

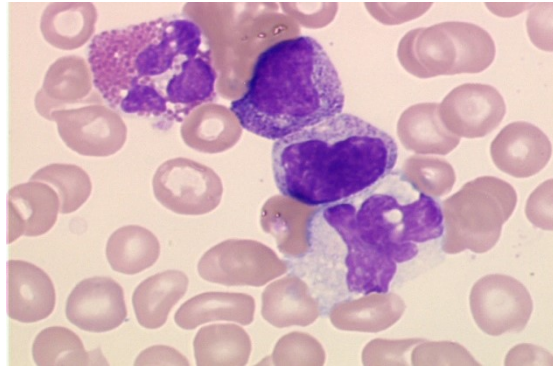
A novel t(3;13)(q13;q12) translocation fusing FLT3 with
GOLGB1: toward myeloid/lymphoid neoplasms with
eosinophilia and rearrangement of FLT3?

Gachard N

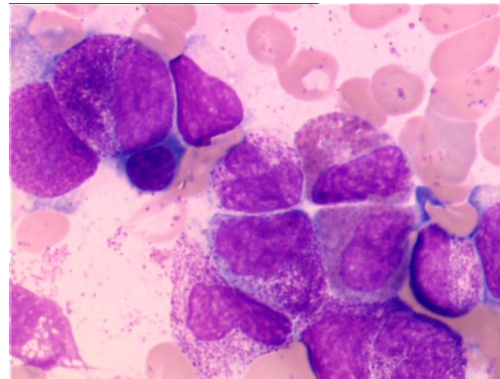
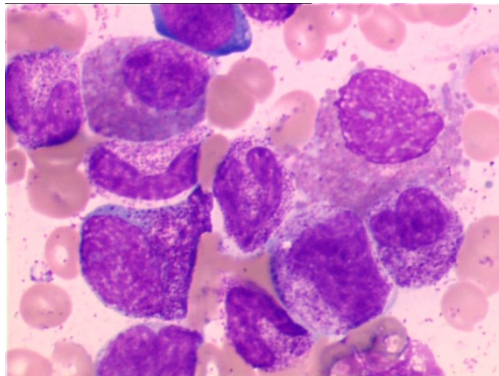
GFCH Oct 2017

Observation clinico-biologique

- ♀ 71 ans, hyperleucocytose, PNN 28G/L, PNE 1G/L, mono 5G/L.



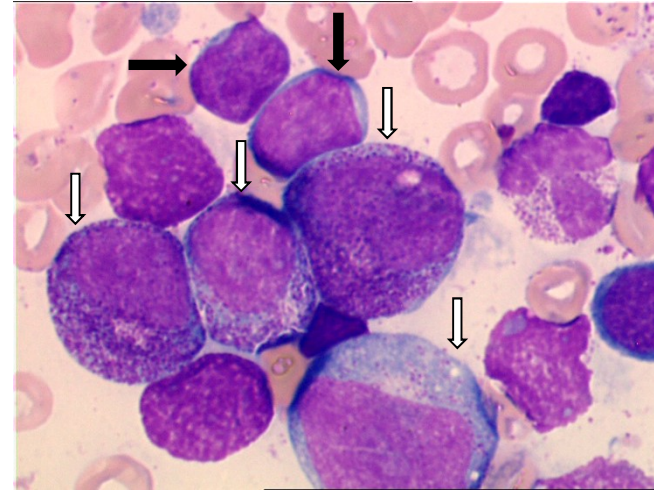
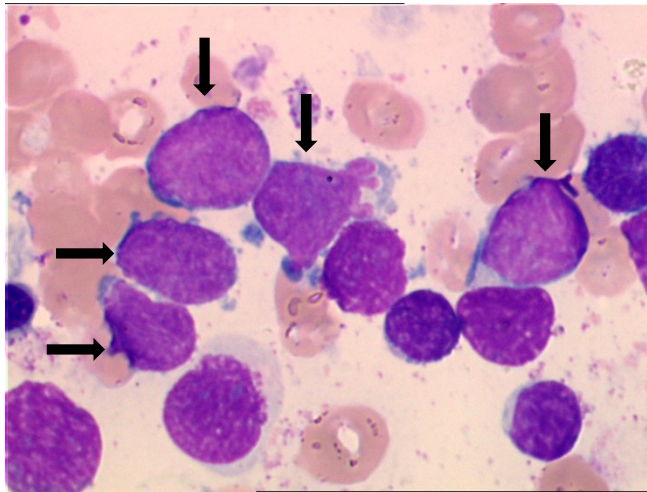
- Myélogramme : hyperplasie granuleuse, hyperéosinophilie, sans excès de blastes, Bcr/Abl négatif → SMP atypique



- La patiente est initialement en abstention thérapeutique.

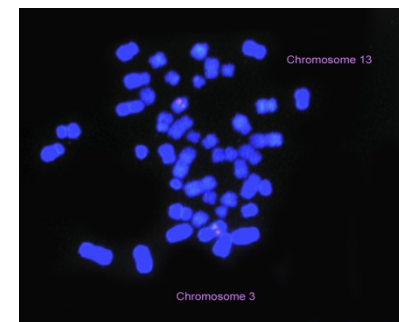
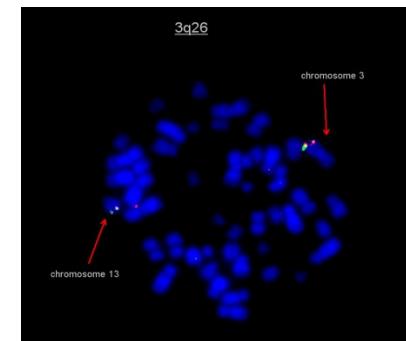
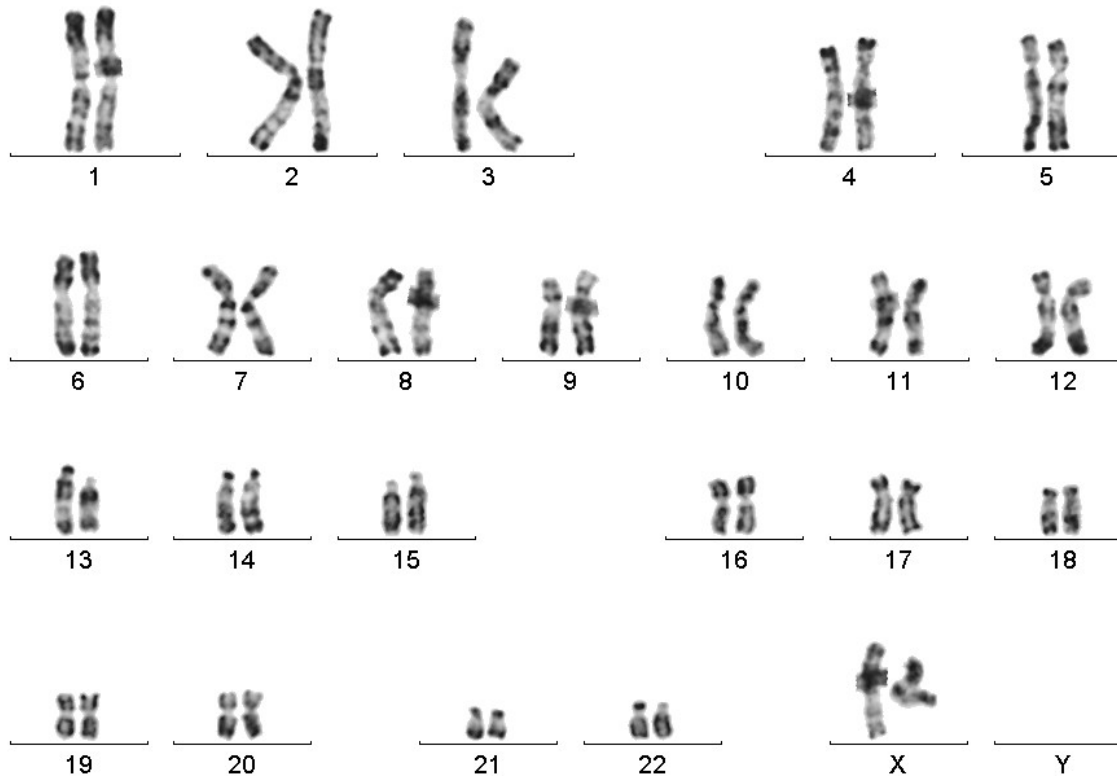
Observation clinico-biologique

- Deux mois après, sd tumoral majeur avec polyadénopathie HMG
- Biopsie ganglionnaire : lymphome lymphoblastique T.
BOM, myélogramme : SMP atypique + amas lymphoïdes T.



- Une polychimiothérapie de type CHOP n'empêche pas l'évolution rapidement fatale par défaillance multiviscérale.

Caryotype

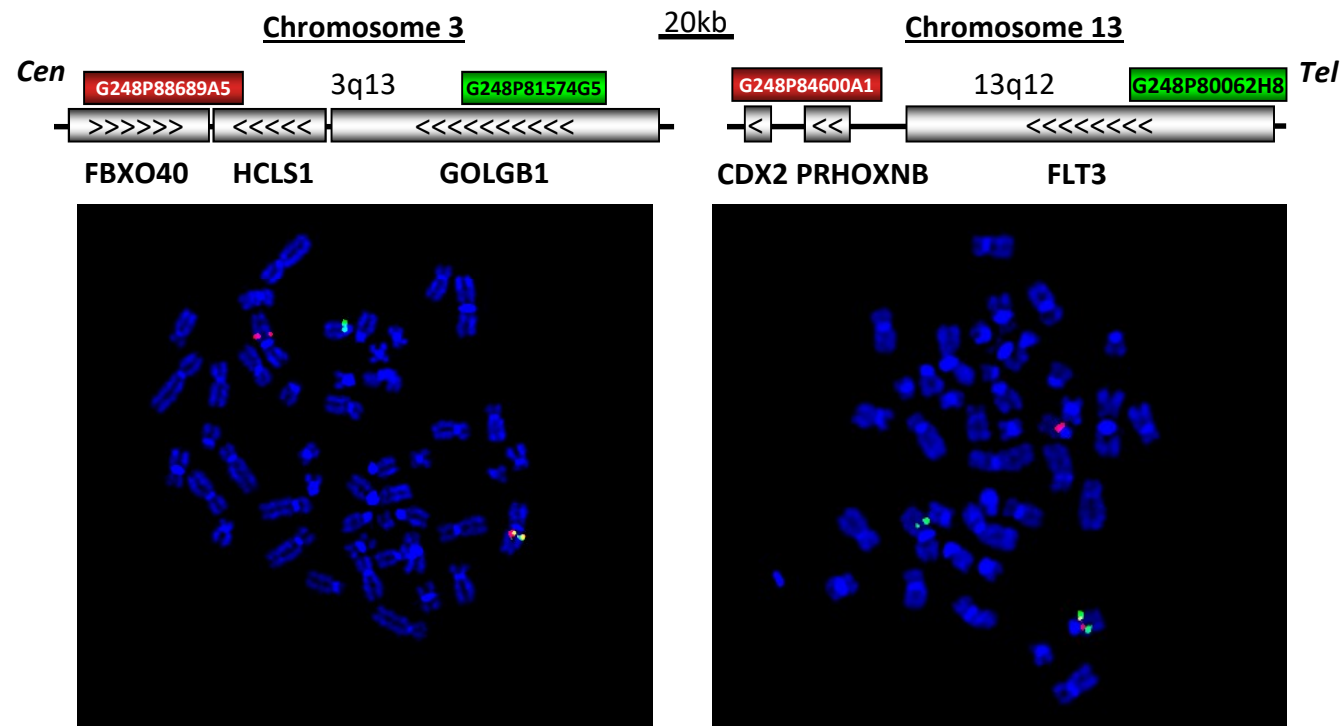


46,XX,t(3;13)(q13q12)[20] sur moelle et ganglion

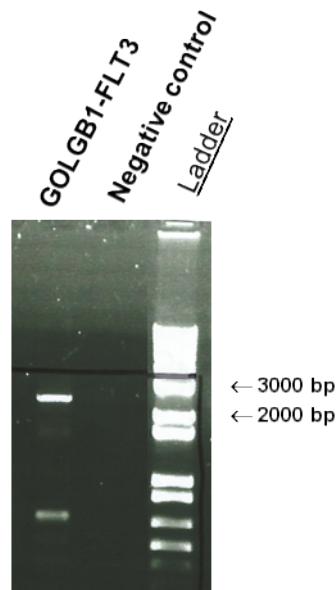
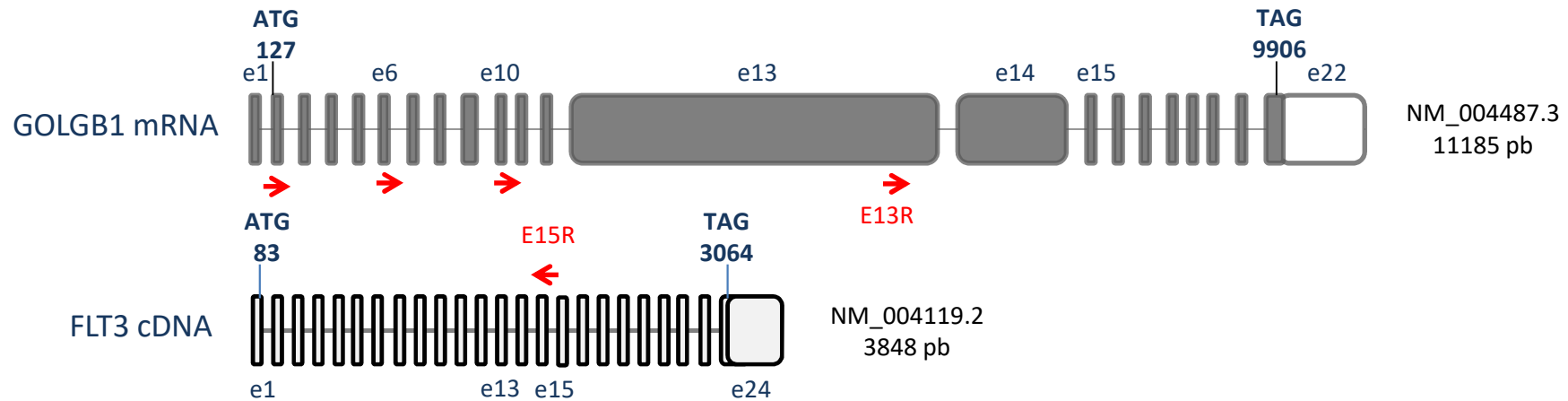
FISH : FIP1L1 PDGFRb FGFR1normaux

PCR FGFR1-ZNF198 négative

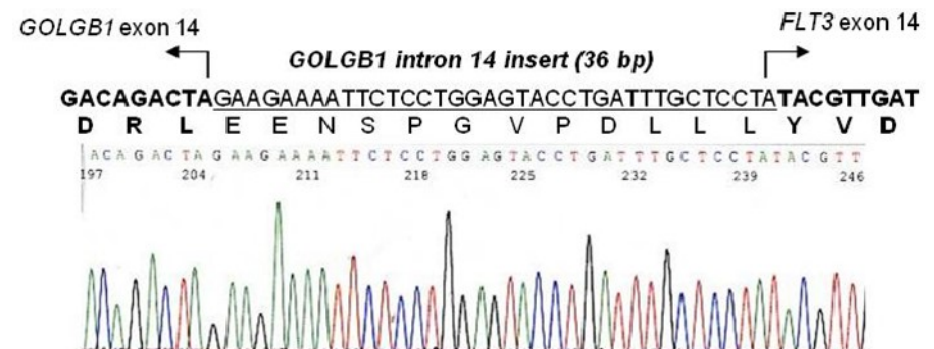
Recherche des points de cassures par FISH



Recherche des points de cassures par RT-PCR

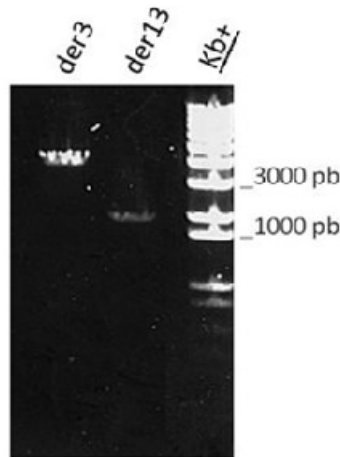


Séquençage de la jonction



Séquençage et clonage

Sur ADN
génomique



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5'- TTCTCCTGGAGTACCTGATTGCTCCTATATCAACCAGTGGCCCTGTACTCCTAG - 3' GOLGB1 intron 14
      |||||
5'- GACCGGCTCCTCAGATAATGAGTACTTCTATCAACCAGTGGCCCTGTACTCCTAG - 3' der(3)
      |||||
5'- GACCGGCTCCTCAGATAATGAGTACTTCTACGTTGATTTCAGAGAATATGAATATG - 3' FLT3 exon 14

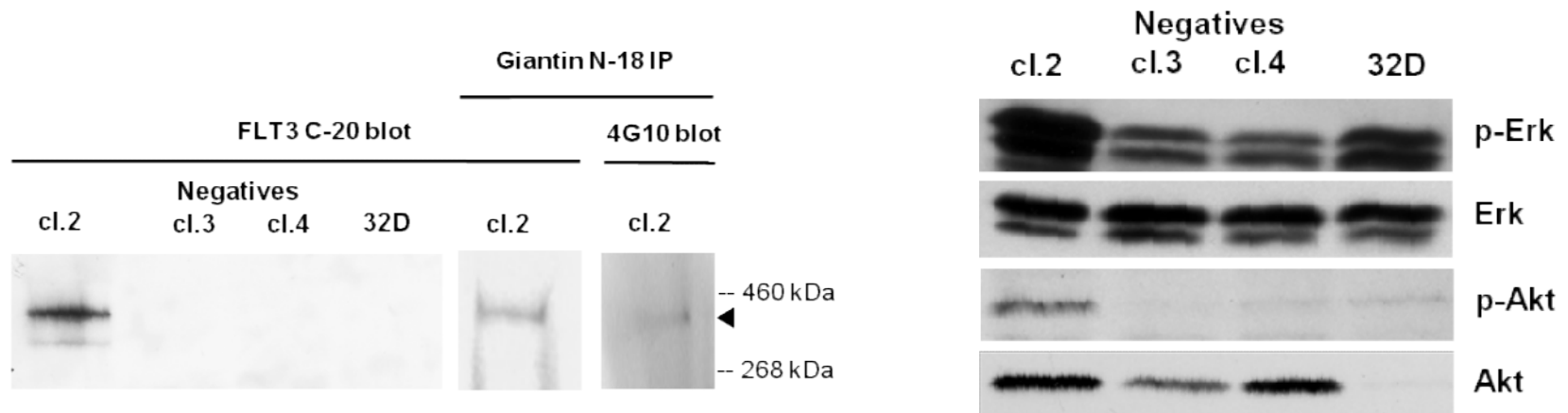
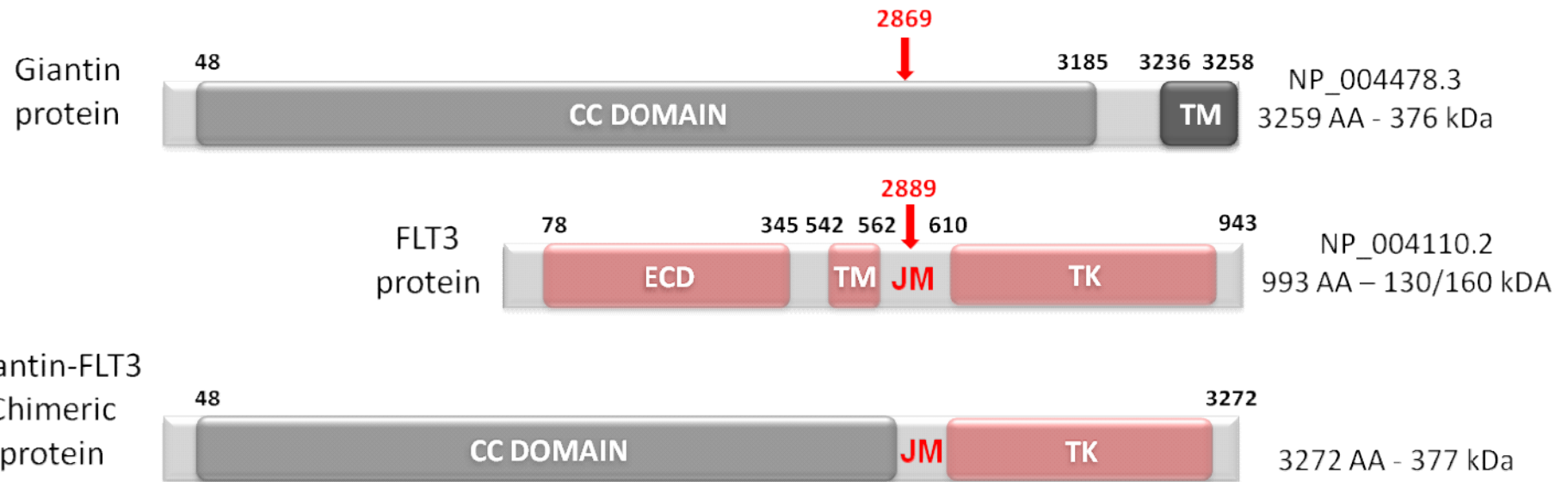
5'- TTCTCCTGGAGTACCTGATTGCTCCTATATCAACCAGTGGCCCTGTACTCCTAG - 3' GOLGB1 intron 14
      |||||
5'- TTCTCCTGGAGTACCTGATTGCTCCTATACGTTGATTTCAGAGAATATGAATATG - 3' der(13)
      |||||
5'- GACCGGCTCCTCAGATAATGAGTACTTCTACGTTGATTTCAGAGAATATGAATATG - 3' FLT3 exon 14
    
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Transcrit de fusion



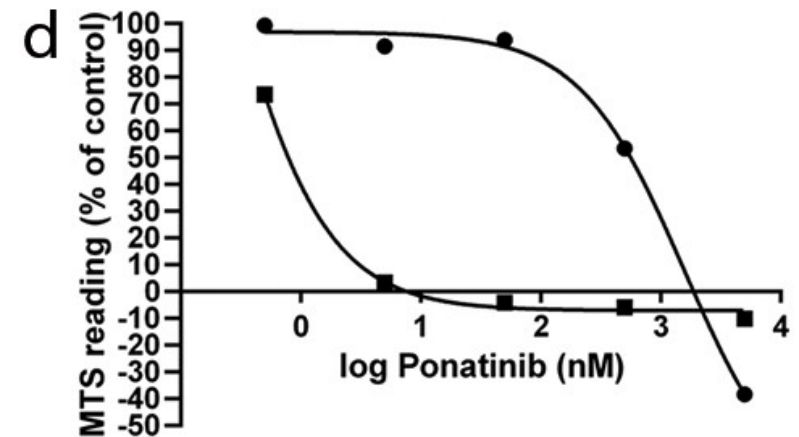
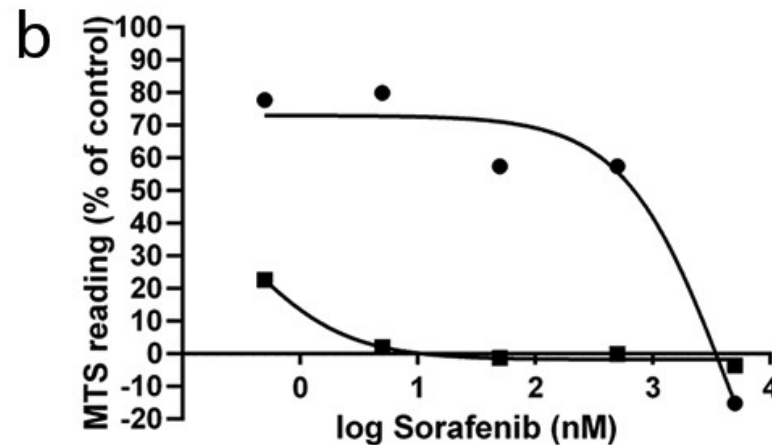
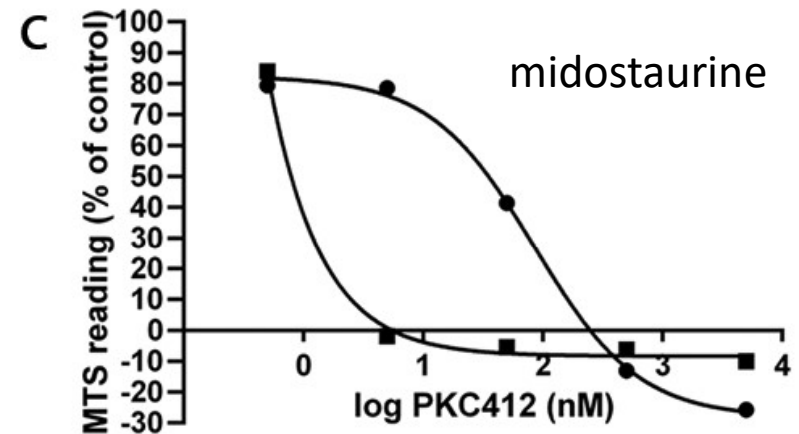
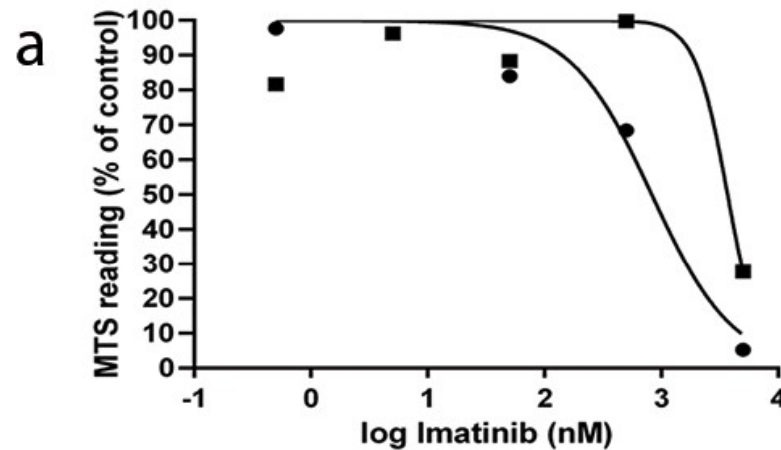
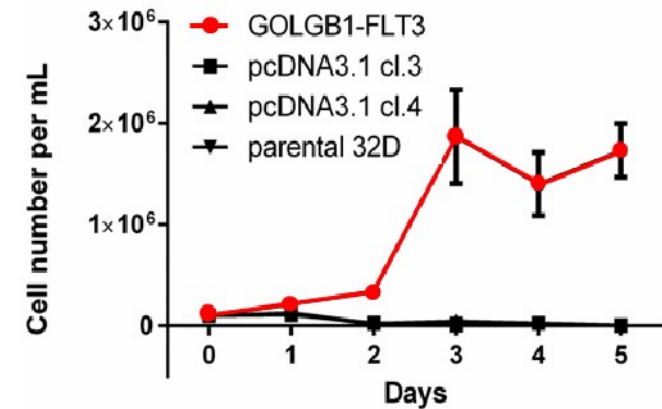
- Séquençage du transcrit : pas de mutation
- Amplification dans TOPO XL et clonage dans pcDNA3.1
- Transfection dans lignée myéloblastique 32D dépendante de l'IL3

Etude protéique



Culture in vitro

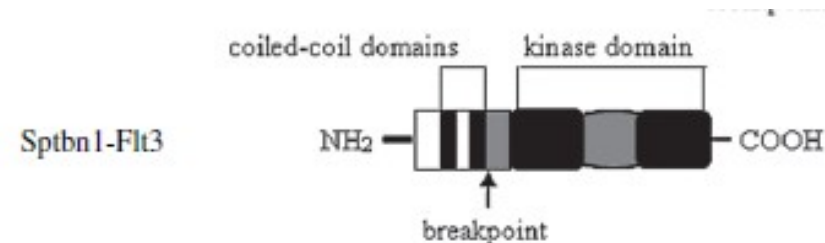
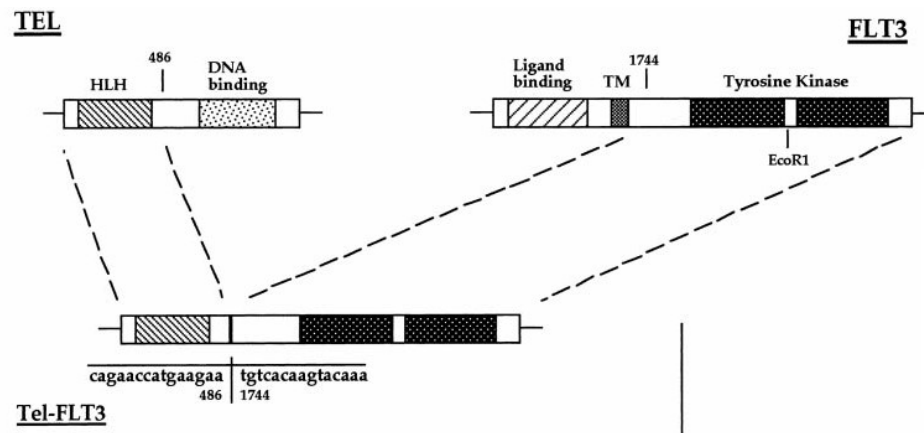
- Vecteur contenant le transcrit
- Vecteur vide



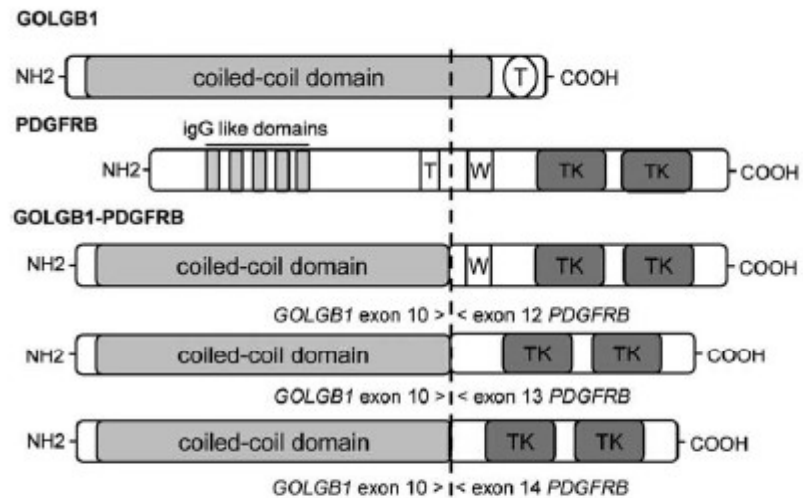
Les translocations impliquant FLT3

Number of cases	Sex	Age (years)	Diagnosis	Cytogenetics	RT-PCR	Sensitivity to new TKI
3 cases	3M	29 - 60	MLN-Eos + PTCL or T-LBL	t(12;13)(p13;q12)	ETV6 exon 4 to 6-FLT3 exon14	multikinase (sunitinib*)
2 cases	2F	68, 40	MLN-Eos	t(12;13)(p13;q12)	ETV6 exon 5-FLT3 exon14 or 15	multikinase (midostaurin [§]) (sorafenib*)
1 case	F	32	aCML	t(2;13;2;21)(p13;q12;q33;q11.2)	SPTBN1 exon 3 – FLT3 exon 13	anti-FLT3 (SU11657 [§]) anti-FGFR (Dovitinib [§])
1 case	M	46	aMPN + B ALL + systemic mastocytosis	t(13;13)(q12;q22)	Not done	Not evaluated
Our case	F	71	MLN-Eos + T-LBL	t(3;13)(q13;q12)	GOLGB1 exon 14 – FLT3 exon 14	Multikinase [§] (Sorafenib, Midostaurine, Ponatinib)

§ in vitro assay; * patient treated with the drug



t(3;5)(q13;q33) : GOLGB1-PDGFRB



D

