MOLECULAR TESTING FOR HEMATOLOGIC MALIGNANCIES

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OUTLINE

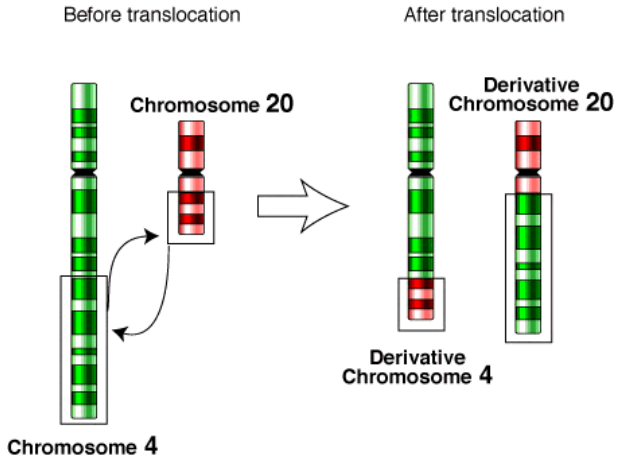
- Introduction (Understand Molecular Testing)
  - When we need to do molecular test (utility)
  - What can be measured (target)
  - How to measure (technology)
- Lymphoma
  - Case 1 – IGH and TCR rearrangement (clonality)
  - Case 2 – Specific translocations (quantitative)
- Myeloid Disorders – MPD, Leukemia, MDS
  - Case 3 – Specific translocations (fusion gene; qualitative)
  - Case 4 – Specific mutations for diagnosis
  - Case 5 – Next generation sequencing

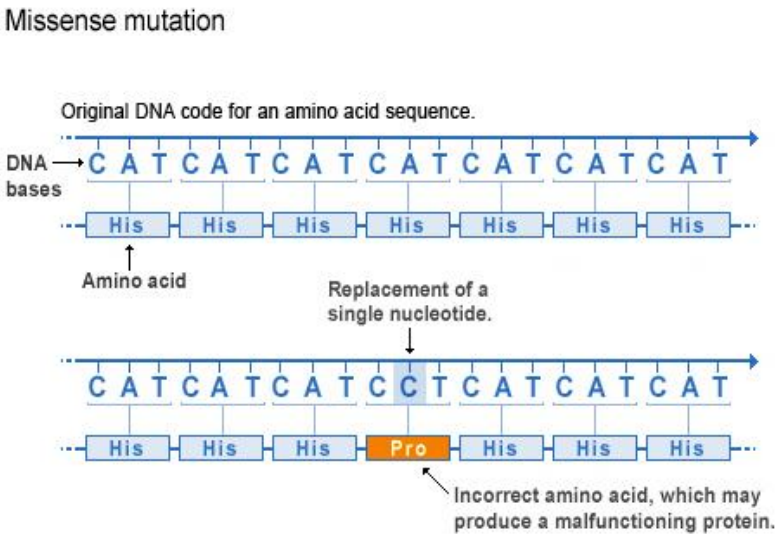
WHEN DO WE TEST – MAJOR INDICATIONS

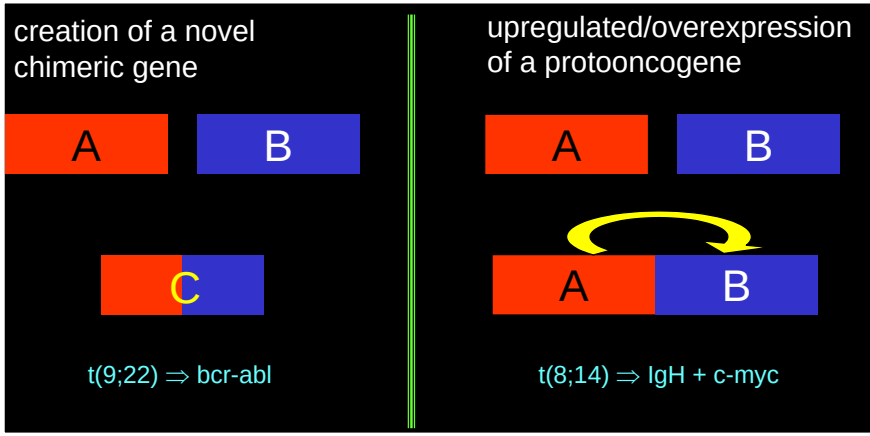
- Diagnosis
  - ✓ neoplastic vs. reactive (and beyond)
  - ✓ lymphoma
- Classification
  - ✓ based upon the genetic abnormalities – AML
- Prognosis
  - ✓ in otherwise homogeneous diseases – CN-AML
- Predictive – Therapeutic choice
  - ✓ Targeted therapy – CML, APL, and more
- Monitoring/MRD
  - ✓ Minimal residual disease monitoring for early recurrence detection – CML

WHAT TO TEST – MOLECULAR TARGETS

- Gene rearrangement (e.g. translocation)
- Mutations (point mutation, insertion, deletion)
- Gain and losses of genetic content
  - Trisomy, duplication, amplification
  - Monosomy, deletion, silencing



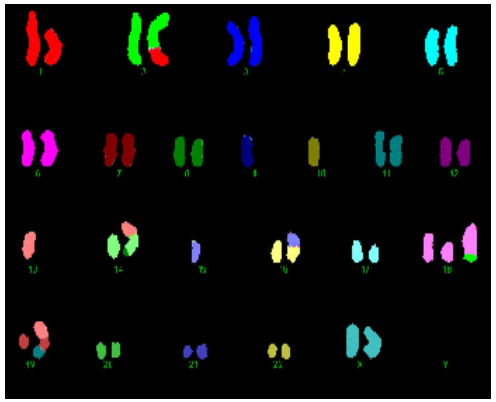


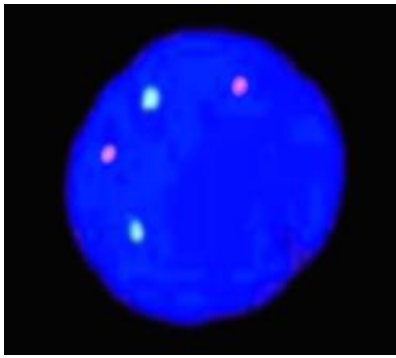


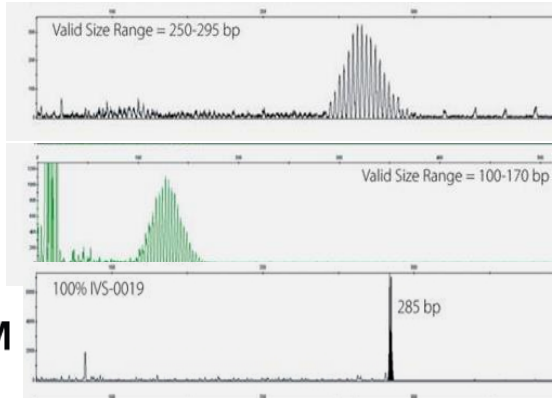
Qualitative Quantitative

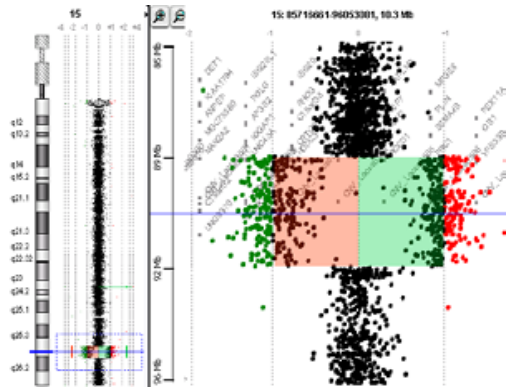
HOW TO TEST – TECHNIQUES

- Chromosomal analysis
  - Cytogenetics (karyogram)
  - FISH
  - Array
    - CGH (Comparative genomic hybridization)
    - SNP array
- Molecular analysis (DNA/RNA)
  - Southern blot
  - PCR based assay
    - Fragment analysis
    - Real-time PCR
    - Sequencing
  - Next Generation Sequencing









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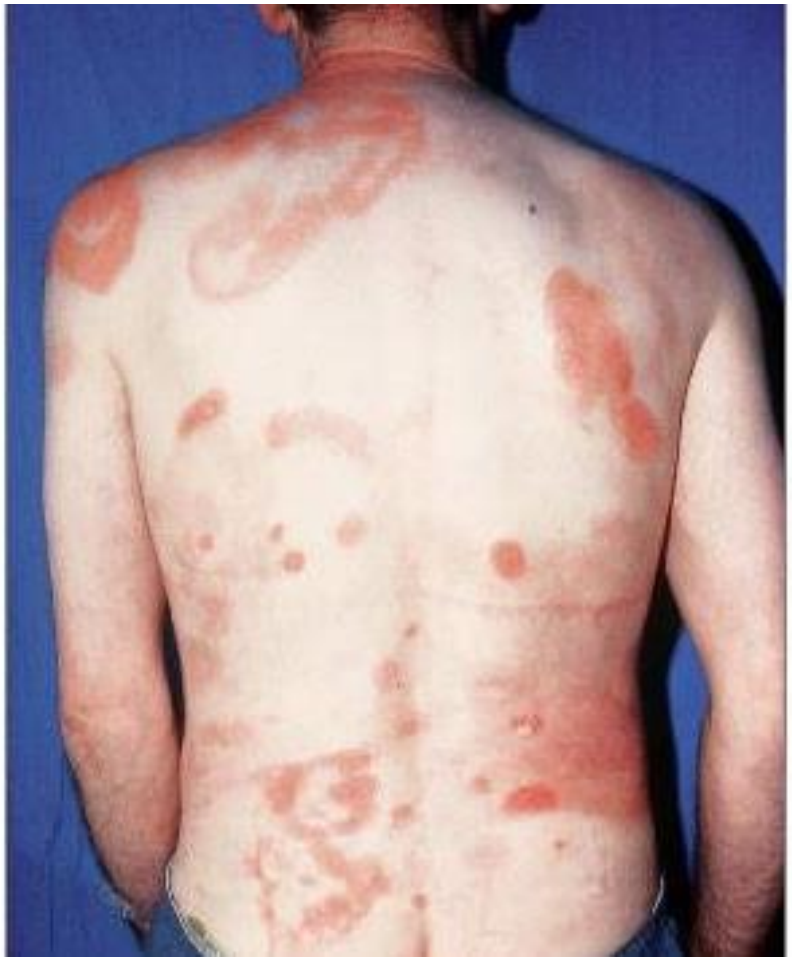
EXAMPLE 1: LYMPHOPROLIFERATIVE DISORDERS – NEOPLASTIC VS REACTIVE

47 year old male with erythematous, finely scaling lesions involving the trunk, buttocks and thighs, sparring .

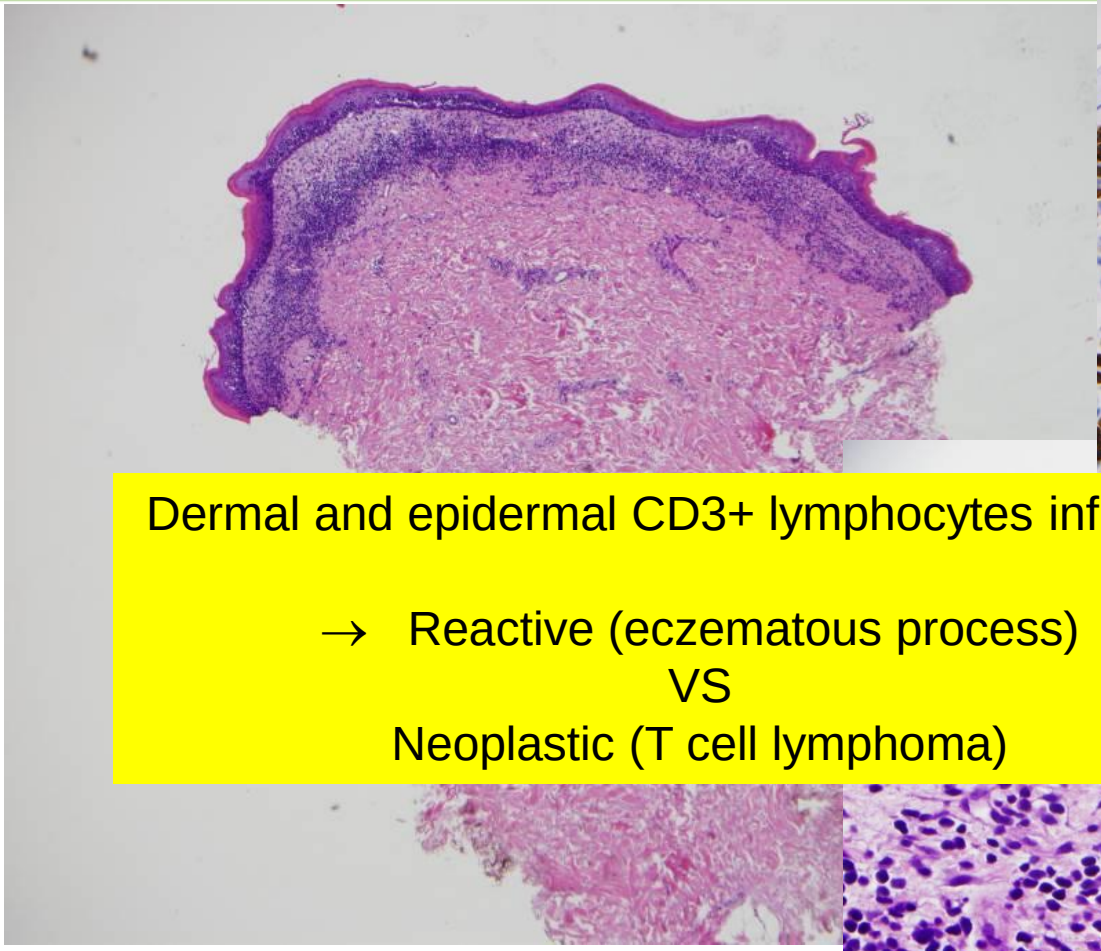
Present for one year and progressing slowly

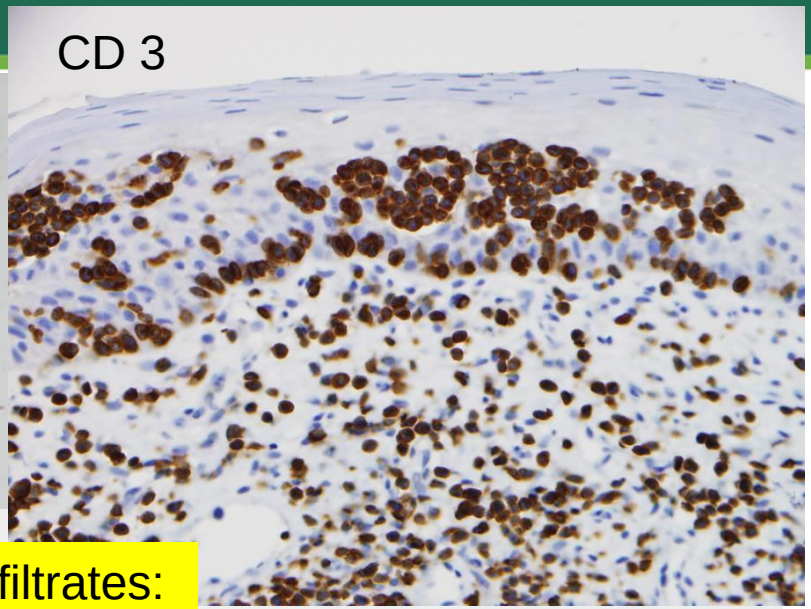
Mildly purpuric

Topical steroid treatment with no improvement



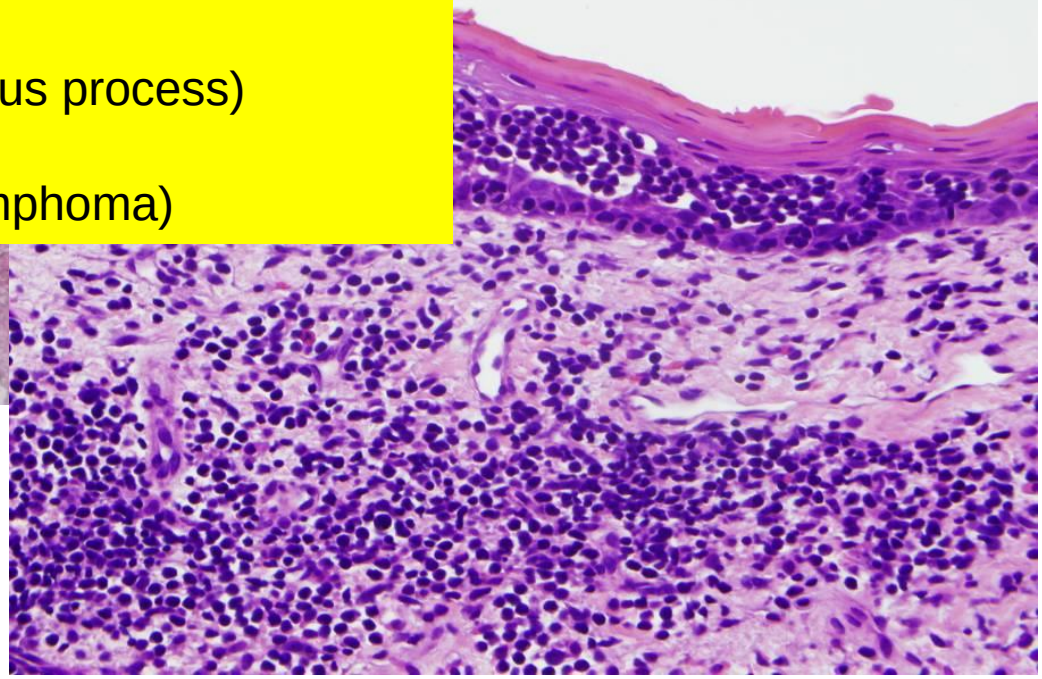
LYMPHOID LESION – SKIN BIOPSY



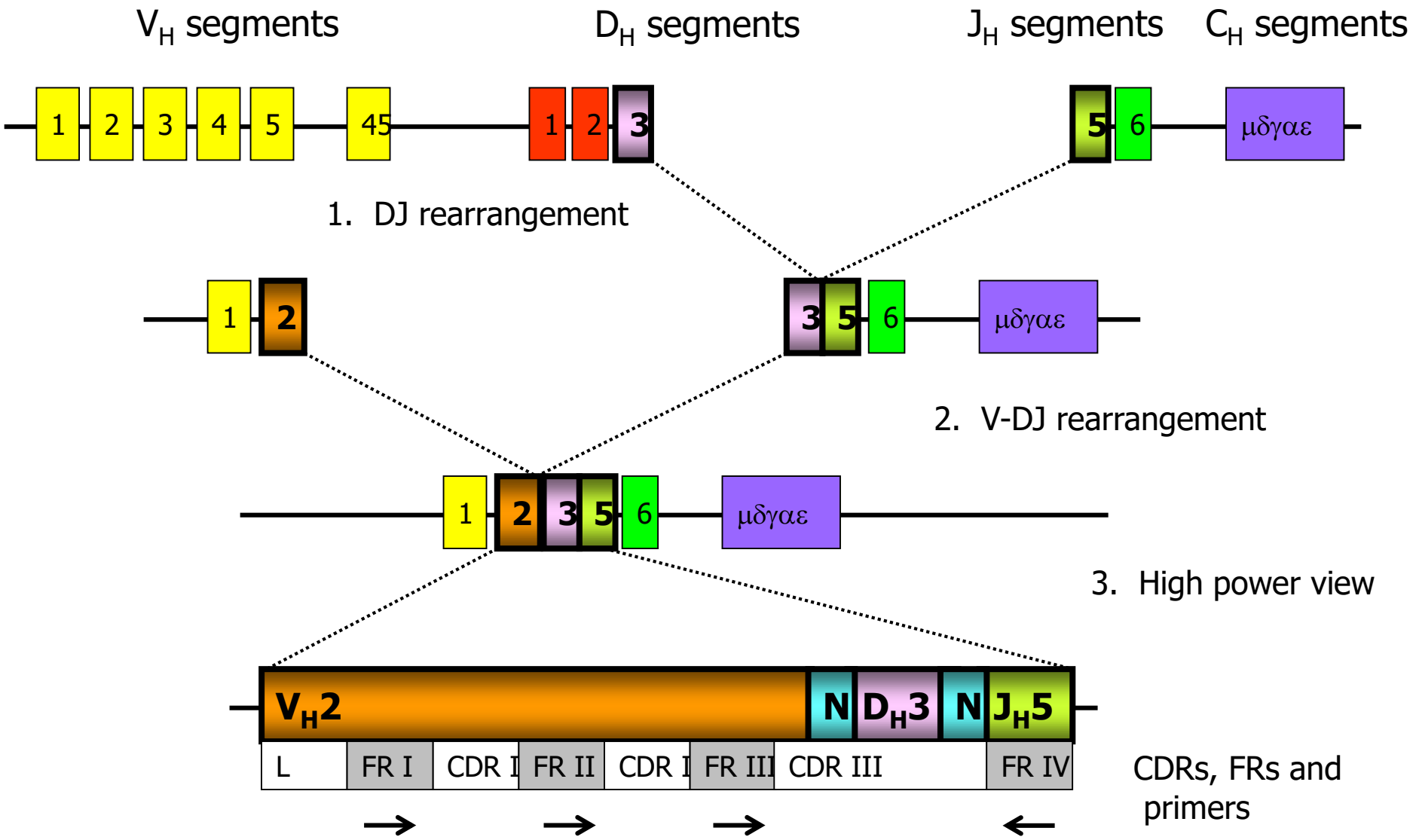


Dermal and epidermal CD3+ lymphocytes infiltrates:

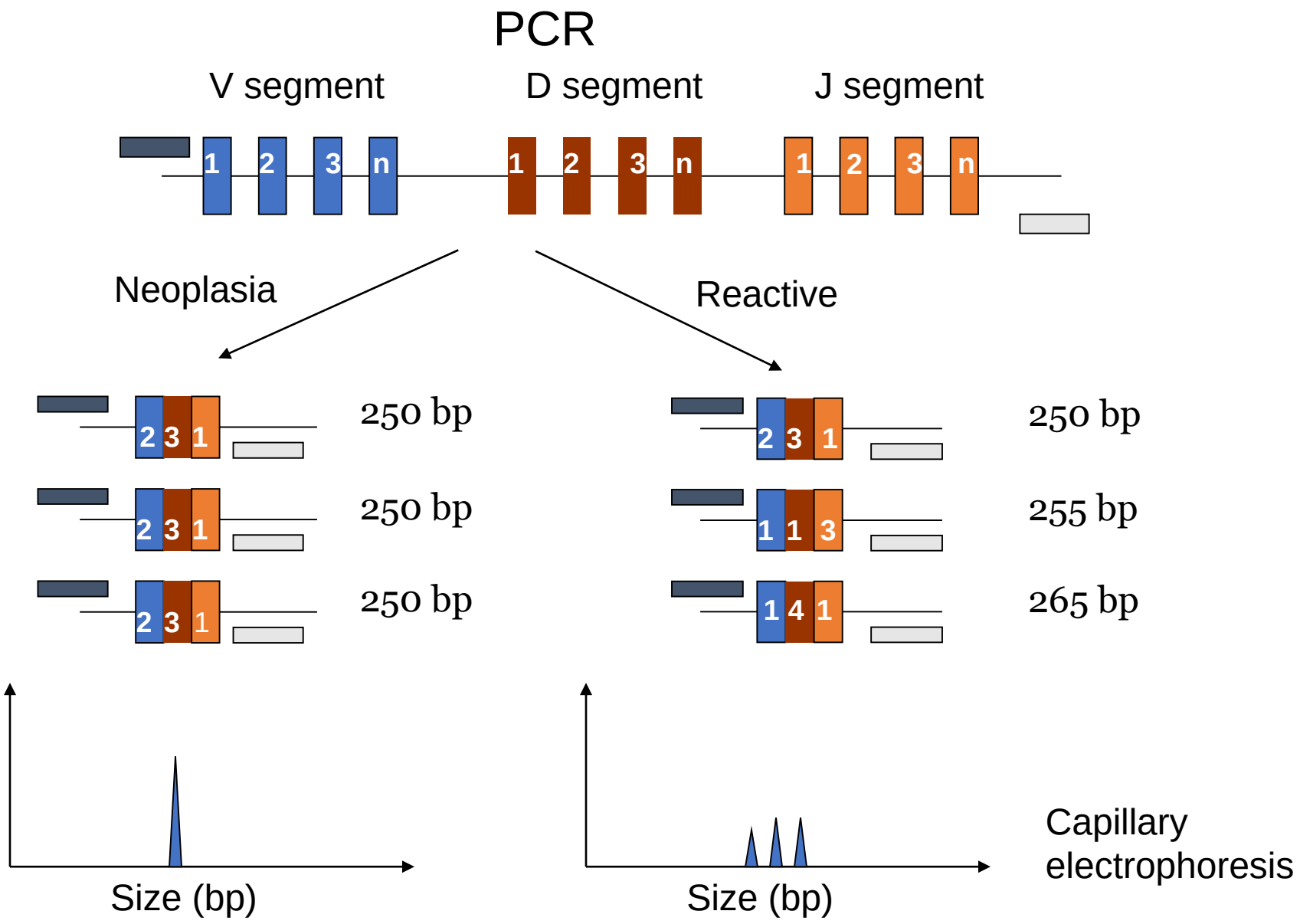
→ Reactive (eczematous process)
VS
Neoplastic (T cell lymphoma)



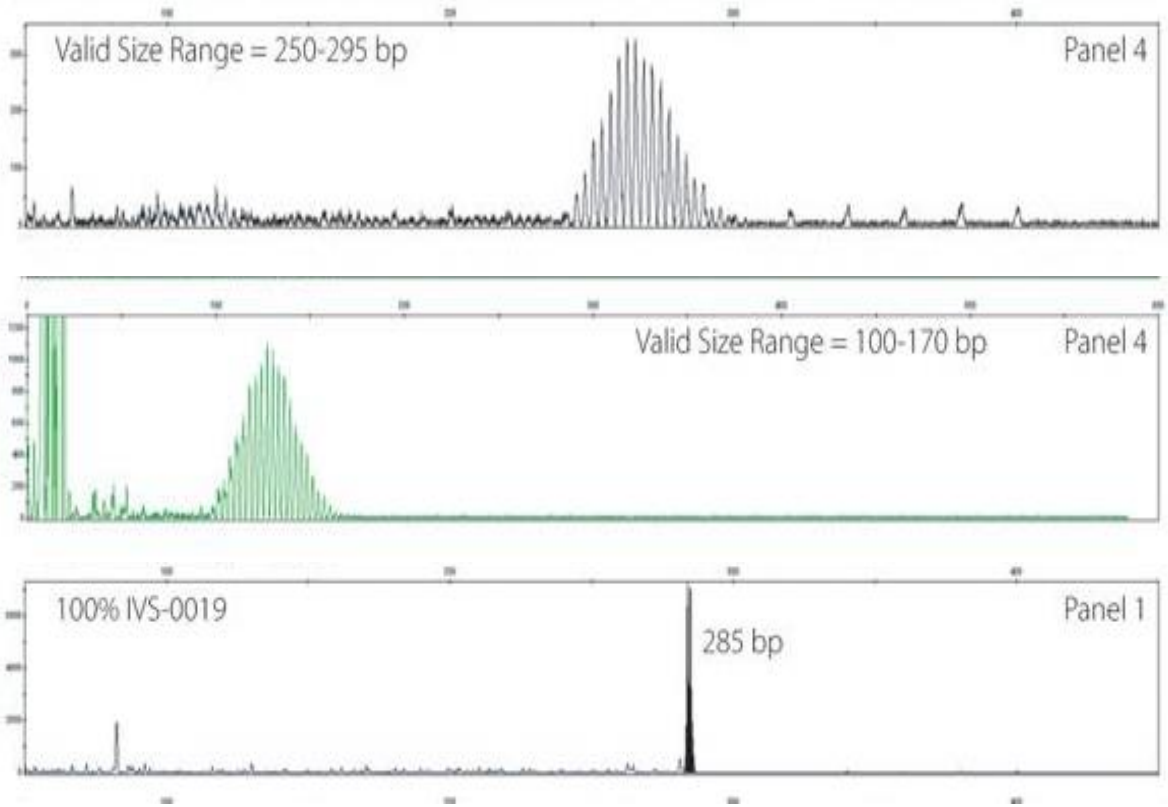
T CELL RECEPTOR GENE REARRANGEMENT

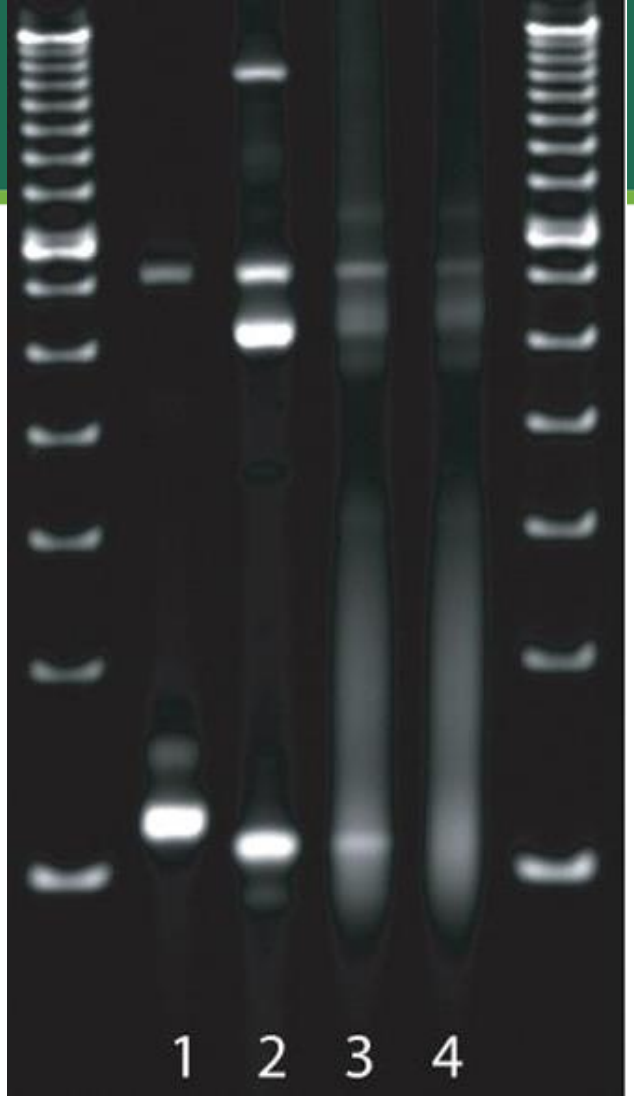


REACTIVE VS NEOPLASTIC



REACTIVE VS NEOPLASTIC (POLYCLONAL VS CLONAL)





1. Clonal
2. Clonal
3. 10% clonal
4. Non-clonal

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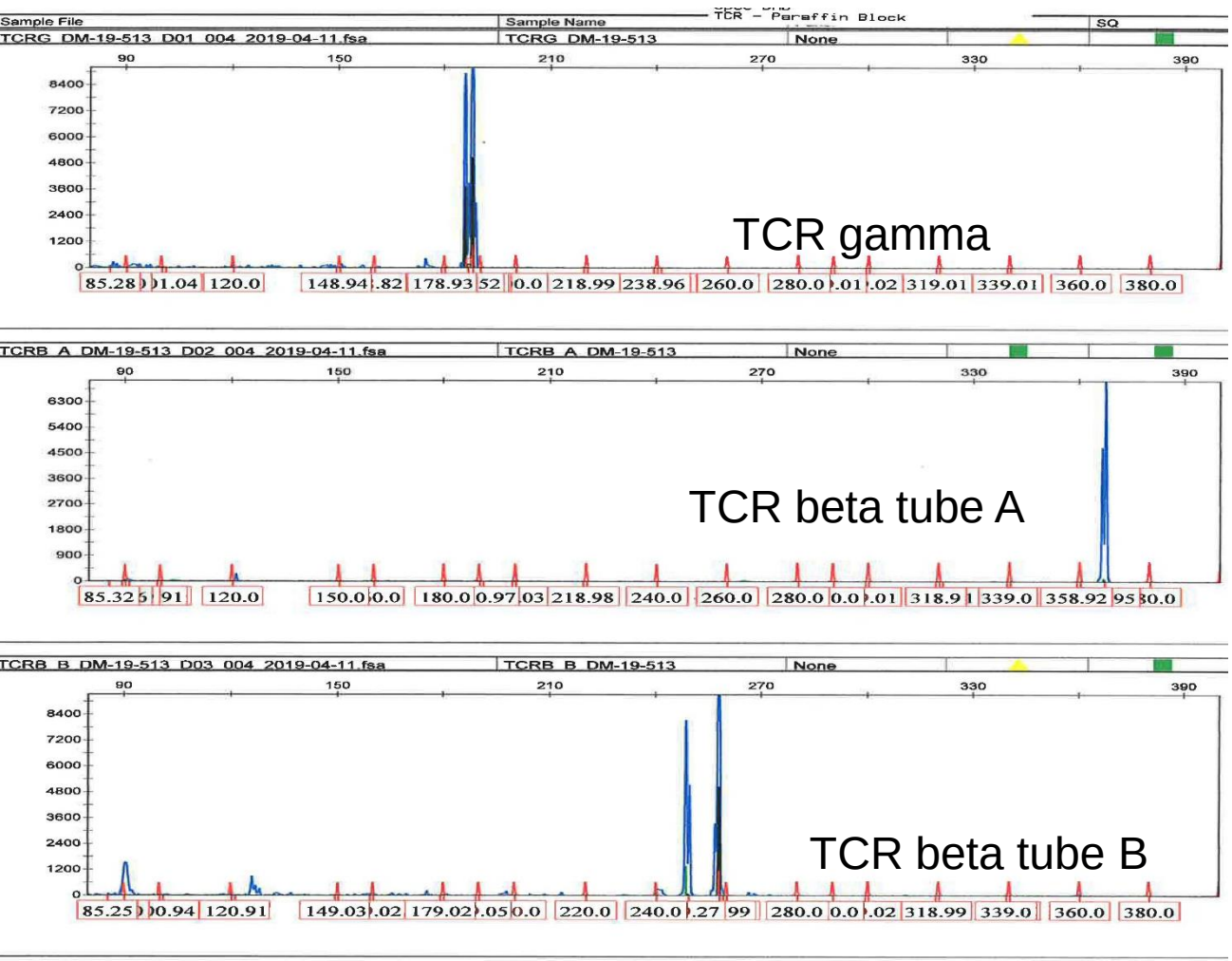
THIS CASE: NEOPLASTIC (LYMPHOMA)



- T cell receptor gene rearrangement – clonal
- Support the diagnosis of Primary cutaneous T cell lymphoma
- Useful in atypical lymphoproliferation with limited tissue
- Not useful in diagnosing specific entities

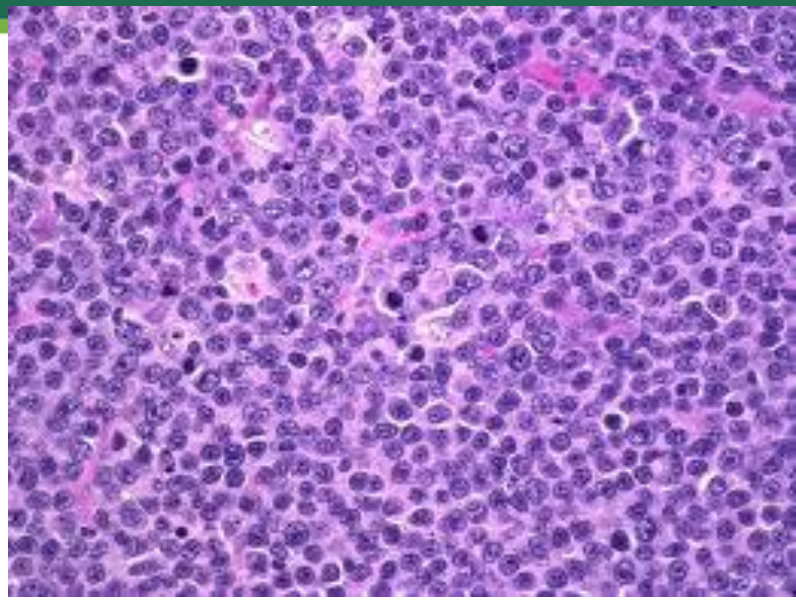
EXAMPLE 2: LYMPHOMA - "QUANTITATIVE" REARRANGEMENT

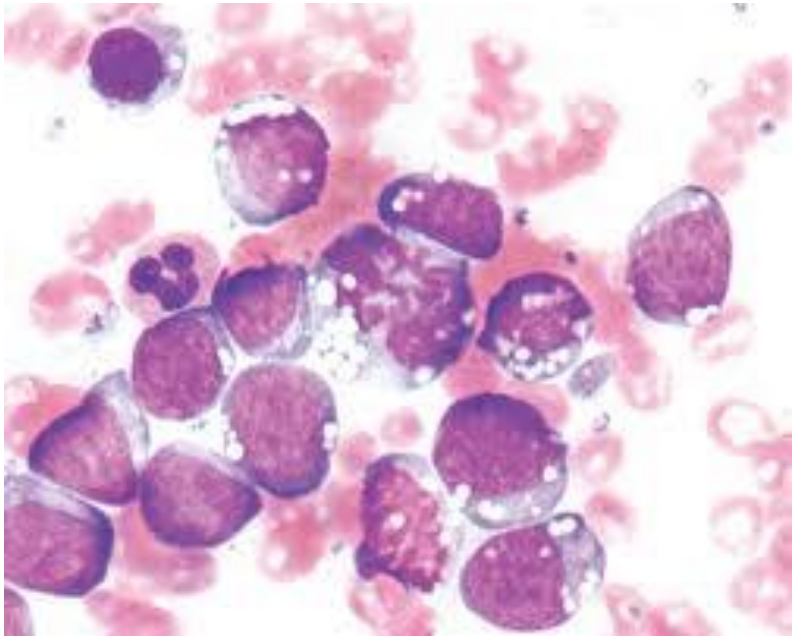
24 year old male with a history of HIV, worsening lymphadenopathy and a new left orbit mass.

Orbit biopsy: extensive infiltrate of mid-size lymphocytes.
BCL6, CD10, CD20 positive; CD5 negative
Ki-67 ~100%, EBER positive

Diagnosis?

What test do you want to order?





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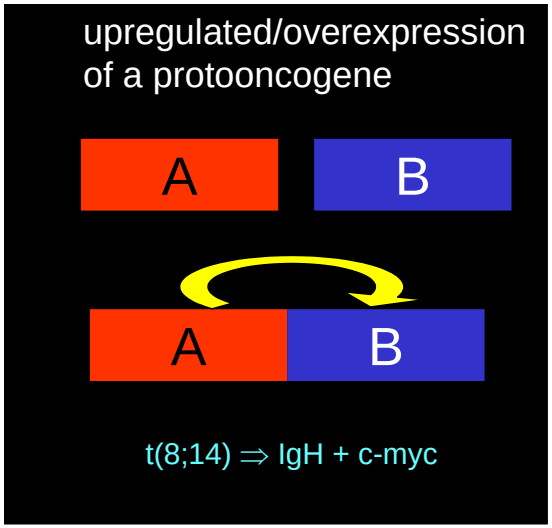
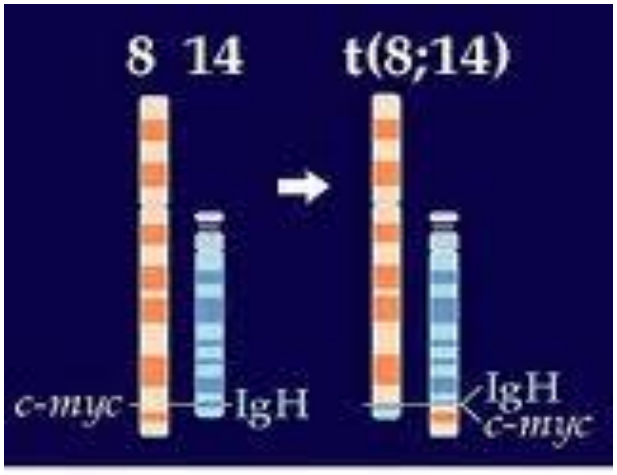
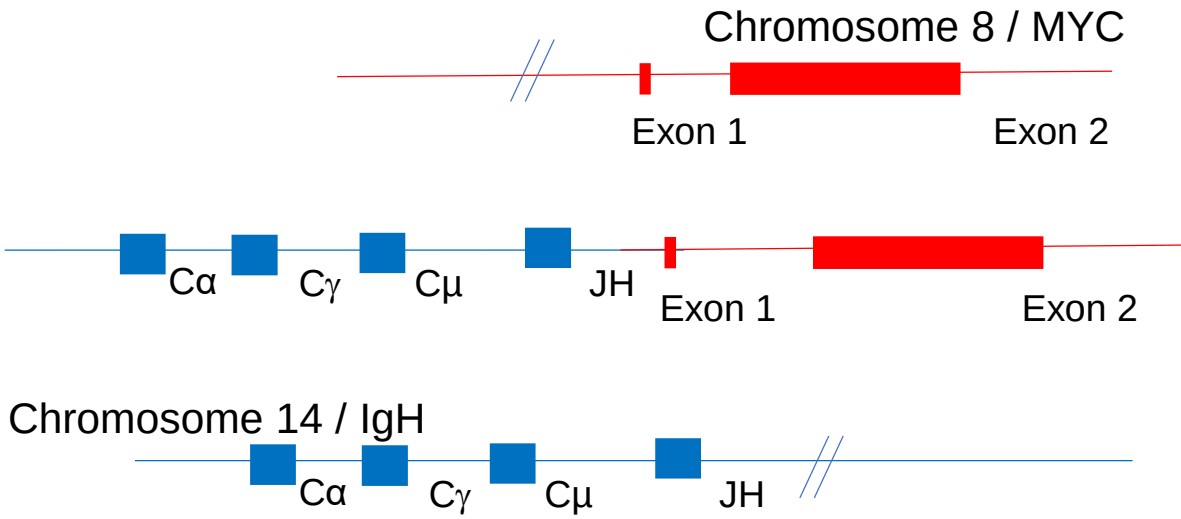
BURKITT LYMPHOMA

- Proto-oncogene *MYC* translocated to Immunoglobulin gene during VDJ recombination, class switching, or somatic hypermutation.
- Controlled by Ig regulatory apparatus, leading to overproduction of protein (c-myc))
- All cases carry translocation between chromosome 8 and 14q32[IgH], 2[kappa] or 22[lambda].



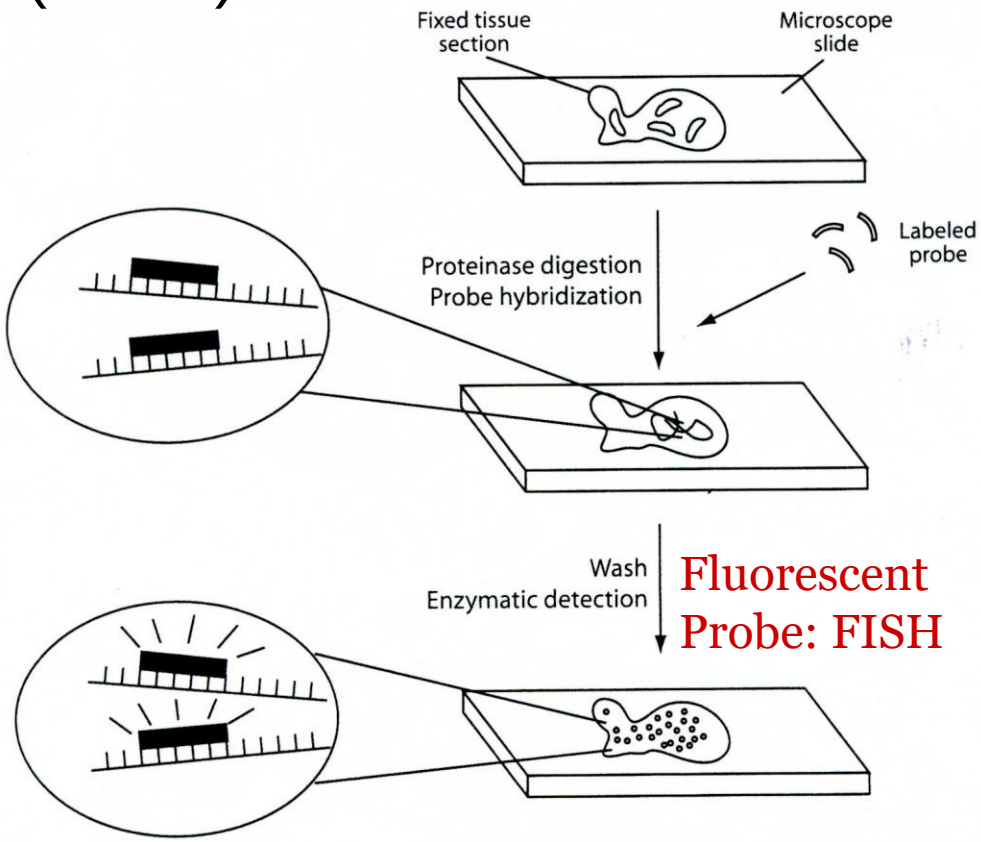




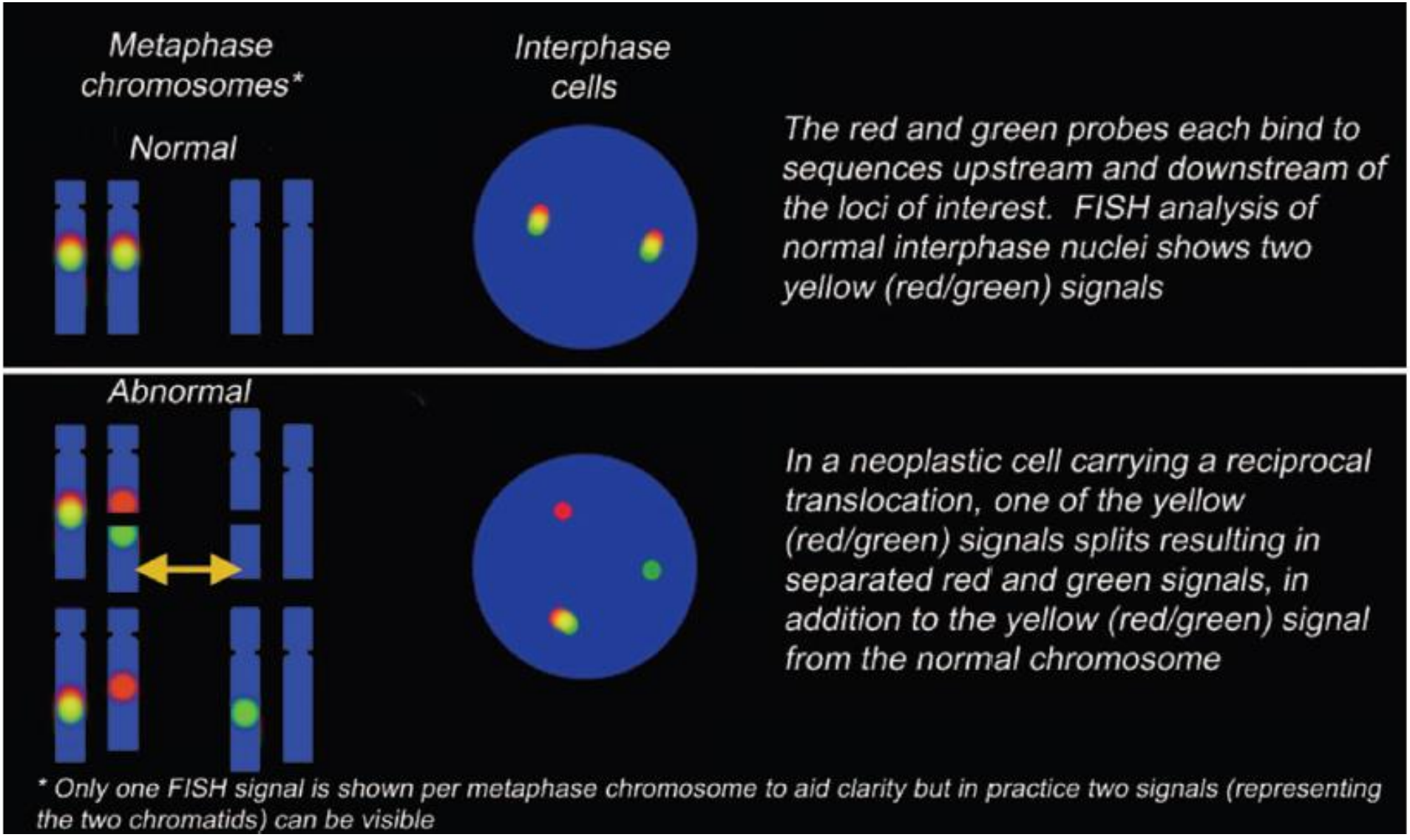
FLUORESCENT IN SITU HYBRIDIZATION (FISH)

- Use a **labeled** complementary DNA or RNA strand (probe) to localize a specific DNA or RNA sequence in a portion or section of tissue (*in situ*)

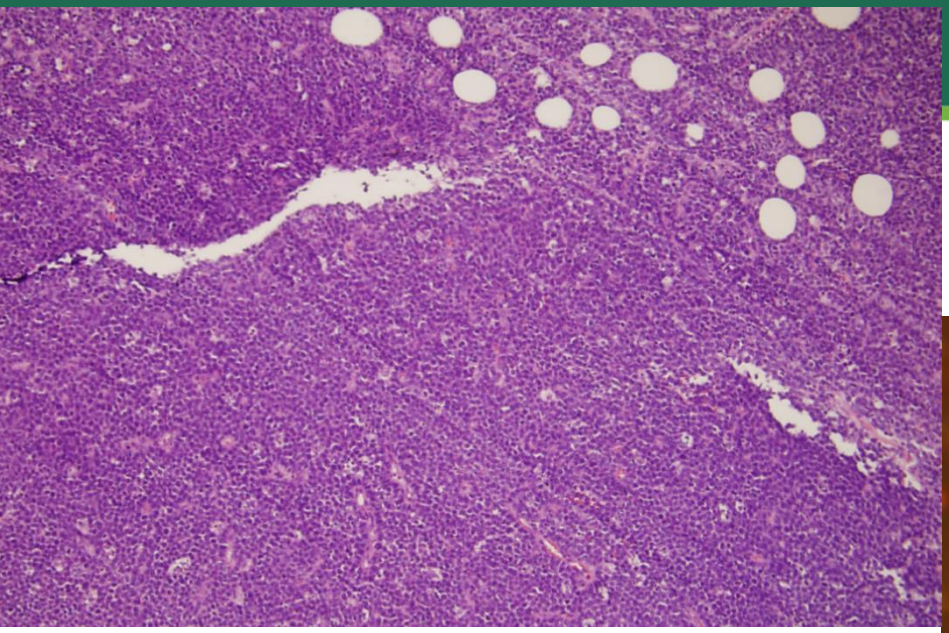
- Fluorescent probe for detection: FISH

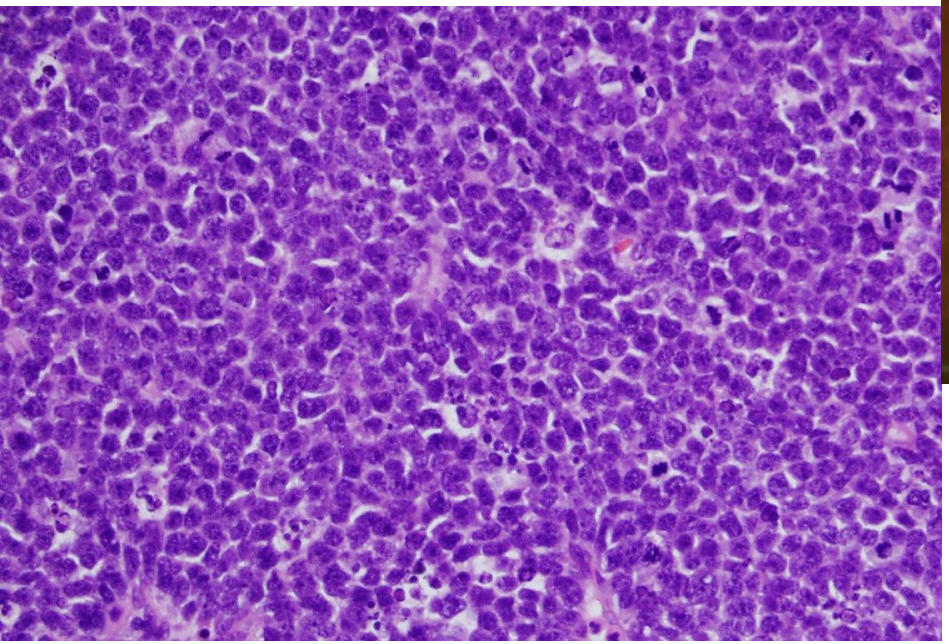


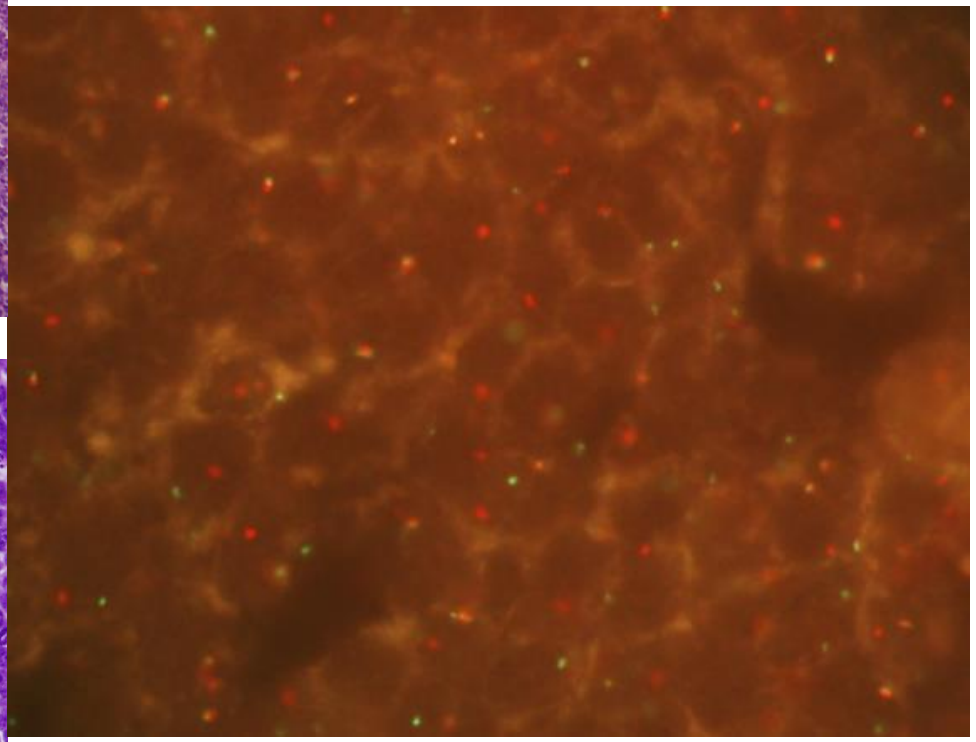
FISH - BREAK APART PROBES



THIS CASE: BURKITT LYMPHOMA







MYC FISH - positive for rearrangement

COMMON ABNORMALITIES IN LYMPHOMA

Mantle cell lymphoma	t(11;14)(q13;q32)	*CCND1 (BCL1)-IGH*
Follicular lymphoma	t(14;18)(q32;q21)	*IGH-BCL2*
MALT/MZL	t(11;18)(q21;q21)	*API2-MALT1* - stomach
	t(14;18)(q32;q21)	*IGH-MALT1*
	also trisomy 3	
DLBL	t(14;18) 30%; abnormalities of 3q27 (BCL6)	
CLL/SLL	del(13q14) – miRNA, 55%, best	
	+12 – ?CDK4, 16%, middle	
	del(11q22) – ATM, 18%, second worst	
	del(17p13) – TP53, 7%, worst	

EXAMPLE 3: LEUKEMIA – "QUALITATIVE" REARRANGEMENT

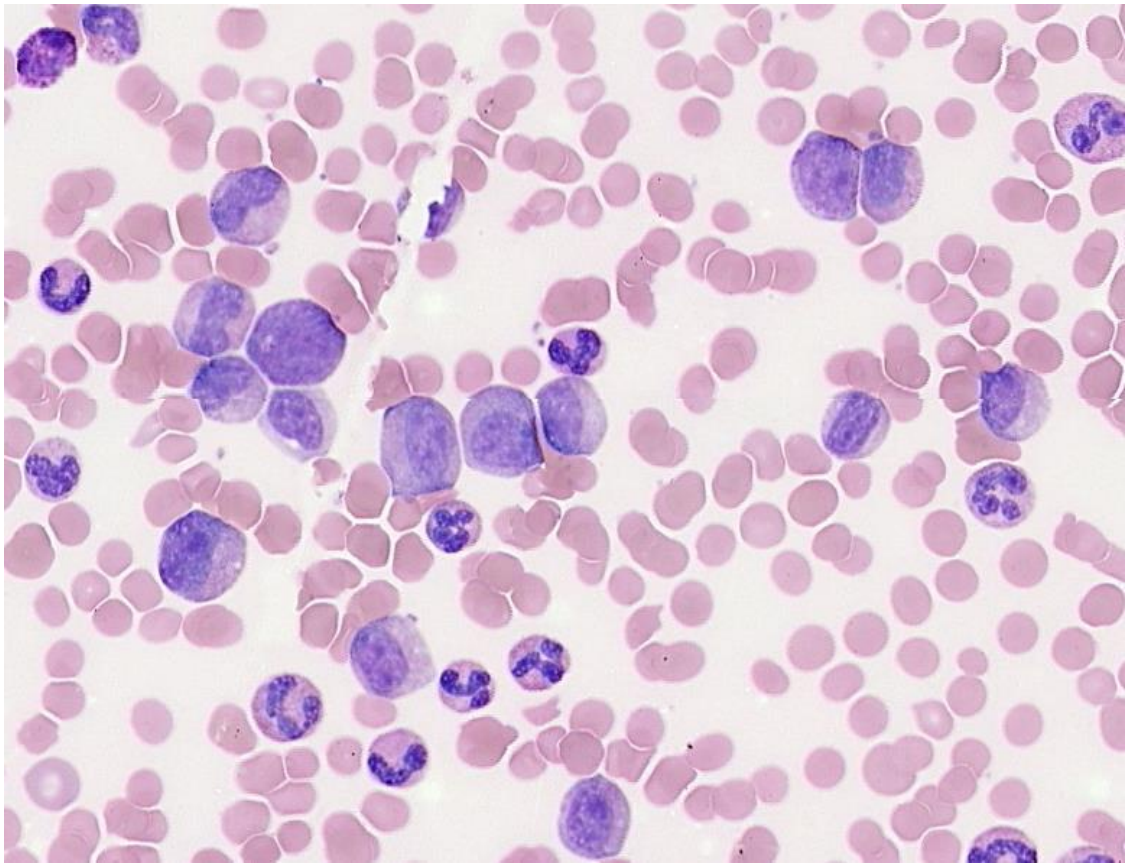
65 year old female with fatigue and weight loss.

CBC: WBC 150,000/ mm^3

Various stage of maturation on differential

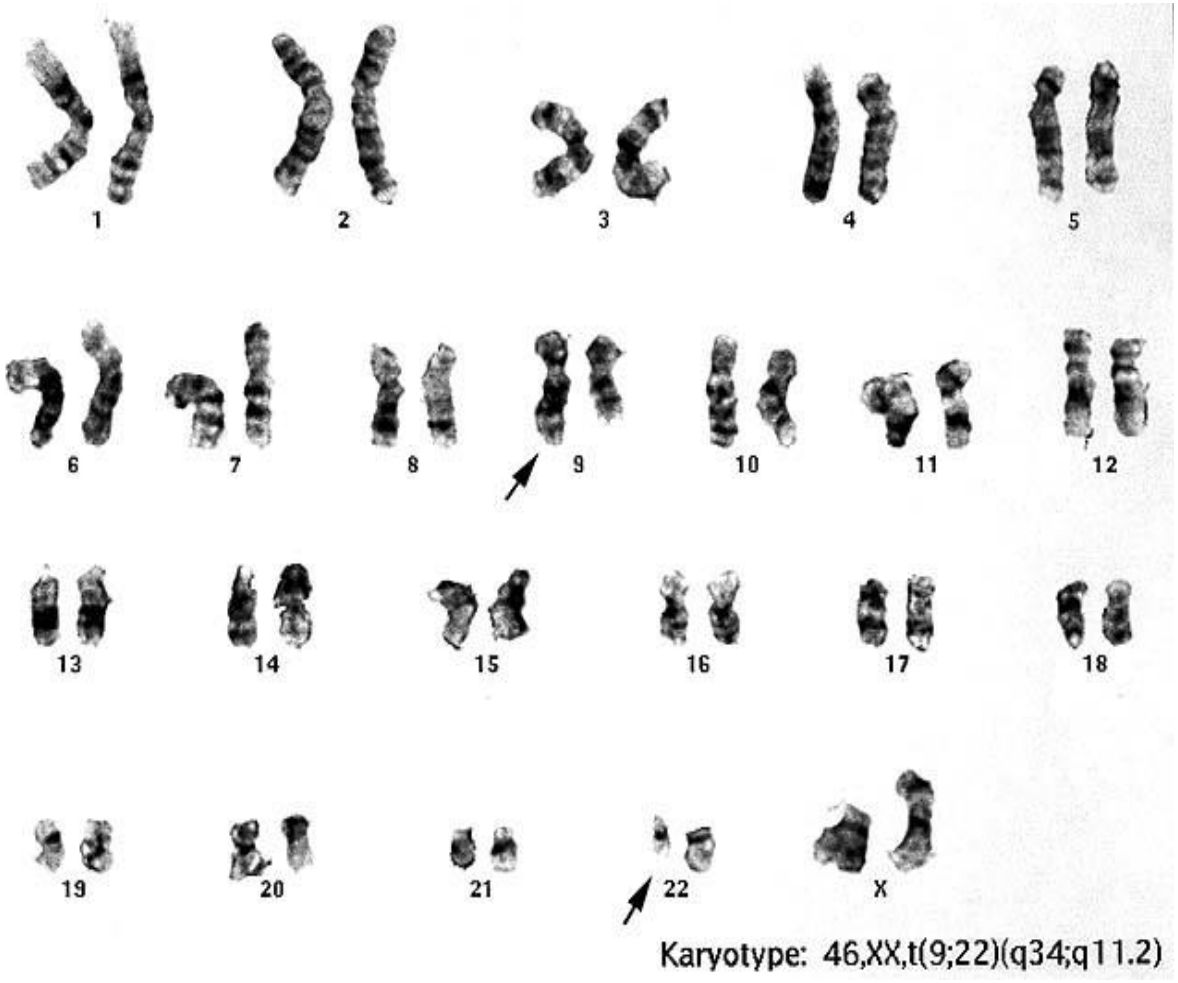
Diagnosis?

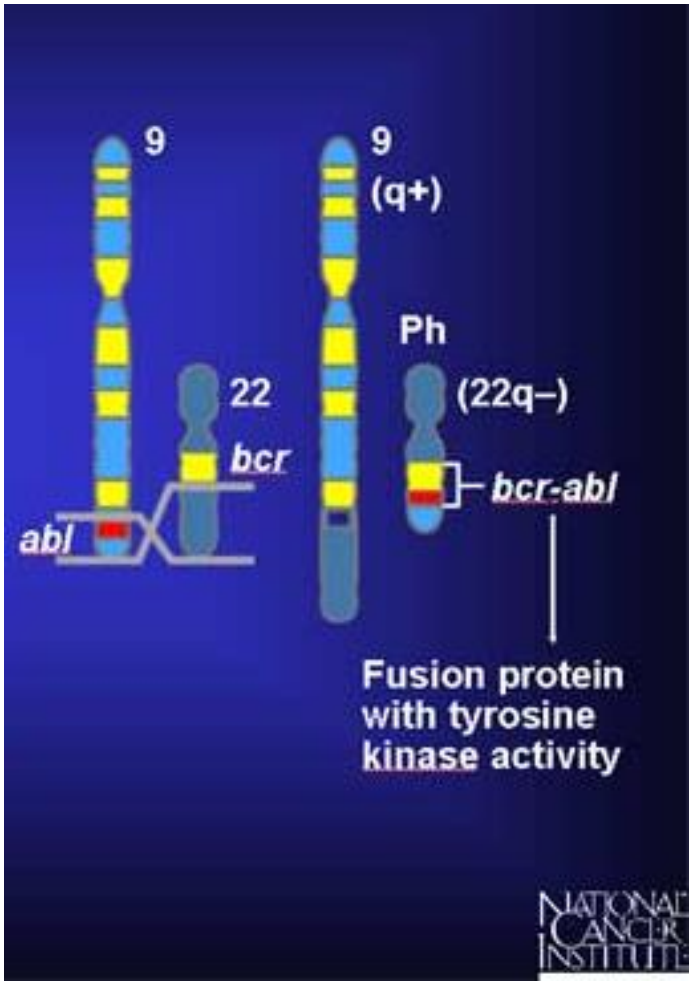
What test do you want to order?



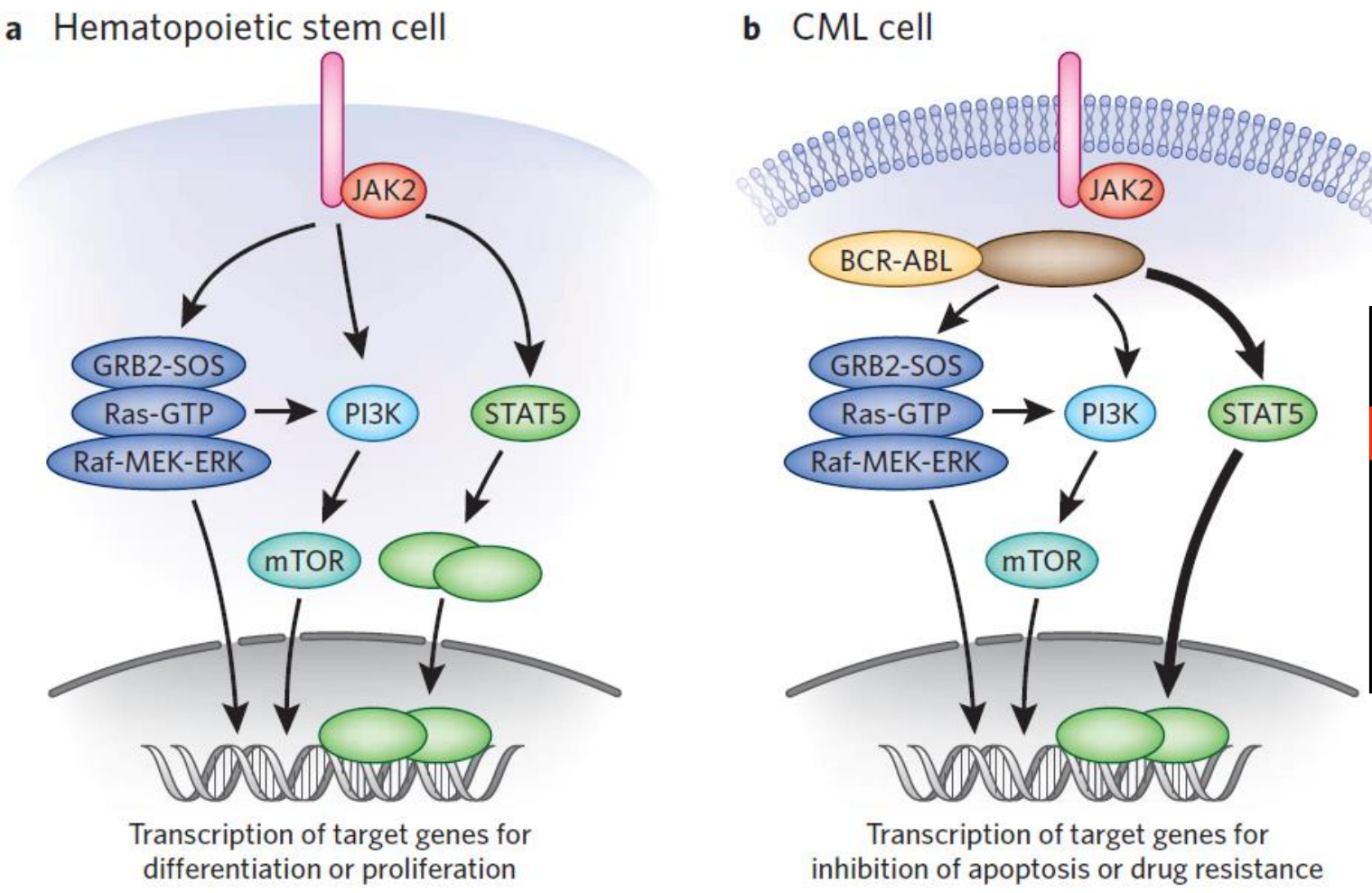
CHRONIC MYELOID LEUKEMIA (CML)

Translocation of *BCR-ABL1* genes - by cytogenetics





FUSION GENE CREATES NEW TYROSINE KINASE: "QUALITATIVE" PROBLEM



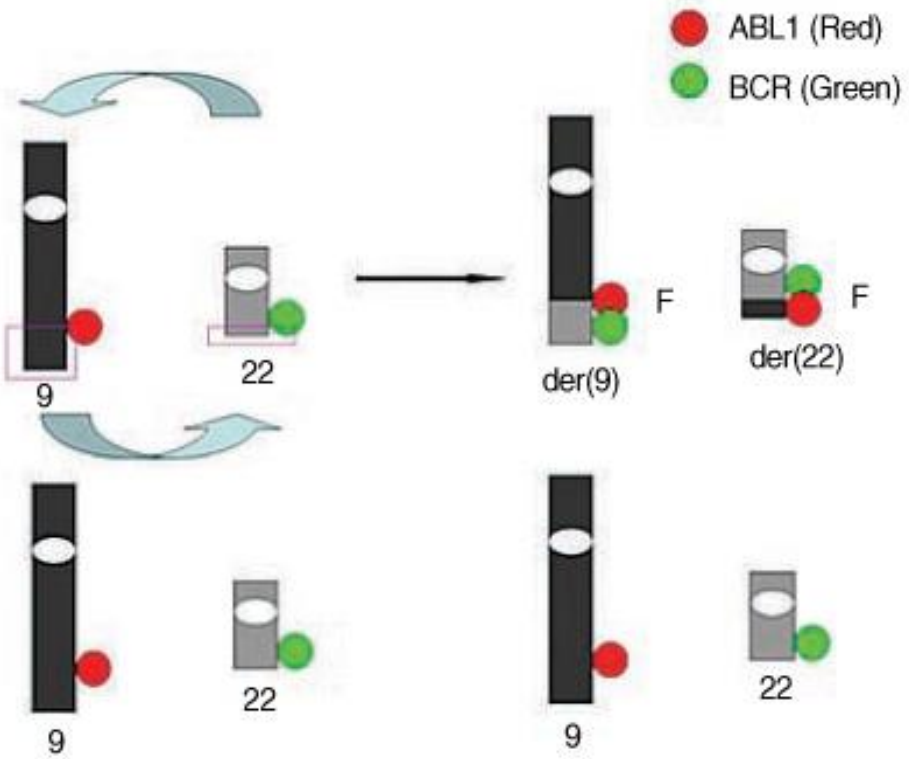
creation of a novel chimeric gene

A B

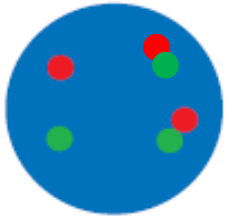
C

t(9;22) ⇒ bcr-abl

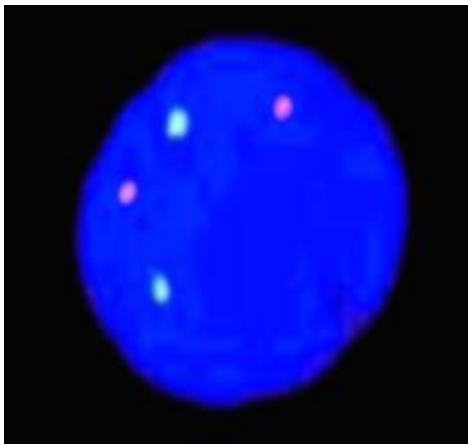
DETECTION OF *BCR-ABL1* BY FISH (FLUORESCENT IN SITU HYBRIDIZATION)

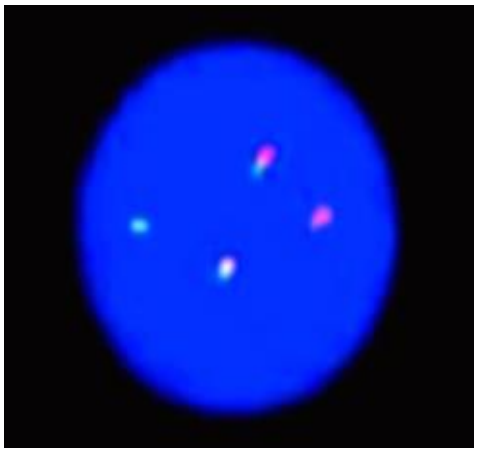


Translocation (–)



Translocation (+)





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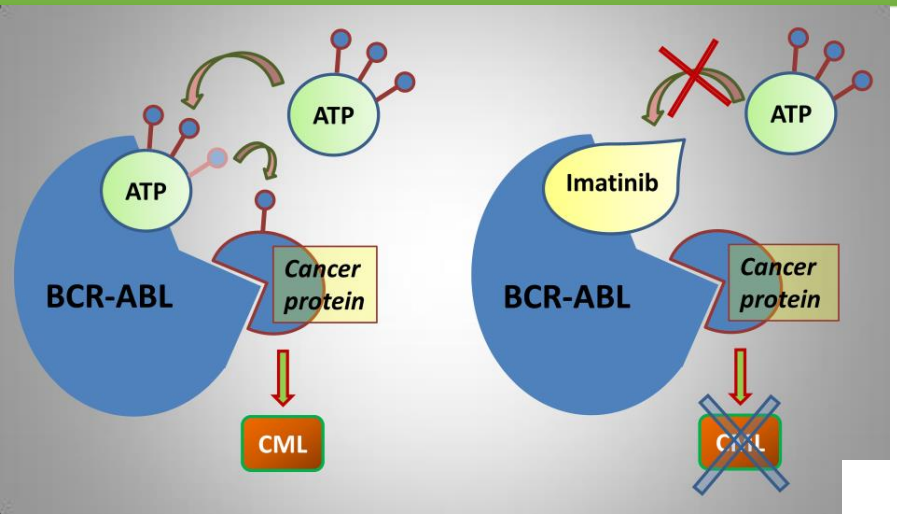
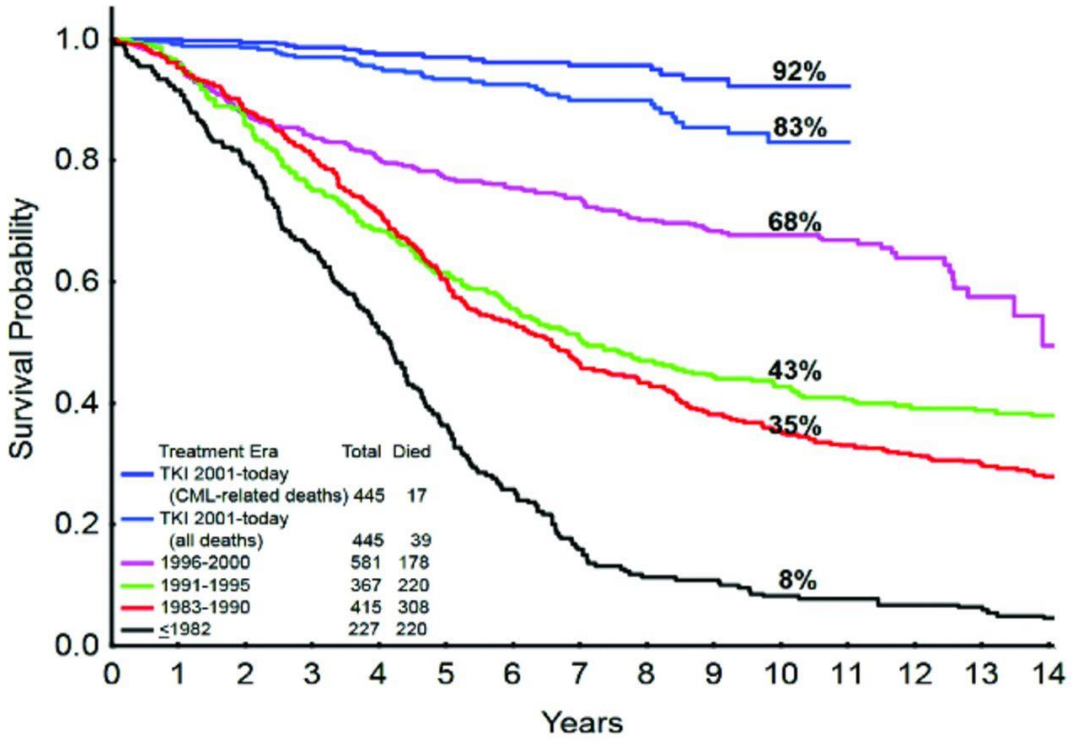
FIRST EXAMPLE OF TARGETED THERAPY





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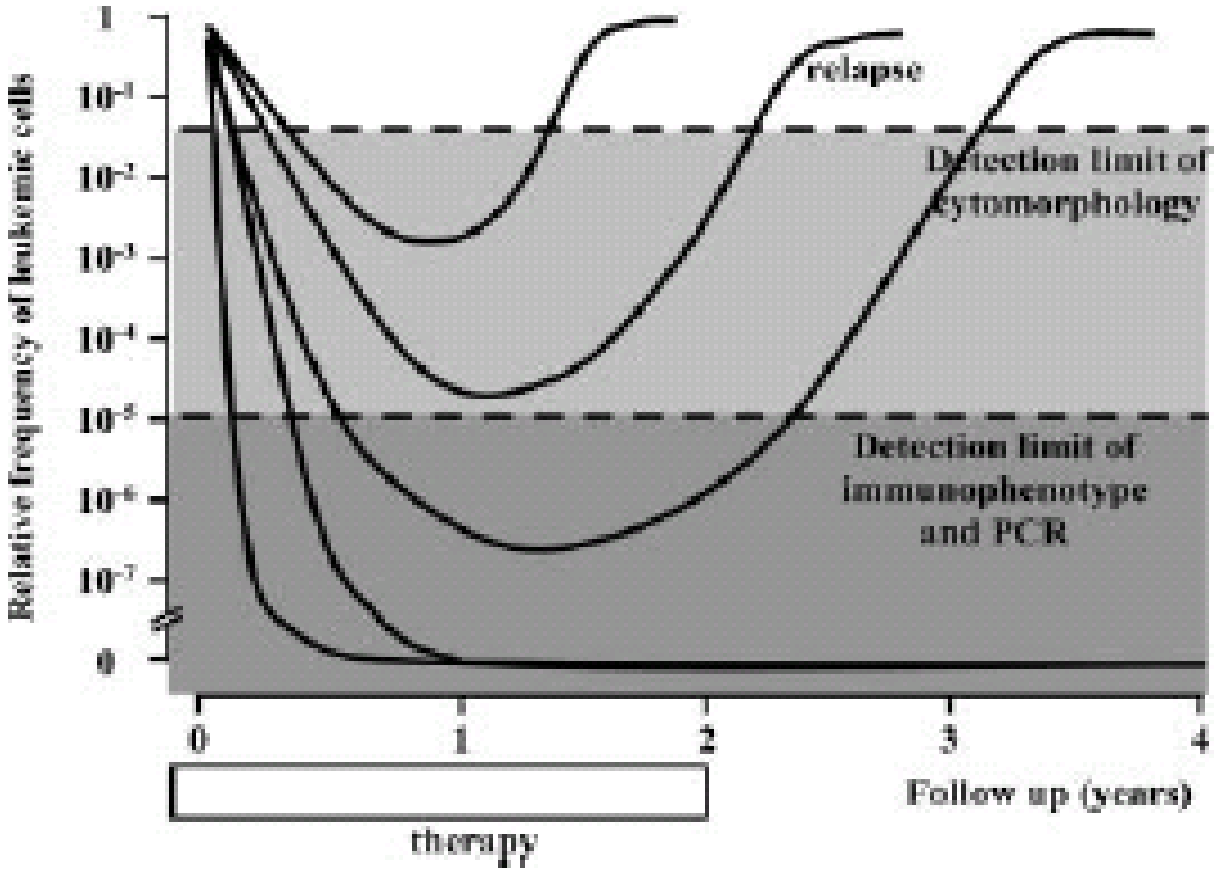
MINIMAL RESIDUAL DISEASE MONITOR – BY QUANTITATIVE RT-PCR



Complete Hematologic Response

Complete Cytogenetic Response

Complete Molecular Response

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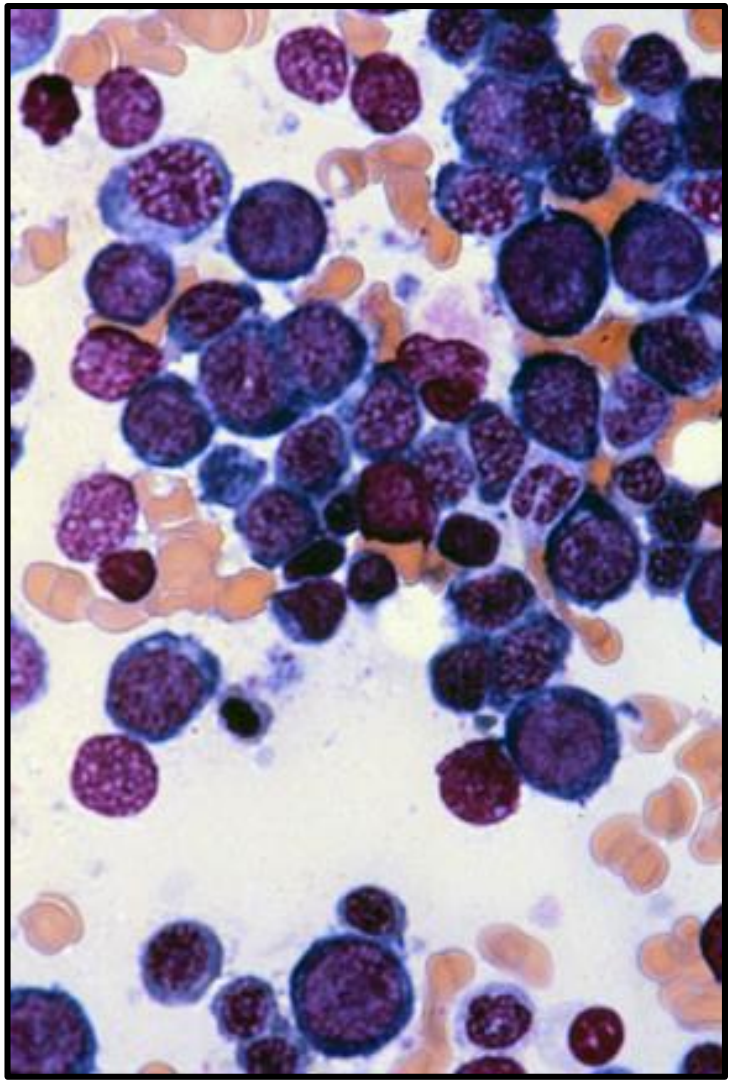
EXAMPLE 4: Myeloproliferative Neoplasms – Specific Mutation For Diagnosis

61 year old female with history of congestive heart failure and osteoarthritis. abnormal CBC was noted.

CBC:
Hb 19.0 g/dL; Hct 61%
WBC 10,060
Platelet 361,0000

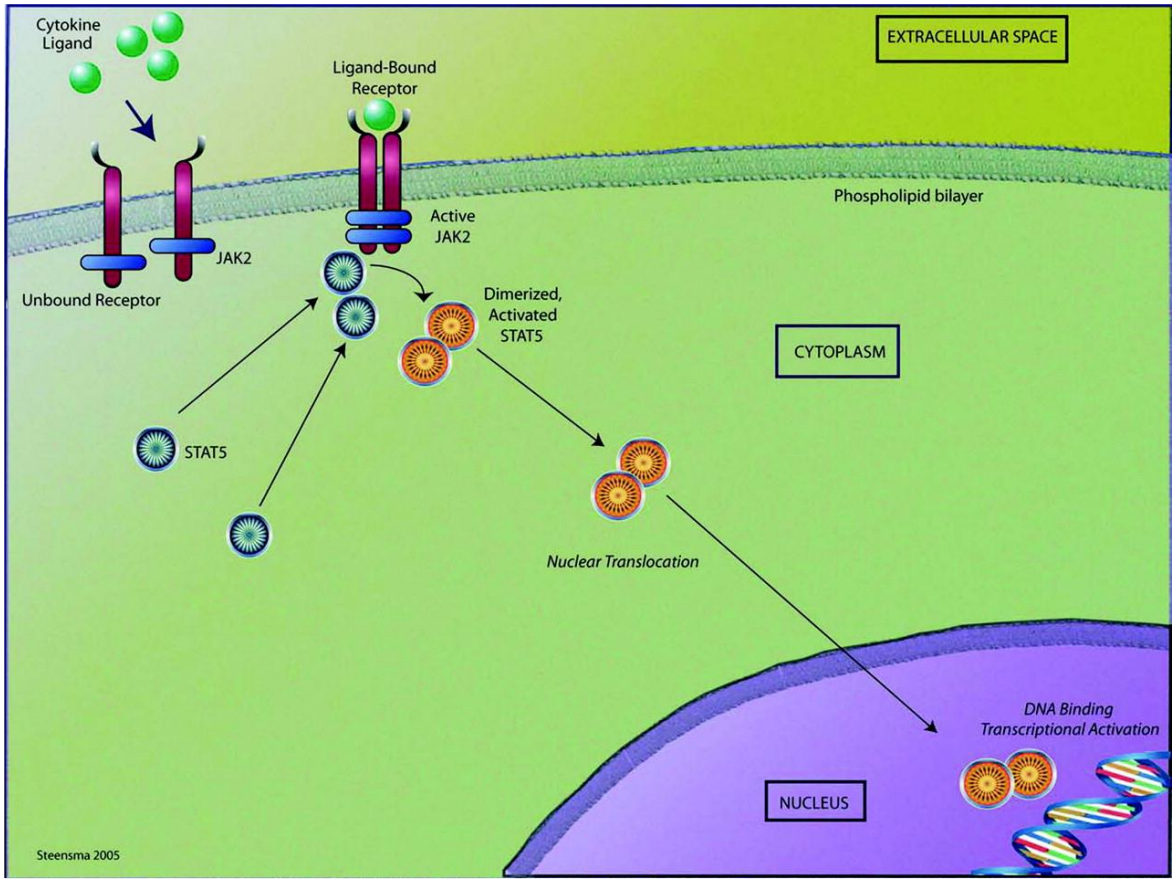
Differential Diagnosis?

What test do you want to order?



MYELOPROLIFERATIVE NEOPLASMS AND *JAK2* MUTATION

- *BCR/ABL* translocation in CML is paradigm for molecular diagnostics
- In 2005, 5 labs simultaneously described a point mutation (V617F) in *JAK2* in most other MPDs
- The next paradigm for CML?
- V617F mutations seen:
  - PV: ~95%
  - CIMF: ~50%
  - ET: ~50%
- Constitutively active JAK2 stimulate cell proliferation



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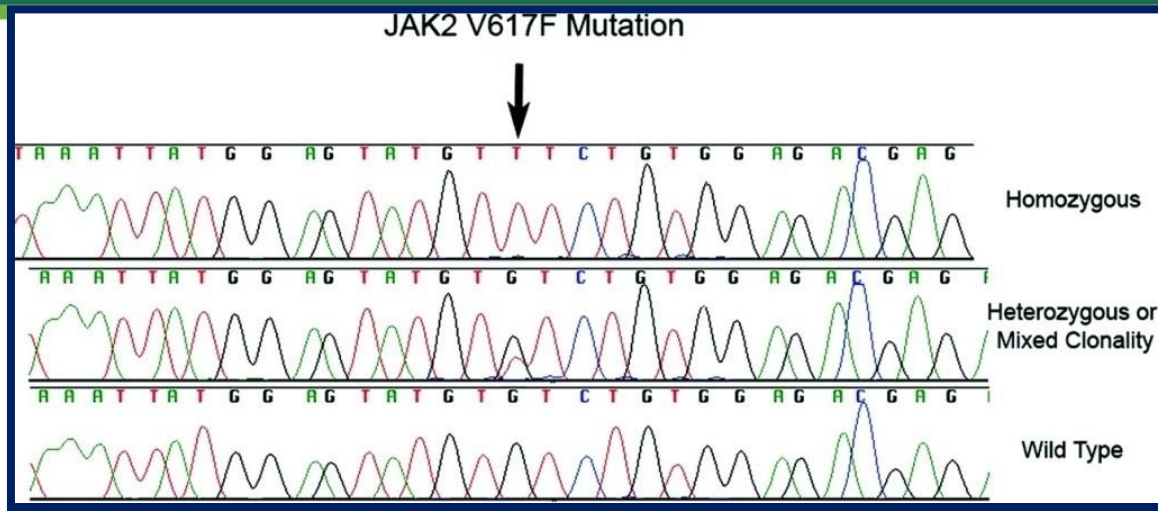
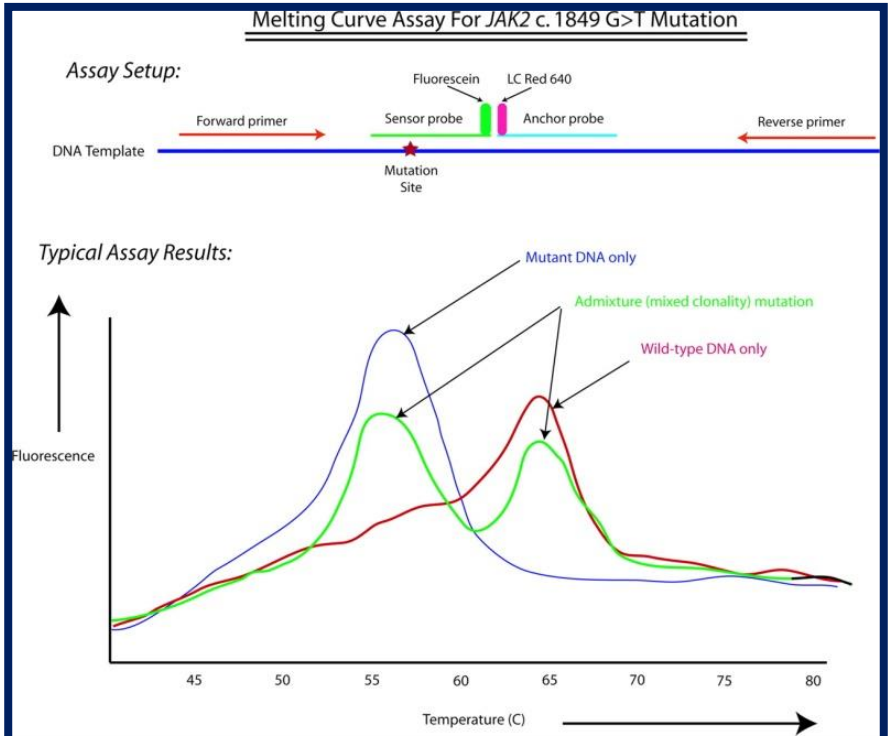
JAK2 V617F MUTATION DETECTION

- Direct Sequencing
- ARMS-PCR / ASO-PCR
- RFLP
- Melt curve analysis
- Pyrosequencing
- Next Generation Sequencing





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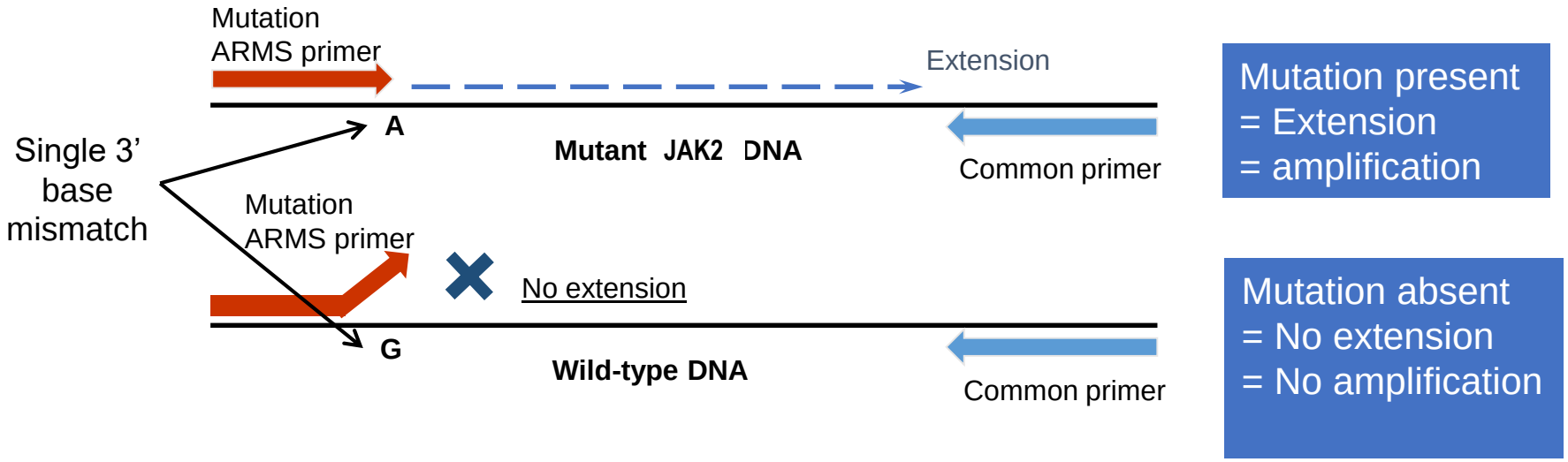
ALLELE SPECIFIC PCR / ARMS (AMPLIFICATION REFRACTORY MUTATION SYSTEM)



This case:

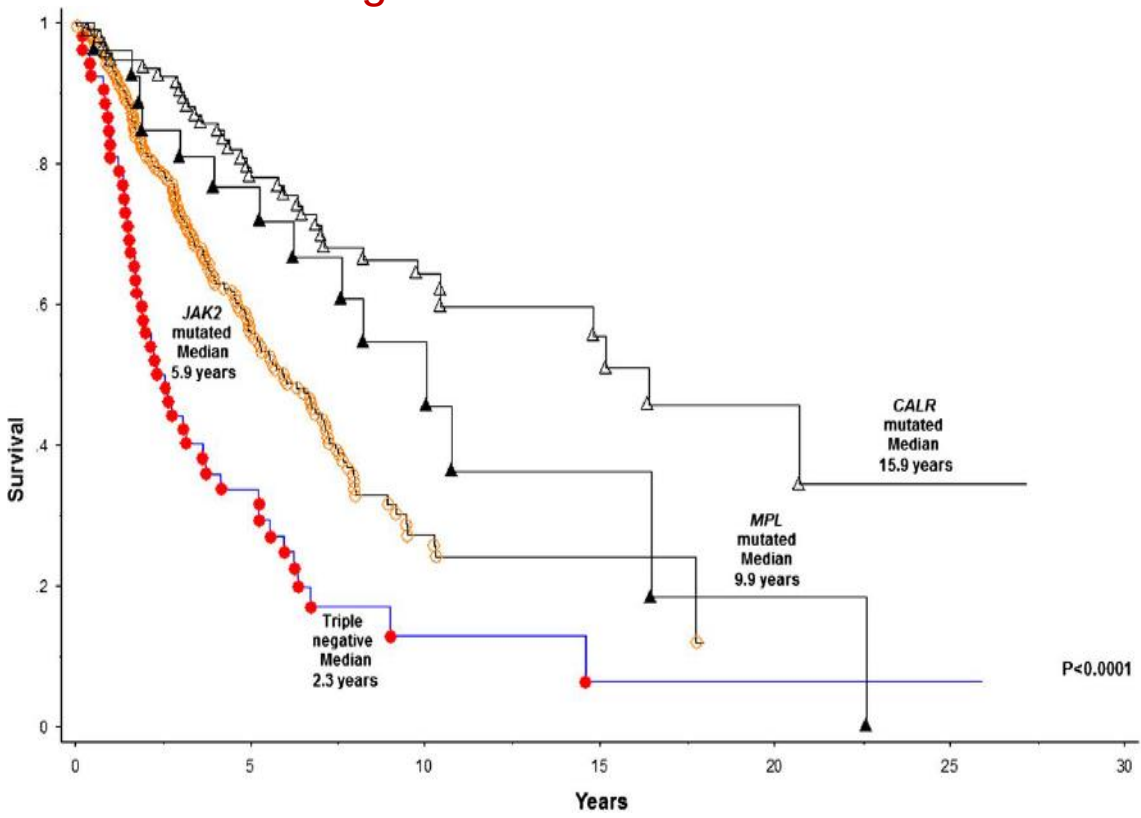
JAK2 V617F 86.5% positive

→ Support the diagnosis of Polycythemia Vera

THERE IS MORE…

- *JAK2* exon 12 mutations
  - only in PV (thus ~100% PV have a *JAK2* mutation)
- *MPL* mutations
  - in rare cases (~5-10%) of PMF and ET, but not PV
- *CALR* (calreticulin) mutations
  - in 25-35% of ET and MF (in 2013)
  - MPL and CALR: new diagnostic criteria for PMF, ET
- "Triple negative"
  – 10-15% of ET, PMF

Prognosis is different depending on which gene is mutated!



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(Tefferi A, et al. Blood 124: 2507-2513, 2014)

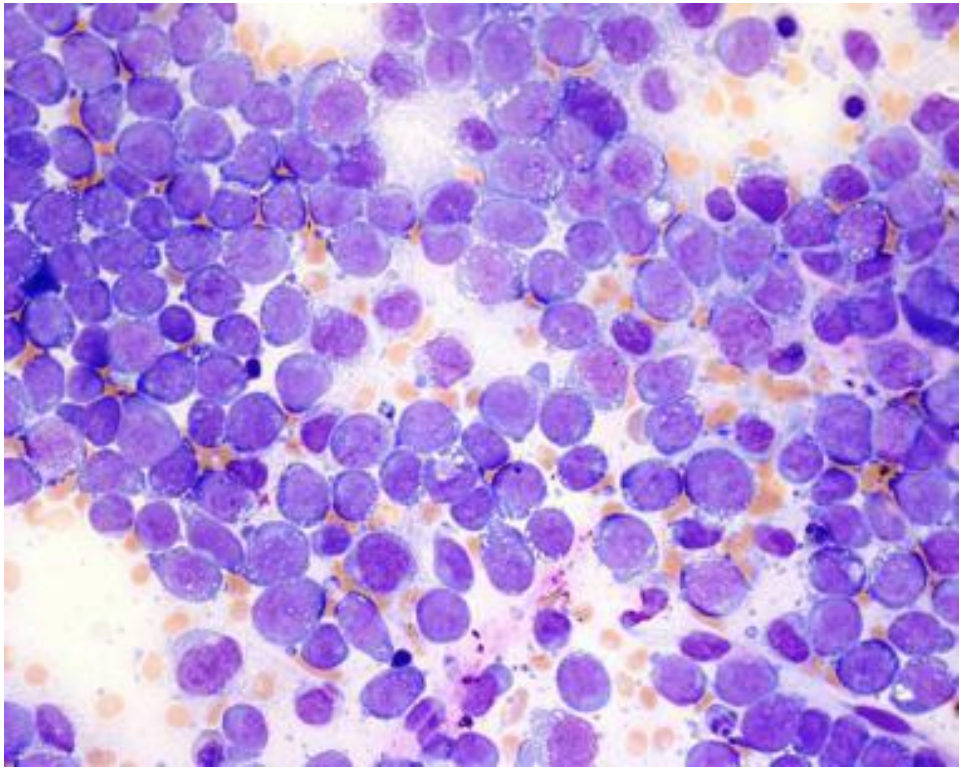
EXAMPLE 5: ACUTE MYELOID LEUKEMIA – NEXT GENERATION SEQUENCING

68 year old female with fatigue and dyspnea.

CBC:
WBC 16,600/ mm^3 with 34% blasts
Hgb 8.5 g/dL
Platelet 80,000/ mm^3

Flow cytometry: 55% myeloblasts (CD34, CD117, CD13, CD33, CD7 and HLA-DR positive)

Bone marrow aspirate and biopsy: AML, NOS, 64% myeloblasts



What test do you want to order?

DIAGNOSTIC: GENETIC ABNORMALITIES IN AML (WHO)

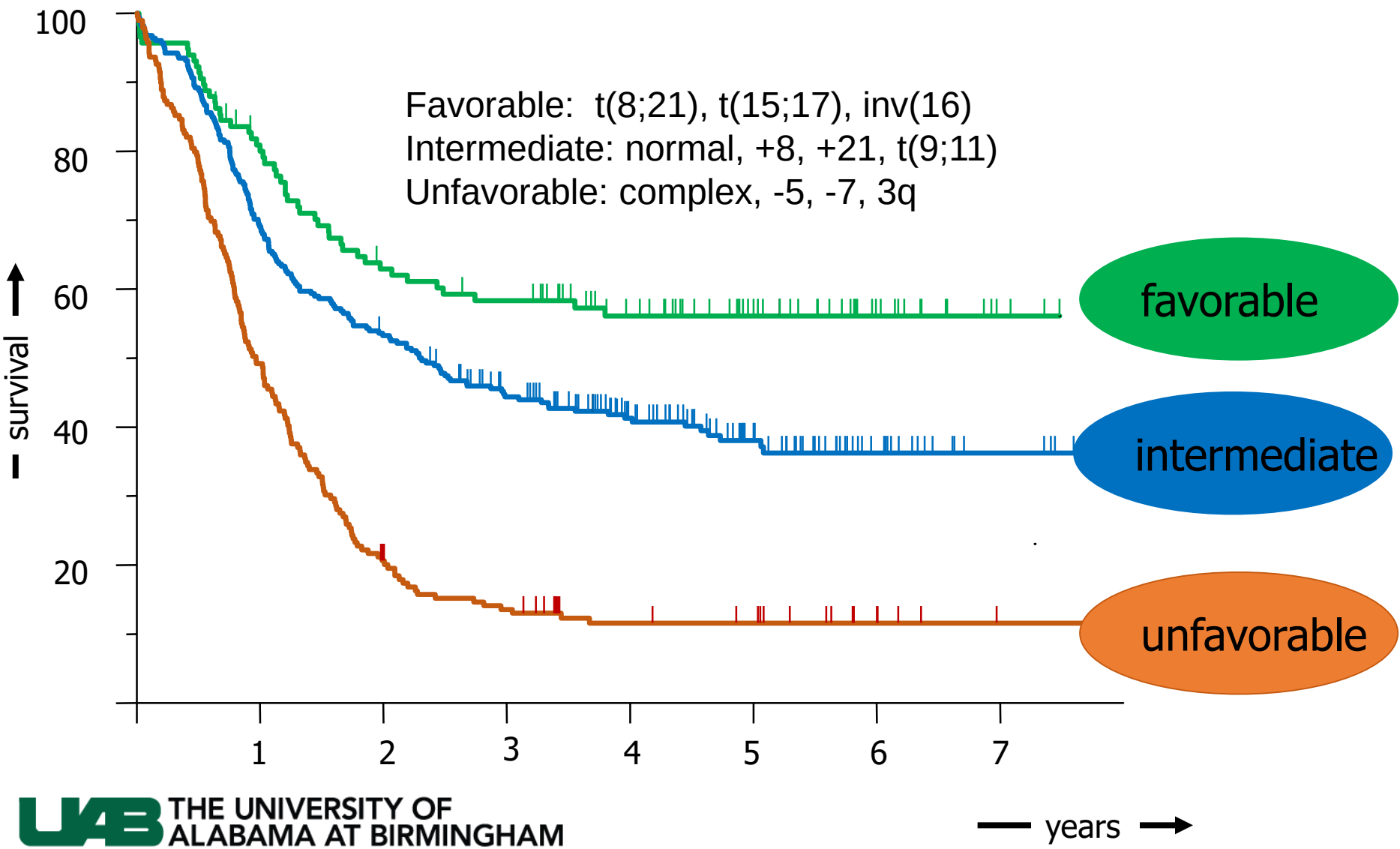
AML with recurrent genetic abnormalities

- AML with t(8;21)(q22;q22) (M2) — *RUNX1-RUNX1T1 (AML1-ETO)*
- AML with inv(16)(p13.1q22) or t(16;16)(p13.1;q22) (M4eo) — *CBFB-MYH11*
- APL with t(15;17)(q22;q12) (M3) — *PML-RARA*
- AML with t(9;11)(p22;q23) (monocytic) — *KMT2A (MLL)-MLLT3*
- AML with t(6;9)(p23;q34) (basophilia and multilineage dysplasia) — *DEK-NUP214*
- AML with inv(3)(q21q26.2) or t(3;3)(q21;q26.2) — *GATA2, MECOM*
- AML (megakaryoblastic) with t(1;22)(p13;q13) — *RBM15-MKL1*
- AML with *BCR-ABL1*

AML with gene mutations

- AML with mutated *NPM1* (nucleophosmin)
- AML with biallelic mutation of *CEBPA*
- AML with mutated *RUNX1*

AML – CYTOGENETIC STRATIFICATION



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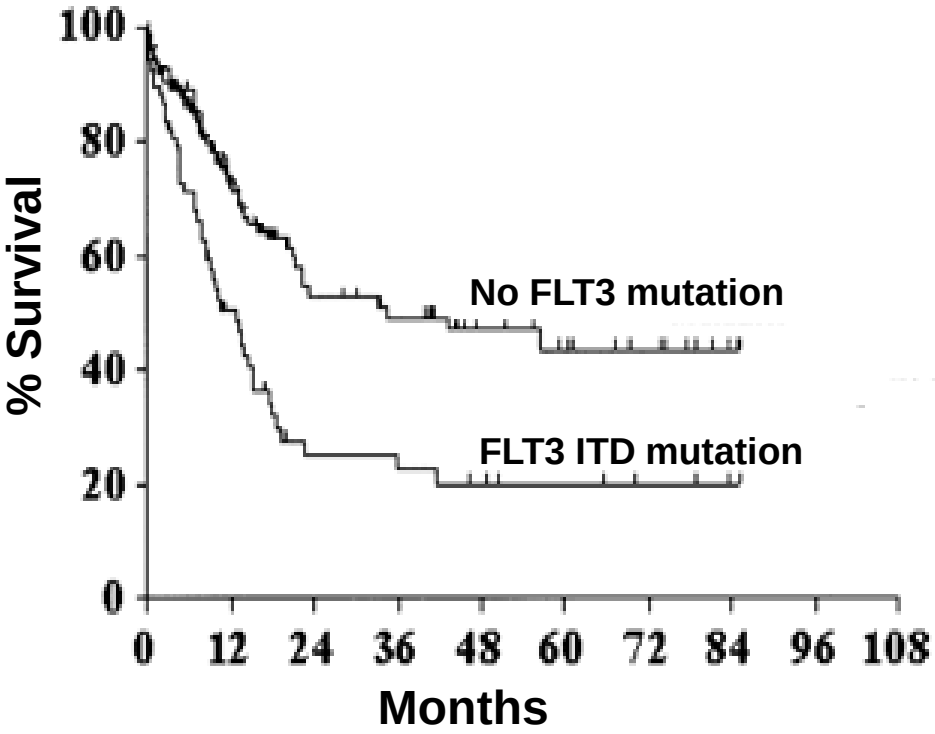
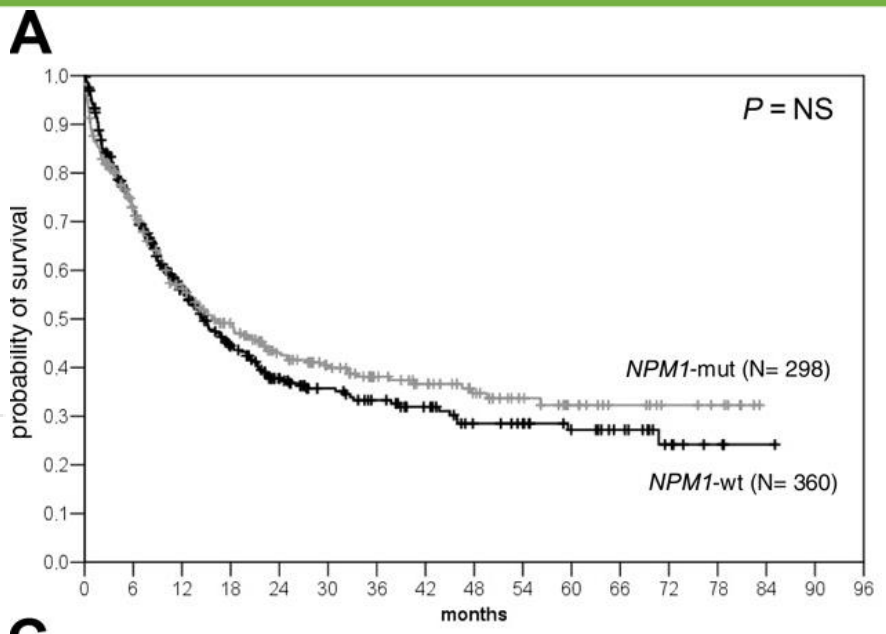
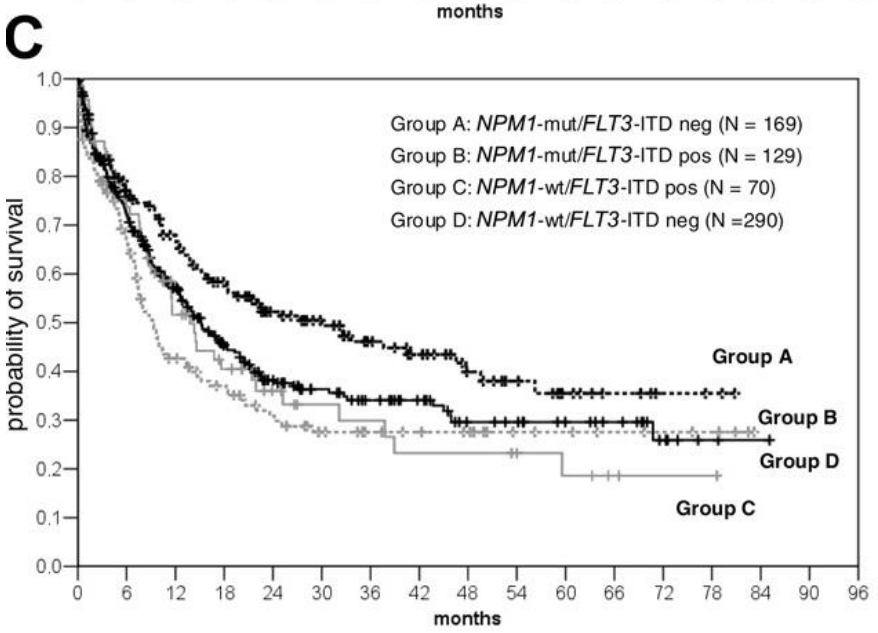
AML – Stratification based on *FLT3* and *NPM1*



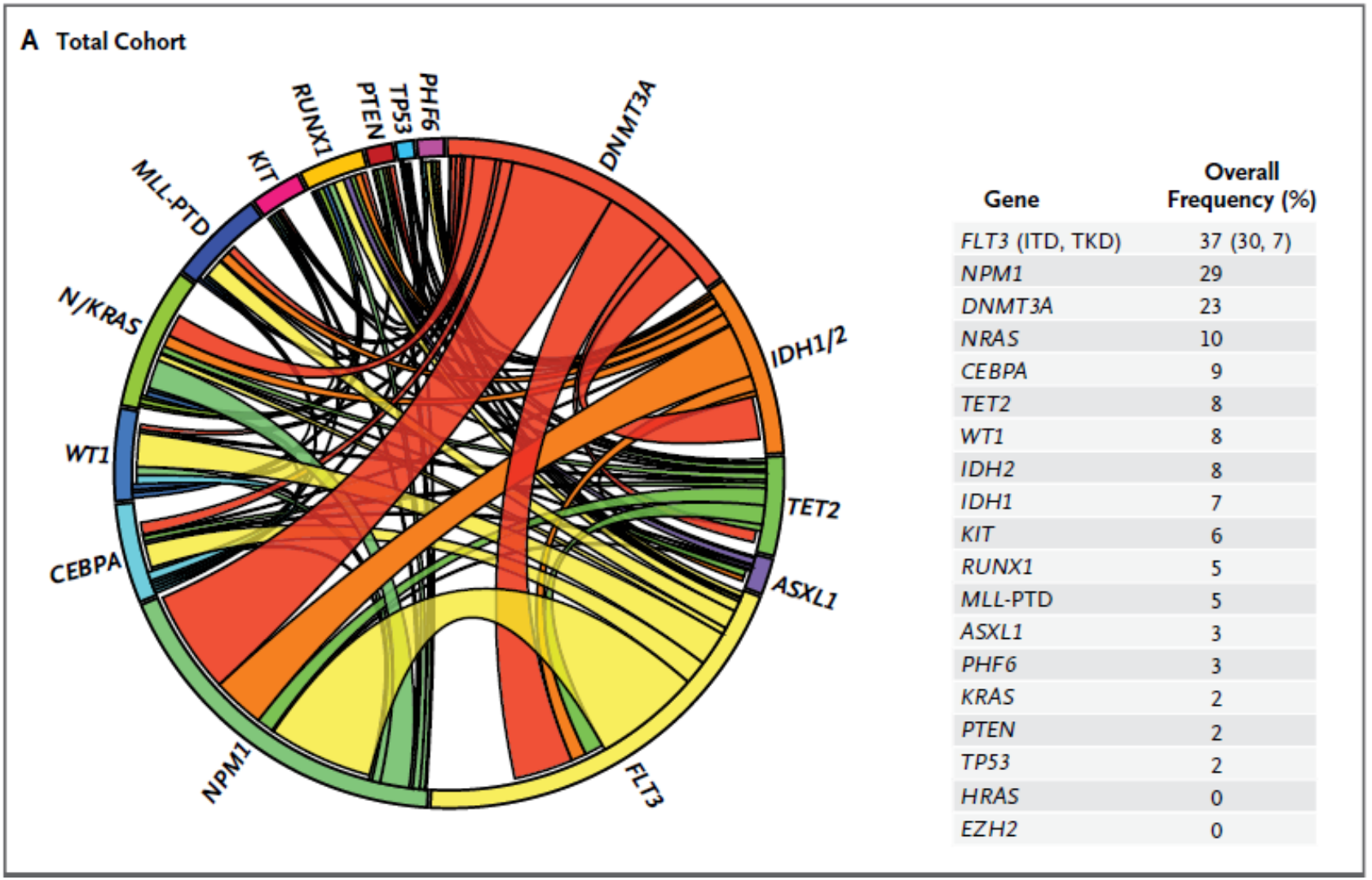
(Frohling *et al*, 2002)





(Thiede C et al. Blood 2006;107:4011-4020)

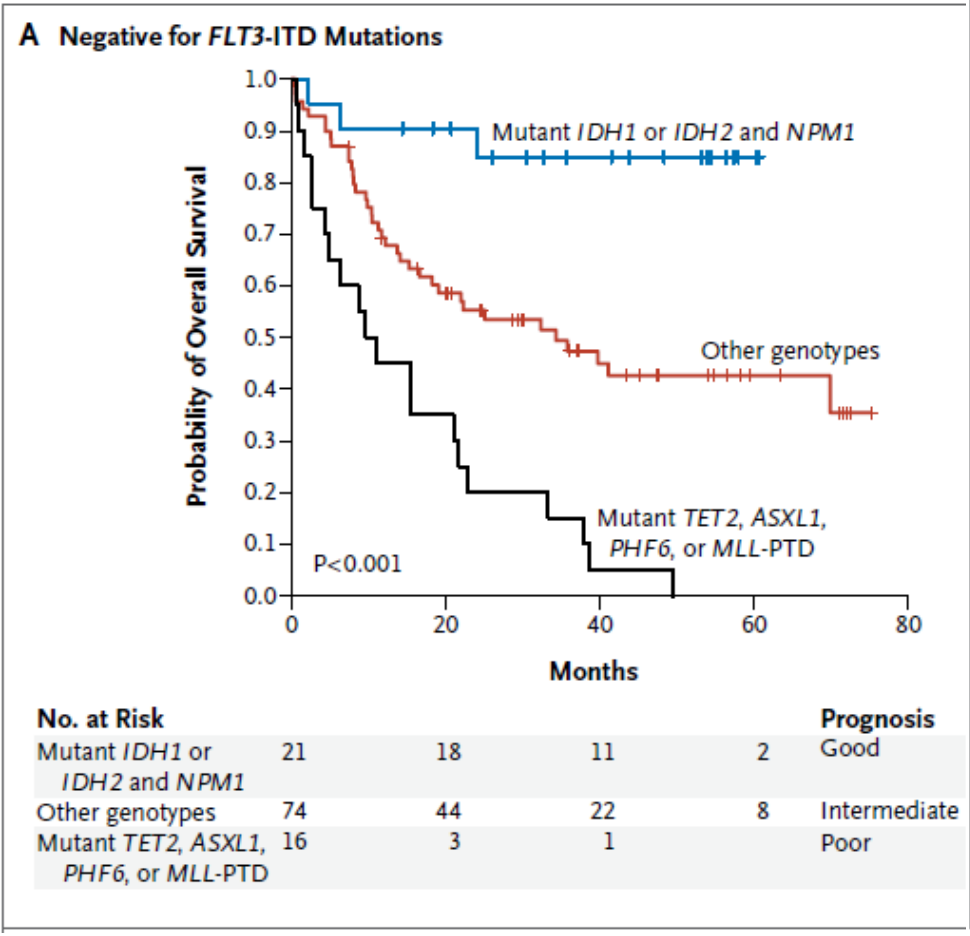
AML – Prognostic Relevance of Integrated Genetic Profiling



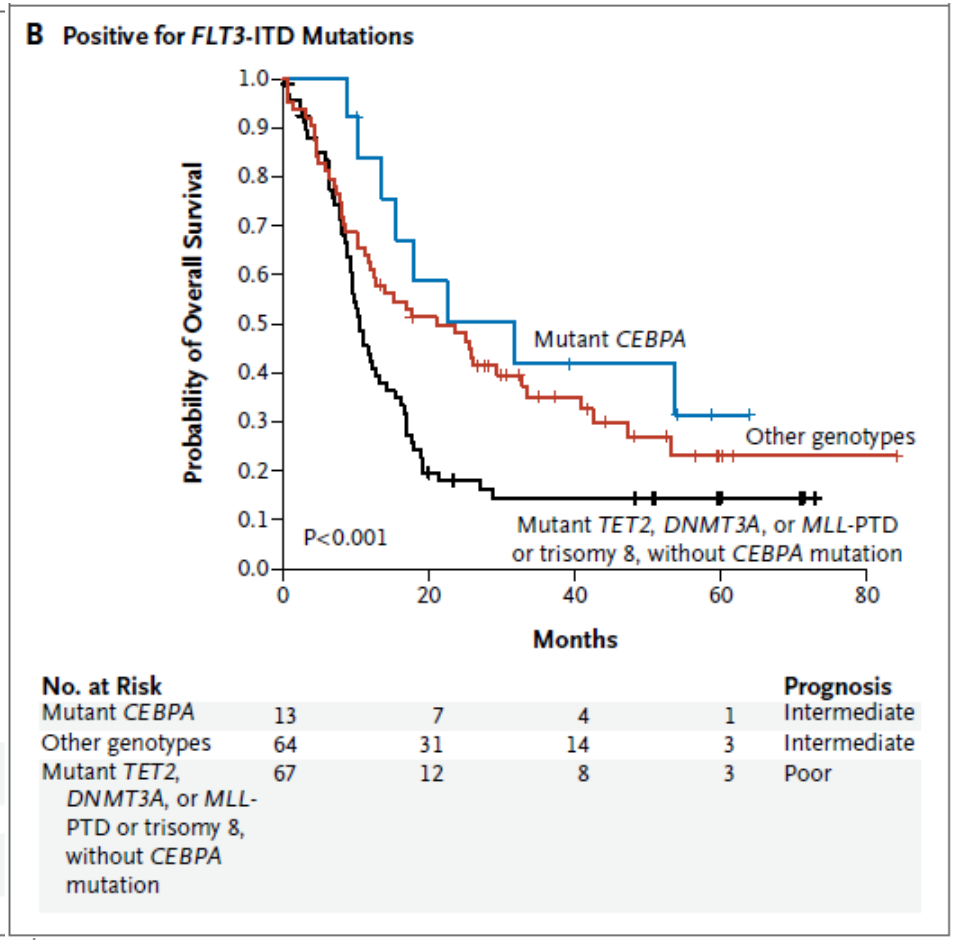
Gene	Overall Frequency (%)
FLT3 (ITD, TKD)	37 (30, 7)
NPM1	29
DNMT3A	23
NRAS	10
CEBPA	9
TET2	8
WT1	8
IDH2	8
IDH1	7
KIT	6
RUNX1	5
MLL-PTD	5
ASXL1	3
PHF6	3
KRAS	2
PTEN	2
TP53	2
HRAS	0
EZH2	0

(Patel JP, et al., NEJM 366 (12): 1079-1089, 2012)

Multivariate Risk Classification of Patients with Intermediate Risk AML



No. at Risk					Prognosis
Mutant *IDH1* or *IDH2* and *NPM1*	21	18	11	2	Good
Other genotypes	74	44	22	8	Intermediate
Mutant *TET2*, *ASXL1*, *PHF6*, or *MLL*-PTD	16	3	1		Poor



No. at Risk					Prognosis
Mutant *CEBPA*	13	7	4	1	Intermediate
Other genotypes	64	31	14	3	Intermediate
Mutant *TET2*, *DNMT3A*, or *MLL*-PTD or trisomy 8, without *CEBPA* mutation	67	12	8	3	Poor

Revised Risk Stratification of Patients with AML on Basis of Integrated Genetic Analysis

A Revised Risk Stratification

Cytogenetic Classification	Mutations		Overall Risk Profile
Favorable	Any		Favorable
Normal karyotype or intermediate-risk ctyogenetic lesions	*FLT3*-ITD-negative	Mutant *NPM1* and *IDH1* or *IDH2*	Favorable
	FLT3-ITD-negative	Wild-type *ASXL1*, *MLL*-PTD, *PHF6*, and *TET2*	Intermediate
	FLT3-ITD-negative or positive	Mutant *CEBPA*	Intermediate
	FLT3-ITD-positive	Wild-type *MLL*-PTD, *TET2*, and *DNMT3A* and trisomy 8–negative	Intermediate
	FLT3-ITD-negative	Mutant *TET2*, *MLL*-PTD, *ASXL1*, or *PHF6*	Unfavorable
	FLT3-ITD-positive	Mutant *TET2*, *MLL*-PTD, *DNMT3A*, or trisomy 8, without mutant *CEBPA*	Unfavorable
Unfavorable	Any		Unfavorable

PROGNOSTIC AND PREDICTIVE: GENETIC ALTERATIONS IN AML

Gene	Frequency in CN-AML	Prognostic Impact	Target Therapy	Drugs
NPM1	30-45%	Favorable		
FLT3-ITD	28-34%	Unfavorable in high allelic ratio	Yes	Sorafenib, Quizartinib, Gilteritinib, Midostaurin
FLT3-TKD	11-14%	Neutral	Yes	Quizartinib, Gilteritinib, Midostaurin
IDH1 or *IDH2*	15-30%	Favorable	Yes	Ivosidenib (IDH1), Enasidenib (IDH2)
Biallelic *CEBPA*	10-18%	Favorable		
RAS	25% NRAS, 15% KRAS	Neutral	Yes	Cobimetinib, other MEK inhibitors
KIT	20-30% of CBF-AML	Unfavorable	Yes	Dasatinib, Imatinib
TET2	15-30%	Possibly worse		
ASXL1	5-16%	Unfavorable		
RUNX1	5-13%	Unfavorable		
KMT2A	5-10%	Unfavorable		
TP53	5-20%	Unfavorable	wild type	Idasanutlin

MYELODYSPLASTIC SYNDROME (MDS)

- Cytogenetic abnormalities:
  - +8, del(7q) or -7, del(5q) or 5-, -Y, del(20q)
  - By karyotyping
- Molecular abnormalities:
  - *EF3B1, RUNX1, TET2, U2AF1, SRSF2, TP53, ASXL1, EZH2, DNMT3A*
  - Mutation alone is not diagnostic
  - *TP53* mutation = aggressive behavior
  - *SF3B1* associated with MDS-RS

GENES FREQUENTLY SOMATICALLY MUTATED IN MDS[a]

This table lists gene mutations likely to be somatic (acquired, not congenital) and disease-related and therefore presumptive evidence of MDS. Other mutations in these genes can occur in MDS, as can mutations in other frequently mutated genes like *TET2* and *DNMT3A*, but these may have less certain significance (ie, possible germline variants or less specific for MDS). All mutated genes are not unique to MDS and must be interpreted in the appropriate clinical context (eg, cytopenias, <20% bone marrow blasts, no other AML defining criteria). Not all MDS patients will have a mutation in one of these genes.

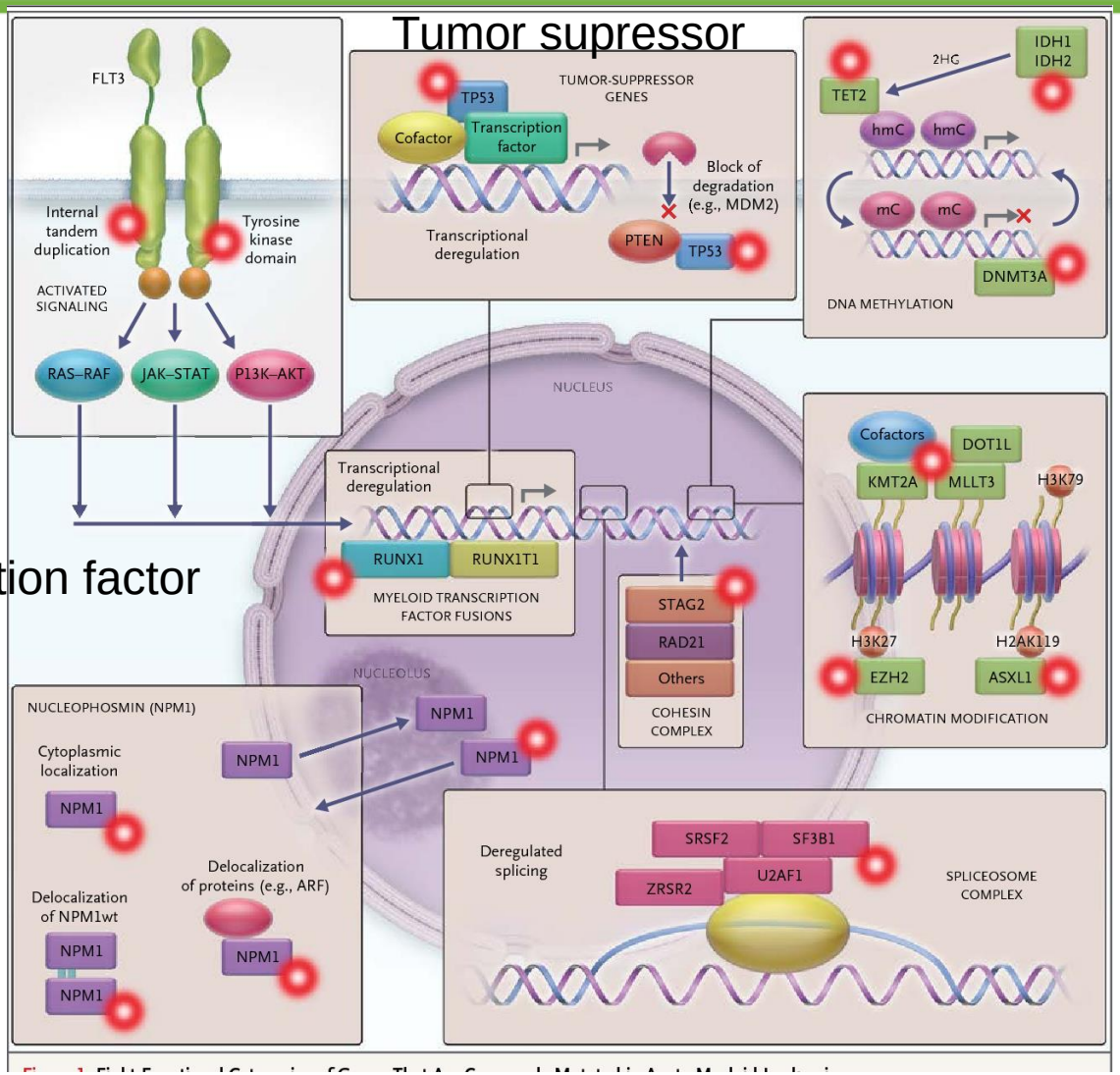
Mutated Gene[b]	Examples of Typical Somatic Mutation Types and Locations in Select MDS-Related Genes[c]	Overall Incidence	Clinical Significance
TET2	Nonsense or Frameshift or Splice Site Missense: any in codons 1134–1444 or 1842–1921	20%–25%	Associated with normal karyotypes. More frequent in CMML (40%–60%). Common in Clonal hematopoiesis of indeterminate potential (CHIP) and Clonal cytopenia of undetermined significance (CCUS).
DNMT3A	Nonsense or Frameshift or Splice Site Missense in codons G543, R635, S741, R736, R739, S770, M880, R882,W893, P904, A910	12%–18%	More frequent occurrence in AML, particularly R882 mutations. Common in CHIP and CCUS.
ASXL1	Nonsense or Frameshift	15%–25%	Independently associated with a poor prognosis in MDS and CMML. More frequent in CMML (40%–50%). Common in CHIP and CCUS.
EZH2	Nonsense or Frameshift	5%–10%	Independently associated with a poor prognosis in MDS and MDS/MPN. More frequent in CMML (12%).
SF3B1	Missense: E622, Y623, R625, N626, H662, T663, K666, K700E, I704, G740, G742, D781	20%–30%	Strongly associated with ring sideroblasts and more frequent in MDS-RS (80%). Independently associated with a more favorable prognosis.
SRSF2	Missense or In-Frame Deletion: involving codon P95	10%–15%	More frequent in CMML (40%) and associated with a poor prognosis.
U2AF1	Missense: S34, Q157	8%–12%	Associated with a poor prognosis.
ZRSR2	Nonsense or Frameshift	5%–10%	Associated with a poor prognosis.
RUNX1[d]	Nonsense or Frameshift	10%–15%	Independently associated with a poor prognosis in MDS.
TP53[d]	Nonsense or Frameshift or Splice Site Missense: any in codons except P47S and P72R	8%–12%	Independently associated with a poor prognosis. More frequent with complex karyotypes (50%) and del(5q) (15%–20%). May predict resistance or relapse to lenalidomide.
STAG2	Nonsense or Frameshift or Splice Site	5%–10%	Associated with a poor prognosis.
NRAS[d]	Missense: G12, G13, Q61	5%–10%	Associated with a poor prognosis, particularly in patients predicted to have lower-risk MDS. More frequent in CMML and JMML (~15%).
CBL[d]	Missense: any in codons 366–420	<5%	More frequent in CMML (10%–20%) and JMML (15%).
NF1[d]	Nonsense or Frameshift or Splice Site	<5%	More frequent in CMML (5%–10%) and in JMML (30%) where it is often germline.
JAK2	Missense: V617F	<5%	More frequent in MDS/MPN-RS-T (50%); can occur in conjunction with *SF3B1*.
CALR	Frameshift: after codon 352	<5%	Observed in MDS/MPN-RS&T where it can occur in conjunction with *SF3B1* mutations.
MPL	Missense: W515L/K	<5%	Observed in MDS/MPN-RS&T where it can occur in conjunction with *SF3B1* mutations.
ETV6[d]	Nonsense or Frameshift	<5%	Independently associated with a poor prognosis.
GATA2[d]	Nonsense or Frameshift or Splice Site Missense: in codons 349–398		Associated with a poor prognosis.
DDX41[d]	Nonsense or Frameshift or Splice Site Missense: in codon R525H		Constitutional (germline) mutations in this gene can occur.
IDH1	Missense: R132	<5%	More frequent in AML.
IDH2	Missense: R140Q, R172	<5%	More frequent in AML. Associated with a poor prognosis.
SETBP1	Missense: E858, T864, I865, D868, S869, G870	<5%	Associated with disease progression. More frequent in CMML (5%–10%) and JMML (7%).
PHF6	Nonsense or Frameshift or Splice Site	<5%	More frequent in cases with excess blasts, but no association with survival.
BCOR	Nonsense or Frameshift or Splice Site	<5%	Associated with a poor prognosis. More frequent in CMML (5%–10%).
FLT3	Internal Tandem Duplication or Missense: in codon D835		Associated with a poor prognosis.
WT1	Nonsense or Frameshift or Splice Site		Associated with a poor prognosis.
NPM1	Frameshift: W288fs*12		Associated with a poor prognosis.
STAT3	Missense: any codons 584-674	<5%	Occurs in large granular lymphocyte leukemia (LGL) associated with MDS; associated with immune bone marrow failure.
PPM1D	Nonsense or Frameshift	~5%	Associated with therapy-related MDS, but not associated with adverse prognosis independent of *TP53*. Common in CHIP and CCUS.

EIGHT FUNCTIONAL CATEGORIES OF GENES MUTATED IN AML

Signaling

Transcription factor

Nucleo-phosmin



Epigenetic
- Methylation
- Chromatin modification

Cohesin

Spliceosome

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(Dohner H. et al. NEJM 373: 1136-1152, 2015)

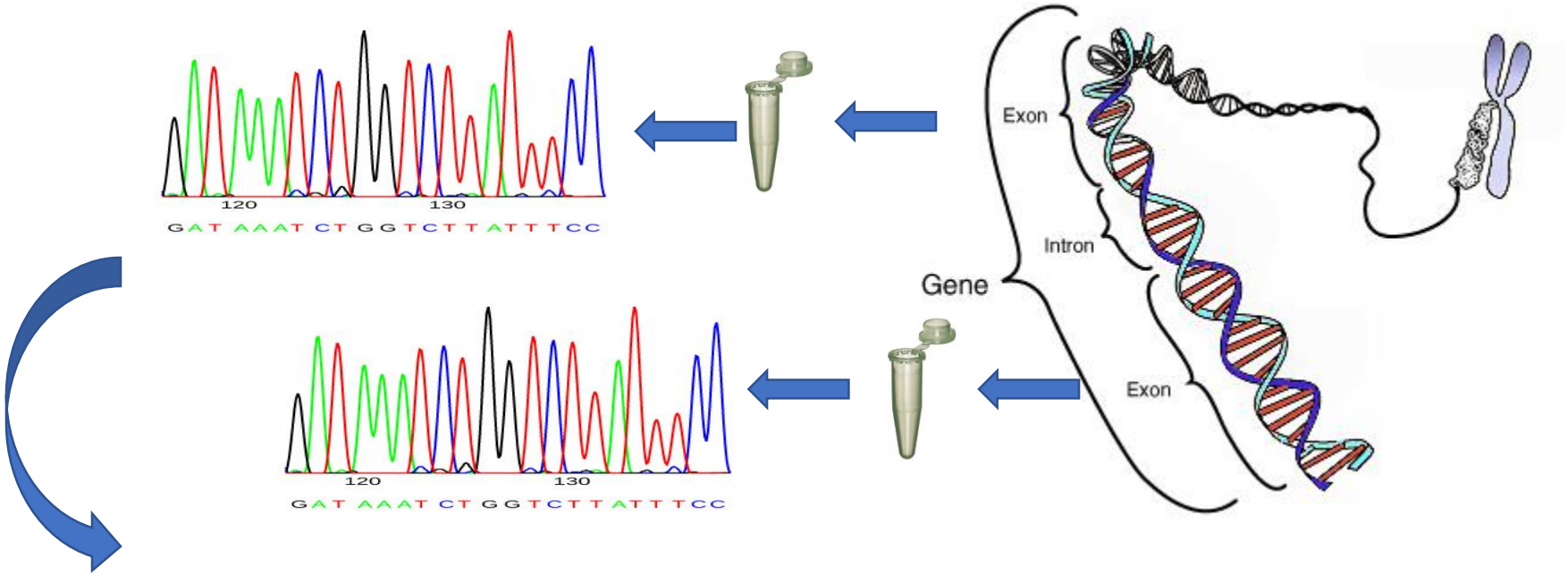
FUNCTIONAL GROUP

Functional class	Specific example mutations
Signaling and kinase pathway	*FLT3, KRAS, NRAS, KIT, PTPN11, NF1*
Epigenetic modifiers (DNA methylation and chromatin modification)	*DNMT3A, IDH1, IDH2, TET2, ASXL1, EZH2, MLL/KMT2A*
Nucleophosmin	*NPM1*
Transcription factors	*CEBPA, RUNX1, GATA2*
Tumor suppressors	*TP53, WT1, PTEN, ETV6, PFP6*
Spliceosome complex	*SRSF2, U2AF1, SF3B1, ZRSR2*
Cohesin complex	*RAD21, STAG1, STAG2, SMC1A, SMC3*

Need to test mutation status of all of these genes.
→ Next generation sequencing panel does make more sense

WHAT IS NEXT GENERATION SEQUENCING? – MASSIVELY PARALLEL SEQUENCING

First, think about sequencing entire genome



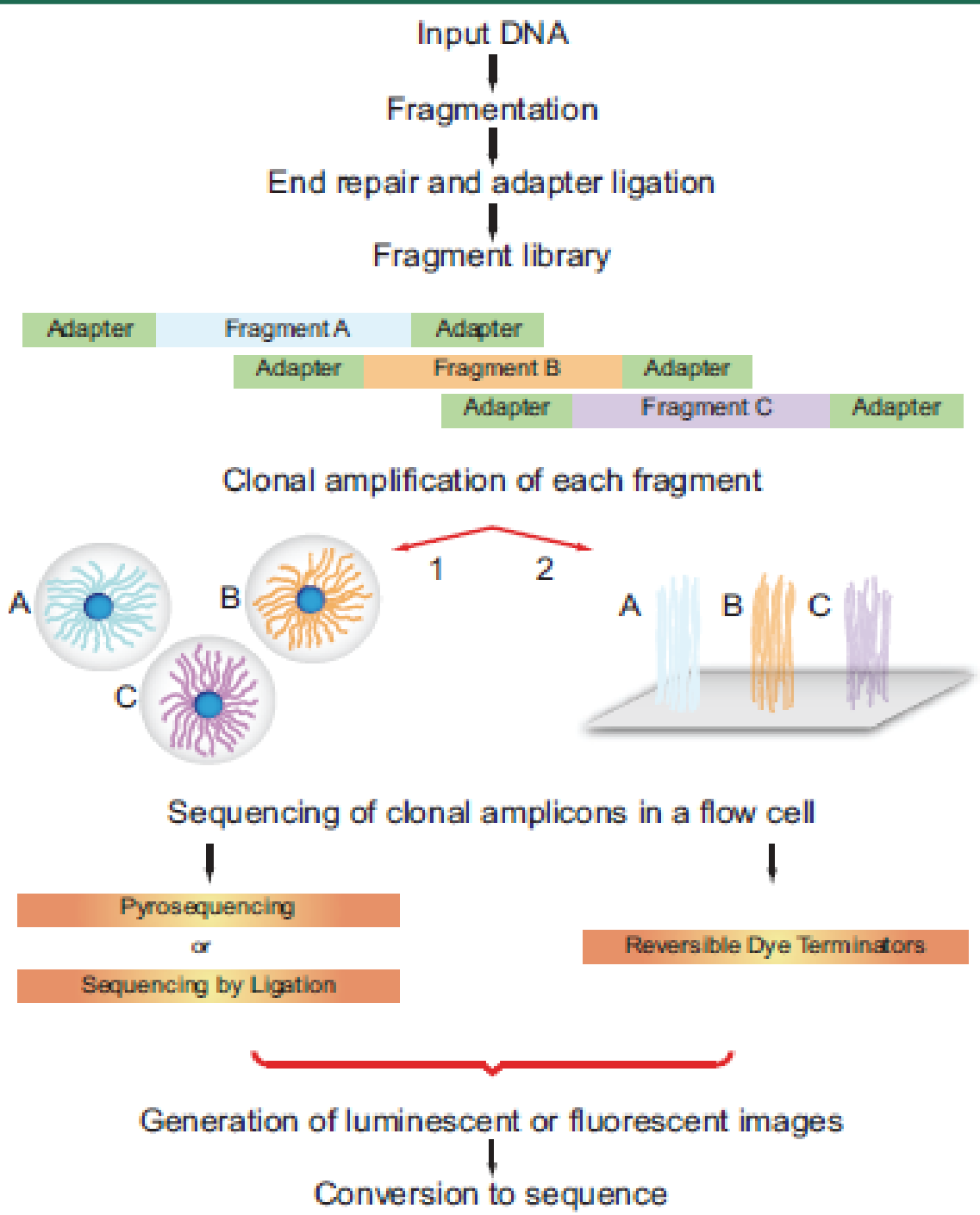
X Number of exon / gene **X** Number of gene

~20,000 coding genes
Less than 5% of whole genome is coding region

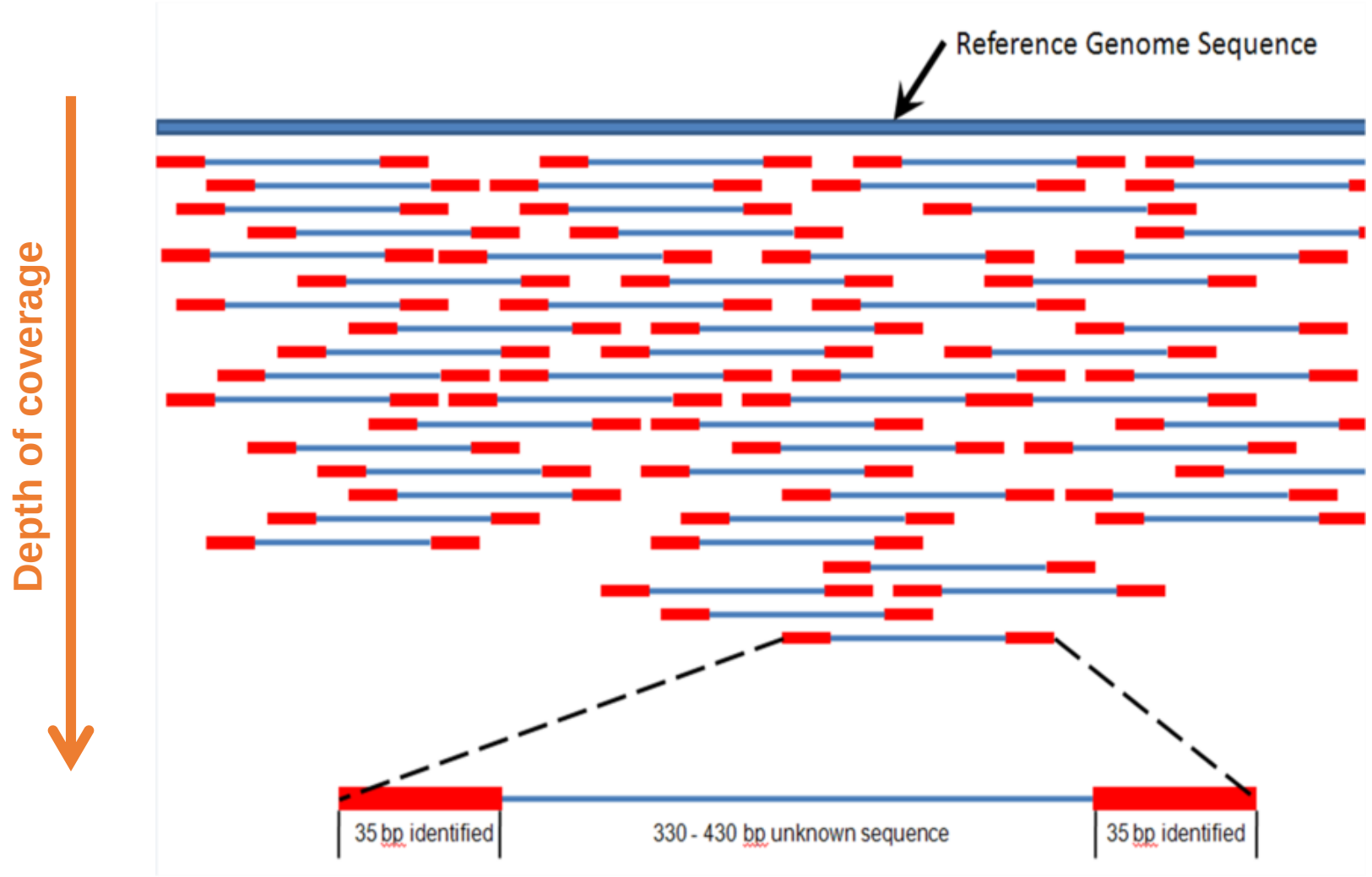
NGS

Just think about “Multiple (MASSIVE) PCR in one tube (PARALLEL)”

Fragmentation →
Ligation →
Amplification →
Sequencing →
Analysis



RESULTS: BIOINFORMATICS PIPELINE NEEDED



MYELOID COMPREHENSIVE PANEL BY NEXT GENERATION SEQUENCING AT UAB

- 50 gene panel (comprehensive)

ABL1, ASXL1, ATRX, BCOR, BRAF, CALR, CBL, CEBPA, CSF3R, CUX1, DNMT3A, ETV6, EZH2, FBXW7, FLT3, GATA1, GATA2, GNAS, HRAS, IDH1, IDH2, IKZF1, JAK2, JAK3, KDM6A, KIT, KRAS, KMT2A (MLL), MPL, NF1, NOTCH1, NPM1, NRAS, PDGFRA, PHF6, PTEN, PTPN11, RAD21, RUNX1, SETBP1, SF3B1, SMC1A, SMC3, SRSF2, STAG2, TET2, TP53, U2AF1, WT1, ZRSR2

- Agilent HaloPlex HS Custom Panel, started in August 2016
  - ✓ Improved base-call accuracy and sensitivity by Molecular Bar Code.
  - ✓ Amplicon redundancy (each target base is covered by multiple amplicons) increases accuracy and even coverage.
- Bioinformatics pipeline and reporting tool by PierianDX
- Sequencing ~300 myeloid cases per year

THIS CASE: MYELOID PANEL RESULTS

TEST PERFORMED

Myeloid Comprehensive panel. Targeted next-generation sequencing was performed on this sample of Bone marrow. See under Test Details for more information.

RESULT SUMMARY

Variants Detected	Therapies or Prognostic Indication (in patient's malignancy)	Therapies or Prognostic Indication (in another malignancy)	Clinical Trial Opportunity
CEBPA p.Q83Sfs*77	! Favorable Prognosis in Acute myeloid leukemia, Acute myeloid leukemia, disease	No	Yes
CEBPA p.G223Vfs*95	! Favorable Prognosis in Acute myeloid leukemia	No	Not evaluated

CLINICALLY RELEVANT RESULTS

FDA Approved Therapies, Prognostic Indication, or Other Course of Action **in patient's tumor type** or **in another tumor type**

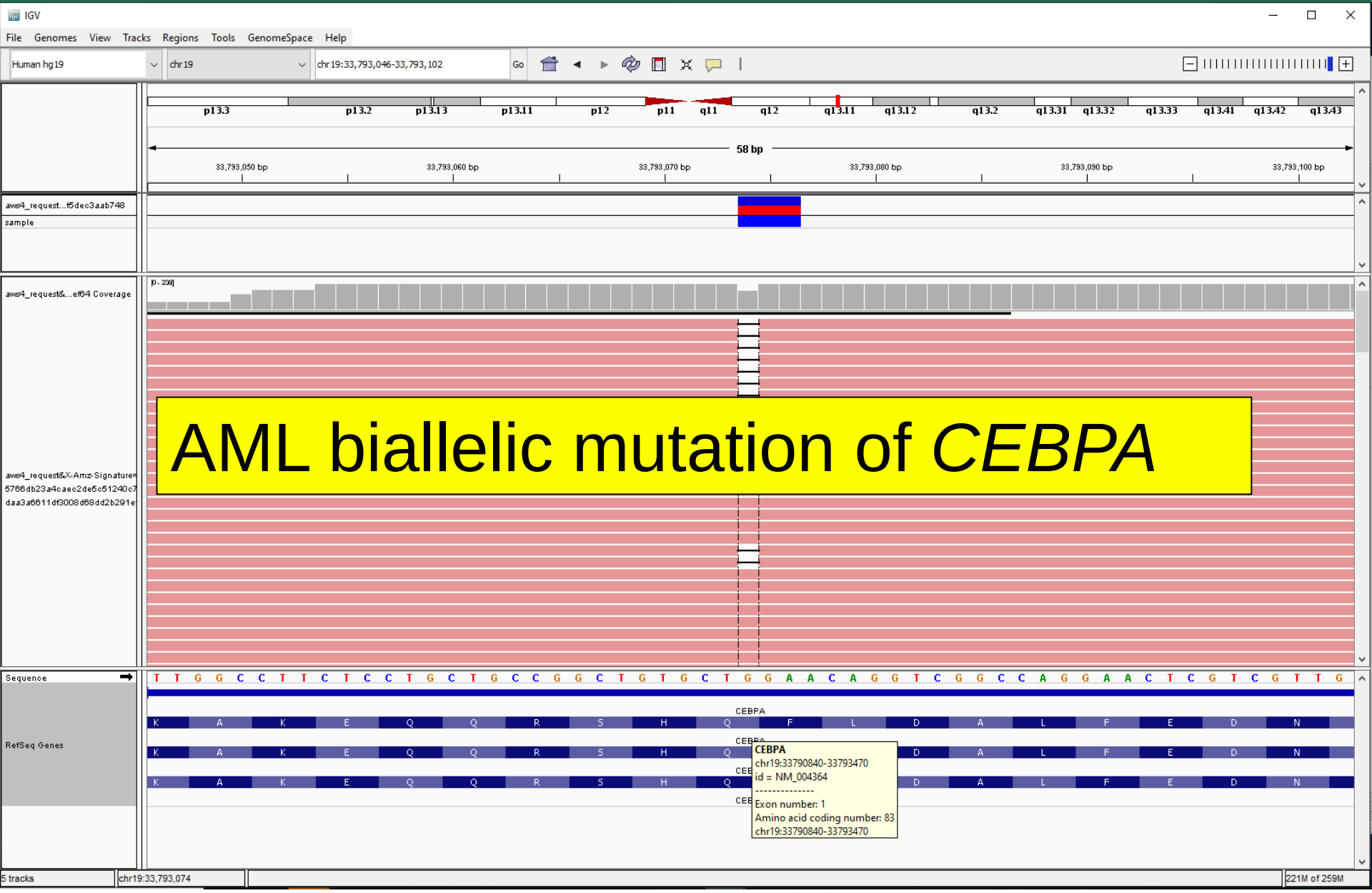
CEBPA
p.Q83Sfs*77

Interpretation: A ***CEBPA* p.Q83Sfs*77** variant has been detected at the allelic fraction of 20-30%

CEBPA gene encodes for CCAAT/enhancer binding protein alpha, a transcription factor that plays a key role in the differentiation of granulocytes. Mutations of CEBPA have been reported in 7% to 11% of patients with AML and the biallelic CEBPA mutations have been associated with a favorable outcome in patients with normal cytogenetics and who lack FLT3-ITD mutations (Renneville A, et al. Blood. 113(21):5090-3; 2009. Fröhling S, et al. J Clin Oncol. 22(4):624-33; 2004. Patel JP, et al. N Engl J Med. 366(12):1079-89; 2012. Preudhomme C, et al. Blood. 100(8):2717-23; 2002, Wouters BJ, et al.; Blood 113; 3088-91; 2009 Mar 26, Blood. 2016;127(20):2391-2405).

Mutations in CEBPA have been reported in 7% to 11% of patients with AML (or 13%-15% of those with NK-AML) and has been associated with a favorable outcome (similar to patients with CBF translocations) with regard to increased remission duration and OS outcome

IGV (INTEGRATIVE GENOMICS VIEWER)



TAKE HOME MESSAGES

- Different molecular techniques can be used to aid diagnosis, prognostication, and to guide therapeutic options (predictive marker) in hematologic malignancy.
- Each techniques (FISH, PCR & fragment analysis, single gene testing, next generation sequencing) has pros and cons and it is important to understand its strengths and limitations.
- Molecular and genomic testing will become a part of the standard of care for the management of many hematologic diseases.

HOPE NOT…..


Drowned in next generation sequencing data
HELP!
QUESTIONS?
http://biocomicals.blogspot.com