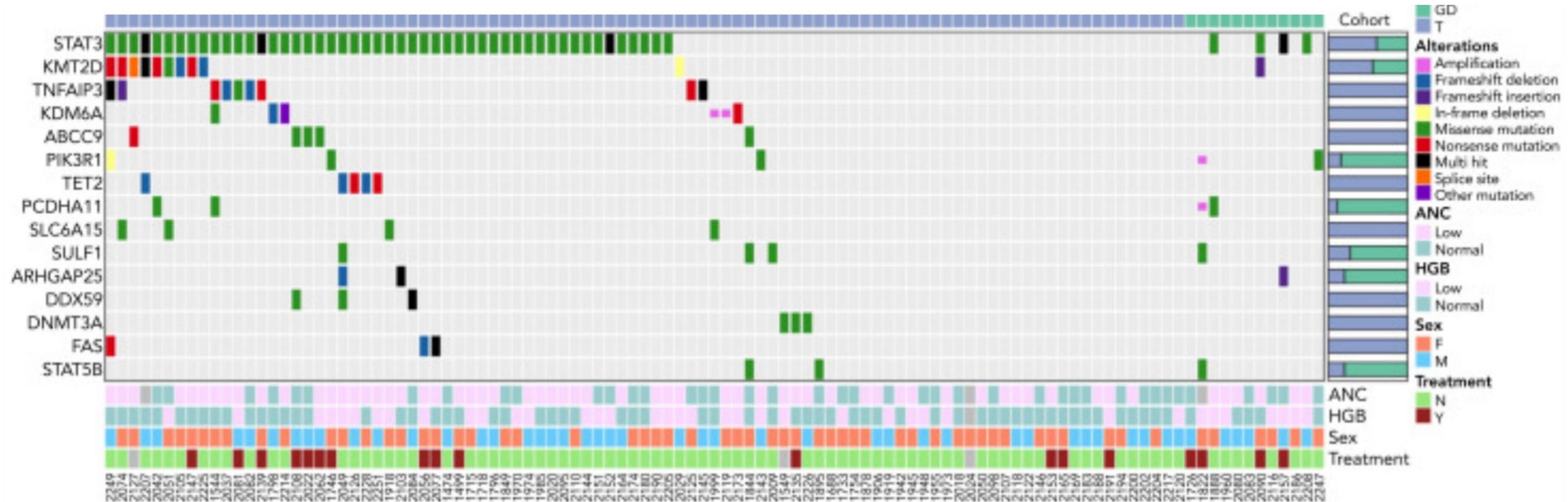
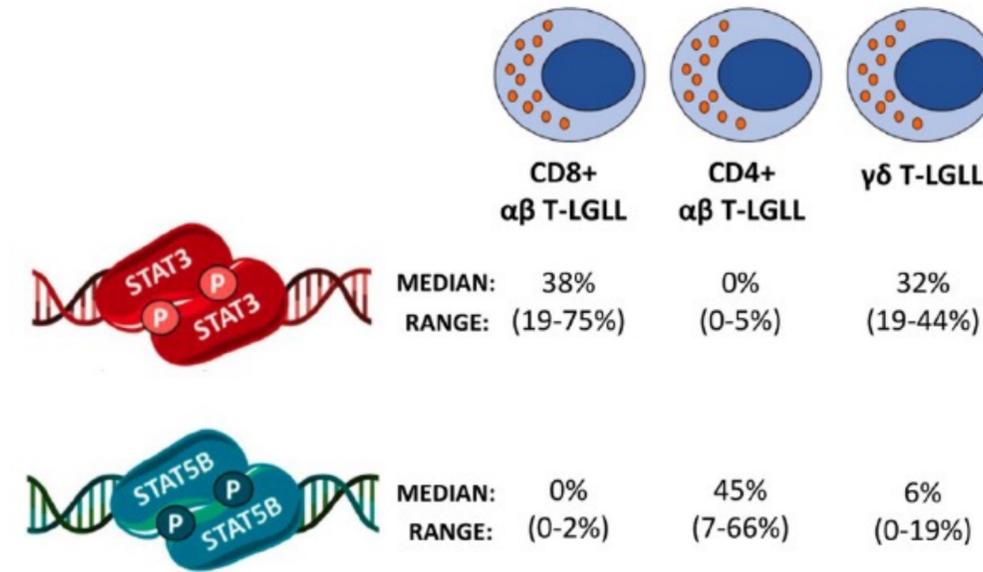
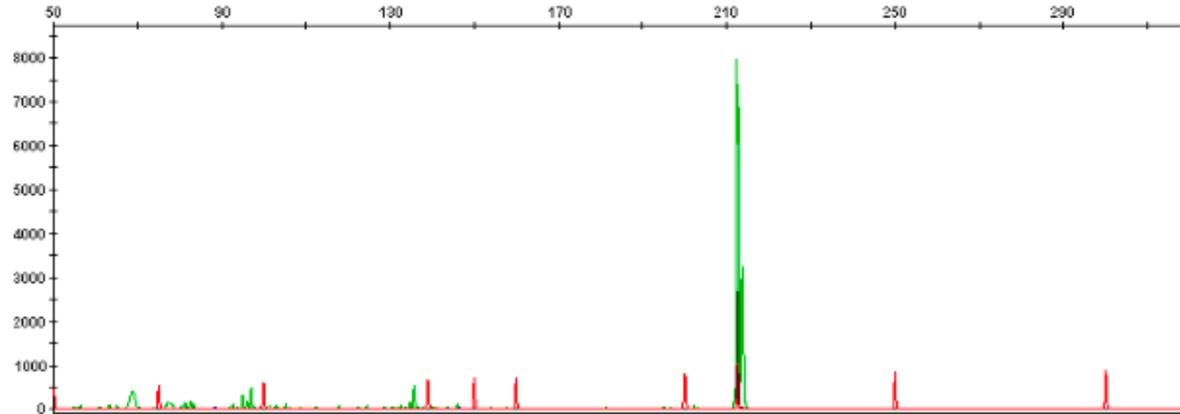
# Leucémie à grands lymphocytes à grains

- Pathologie rare (2,5% des syndromes lymphoprolifératifs)
- Diagnostic
  - Présence de LGL sur frottis sanguin (>0,5G/L chronique)
  - Présentation clinique
    - Cytopénie : neutropénie (infections)
    - Auto-immunité : polyarthrite rhumatoïde++
    - Splénomégalie
- 2 sous types
  - LGL-T : CD3+, CD5low, CD8+, CD57+
  - LGL-NK : CD3-, CD56, CD16, CD57+
- Intérêt de la biologie moléculaire pour confirmer la clonalité des LGL
- Eliminer les causes réactionnelles (virale, OH, greffe organe ou CSH, splenectomie)



# Leucémie LGL-T

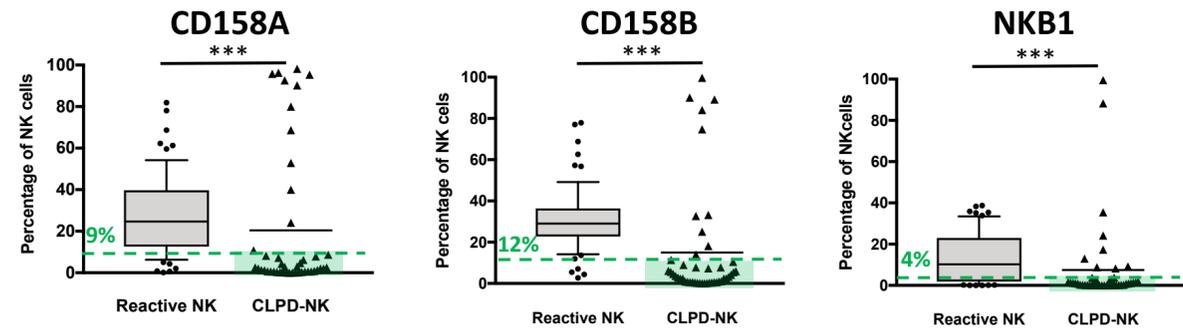
**b** LGL-leukemia patient



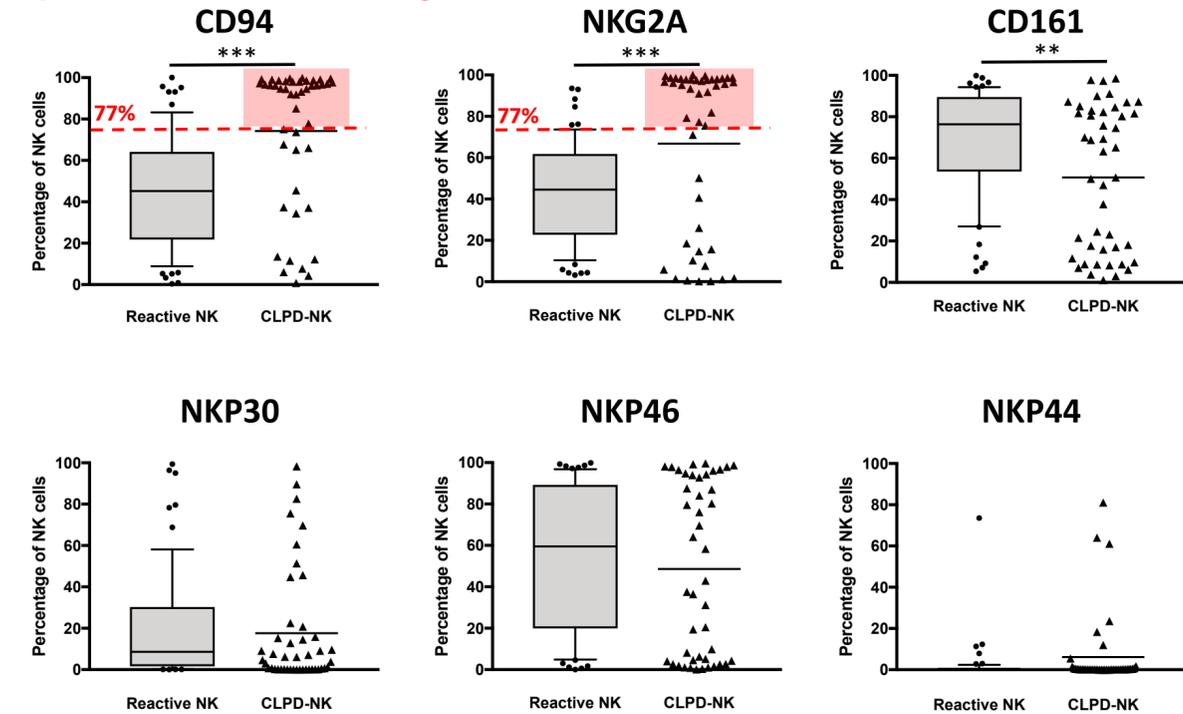
# Leucémie LGL-NK

## Cytométrie et clonalité NK

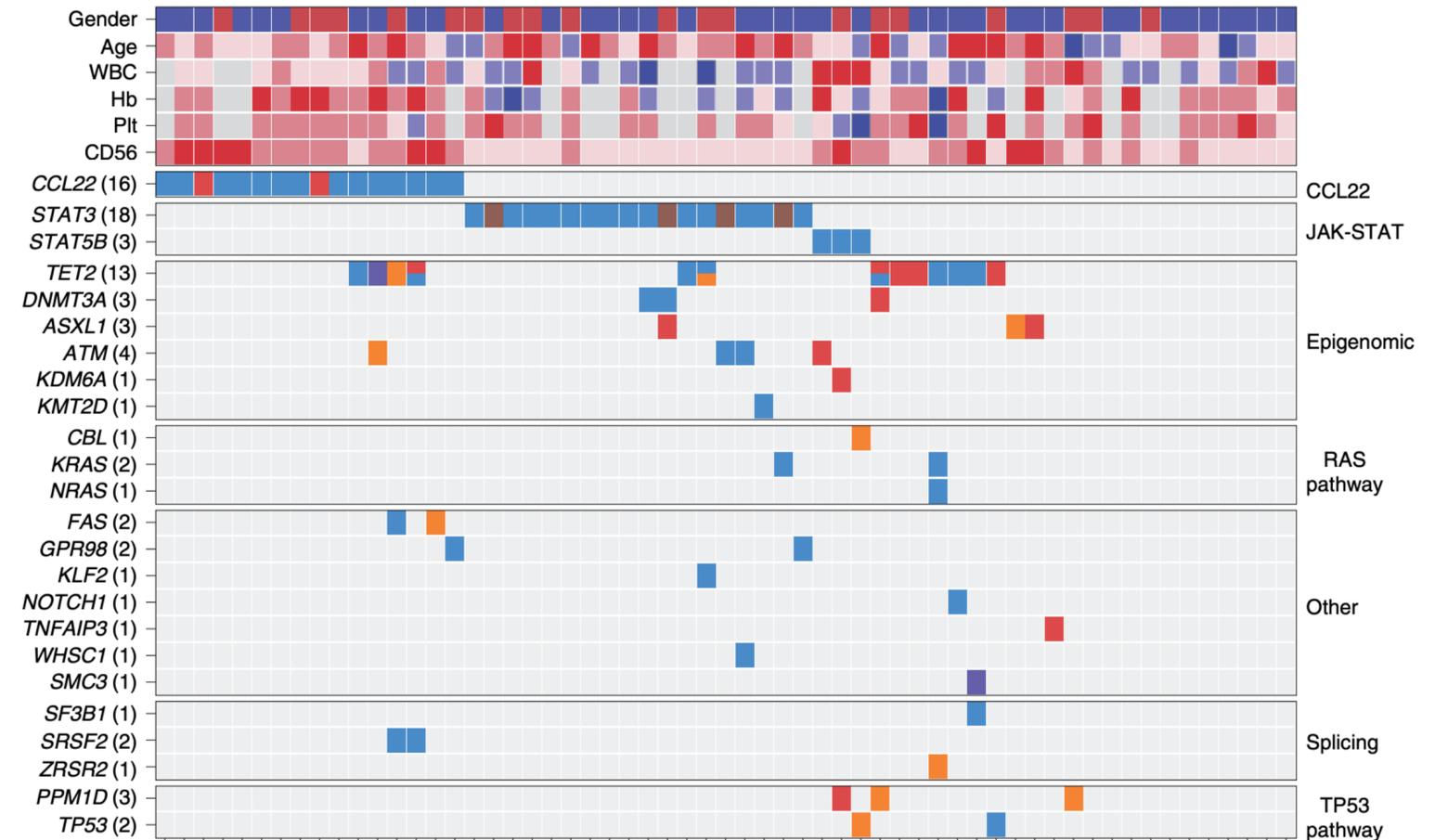
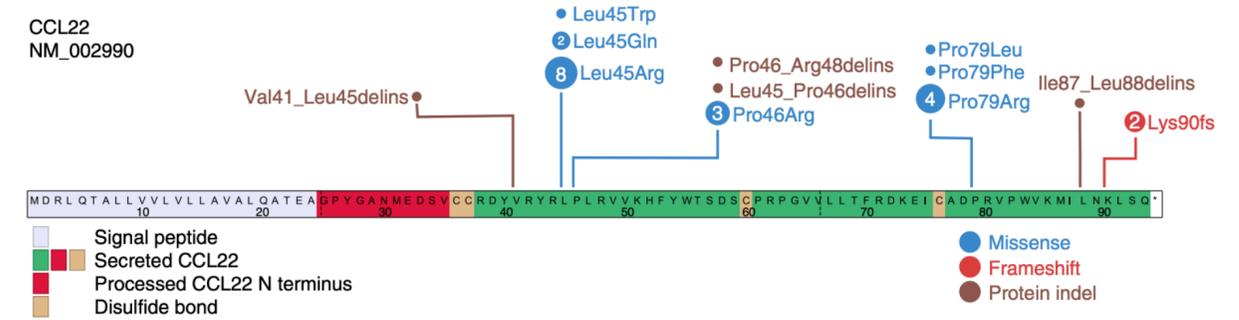
### Restriction répertoire KIR



### Expression forte et homogène CD94/NKG2A



## Mutations STAT3, TET2 et CCL22



# Leucémie prolymphocytaire T

- Leucémie T mature agressive
- Présentation clinique
  - Hyperlymphocytose extrême
  - Anémie, thrombopénie
  - Hépatosplénomégalie
- CMF : CD3+, CD4+, CD8+/-, CD52+

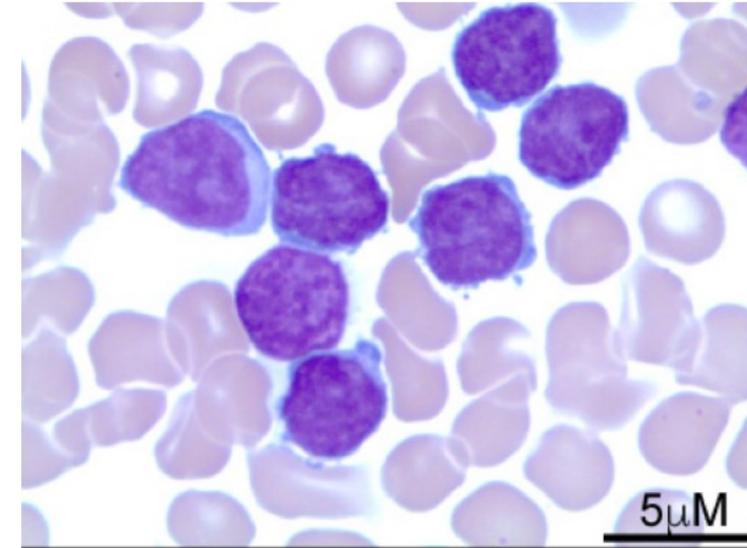


Table 2. Major and minor diagnostic criteria for T-PLL defined by TPLL-ISG \*.

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## Major Criteria

---

1.  $>5 \times 10^9$  /L cells of T-PLL phenotype in peripheral blood or bone marrow
  2. T-cell clonality (by polymerase chain reaction for T-cell receptor beta or gamma, or by flow cytometry)
  3. Abnormalities of 14q32 or expression of *TCL1A/B* or *MTCP1*
- 

## Minor Criteria

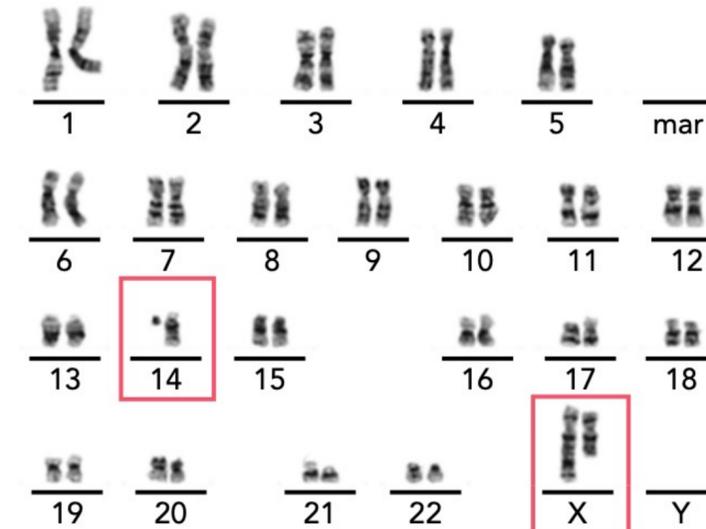
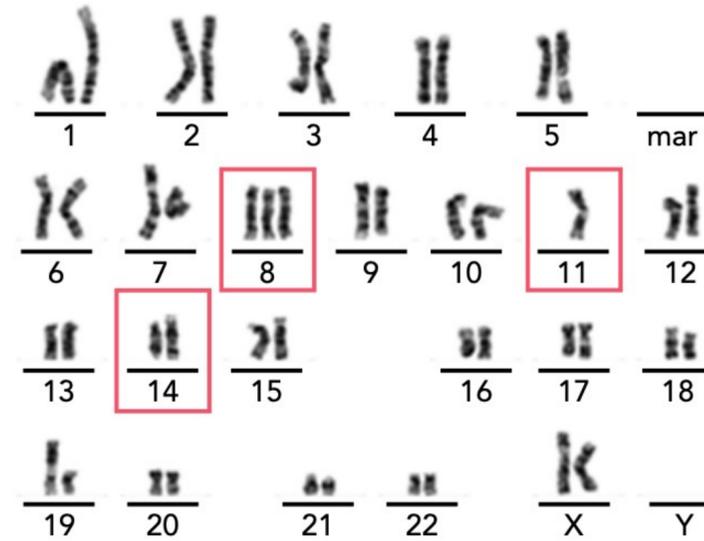
---

1. Abnormalities of chromosome 11 (11q22.3, *ATM*)
  2. Abnormalities of chromosome 8 [idic(8)(p11), t(8;8), or trisomy 8(q)] chromosome 5, 12, 13, or 22
  3. Complex karyotype
  4. Involvement of T-PLL specific site (e.g., splenomegaly or pleural effusions)
-

# Leucémie prolymphocytaire T

## Cytogenetic features

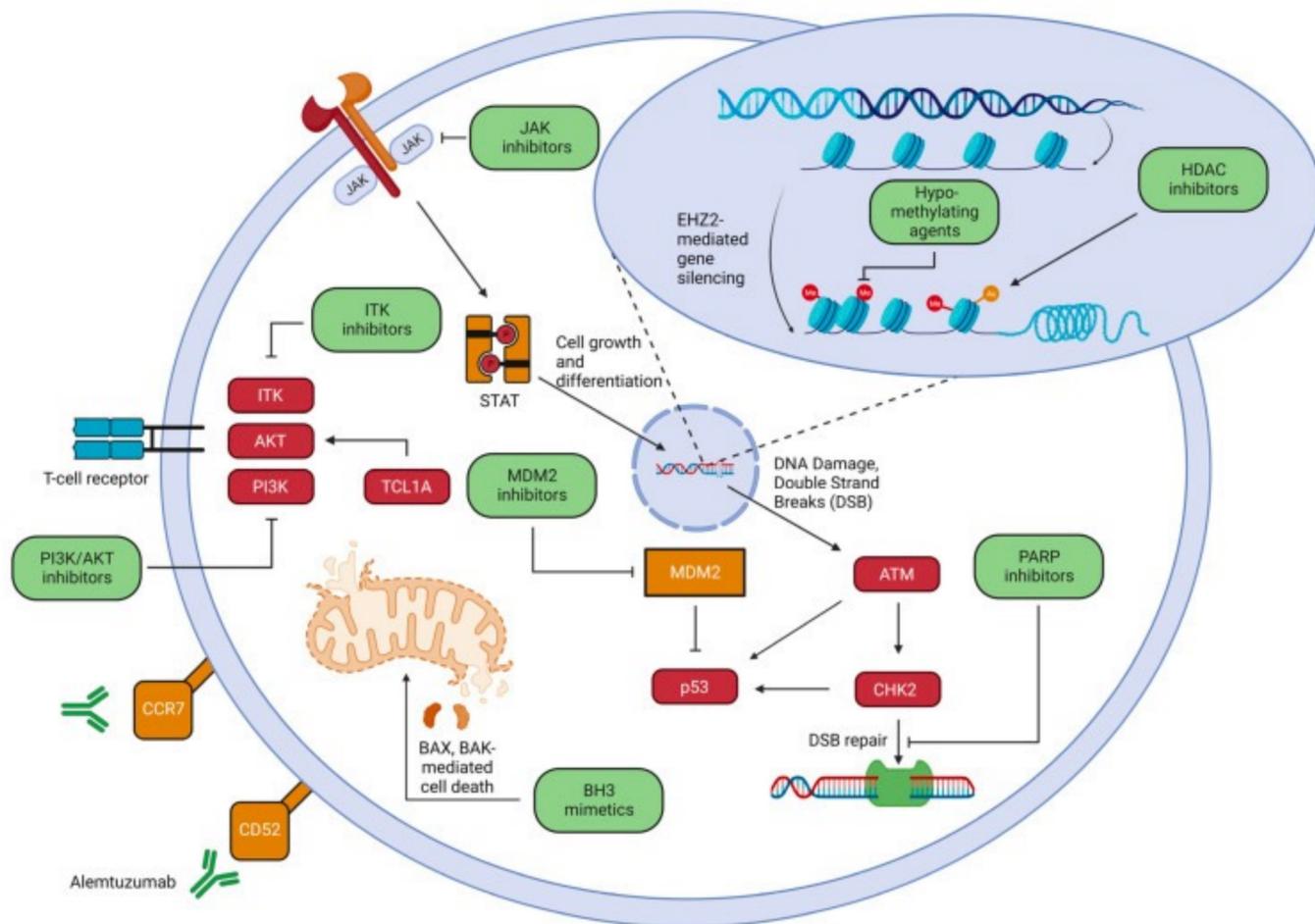
(inv14)(q11;q32.1) or t(14;14)(q11;q32.1)/total cases analyzed (%)	24/60 (40.0)	<b>TCL1 hyperexpression</b>
Trisomy 8 or isochromosome 8q/total cases analyzed (%)	21/60 (35.0)	
-11 or deletion 11q22-23/total cases analyzed (%)	20/60 (33.3)	
-17 or isochromosome 17q or deletion 17p/total analyzed cases	8/60 (13.3)	



46,XX,der(7;11)(q10;q10),der(8)t(8;11)(p11;p11),  
+der(8)t(8;11)(p11;p11),inv(14)(q11q32),  
der(19)t(3;19)(q21;p13)

46,X,t(X;14)(q28;q11.2),inv(10)(p12q21)

**NGS : STAT5B, ATM mutations**



# Lymphomes/Leucémies T : synthèse

- Intérêt majeur de la clonalité T
  - *TCRG* en première intention
  - *TCRB* si doute diagnostique (+/- *TCRD* si suspicion de lymphome TGD)
- Intérêt du NGS
  - Leucémies LGL (STAT3, STAT5B, TNFAIP3, CLL22, TET2...)
  - Leucémie prolymphocytaire T (STAT5B, ATM)
  - Autres lymphomes (hors lymphocytose)

		PTCL-NOS	AITL	ALCL	HSTL	NKTCL	EATL	MEITL	Sezary	ATLL
apoptosis	TP53									
epigenetics	DNMT3A									
	TET2									
	IDH2									
signalling pathways	STAT5B									
	STAT3									
	RHOA									
	PLCG1									
	JAK3									
	CD28									
	CARD11									

# Conclusion

- Hyperlymphocytose est une situation fréquente
- Eliminer les causes réactionnelles
- Essor des indications de la biologie moléculaire (prise en charge des patients?)

