Haematology Cancer Consortium (HCC)

What can our chromosomes tell us?

Relevance of cytogenetic assessment in hematological malignancies.

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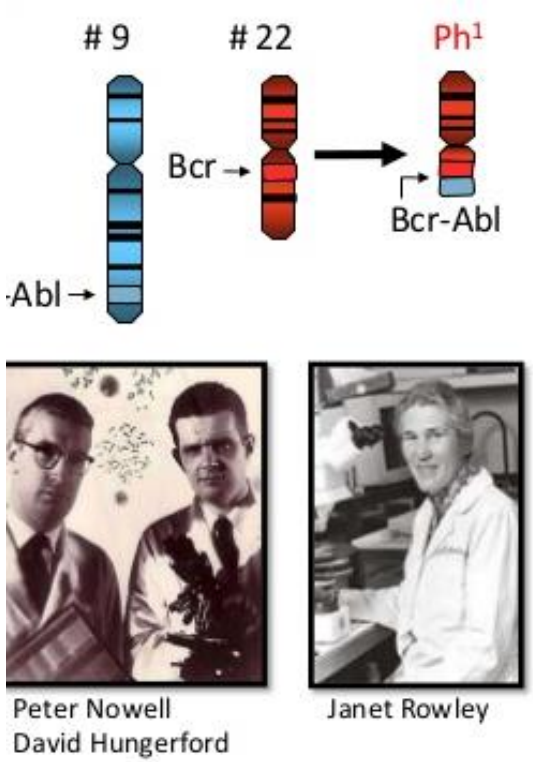
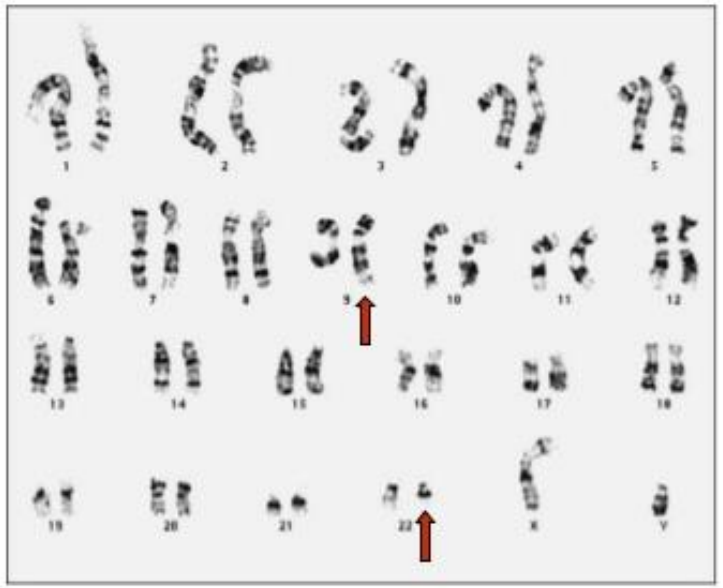
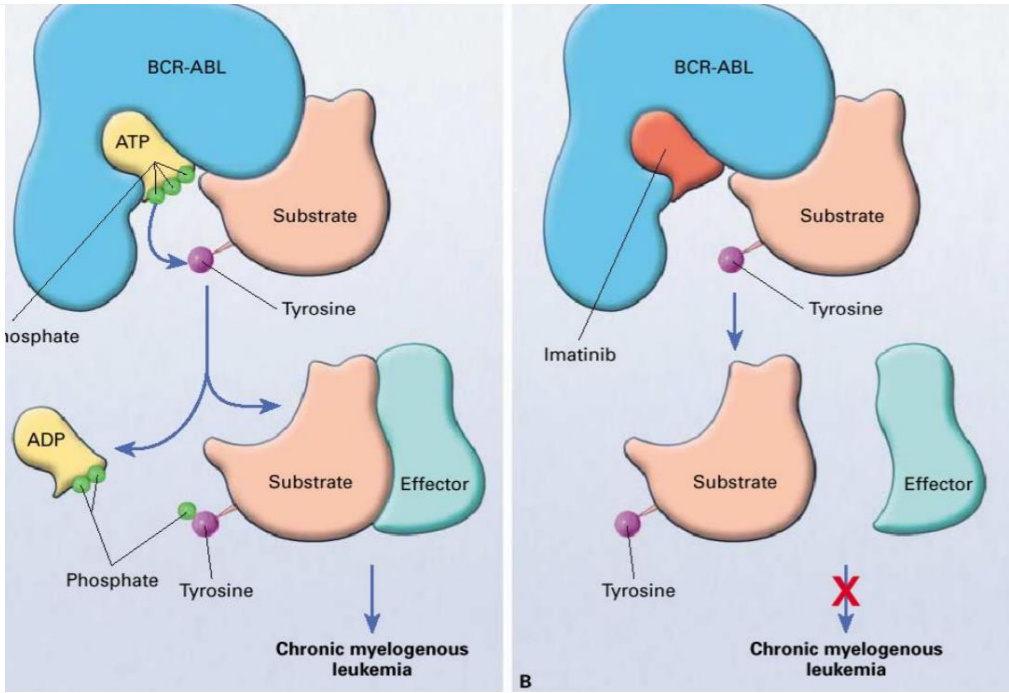
Origins of cancer: From viruses to oncogenes

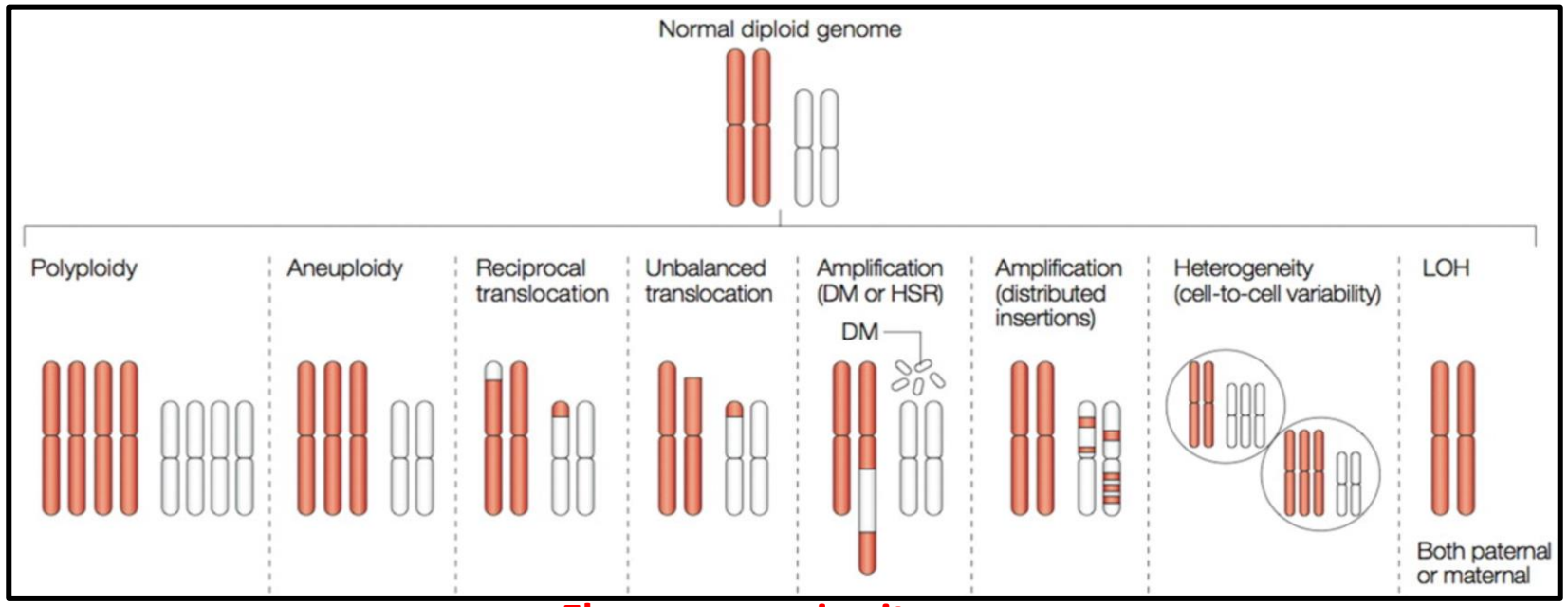




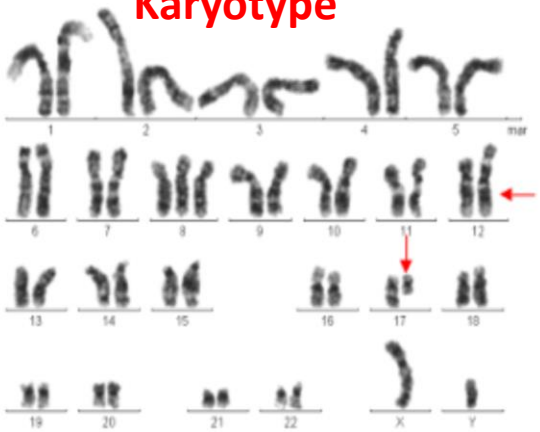


Haematologica 2016 Volume 101(5):541-558
J Clin Invest. 2007 Aug 1; 117(8): 2033–2035
Science 1960,132:1497
Nature 1973,2343,290-293

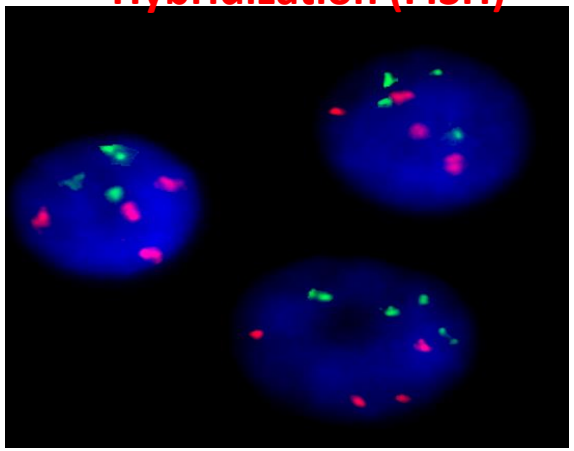
Chromosomal abnormalities in Cancer



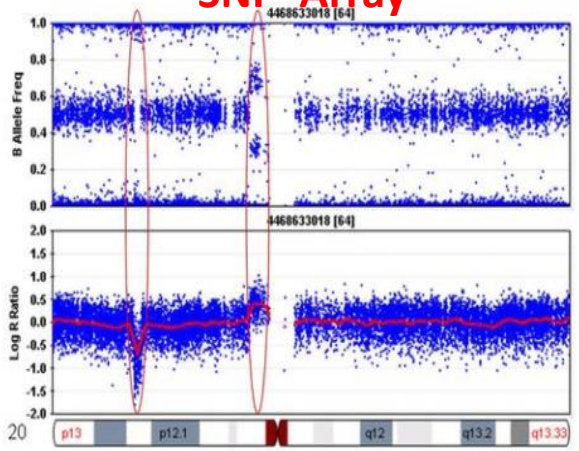
Karyotype



Fluorescence in situ Hybridization (FISH)

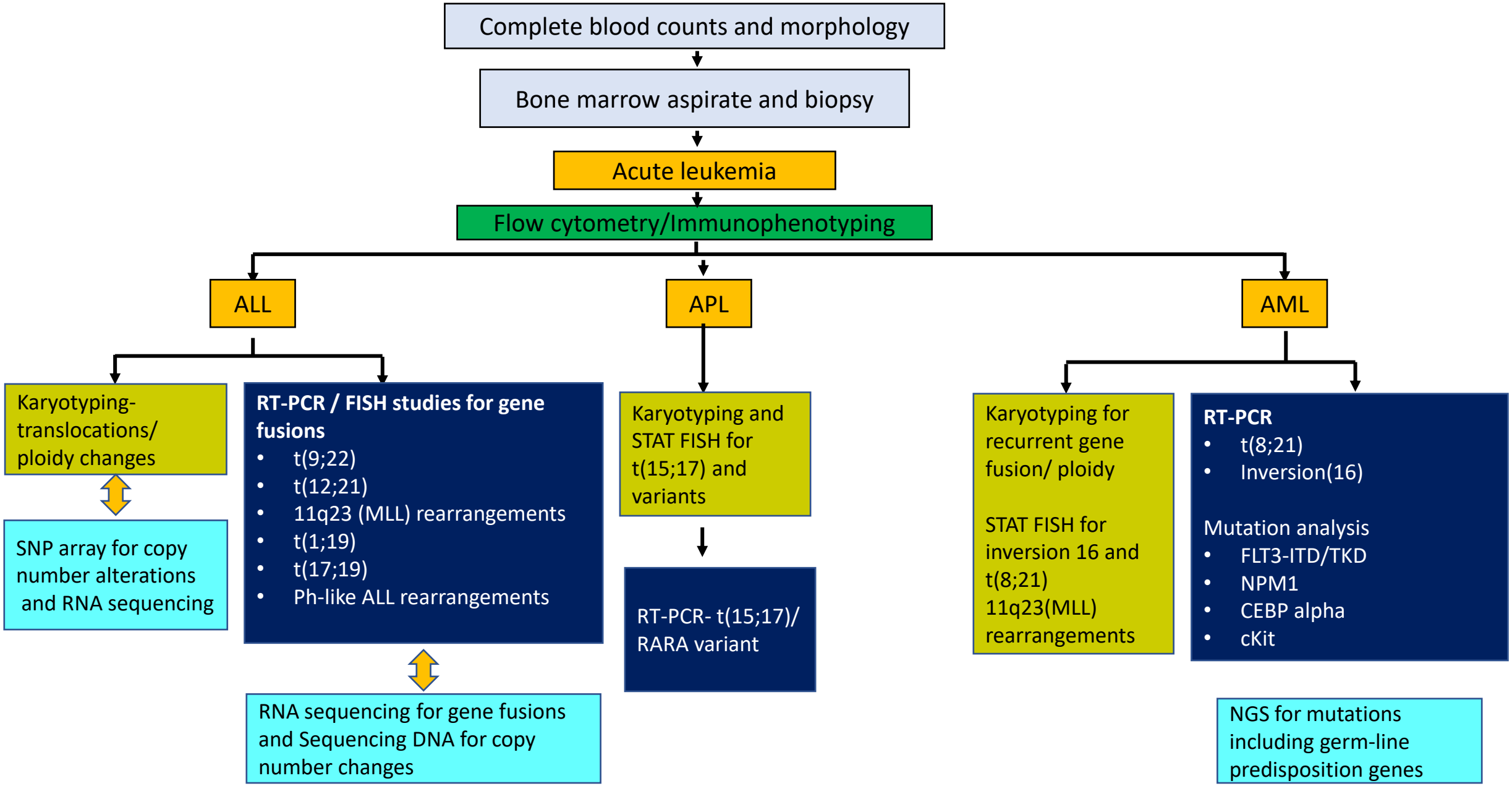


SNP Array

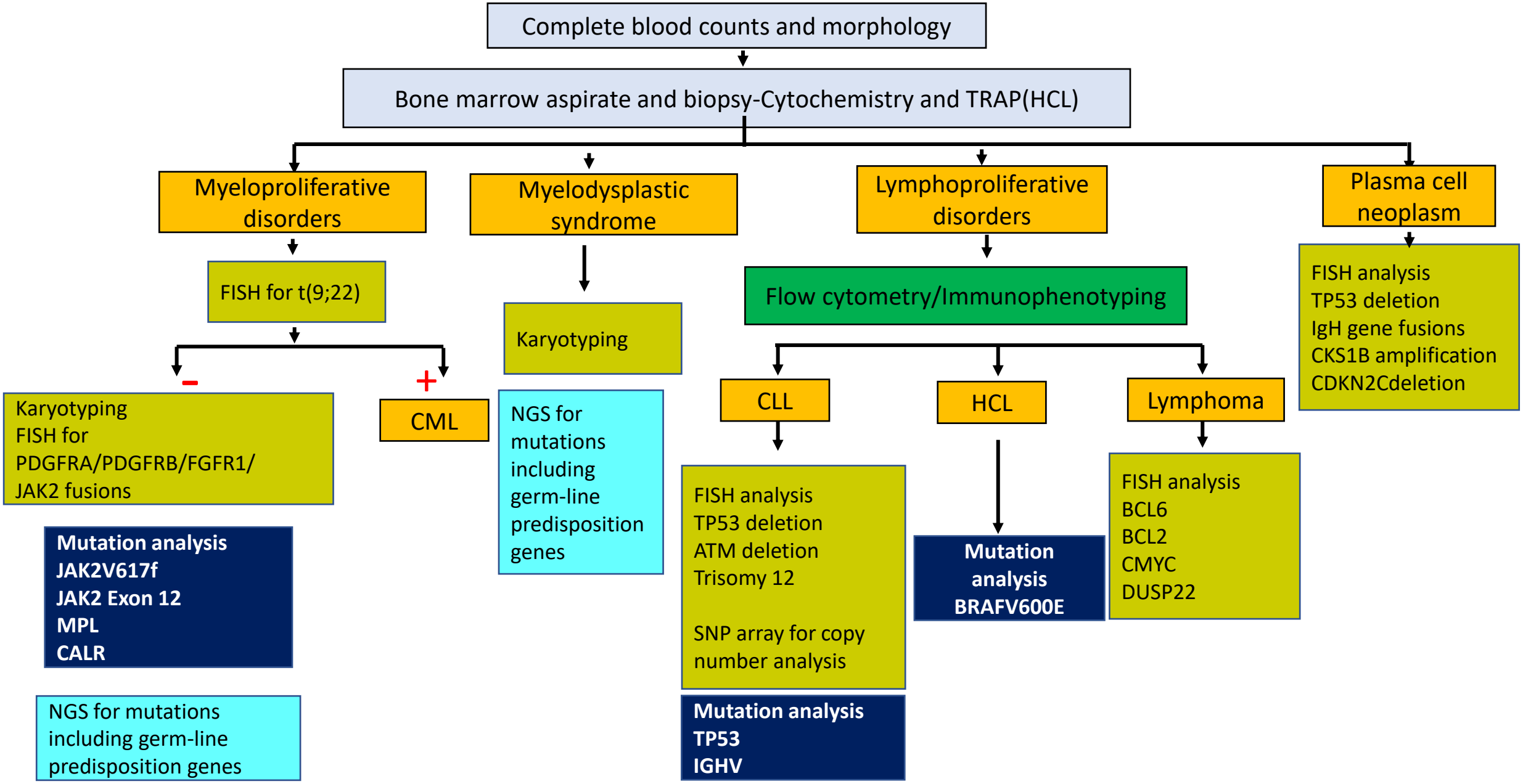


Chromosome abnormalities and cancer cytogenetics. Nature Education 1(1):68

Laboratory work up for haematological malignancies -I



Laboratory work up for haematological malignancies -II



Why should we test for chromosomal abnormalities?

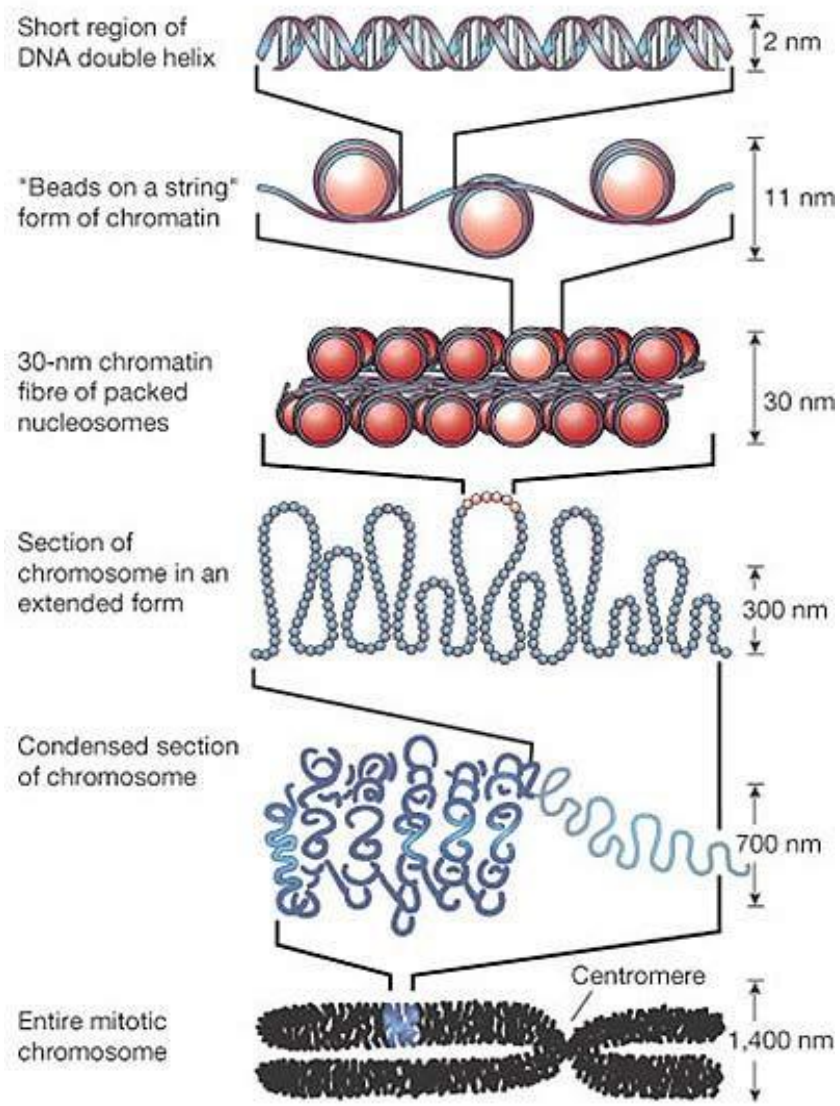
To establish the specific diagnosis

To estimate prognosis, based on the presence of a recurring abnormality, appearance of new karyotypic abnormalities, or the existence of clonal heterogeneity/evolution, which often signal a change in the pace of the disease, usually to a more aggressive course

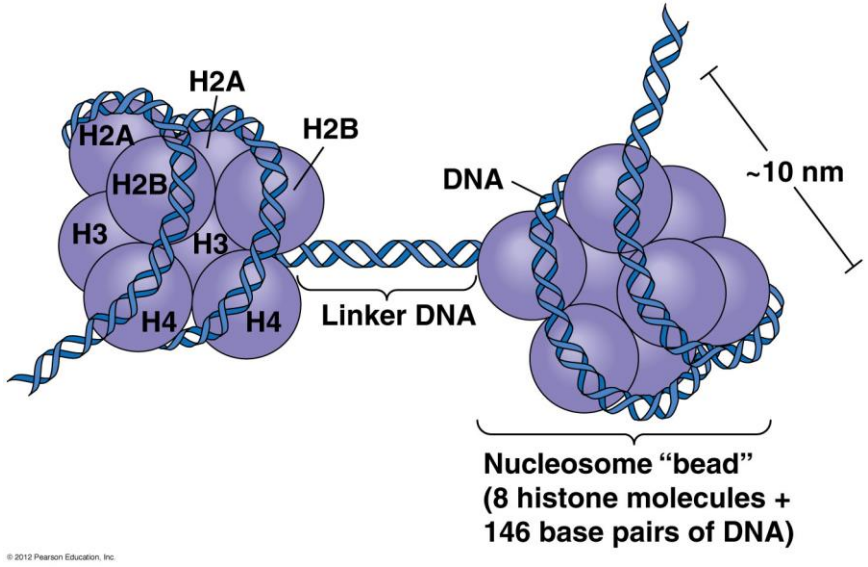
To help in the planning of treatment, since some chromosomal changes predict for response (or nonresponse) to specific therapies, or to inform the selection of a targeted therapy

To distinguish between benign reactive lymphoid or myeloid hyperplasia and a monoclonal malignant proliferation

DNA is packaged into chromosomes



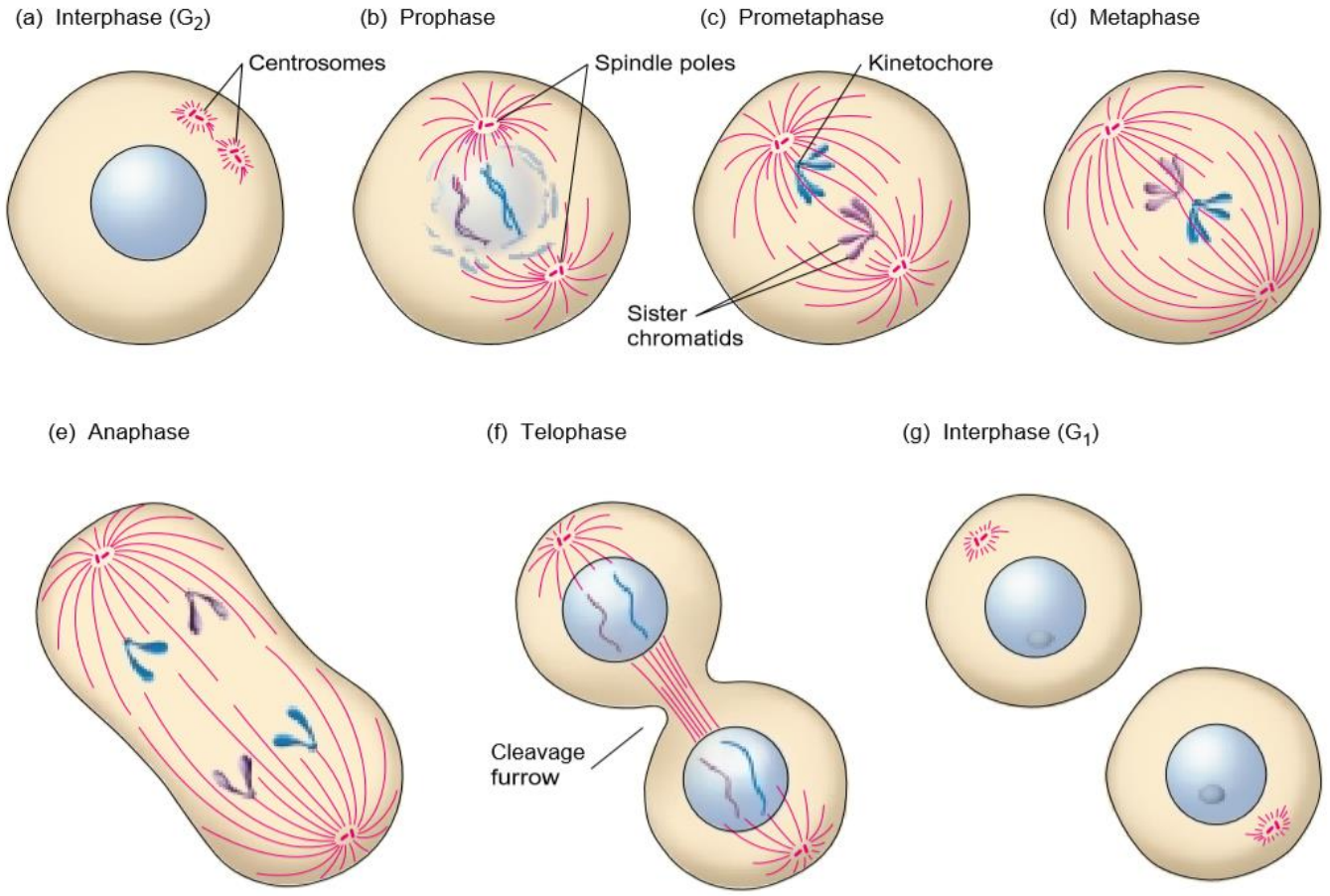
Coiling and packing at multiple level make chromosome condensed which is about 1metre long to fit into a nucleus of 5 micron in diameter.



The basic structural unit of chromatin, the nucleosome, was described by Roger Kornberg in 1974

Molecular Biology of the Cell Alberts, Bruce; Johnson, Alexander; Lewis, Julian; Raff, Martin; Roberts, Keith; Walter, Peter New York and London: Garland Science;

Chromosomes are best visualized during the metaphase stage of the cell cycle



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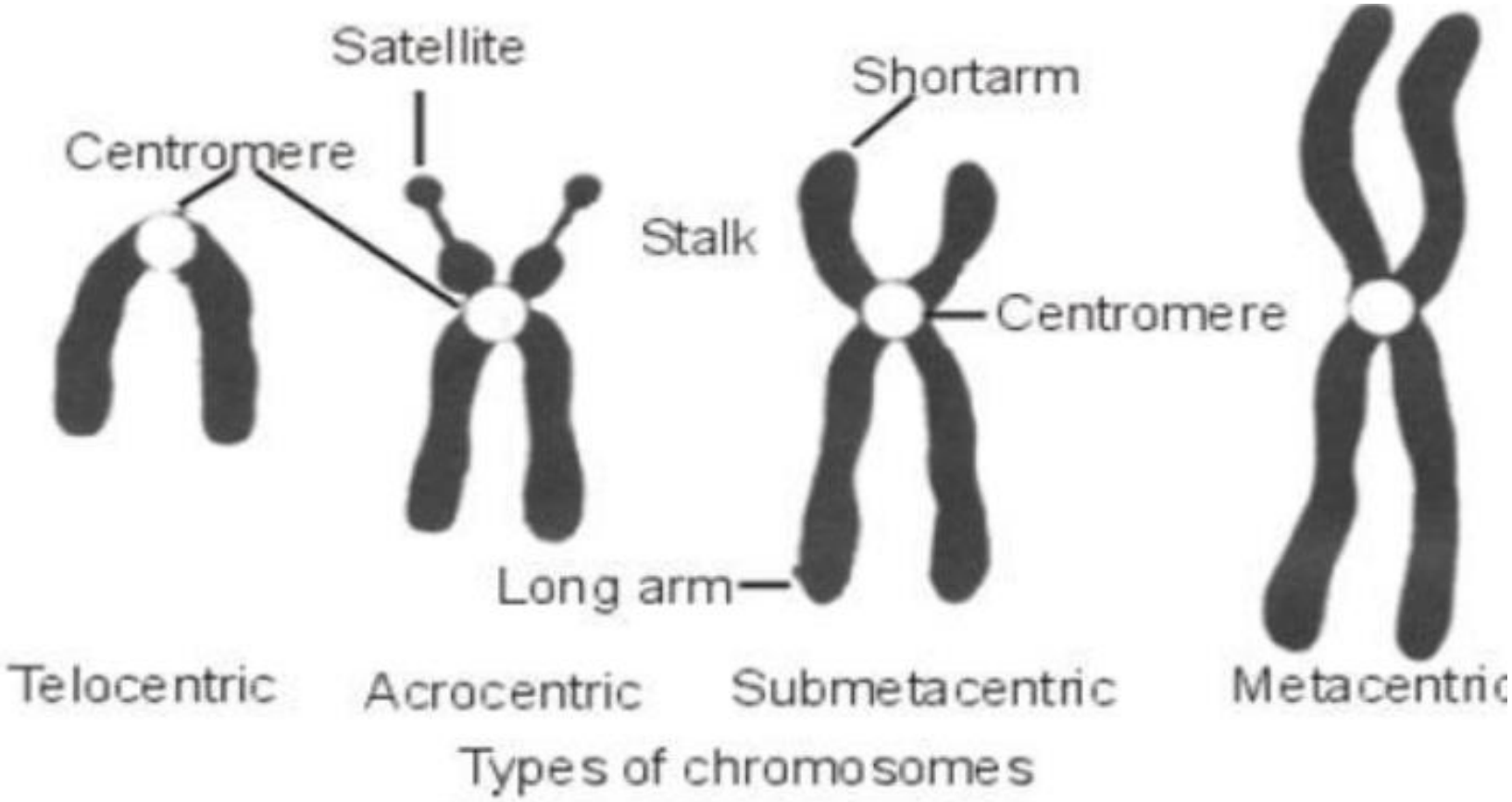
Chromosome identification and karyotype description



Stevens-Kroef M., Simons A., Rack K., Hastings R.J. (2017) Cytogenetic Nomenclature and Reporting. In: Wan T. (eds) Cancer Cytogenetics. Methods in Molecular Biology, vol 1541. Humana Press, New York, NY

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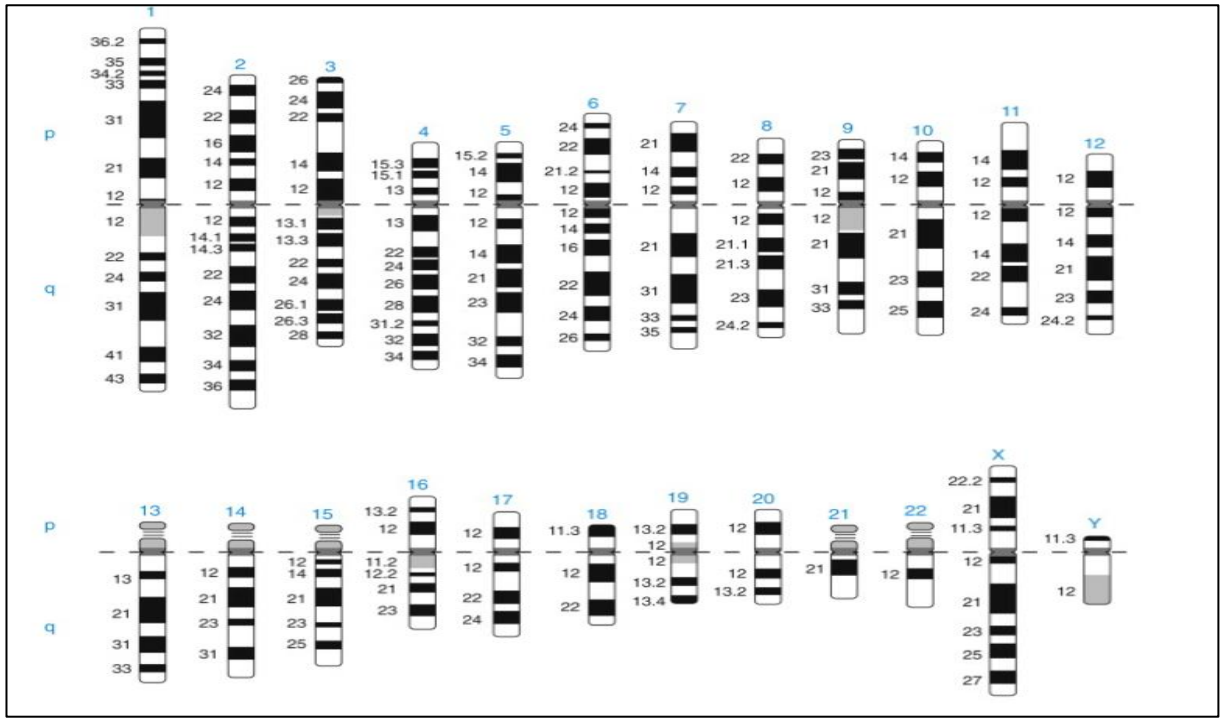

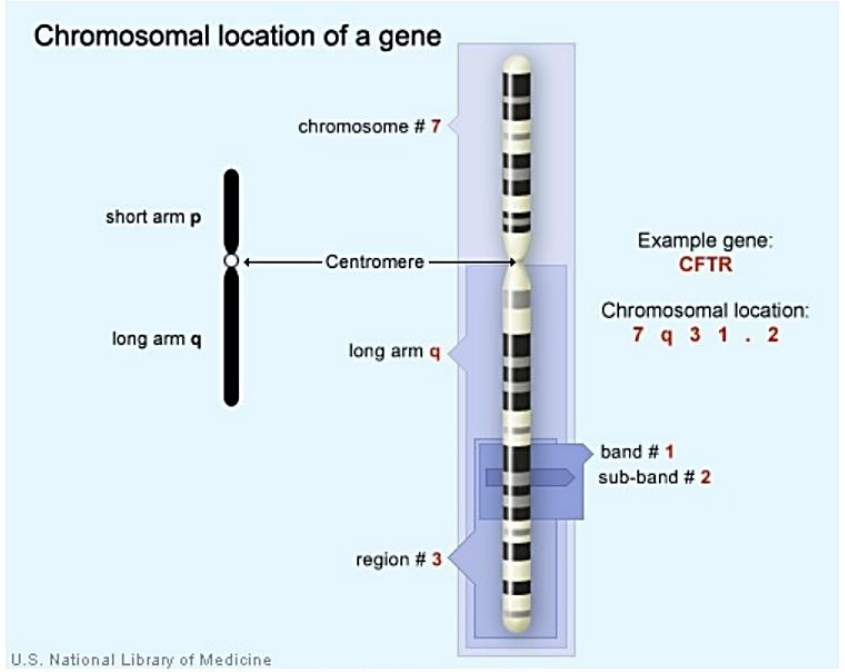

Credit: U.S. National Library of Medicine

Abnormalities are described according to ISCN standards:
Deletion- del : Translocation – t : Derivative- der : Inversion- inv : loss of one chromosome – minus(-):
Chromosome gain : plus symbol(+)

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To distinguish between benign reactive lymphoid or myeloid hyperplasia and a monoclonal malignant proliferation

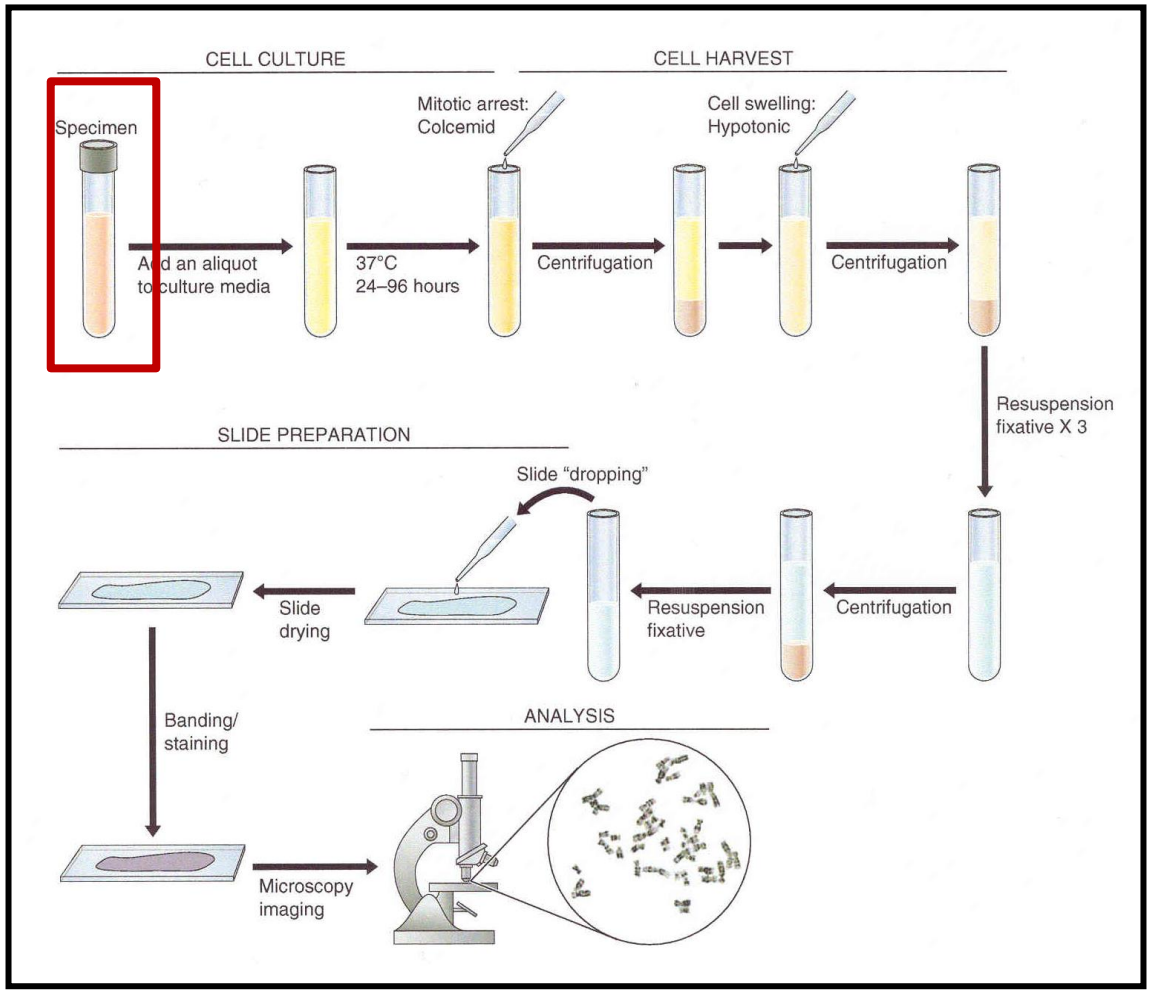
49 year old male presented with fever since 2 weeks. He was noted to have hepatosplenomegaly. Investigations revealed WBC count of 1.87 lac per cu.mm with 67% blasts. Diagnosed to have CML in blast crisis.

Aspirate :Acute myeloid Leukemia (81% blasts strongly positive for SBB).In view of increased basophils in the peripheral blood and bone marrow a possibility of CML in blast transformation should be considered. Also kindly exclude the possibility of an APML in view of the blast morphology and cytochemistry.

Trephine:
Acute leukemia consistent with acute myeloid leukemia

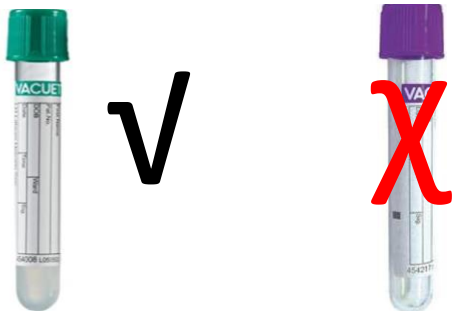
IPT :
Consistent with AML

Do's and Don'ts of sample requirements for karyotyping



Sample: Bone marrow

Collection tube: Heparin ! Heparin! Heparin!



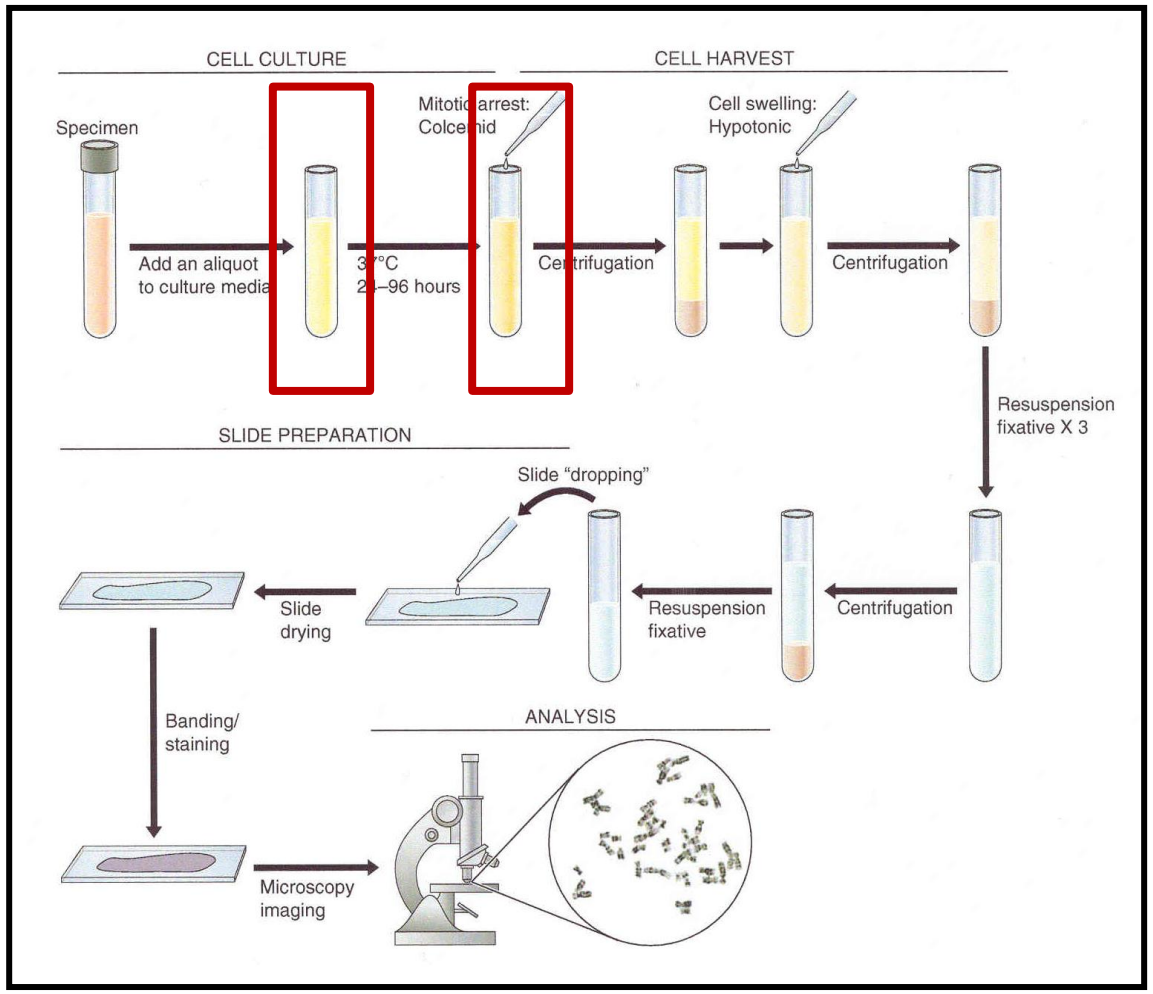
Transport

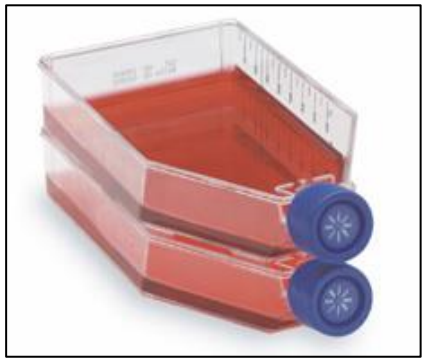
<48 hrs if being shipped(Myeloma – same day)

Do **NOT** freeze- Transport in room temperature

The AGT Cytogenetics Laboratory Manual, Fourth Edition. Page 26-60
General Guidelines and Quality Assurance for Cytogenetics, E.C.A. Newsletter, January 2012

Karyotyping workflow : Culture initiation and mitotic arrest



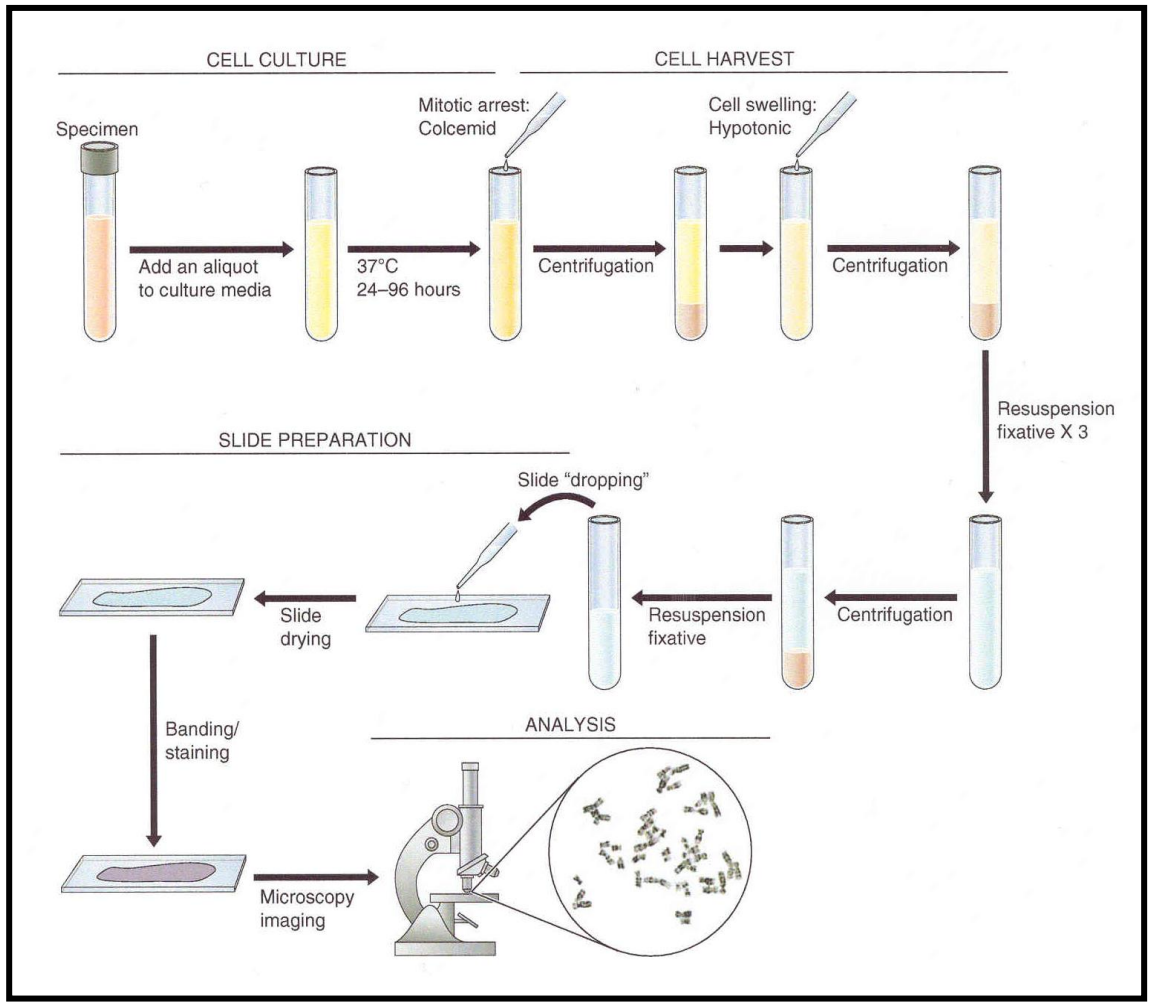


- Rapidly proliferating cells
- Unstimulated except in myeloma and chronic lymphocytic leukemia
- 1.5 x 10^6 /ml of medium

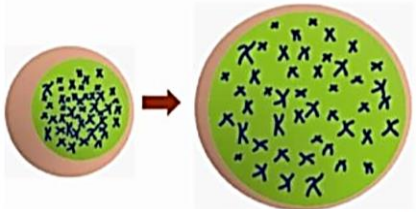
- Mitotic Inhibitor
- Disrupts spindle tubules
- Morphology of chromosomes varies according to colcemid conc and duration of treatment

The AGT Cytogenetics Laboratory Manual, Fourth Edition. Page 26-60

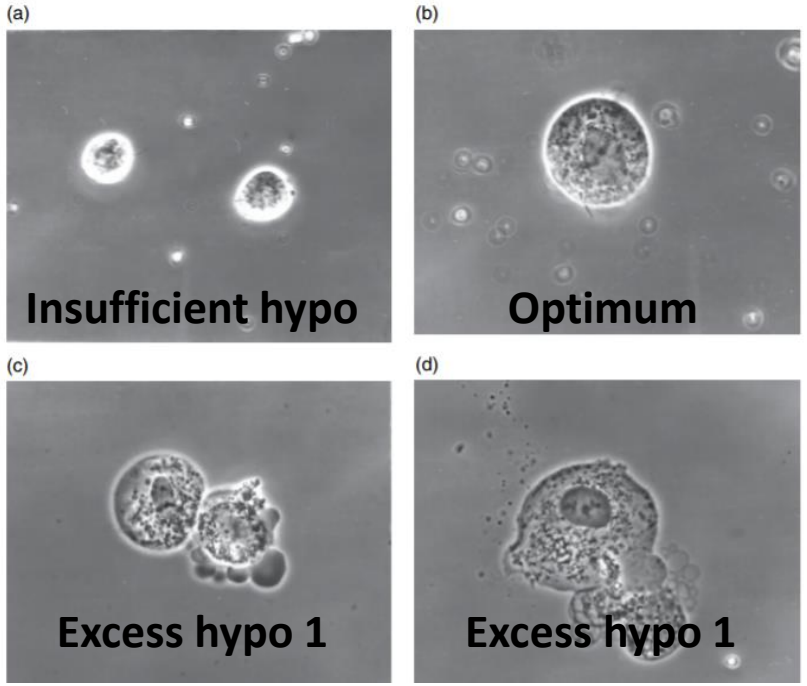
Karyotyping workflow: harvest



Hypotonic - 0.075 M Potassium chloride

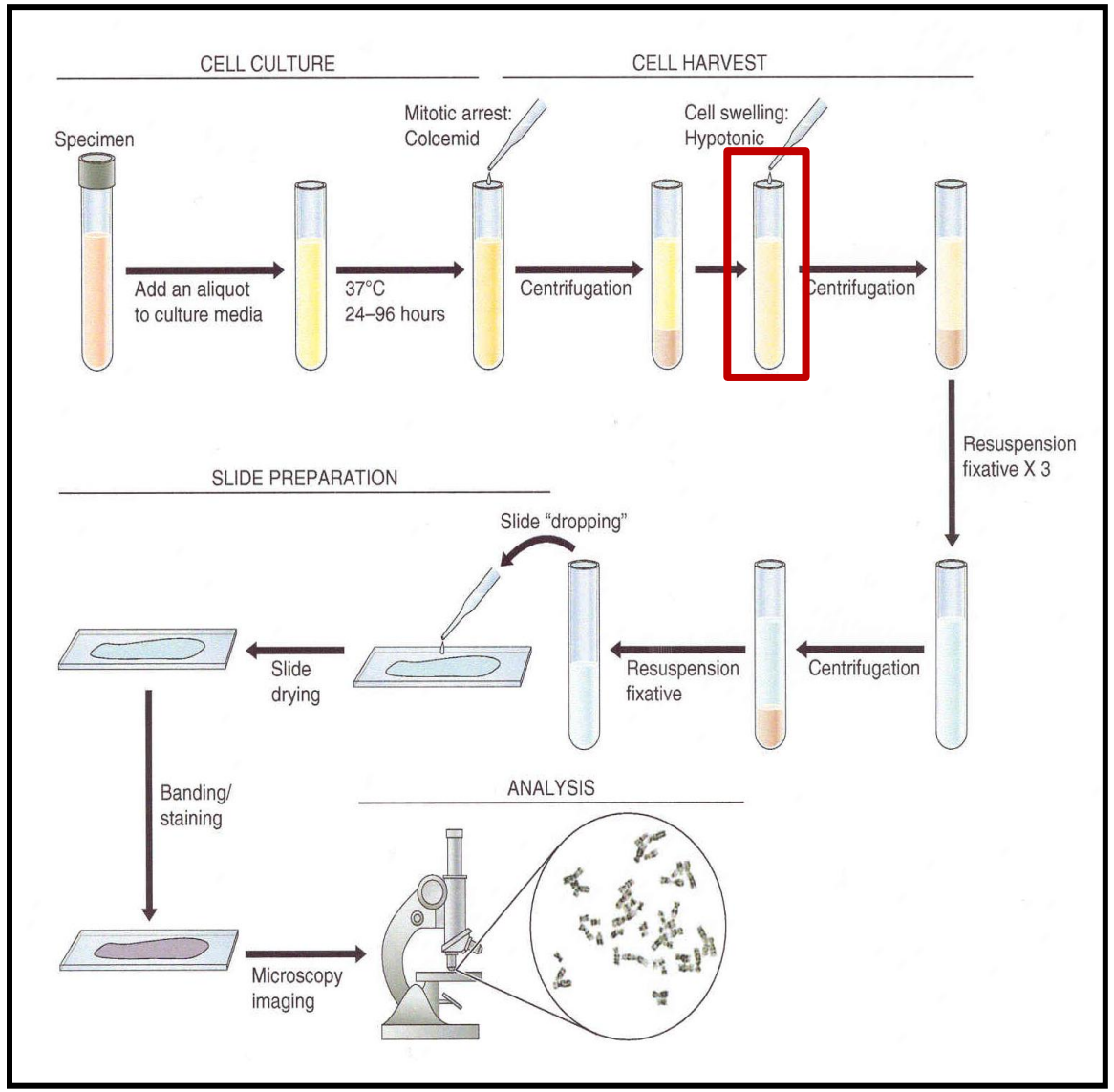


Cells swell enabling chromosomes to spread



The AGT Cytogenetics Laboratory Manual, Fourth Edition. Page 39

Karyotyping workflow



Fixation- Modified Carnoy's fixative
Methanol:acetic acid 3:1

- removes water from the cells
- kills and preserves them,
- hardens membranes and chromatin and preparing the chromosomes for the banding procedure.

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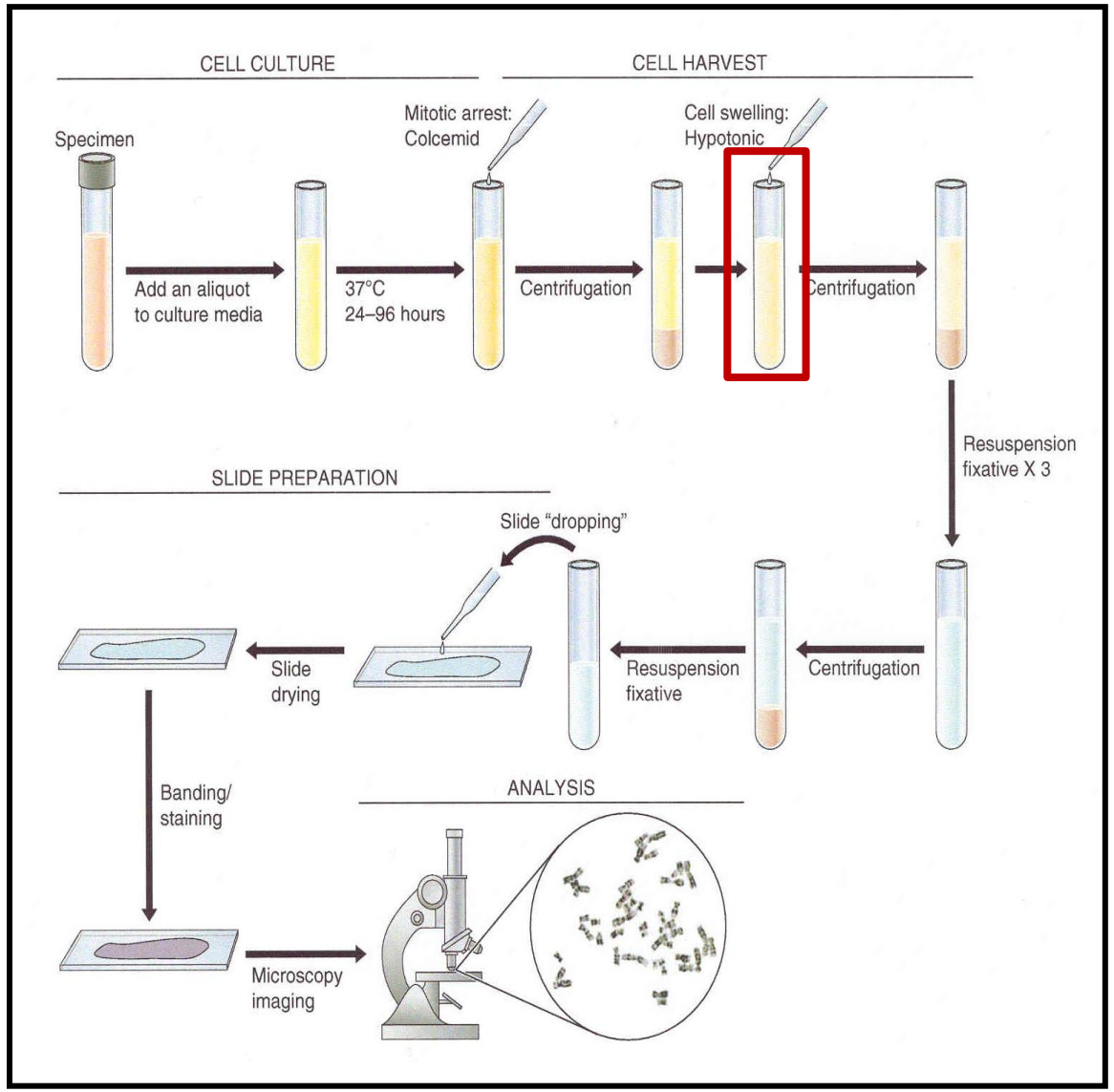
Karyotyping workflow



Slide making and banding

- Slide prepared under controlled environment conditions
- Slides are treated with trypsin to degrade scaffold proteins
- stained with Geimsa / Leishman's

Capture and analysis

- 20 cells per sample
- Software aided analysis

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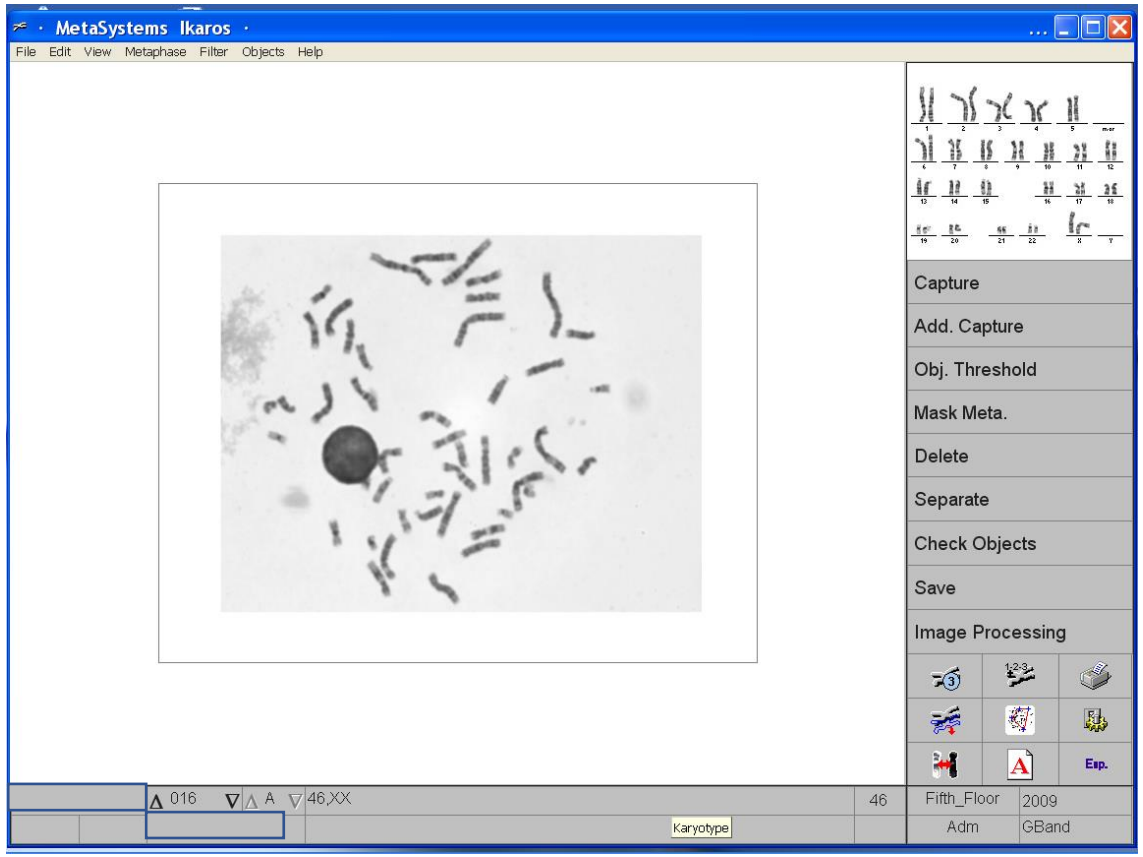
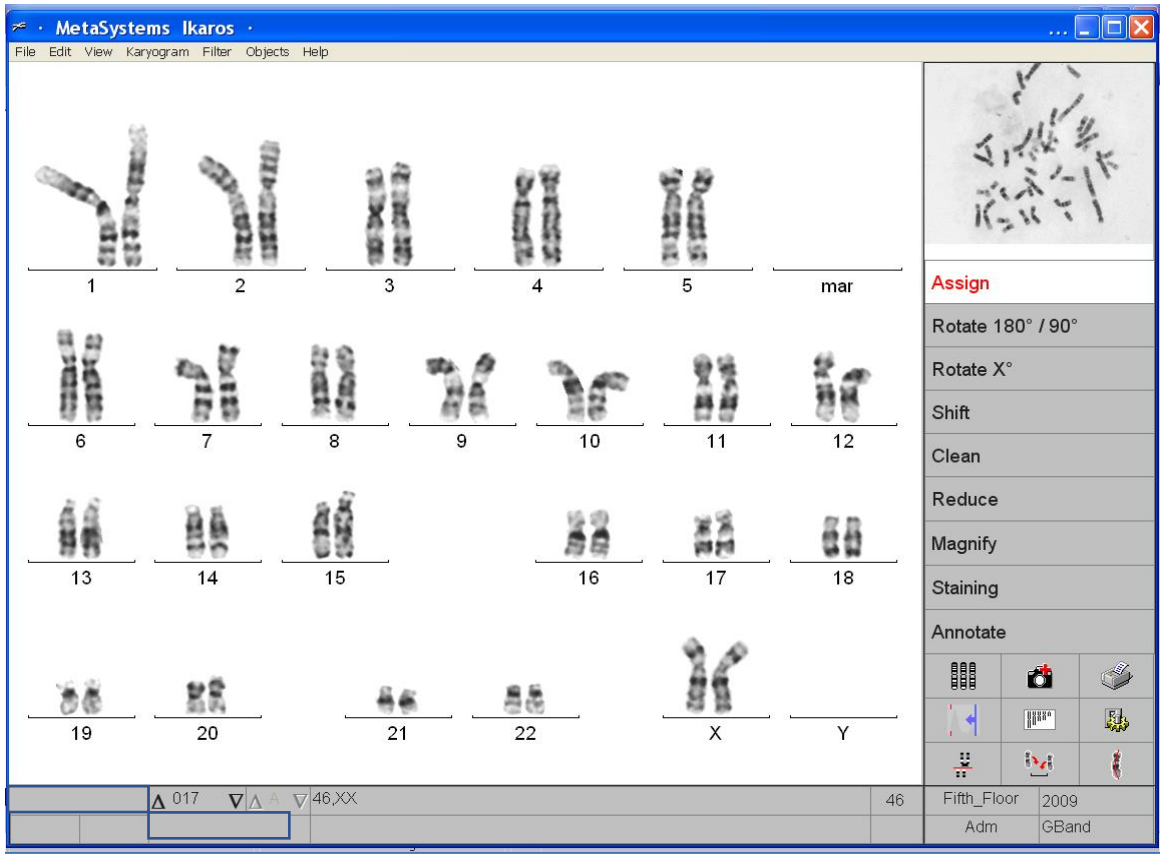
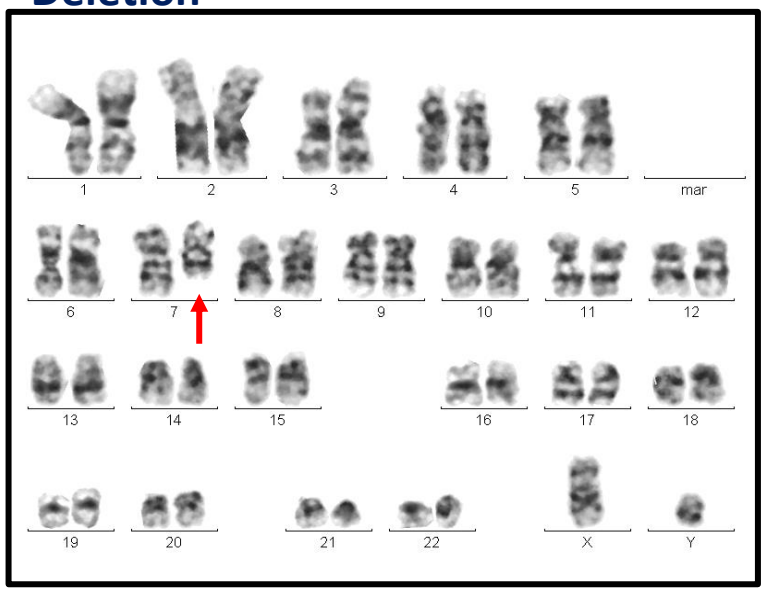
Analysis workstation



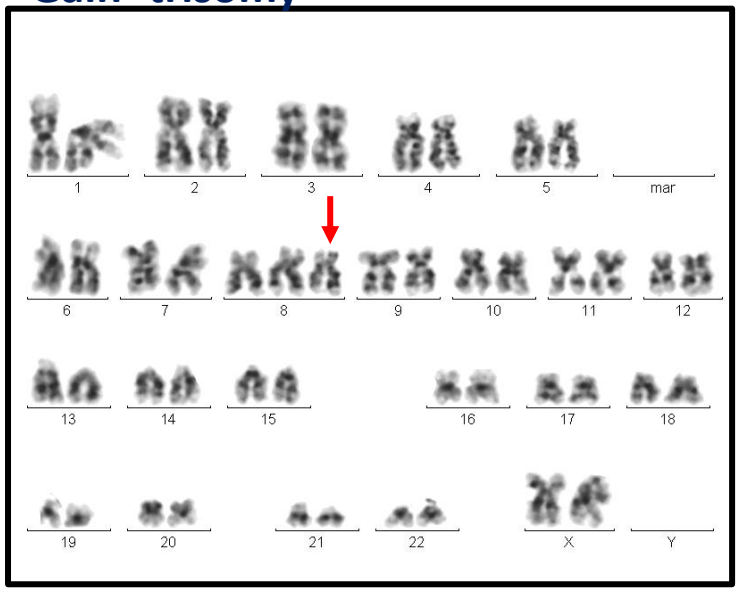


What is a clonal abnormality?

Deletion



Gain- trisomy



Loss- Monosomy

- **Structural aberrations:** 2 out of 20 cells should have same abnormality
- **Numerical Gain (trisomy): 2 out of 20 cells** should show gain of the same chromosome
- **Numerical loss(monosomy): 3 out of 20 cells** should show loss of the same chromosome

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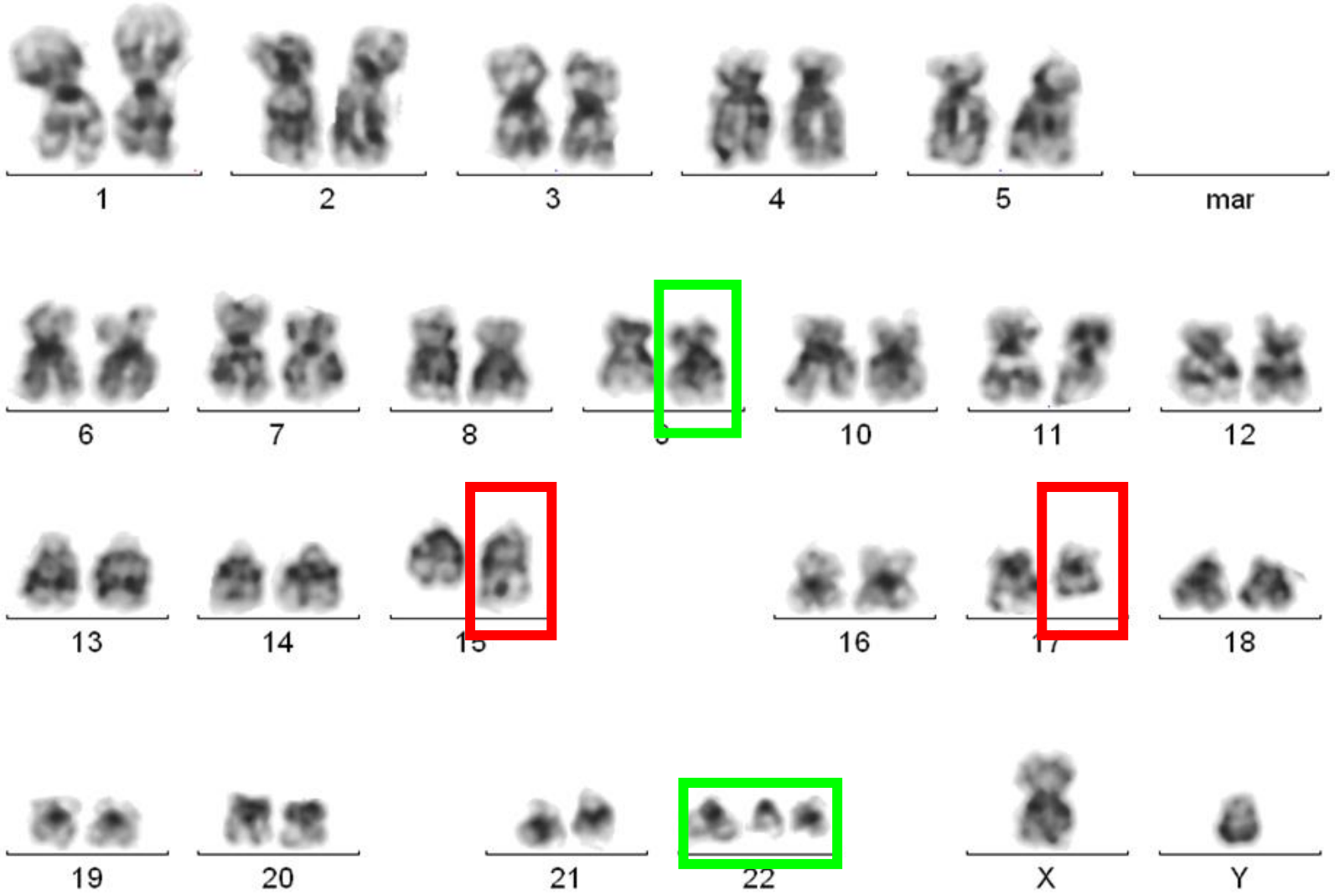
Karyotyping - a whole genome scan



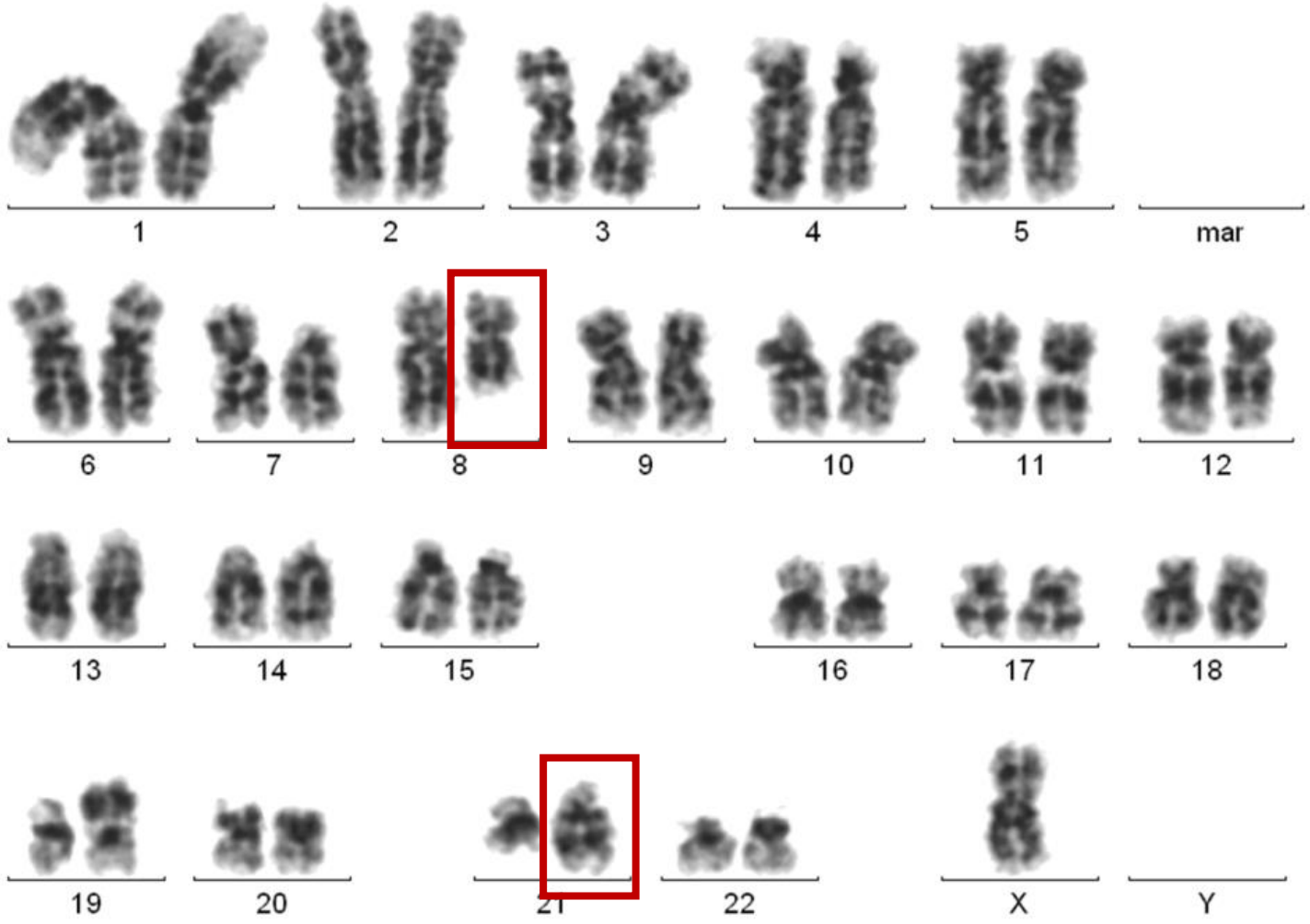
40 year old male was evaluated for fatigue and weight loss – noted to have pancytopenia. On further evaluation, diagnosed to have chronic myelomonocytic leukemia – 1 (5% blasts) on the basis of bone marrow morphology and he was started on decitabine.

Aspirate :
Solidly cellular marrow with multilineage dysplasia with 5% blasts and decreased megakaryocytes. Note: peripheral blood shows leukocytosis(3%blasts), leukoerythroblastic blood picture, severe dysplasia and monocytosis.

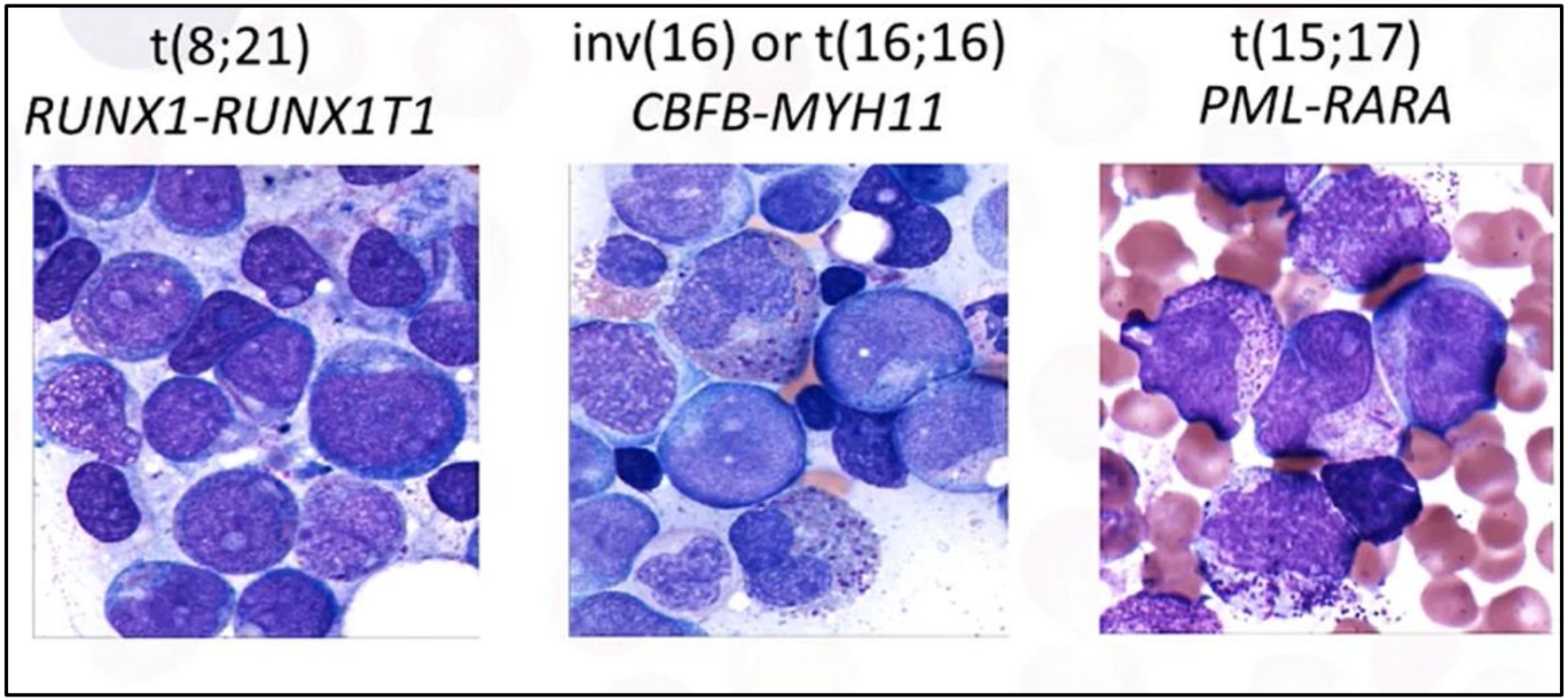
Trephine:
Moderately hypercellular marrow with myeloid hyperplasia, shift to left and mild dysmegakaryopoiesis and mild increase in immature precursors (~5-6%).

IPT :
Consistent with myeloid blast with aberrant CD19.
NGS :
NRAS mutation

Karyotype : 45,X,-Y,del(7)(p12),t(8;21)(q22;q22),add(19)(p13.3)[19]/46,XY[1cell]
FISH : 93% positive for RUNX1/RUNX1T1



Cytogenetic abnormalities that define AML (Blasts<20%)



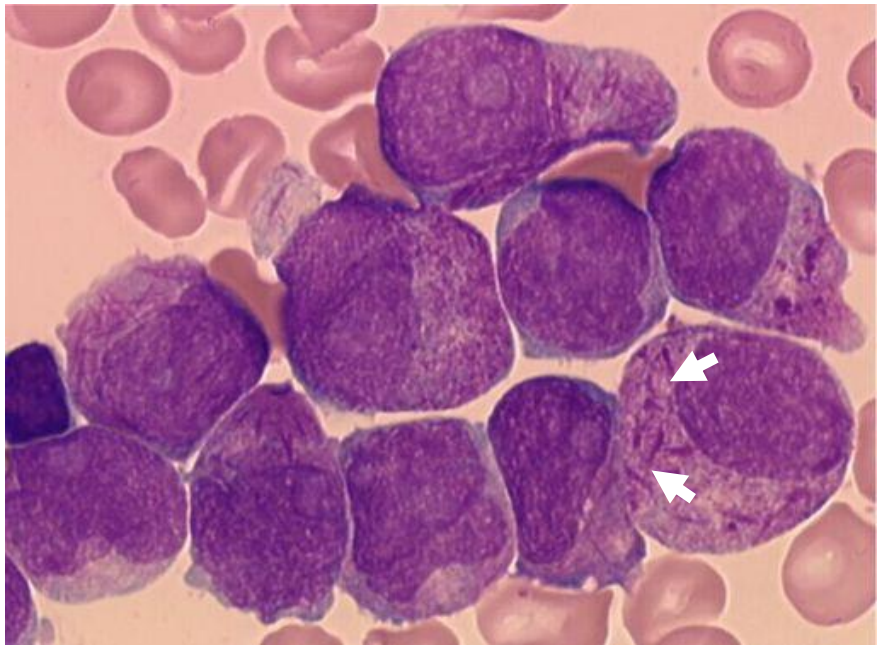
Blood (2016) 127 (20): 2391–2405

Probing deeper : Fluorescence *in situ* hybridisation

20 year male with fever, spontaneous bleeds from nose over 1 week.o/e : No hepatosplenomegaly, no lymphadenopathy

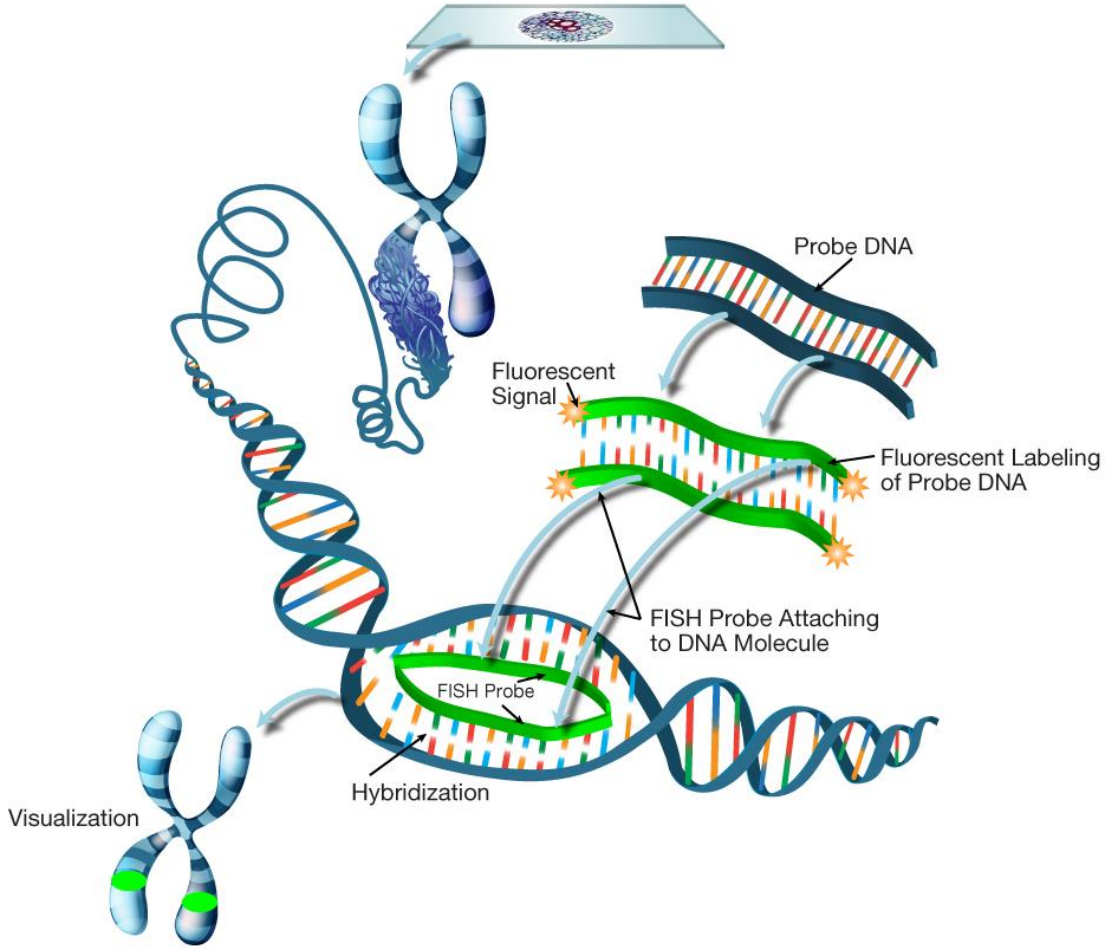
Total leucocyte count : 10,000/cc with 60% promyelocytes. Platelets reduced markedly (10,000/cc)

“Bunch of sticks” appearance of Auer rods in promyelocytes



Principle of FISH and advantages over karyotyping

Based on the hybridization of a fluorescently labelled probe binding to a complementary region on the patient's DNA



- Does not need dividing cells- applied widely in myeloma where plasma cells are slow to divide
- Probe size is small- can detect abnormalities upto 50kb whereas resolution of G banded chromosome in 5-10mb.
- Analyze 200 cells whereas in karyotyping we analyze only 20

FISH probes-points to remember

Probe design

1. Dual color dual fusion
2. Dual color break apart
3. Locus specific identifier
4. Chromosome enumeration probe
5. Whole chromosome paint

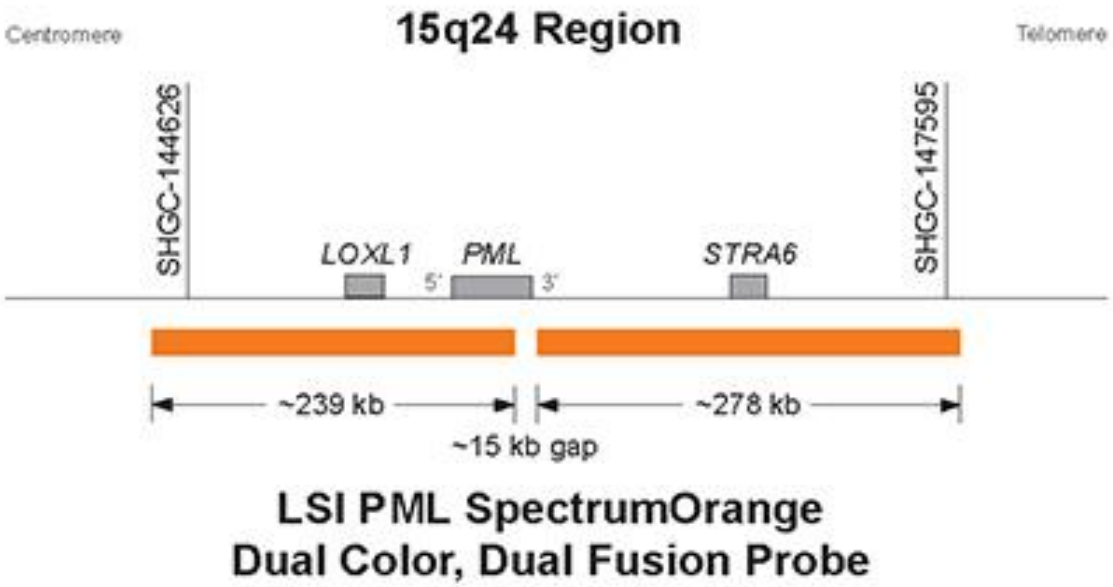
Fluorochromes

1. FITC
2. Texas red
3. Aqua
4. Gold

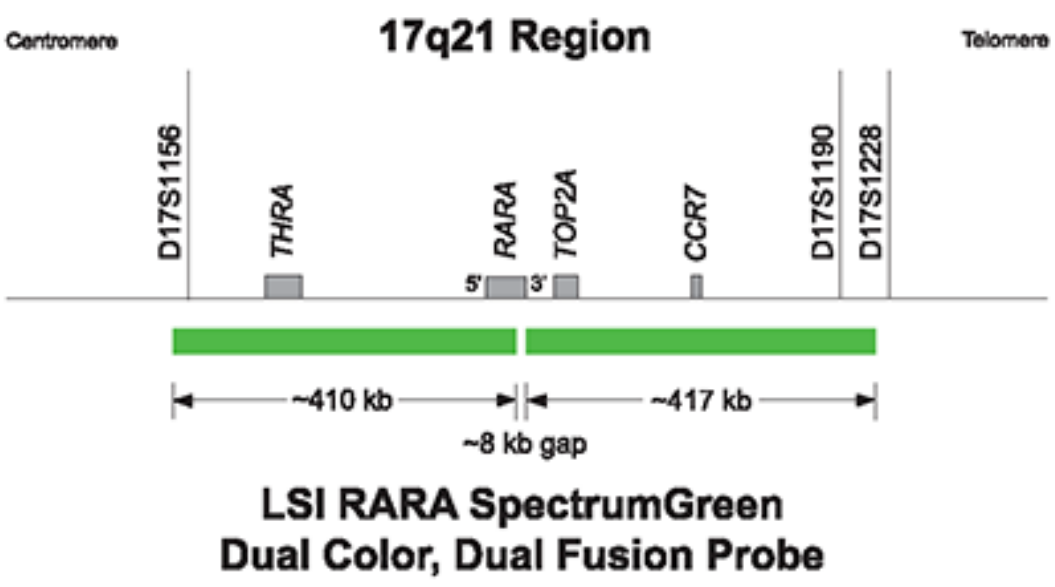
Reaction conditions

Specific to manufacturer

Probe design- Dual color dual fusion



LSI PML SpectrumOrange
Dual Color, Dual Fusion Probe



LSI RARA SpectrumGreen
Dual Color, Dual Fusion Probe

STAT FISH: Results provided in 4 hours!

FISH-Workflow

Pretreatment

Denaturation and Hybridization

Post Hybridization wash

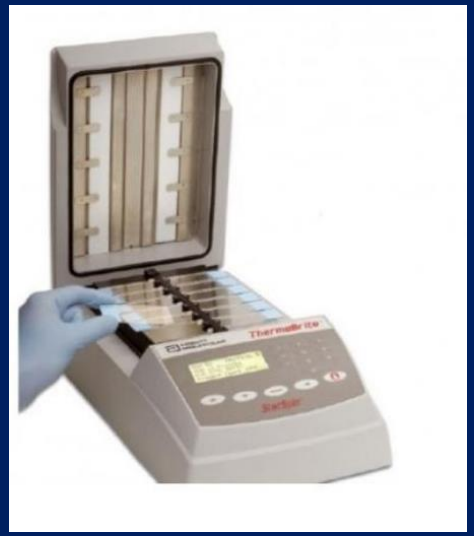
FISH-Workflow

Pretreatment

2XSSC

- condensing effect on chromatin,
- more discrete FISH signals,
- hardens the chromatin to prepare it for the harsh treatment during denaturation

Formamide/ Thermobrite

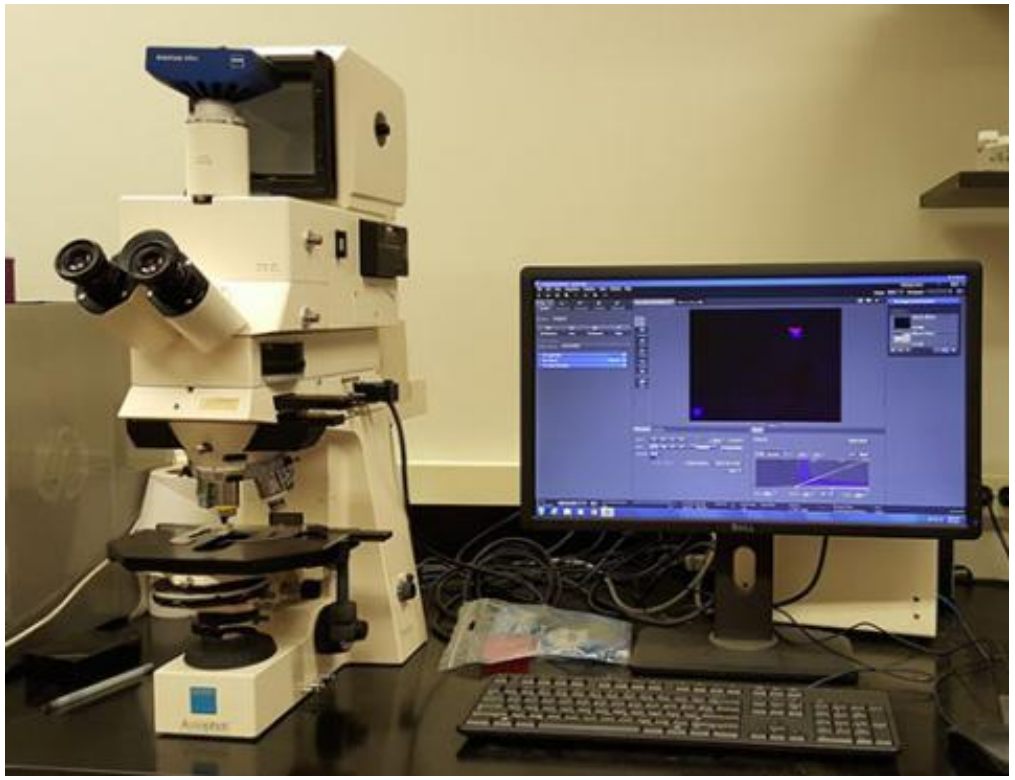


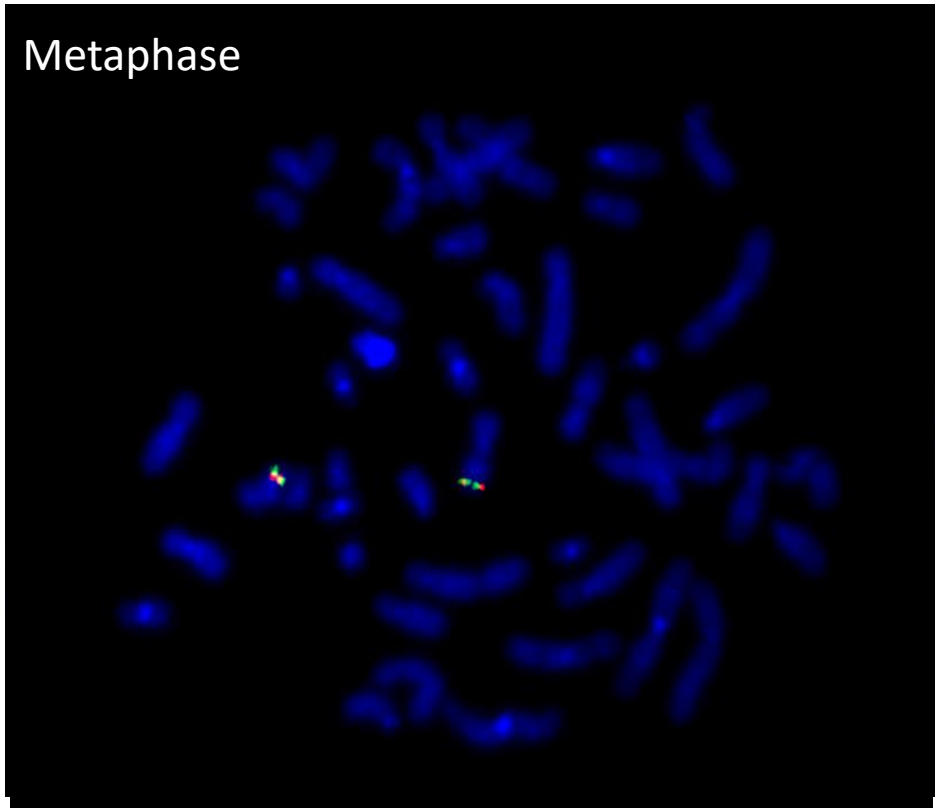
Post Hybridization wash

high temperature, low salt

0.4 X SSC with 0.3% NP 40
2 X SSC with 0.1%NP 40

FISH analysis

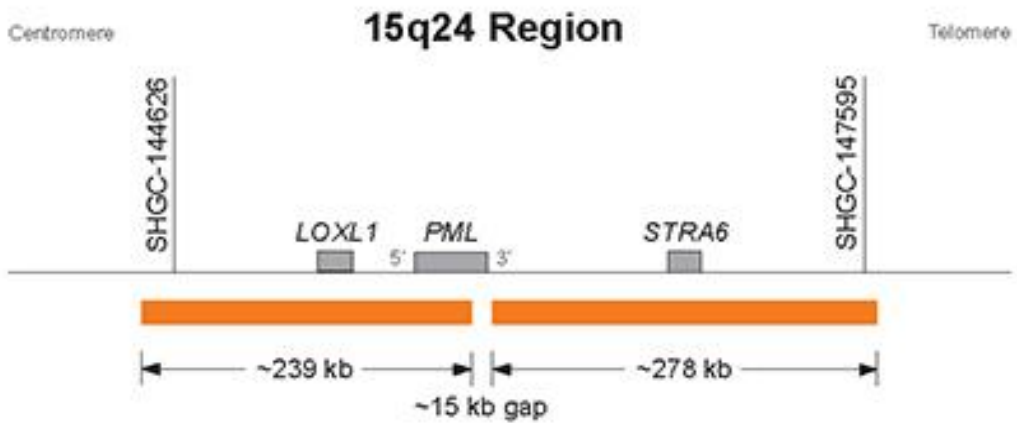




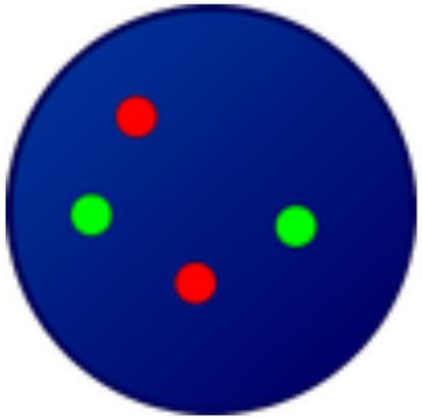
Total number of cells counted= 200

2 FISH readers count 100 cells each- result is reported as an average of the two readings.

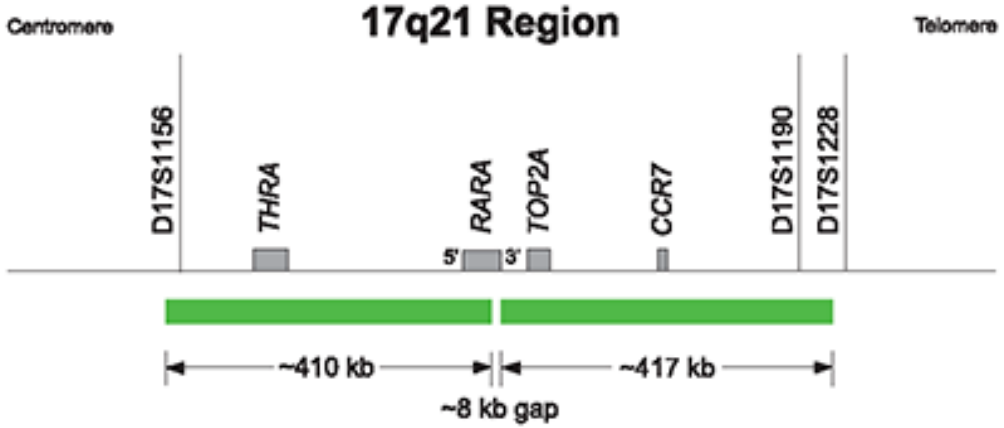
PML/RARα probe



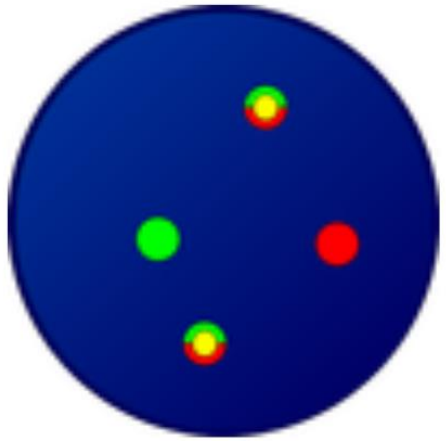
LSI PML SpectrumOrange
Dual Color, Dual Fusion Probe



Negative

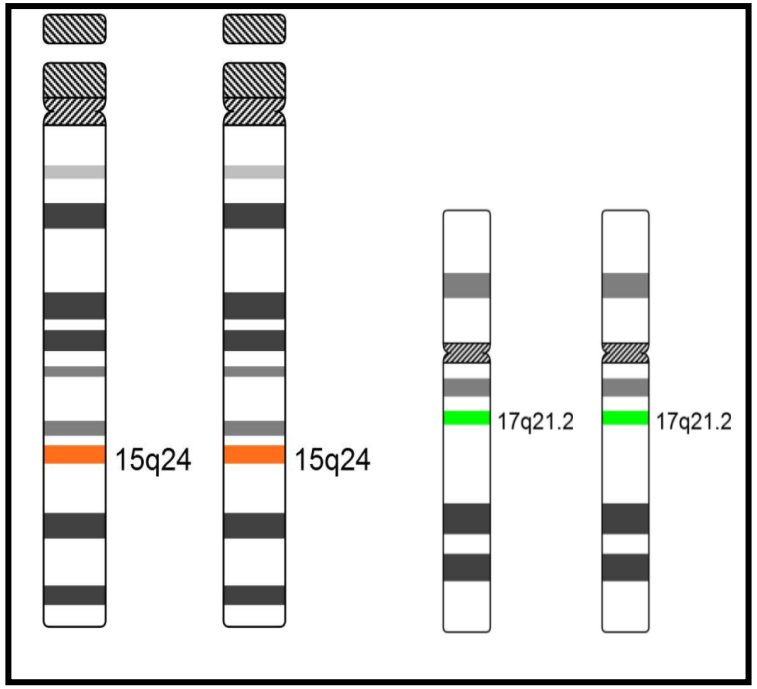


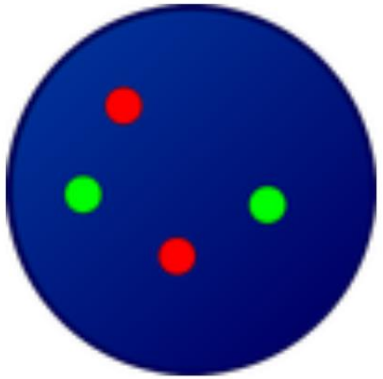
LSI RARA SpectrumGreen
Dual Color, Dual Fusion Probe



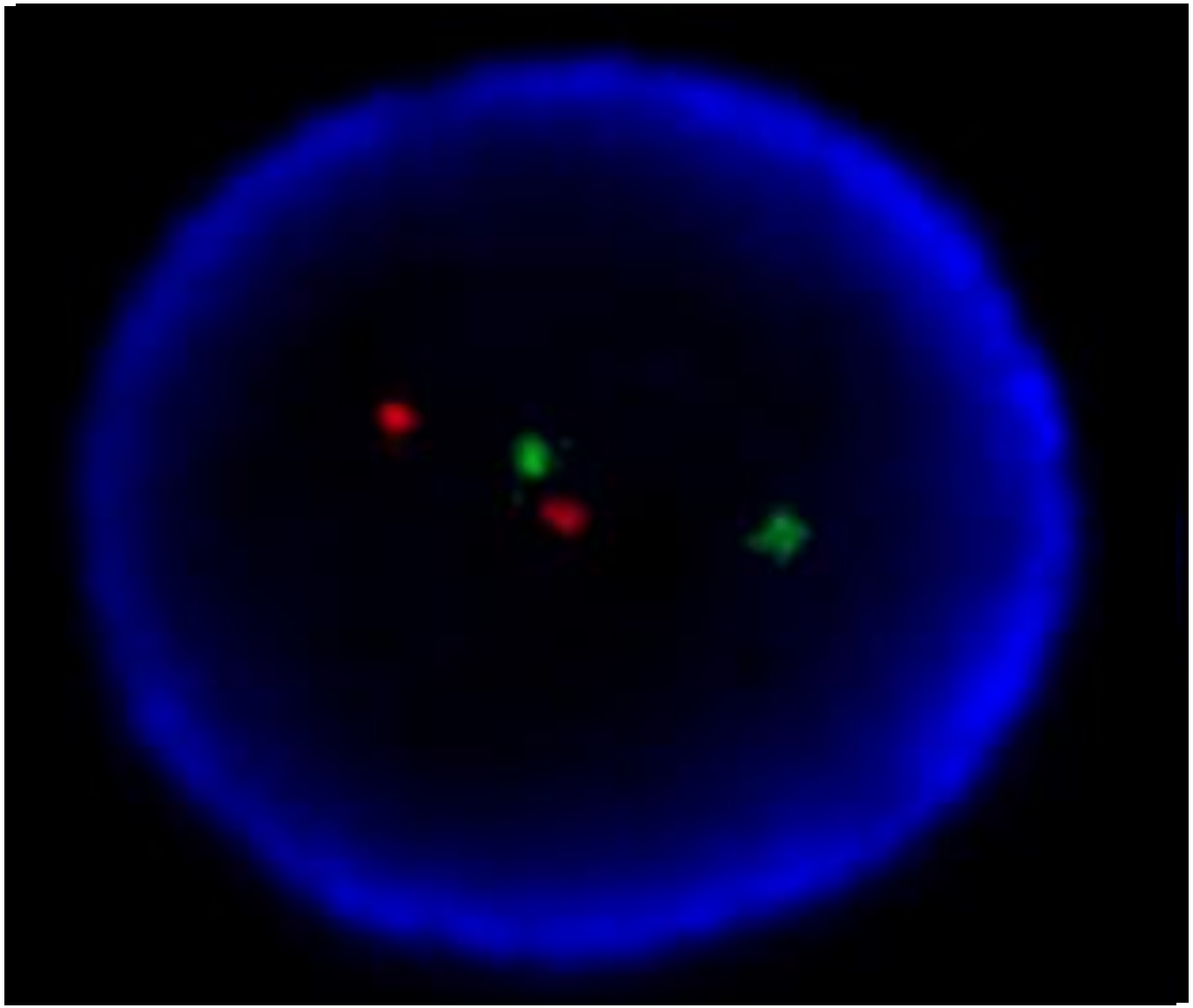
Positive

Negative for PML/RARA fusion

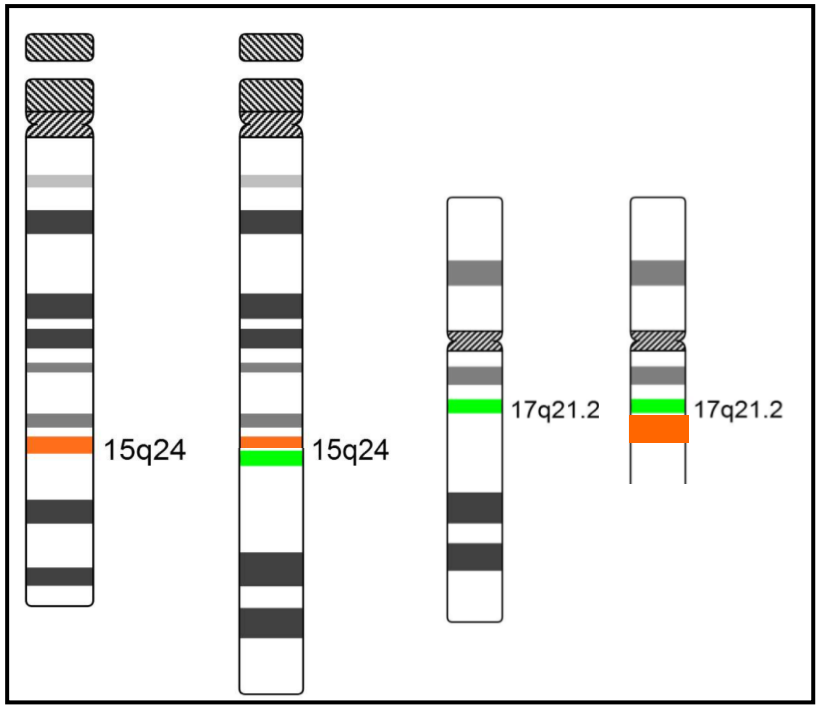


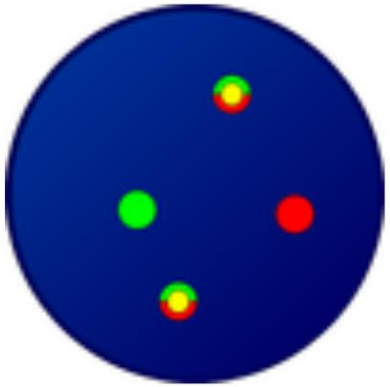


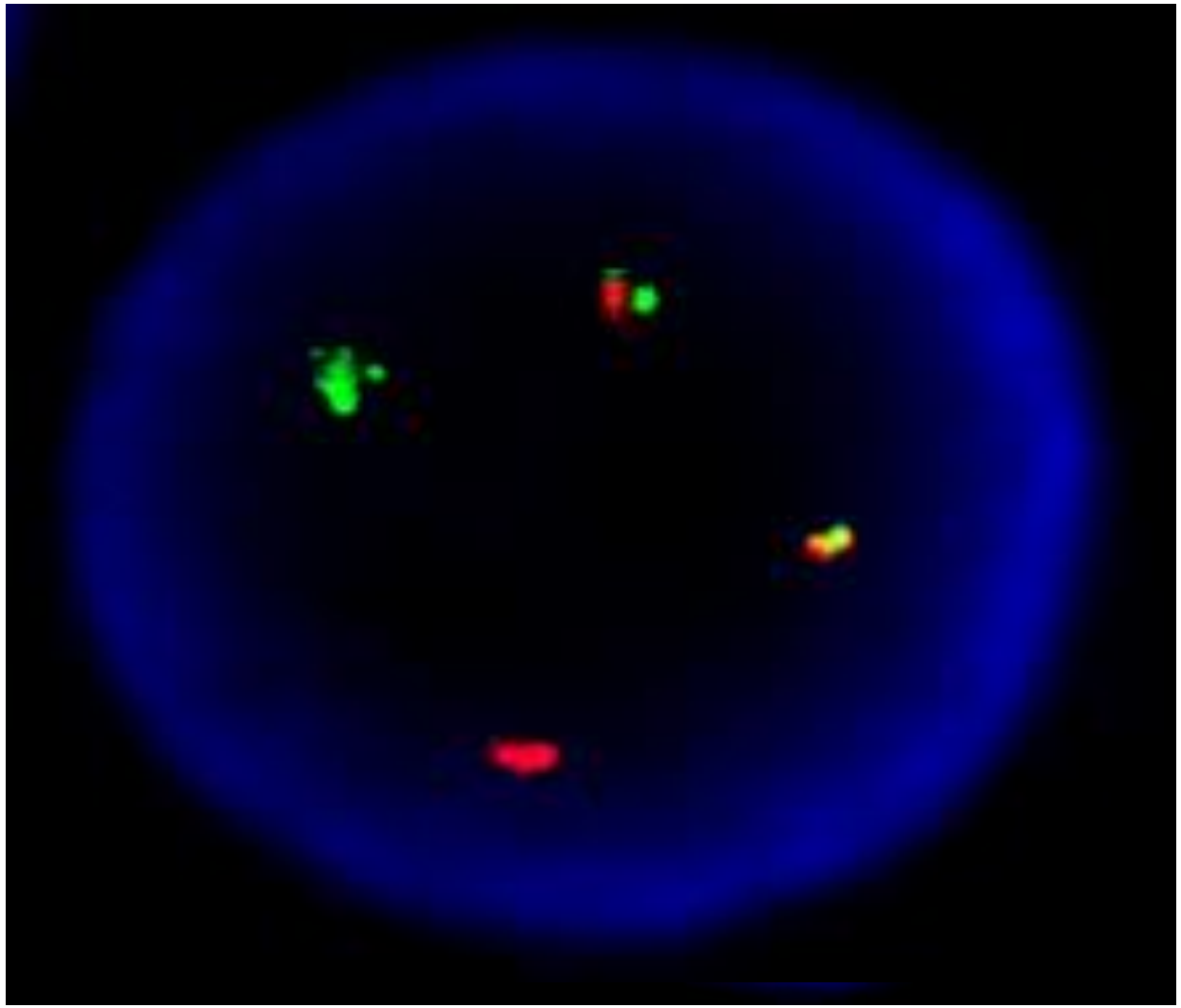
Negative:2 Red 2 Green: 2R2G



Positive for PML/RARA fusion

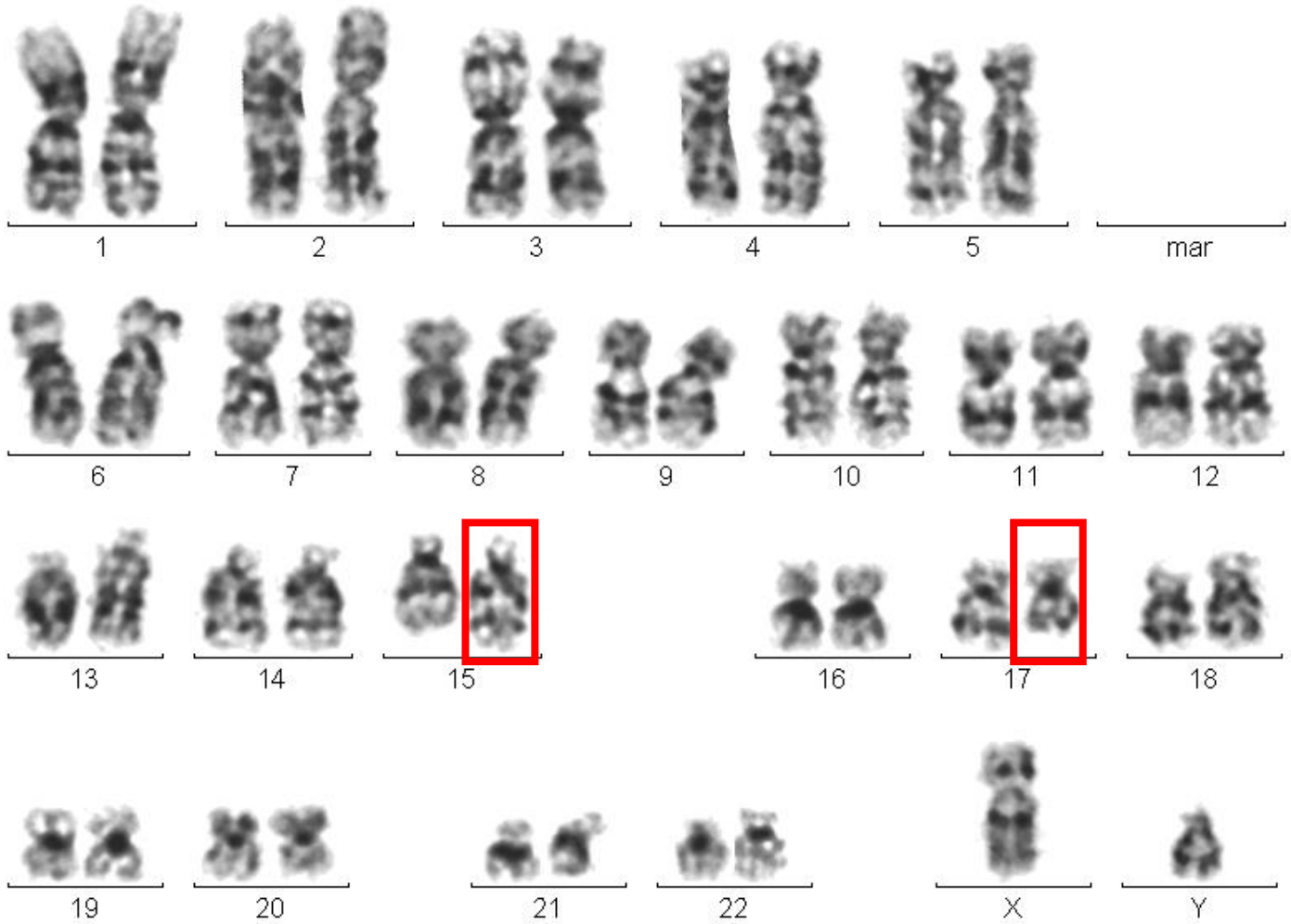






t(15;17)- 2 Fusion 1Red1Green: 2F1R1G

Karyotype showing the t(15;17)

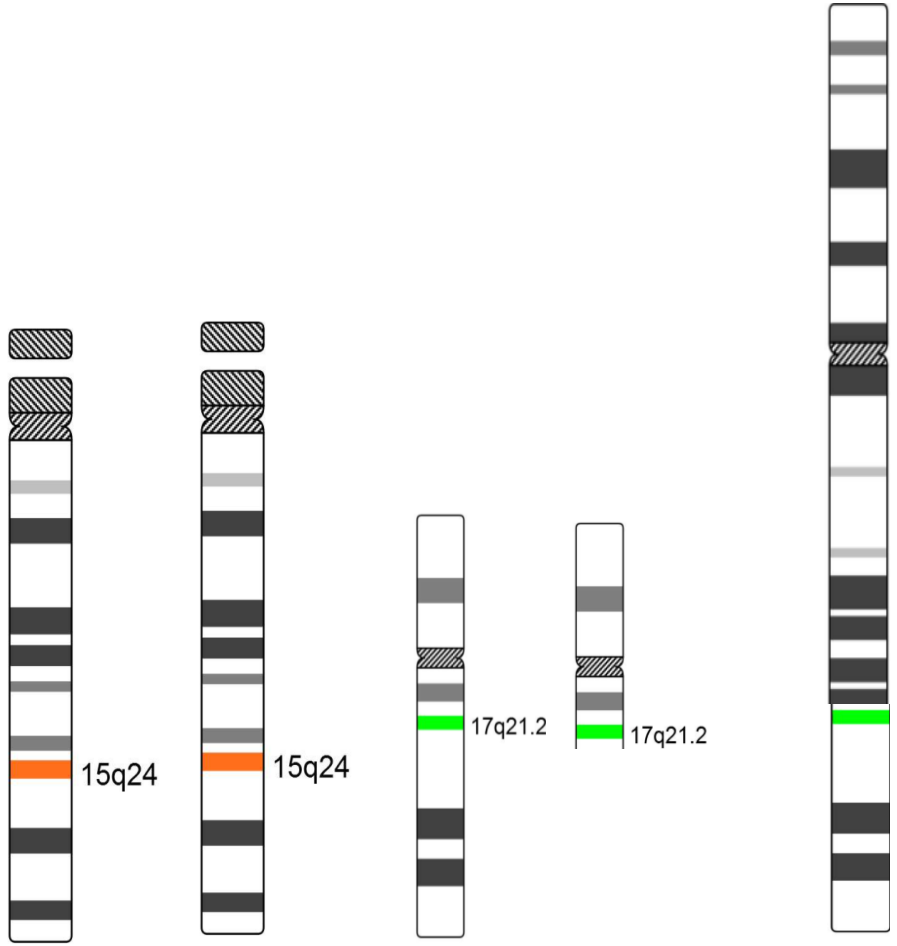


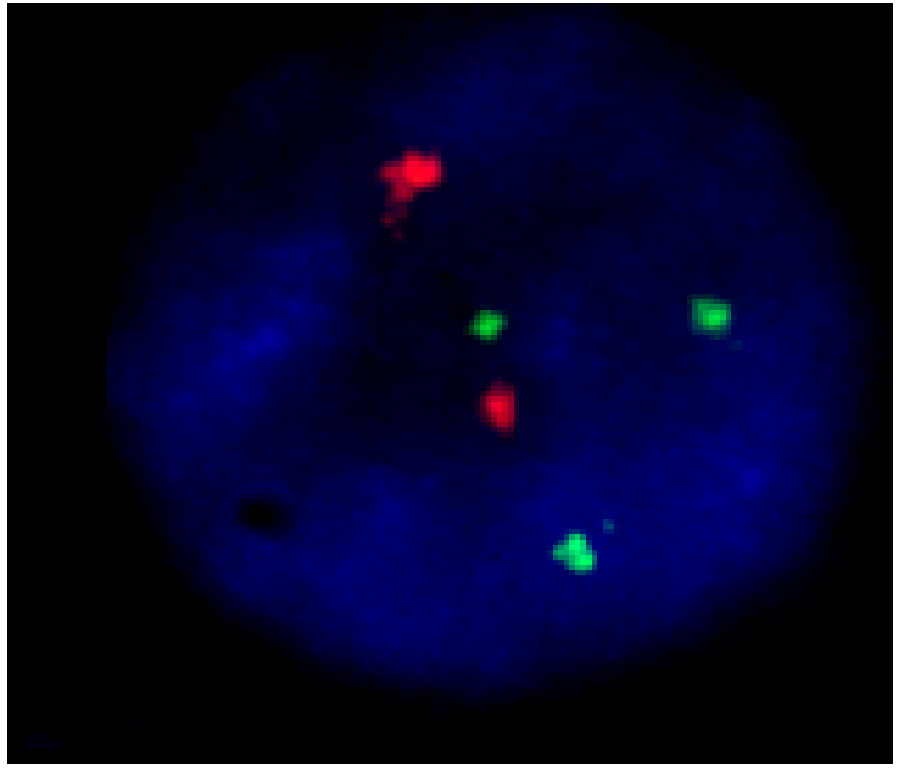
What about a variant RARα translocation?

- NPM1 t(5;17)(q35;q21)
- NUMA1 -(11;17)(q13;q21)
- ZBTB16 t(11;17) (q23;q21)
- NABP1- t(2;17)(q32;q21)
- FIP1L1- t(4;17)(q12;q21)
- BCOR- t(X;17)(p11;q21)
- TBLR1 t(3;17)(q26;q21)
- PRKAR1A t(17;17) (q21;q24)
- STAT5B [rearrangement within 17q21]

Aspirate	: Acute promyelocytic leukemia (62% abnormal promyelocytes, faggot cells seen.)
Trephine	: Acute leukemia
IPT	: Consistent with acute promyelocytic leukemia

FISH results using dual color dual fusion probe shows atypical results

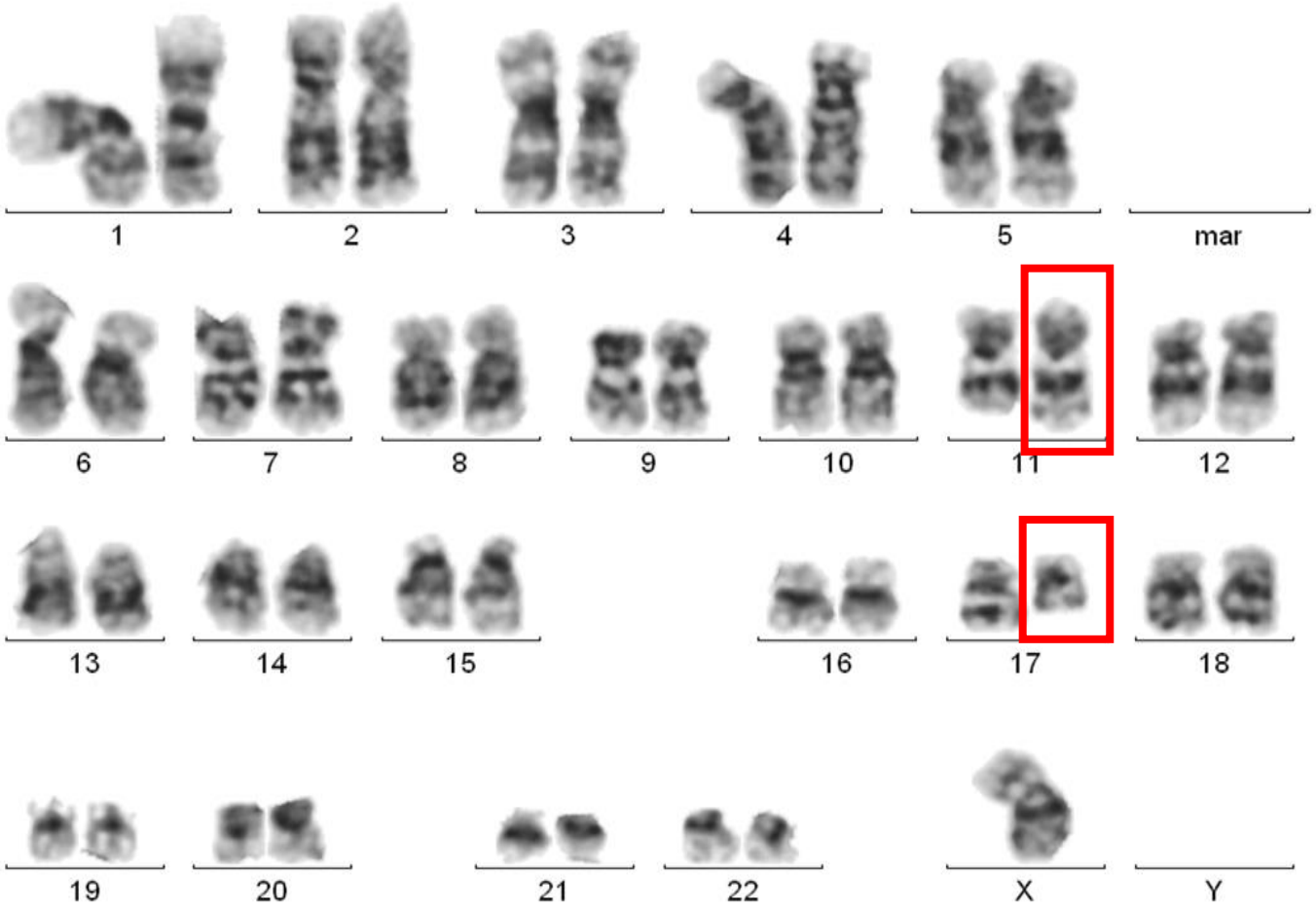




2Red 3Green signals

RARα signal(Green) is present on a 3rd chromosome

Karyotype showed a t(11;17) involving the RARα gene

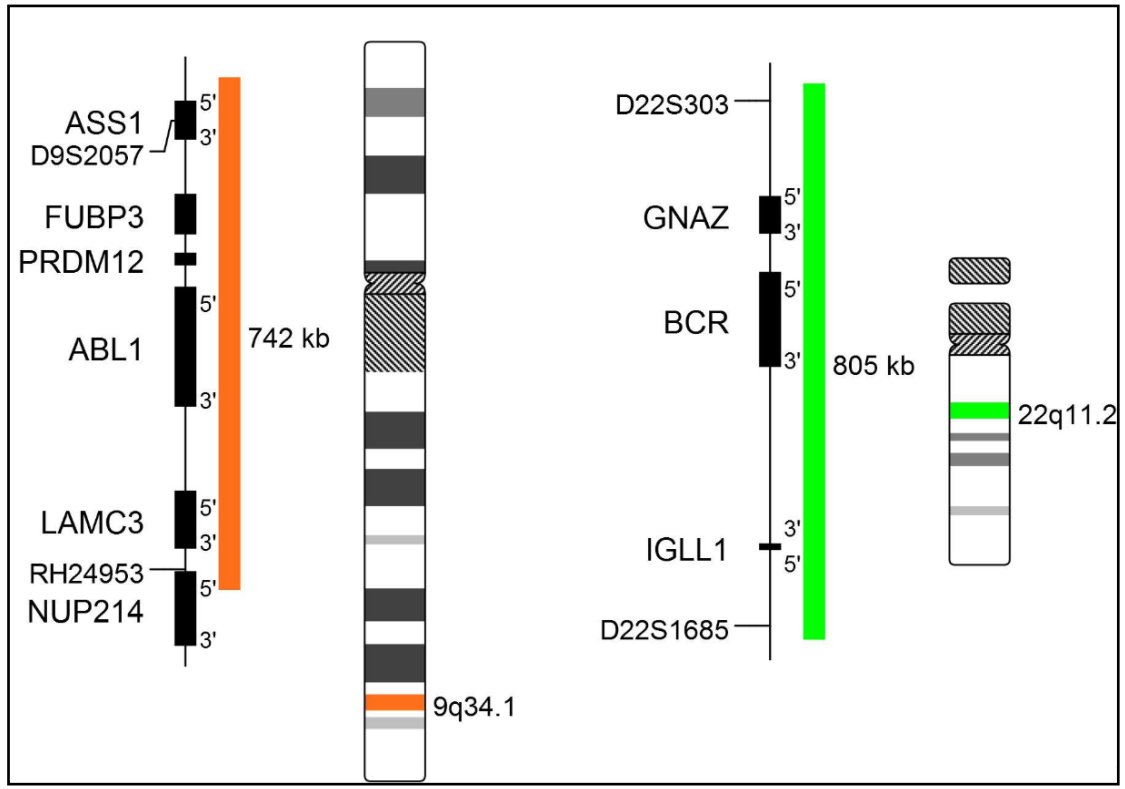


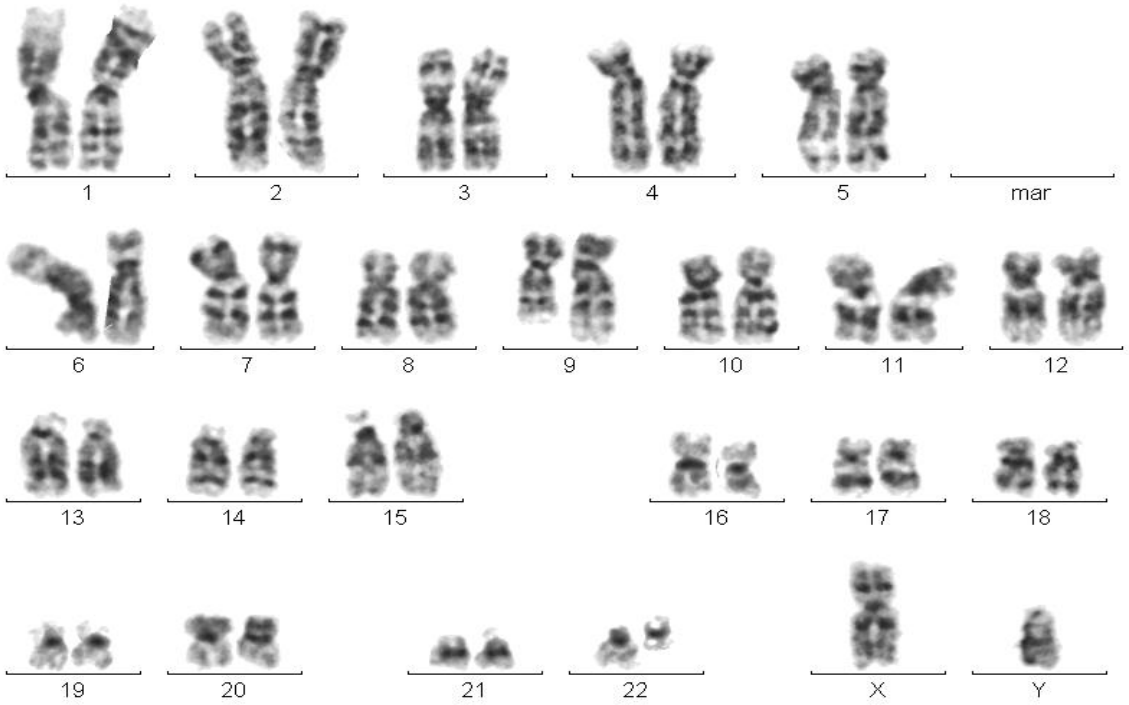
45,X,-Y,t(11;17)(q23;q21)[20]

Counting and interpretation of FISH signals- a word of caution

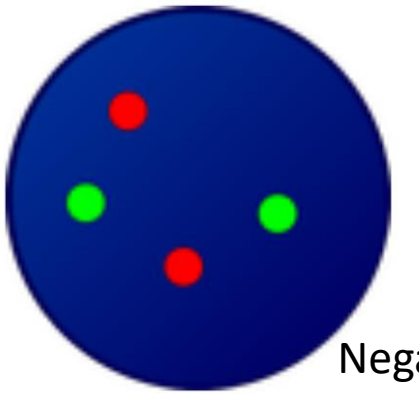
S.NO	Probe name	Fusion pattern	No.of controls	Confidence Interval	False positive cells plus 1	No. cells analysed	Beta Inverse	Cut off values
1	BCR/ABL	2F1R1G	10	0.95	1	200	1.49%	1.5%
		1F1R1G		0.95	17	200	11.03%	11.0%
2	PML/RARA	2F1R1G	10	0.95	1	200	1.49%	1.5%
		1F1R1G		0.95	15	200	10.04%	10.0%
3	CEP7/ 7q	1R2G	10	0.95	8	200	6.26%	6.3%
		1R1G		0.95	7	200	5.67%	5.7%
4	IGH/FGFR3	2F1R1G	10	0.95	1	200	1.49%	1.5%
		IF1R1G		0.95	10	200	7.39%	7.4%
		4R4G		0.95	3	200	3.08%	3.1%
5	IGH/CCND1	2F1R1G	10	0.95	1	200	1.49%	1.5%
		1F1R1G		0.95	9	200	6.83%	6.8%
		1R2G		0.95	8	200	6.26%	6.3%
		2R1G		0.95	6	200	5.06%	5.1%
6	TP53/CEP17	1R2G	10	0.95	11	200	7.94%	7.9%
		1R1G		0.95	14	200	9.53%	9.5%
		2R1G		0.95	5	200	4.43%	4.4%
		4G4R		0.95	8	200	6.26%	6.3%

Counting and interpretation of FISH signals- a word of caution

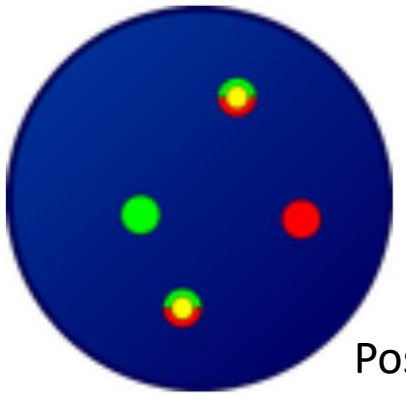




46,XY,t(9;22)(q34;q11.2)



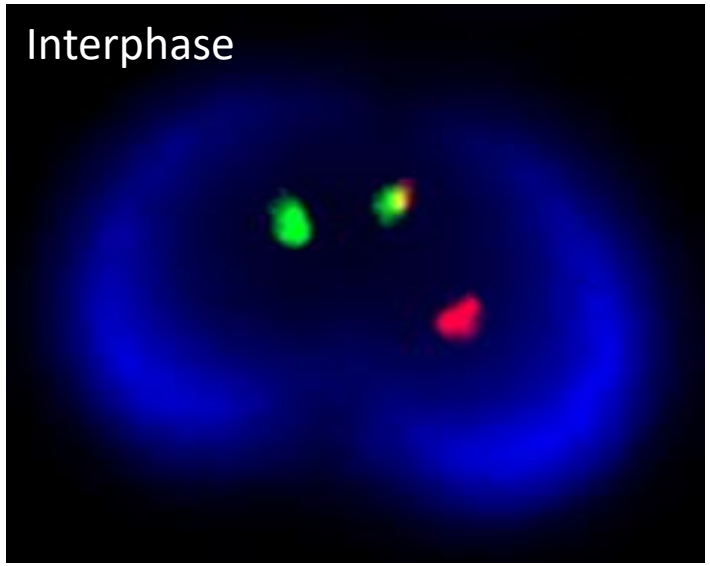
Negative



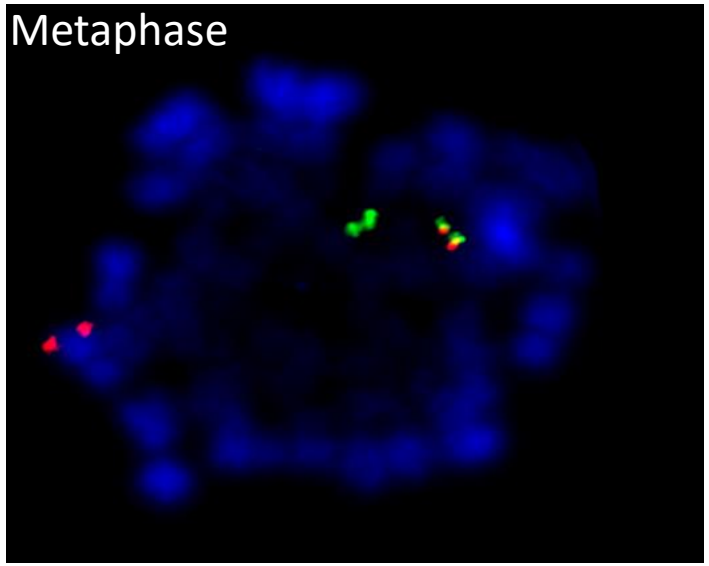
Positive

Counting and interpretation of FISH signals- a word of caution

CML- BCR/ABL1 SINGLE FUSION

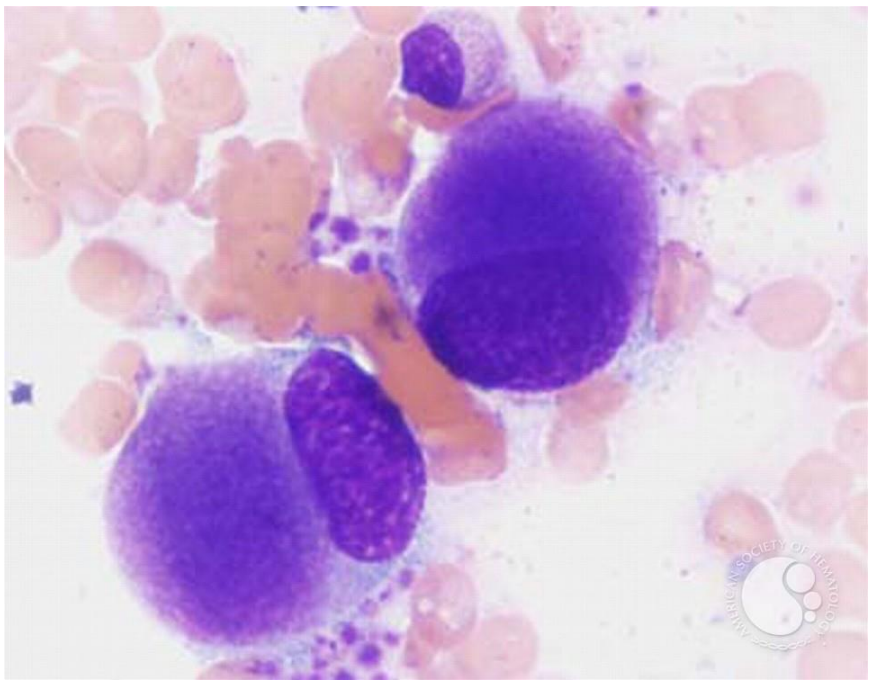


CML- BCR/ABL1 SINGLE FUSION

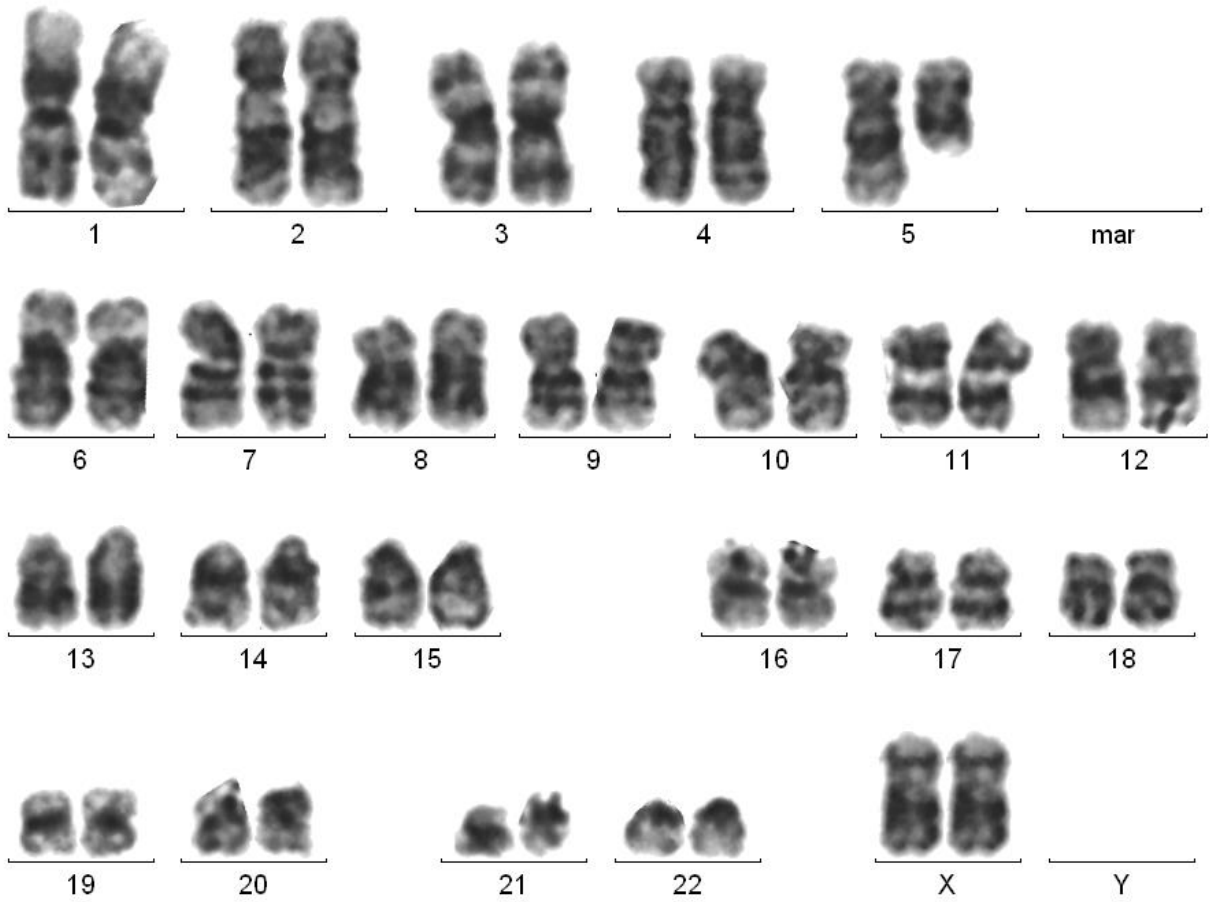


- Atypical single fusion signals are seen in upto 20% of cells in **normal controls/ essential thrombocythemia/polycythemia vera.**
- Caution to be exercised when calling this pattern positive **if seen only in a small population of cells(20%).**
- Diagnostic conundrum when this pattern is seen in a post treatment sample who has not been tested in the same centre previously.
- Atypical single fusion if present in a metaphase can be confirmed as positive.

40 year female with refractory anemia not responding to Iron and Vitamin B12 supplements for 3 months.
o/e : mild hepatosplenomegaly, no lymphadenopathy
Provisional clinical diagnosis : Myelodysplastic syndrome
Macrocytic anemia (Hb = 6g/dl), Total count of 6,000/cc (mild leucopenia) with elevated platelet counts of 6 lakh/cc.
Aspirate : Varyingly cellular marrow with relatively poor cell trails, myeloid and megakaryocyte dysplasia, relative erythroid hypoplasia and hypolobate megakaryocytes, consistent with MDS.
Trephine :Consistent with myelodysplastic syndrome



A solitary deletion 5q



46,XX,del(5)(q13q33)

MDS-defining abnormalities(WHO 2016)

- Loss of chromosome 7 or del(7q)
- del(5q)
- Isochromosome 17q or t(17p)
- Loss of chromosome 13 or del(13q)
- del(11q)
- del(12p) or t(12p)
- del(9q)
- idic(X)(q13)
- t(11;16)(q23.3;p13.3)
- t(3;21)(q26.2;q22.1)
- t(1;3)(p36.3;q21.2)
- t(2;11)(p21;q23.3)
- inv(3)(q21.3;q26.2)/ t(3;3)(21.3;q26.2)
- t(6;9)(p23;q34.1)

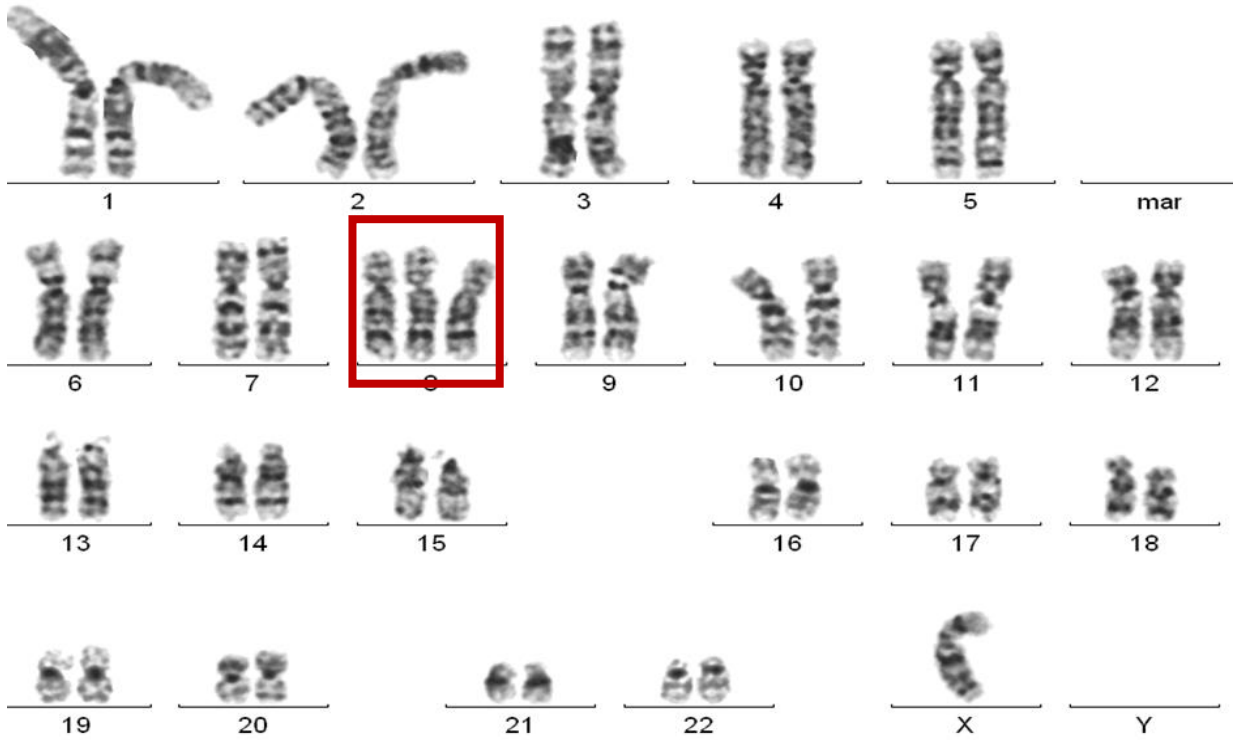
Blood 19 May 2016, Volume 127, Number 20. Page 2391-2405.

79/M – Exclude MDS

Smear : Varyingly cellular marrow (predominantly hypocellular) with scattered dyserythropoieisis and adequate megakaryocytes.

Trephine : Markedly hypercellular marrow with adequate trilineage haematopoiesis and no specific lesion.

When finding a clone does not confirm diagnosis



Karyotype :46,X,-Y,+8[14]/46,XY[6]

The presence of +8, -Y, or del(20q) is not considered to be MDS-defining in the absence of diagnostic morphologic features of MDS.

Blood 19 May 2016, Volume 127, Number 20. Page 2391-2405.

Why should we test for chromosomal abnormalities?

To establish the specific diagnosis

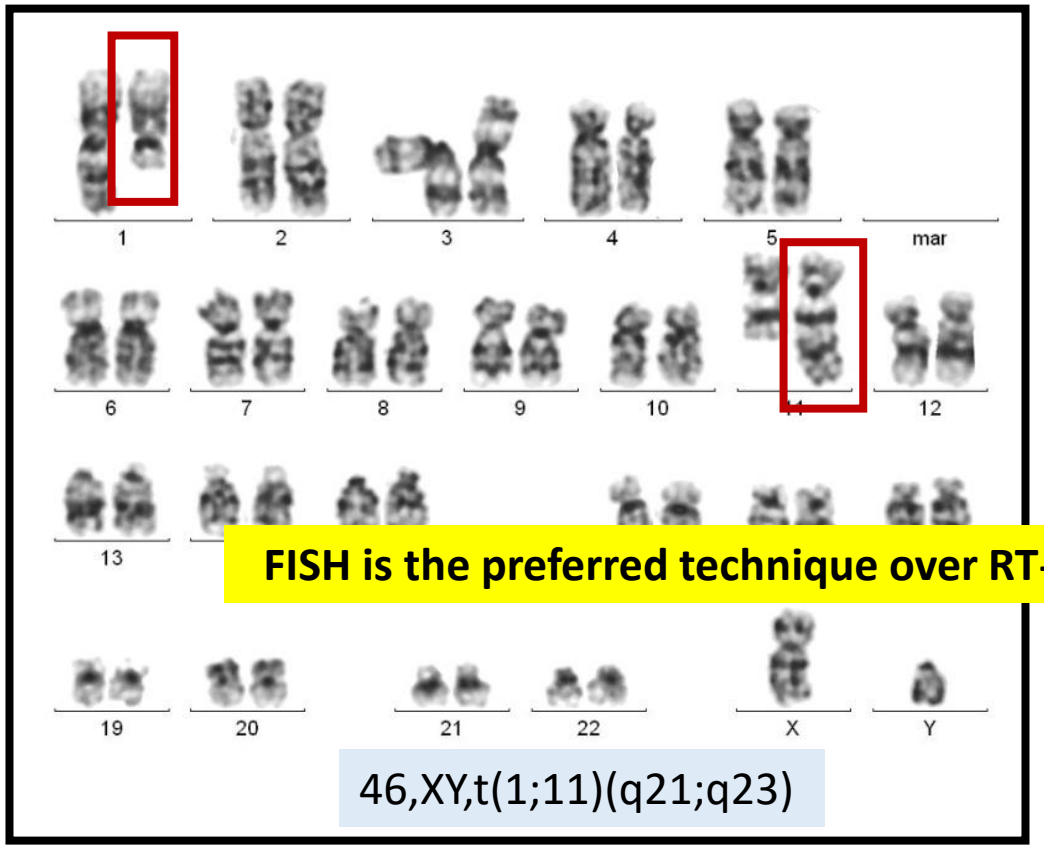
To estimate prognosis, based on the presence of a recurring abnormality, appearance of new karyotypic abnormalities, or the existence of clonal heterogeneity/evolution, which often signal a change in the pace of the disease, usually to a more aggressive course

To help in the planning of treatment, since some chromosomal changes predict for response (or nonresponse) to specific therapies, or to inform the selection of a targeted therapy

To distinguish between benign reactive lymphoid or myeloid hyperplasia and a monoclonal malignant proliferation

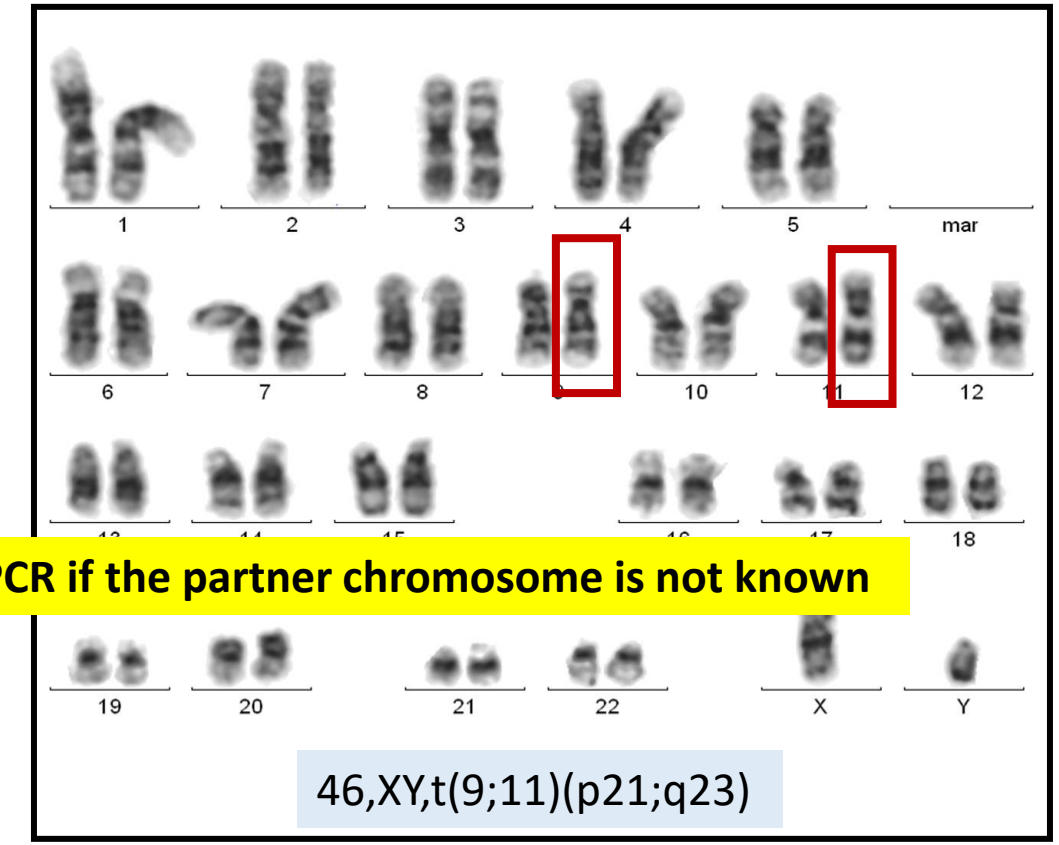
KMT2A(MLL) gene rearrangements in acute leukemia

- KMT2A gene on 11q23.3 fuses with various partner genes: ~ 80 genes have been described
- Usually poor risk except for t(9;11) in AML and the t(1;11) in pediatric AML
- Maybe cryptic/ submicroscopic in most instances



46,XY,t(1;11)(q21;q23)

FISH is the preferred technique over RT-PCR if the partner chromosome is not known



46,XY,t(9;11)(p21;q23)

Blood. 2009 Sep 17; 114(12): 2489–2496
Blood. 2017 Jan 26; 129(4): 424–447

Probe design- Dual color breakapart

When do we use this probe design? → Numerous translocation partners

KMT2A/MLL

RUNX1

RARα

CBFβ

CRLF2

ABL1

ABL2

CSF1R

JAK2

PDGFRα

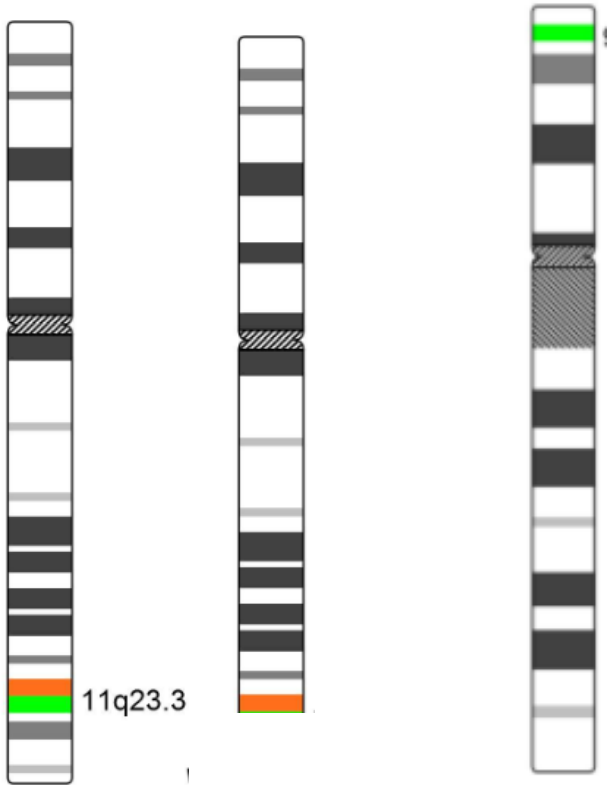
PDGFRβ

FGFR1

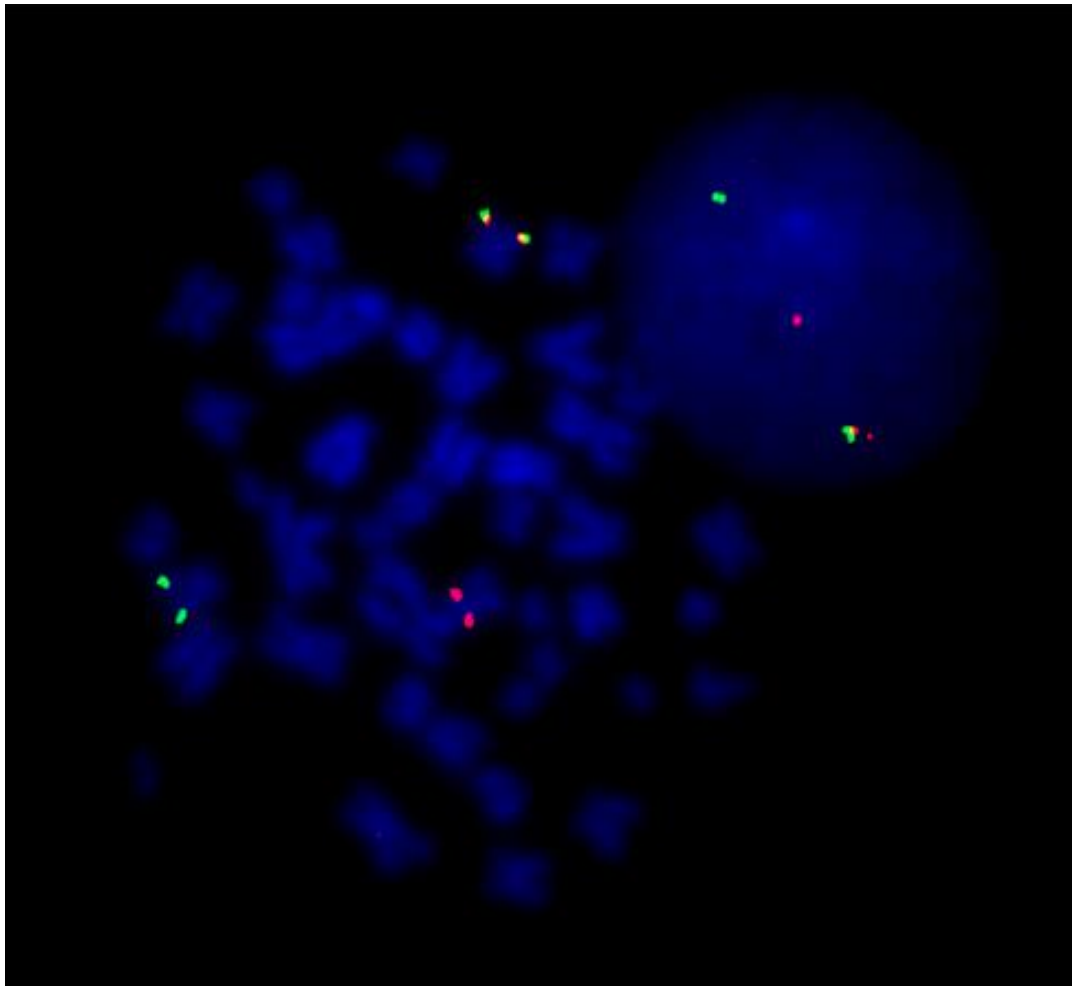
IgH

CMYC

Dual color breakapart probe for KMT2A gene rearrangements

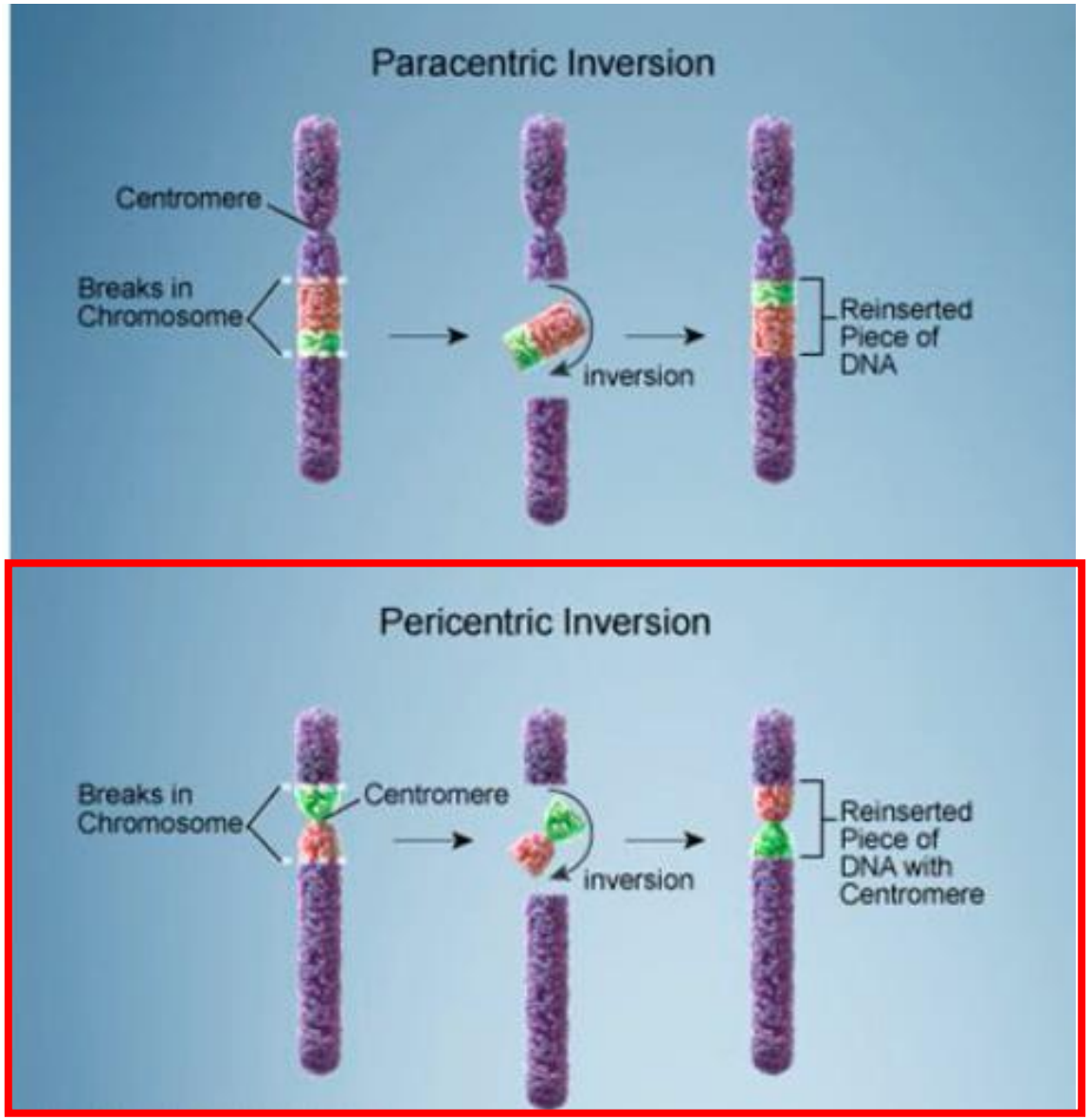


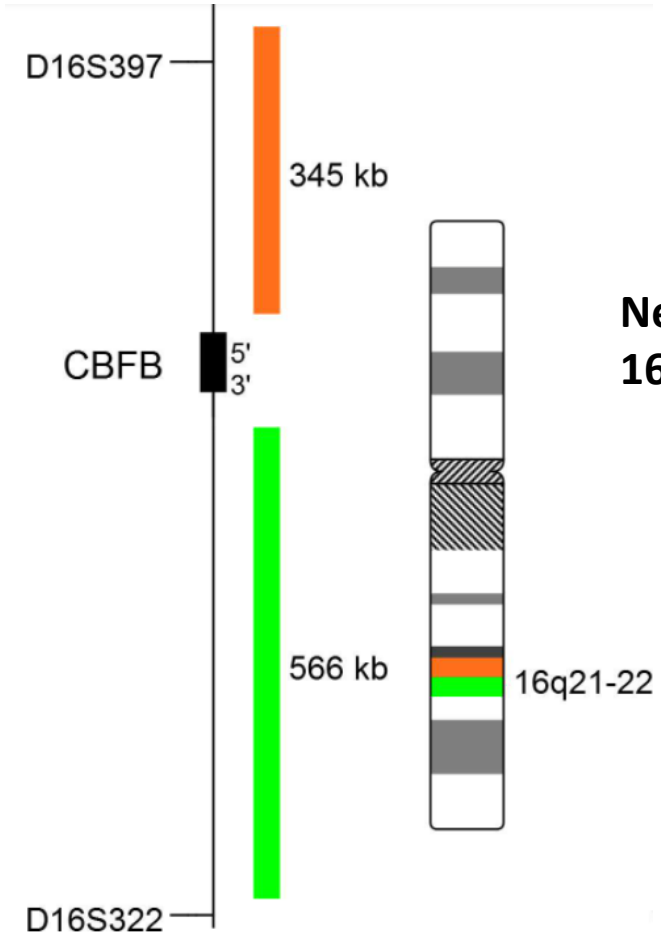
Partner chromosome showing 3’ KMT2A signal

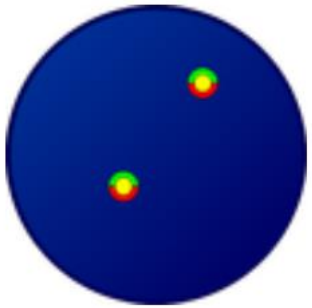


1Fusion1Green1Red showing KMT2A gene rearrangement

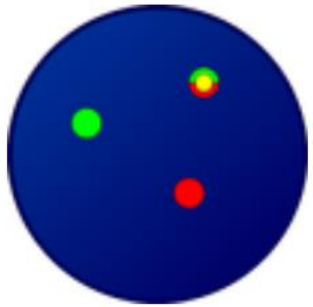
Dual color breakapart probe for CBFβ gene rearrangements





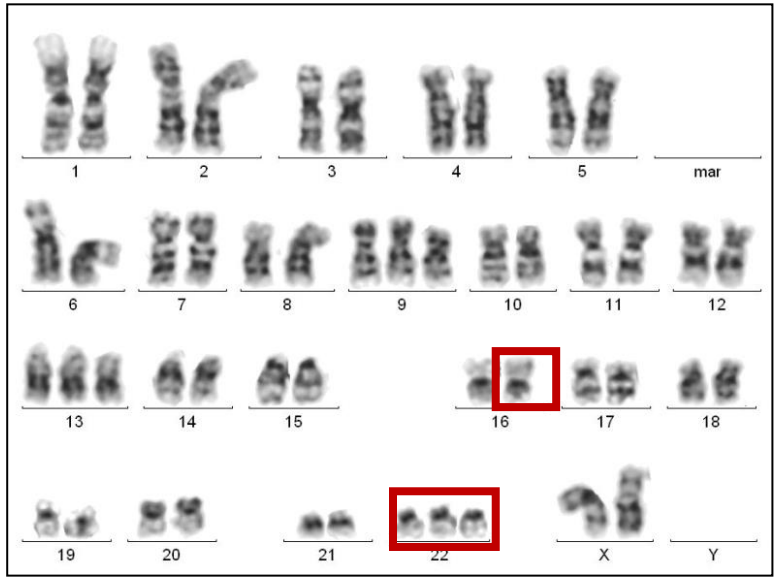


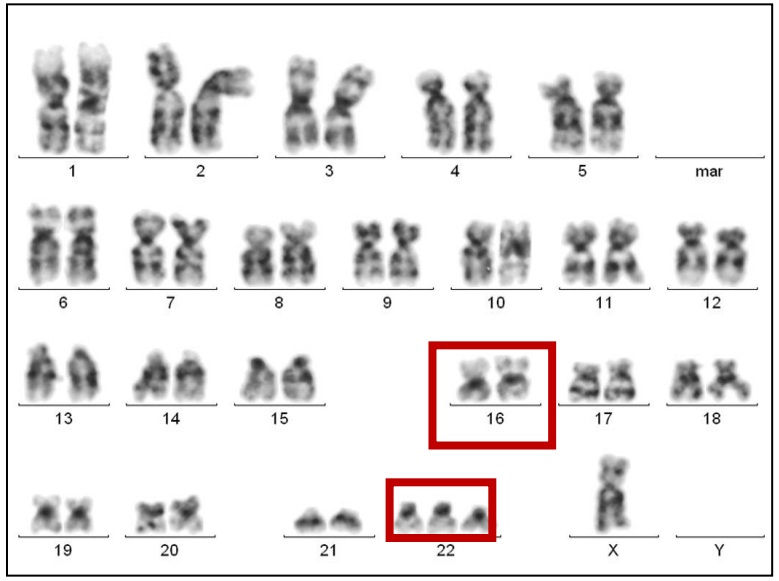
Negative for inversion 16 /t(16;16)

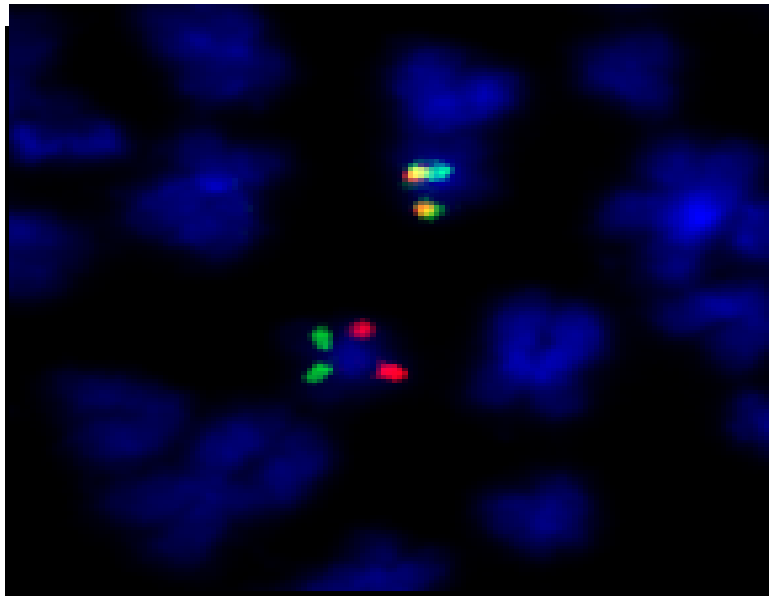


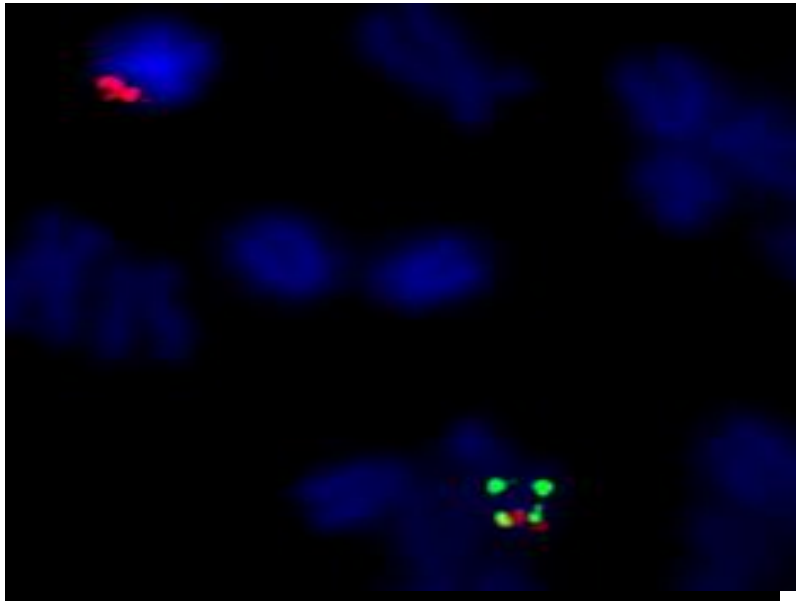
Positive for inversion 16/ t(16;16)

CBFβ gene rearrangements- favorable risk abnormality in AML









Multiple myeloma risk stratification – from CRAB to FISH

MAYO CLINIC

mSMART 3.0: Classification of Active MM

High-Risk

- High Risk genetic Abnormalities [a,b]
  - t(4;14)
  - t(14;16)
  - t(14;20)
  - Del 17p
  - p53 mutation
  - Gain 1q
- RISS Stage 3
- High Plasma Cell S-phase[c]
- GEP: High risk signature

- Double Hit Myeloma: Any 2 high risk genetic abnormalities
- Triple Hit Myeloma: 3 or more high risk genetic abnormalities

Standard-Risk[a]

All others including:

- Trisomies
- t(11;14)[d]
- t(6;14)

[a] Trisomies may ameliorate
[b] By FISH or equivalent method
[c] Cut-offs vary
[d] t(11;14) may be associated with plasma cell leukemia

Dispenzieri et al. Mayo Clin Proc 2007;82:323-341; Kumar et al. Mayo Clin Proc 2009 84:1095-1110; Mikhael et al. Mayo Clin Proc 2013;88:360-376. v14 //last reviewed August 2018

Extensive panel

Minimum panel

TP53 deletion | IgH translocation | Gain 1q

+

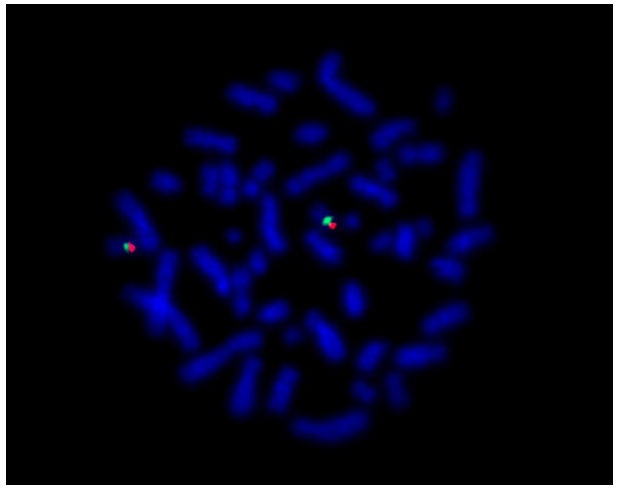
IgH/CCND1: t(11;14)
IgH/FGFR3 :t(4;14)
IgH/MAF :t(14;16)

Why enrich?

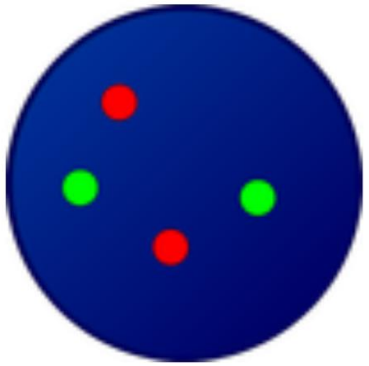
Probe	Total no.of patients tested	% Positive (n)	% Positive after PC enrichment
TP53	752	5%	11%
IgH/FGFR3	204	5%	9 %
IgH/CCND1	201	3%	7.6%
Del 13q/Monosomy 13	188	10%	33.3%

Plasma cell enrichment principle

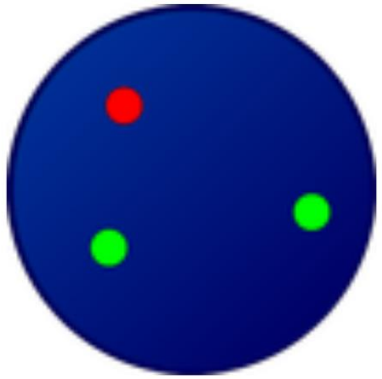
Locus specific identifier- TP53 deletion in myeloma and chronic lymphocytic leukemia



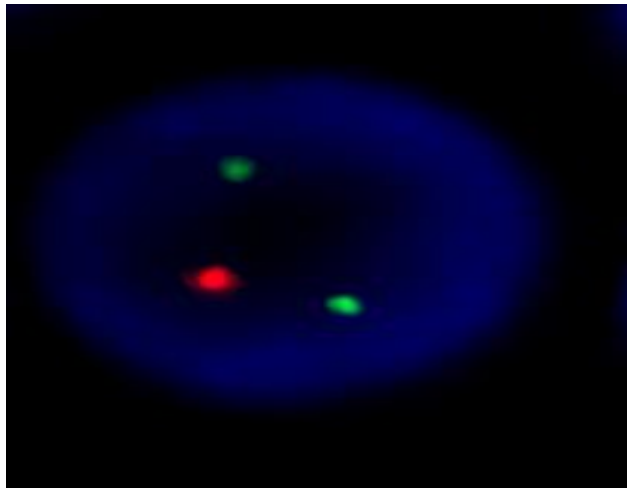
2Green 2Red signals are seen when there is no deletion



Negative

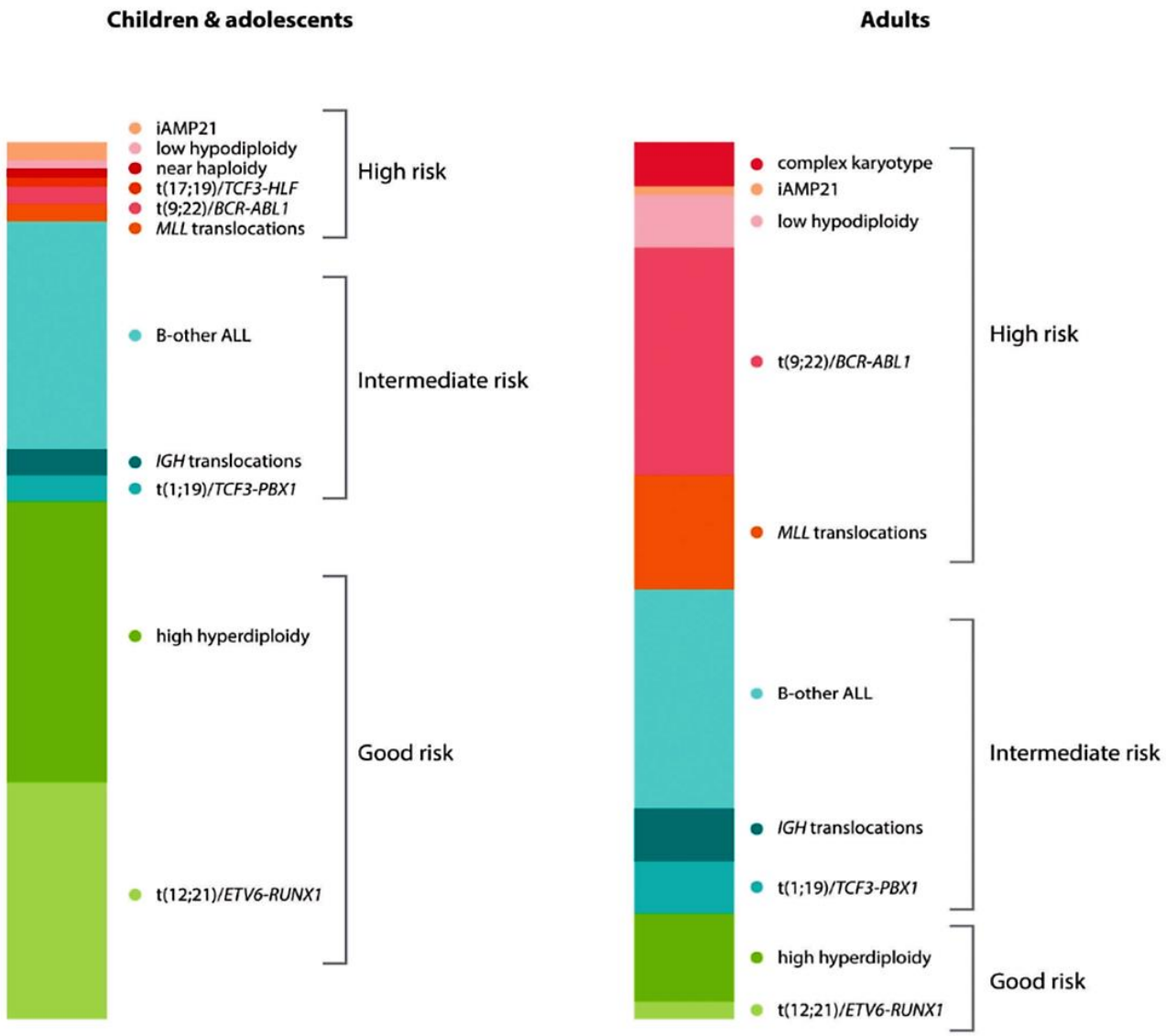


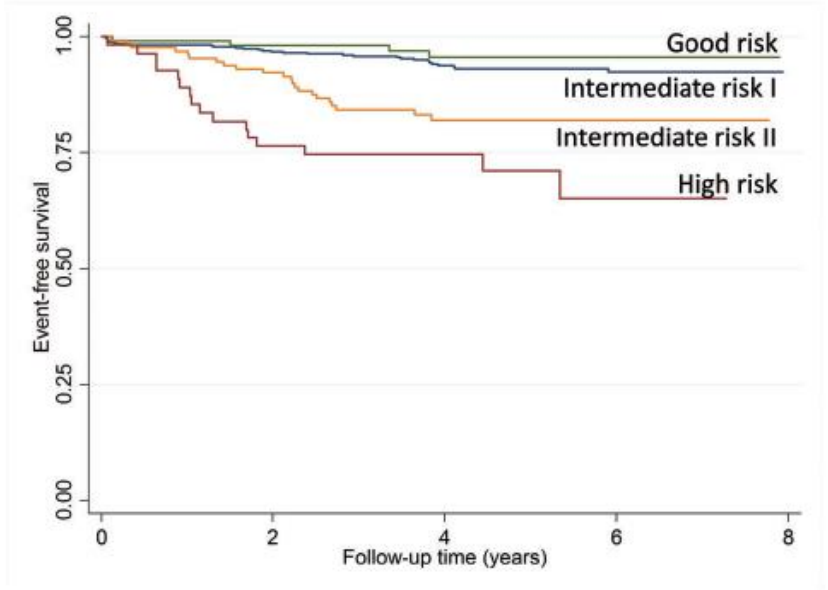
Positive



TP53 gene deletion: 2Green 1Red

B cell acute lymphoblastic leukemia

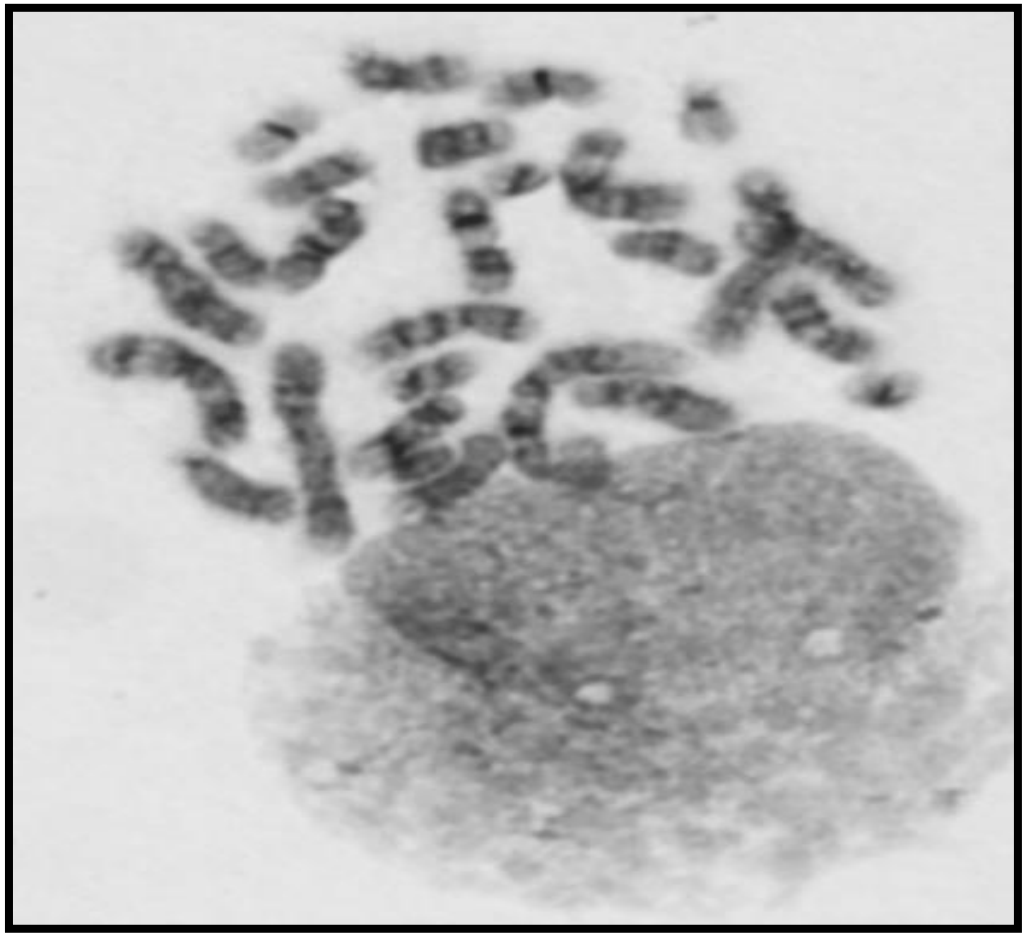


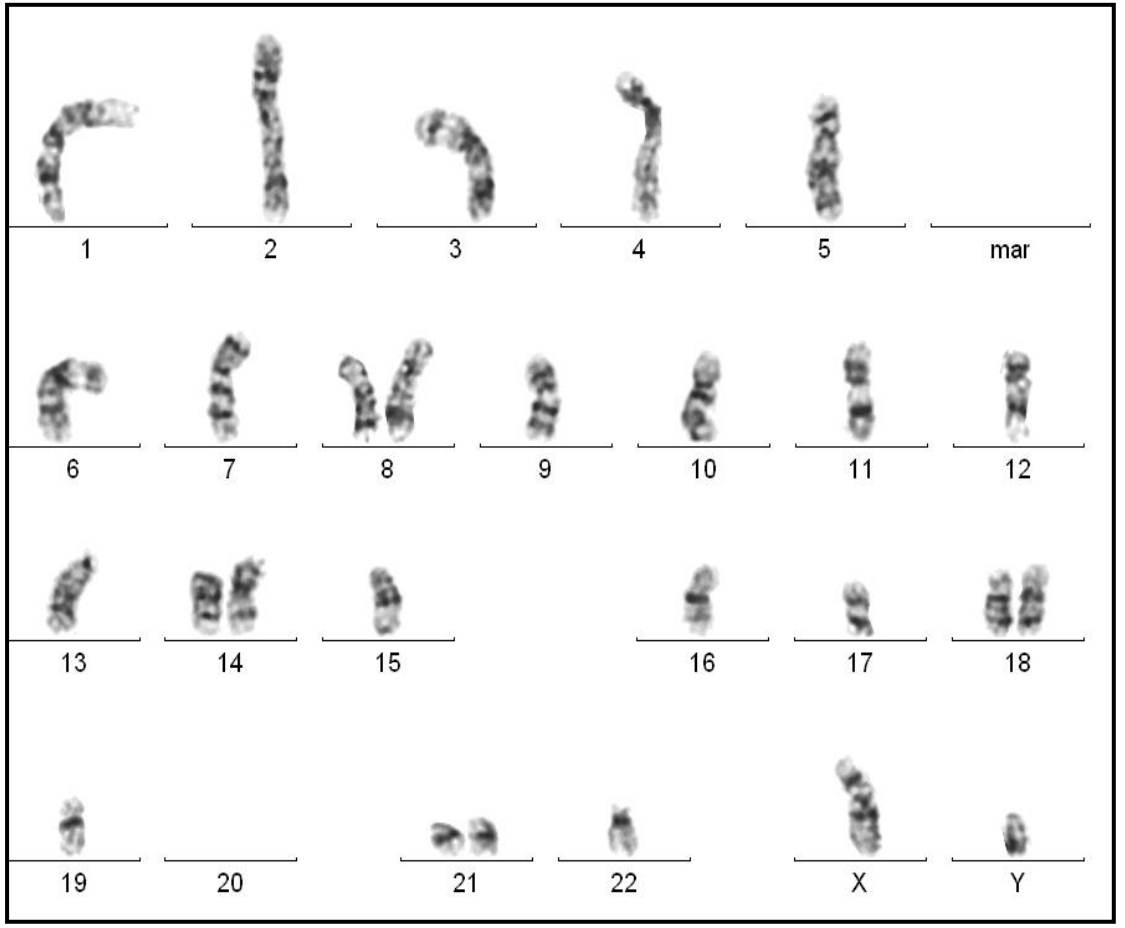


Good risk: t(12;21)/*ETV6-RUNX1*, High hyperdiploidy;
Intermediate Risk: B-other/t(1;19)/*TCF3-PBX1*/*IGH* translocations
I - with good risk copy number alteration profile
II: with intermediate/poor risk copy number alteration profile
High risk: iAMP21, *MLL* translocations, t(17;19)/*TCF3-HLF*, haploidy, low hypodiploidy

Haematologica | 2016; 101(4)

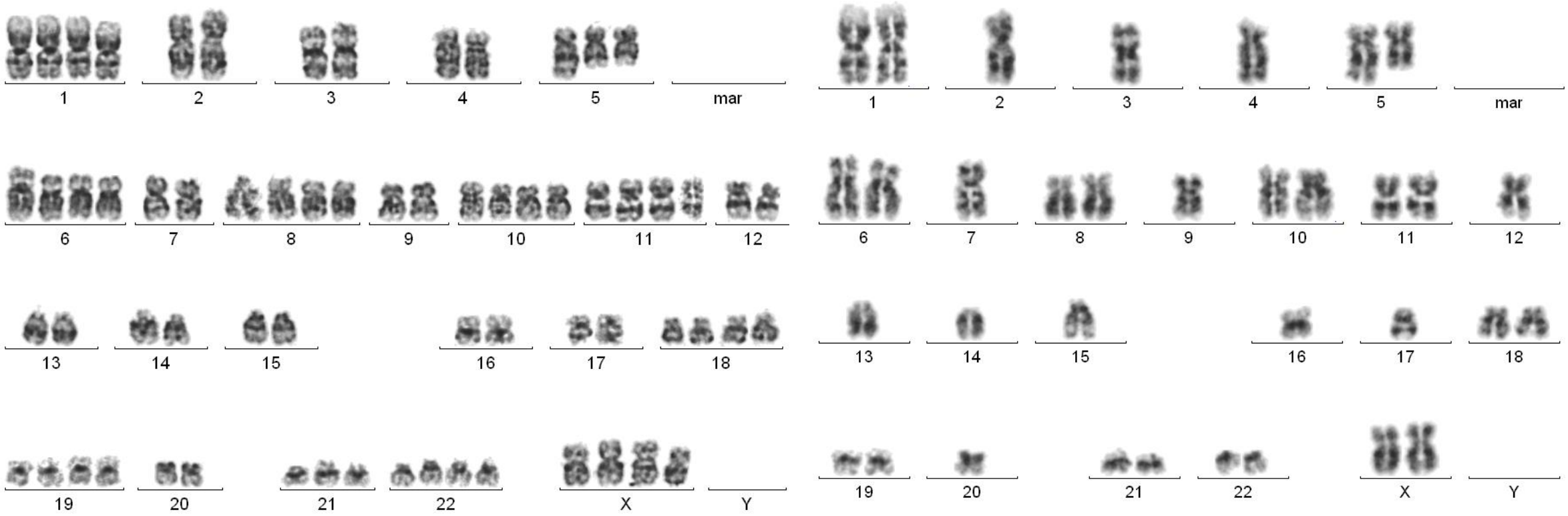
Its all in the numbers!





Ploidy groups representing significant and established cytogenetic entities in ALL high hyperdiploidy (51–65 chromosomes), near haploidy (25–29 chromosomes), low hypodiploidy (30–39 chromosomes), near triploidy (66–79 chromosomes), and near tetraploidy (84–100 chromosomes).

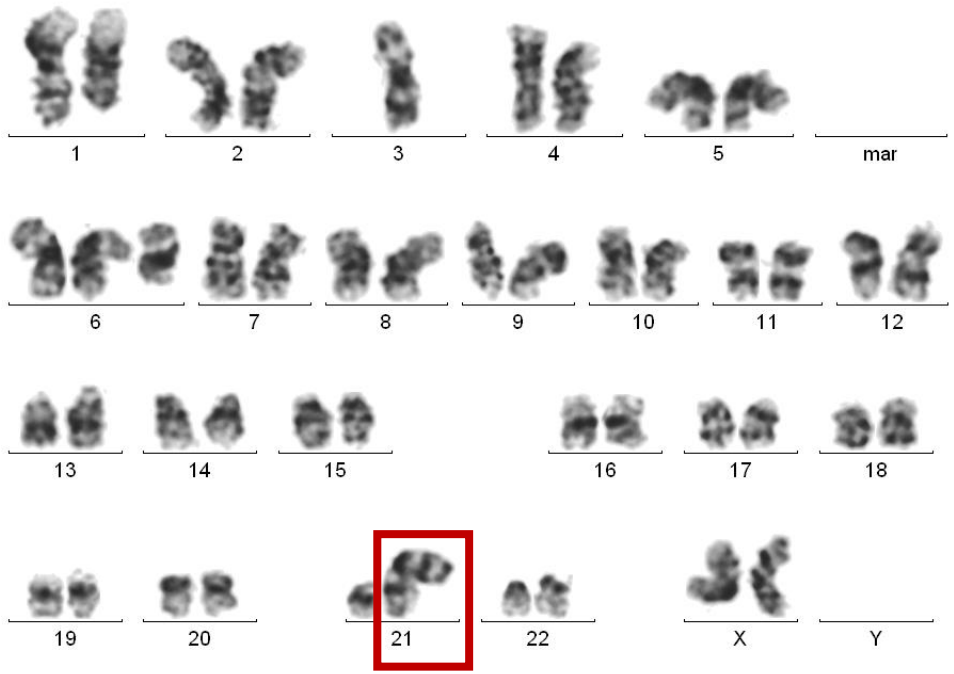
A triploid/ even a high hyperdiploid clone may harbor a hypodiploid clone

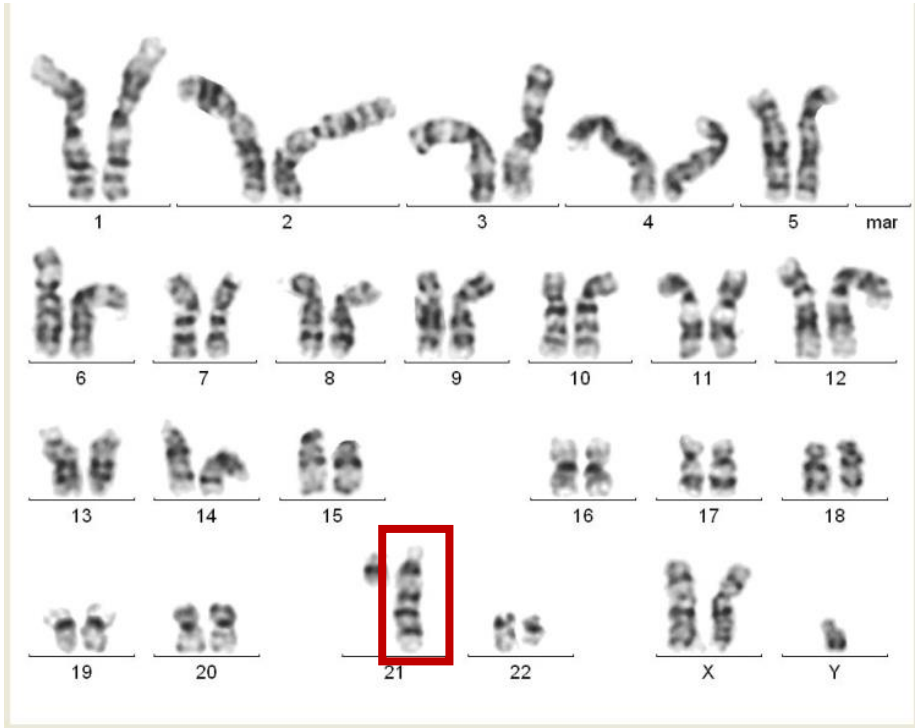


Important to analyse the pattern of gains to exclude this high risk entity- hidden hypodiploidy
Alternative is a Flow analysis for ploidy which will show two populations of cells

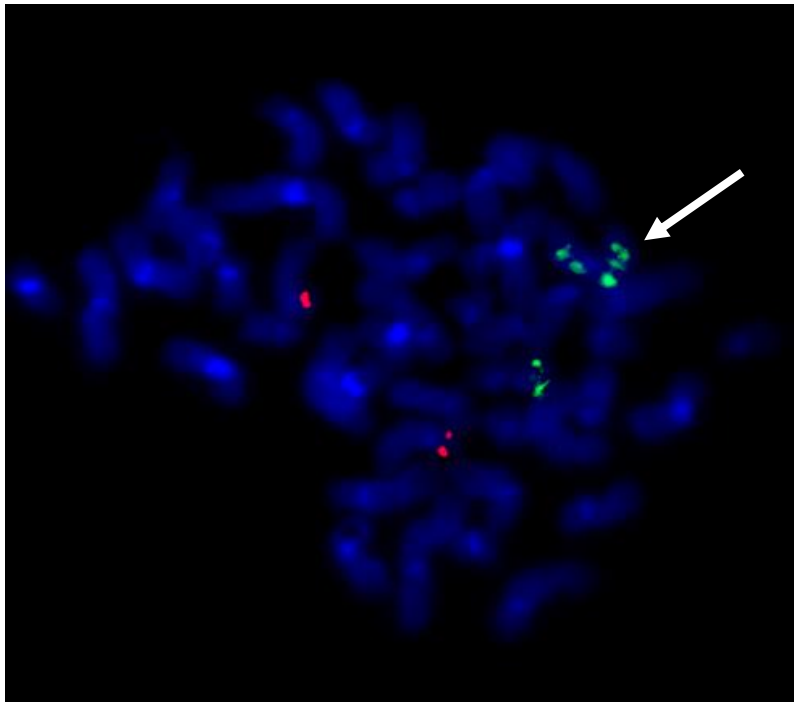
Identification of intra chromosomal amplifications by FISH

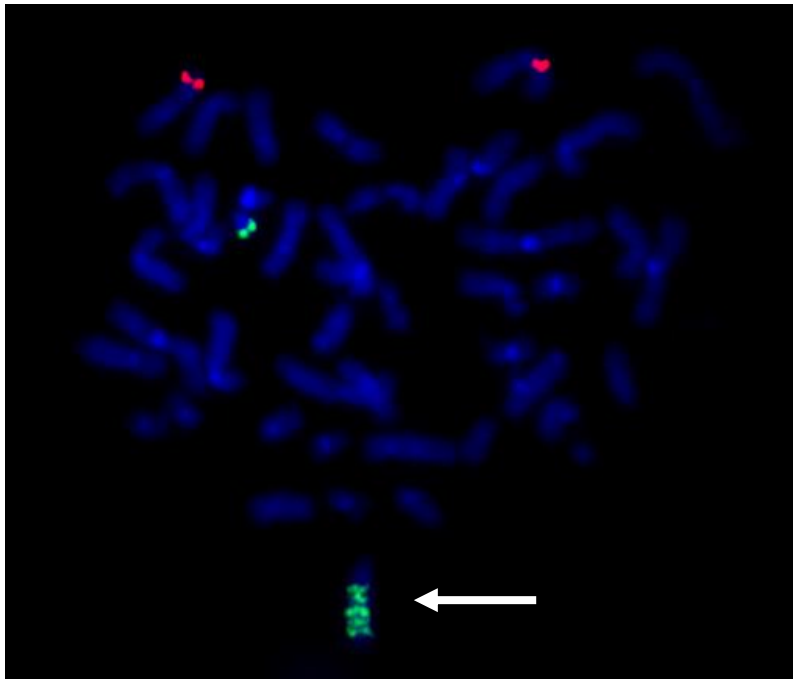
- ~2% of paediatric ALL
- > 5 signals from RUNX1 probe in a single cell by FISH
- **Morphology on karyotype varies**
- If treated as standard risk >80% relapse. Reduced to <20% on intensive arm of UKALL2003,regimen C

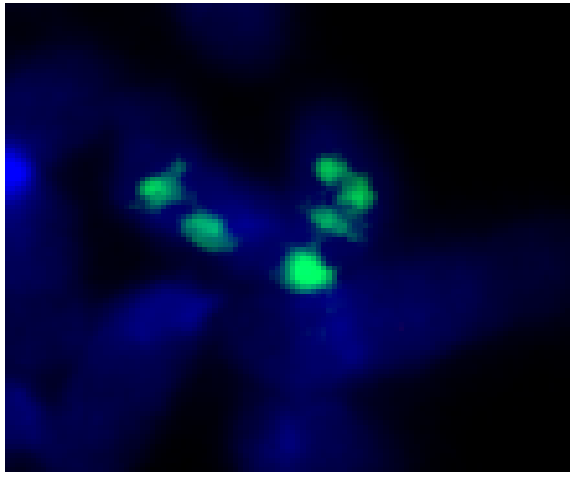




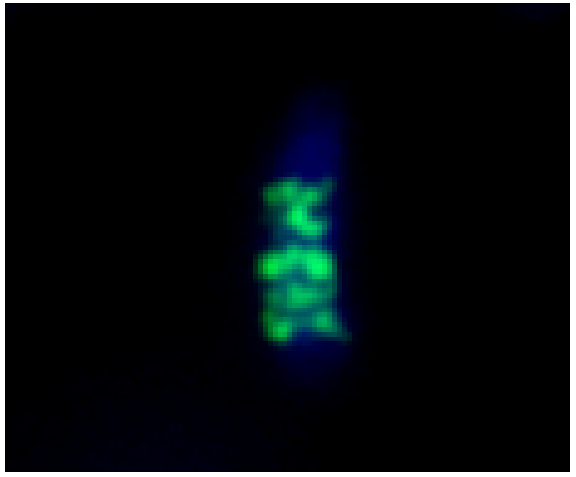
Identification of intra chromosomal amplifications by FISH



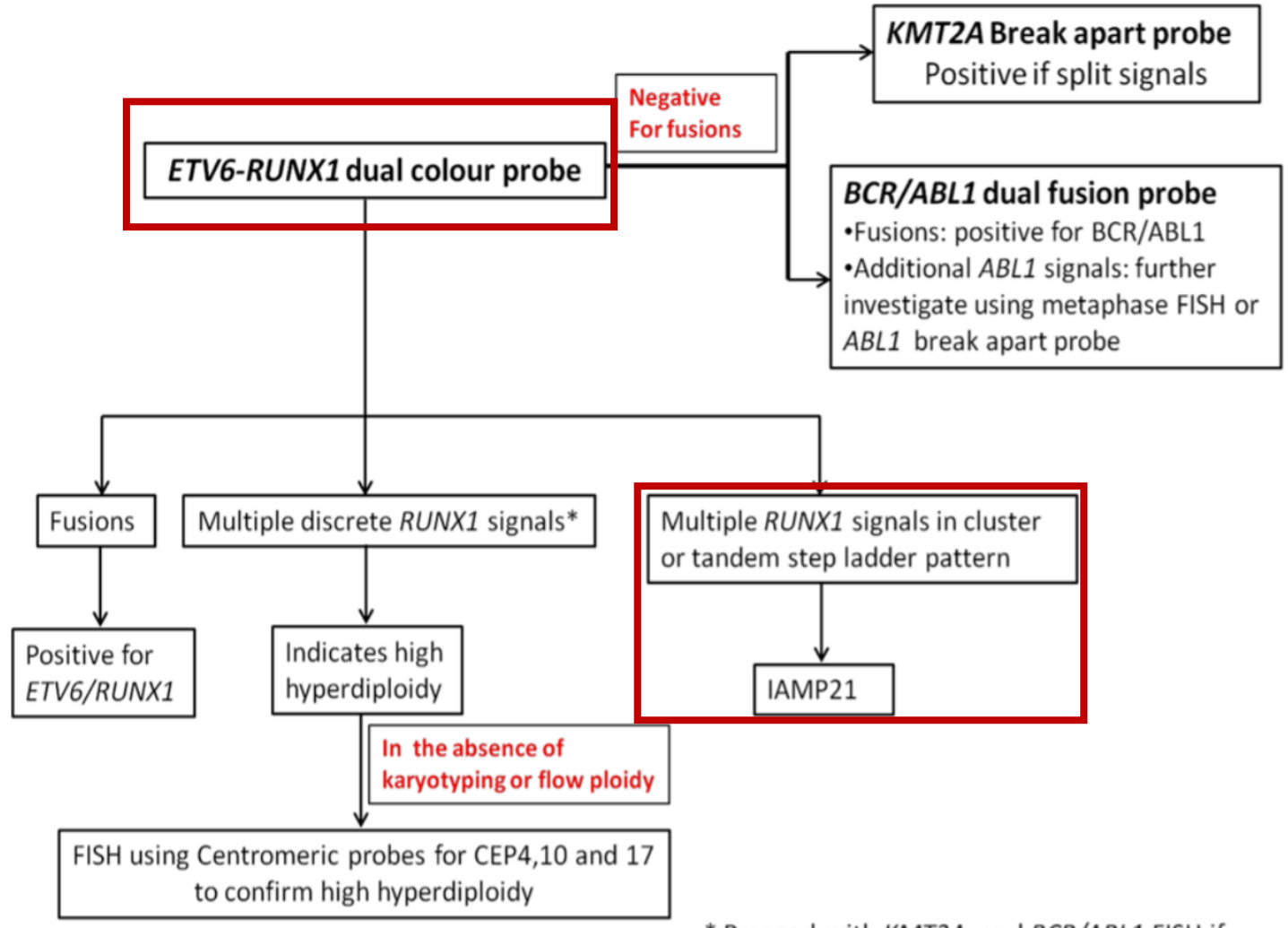




Amplification of RUNX1 gene (green signal) seen on the abnormal chromosome 21

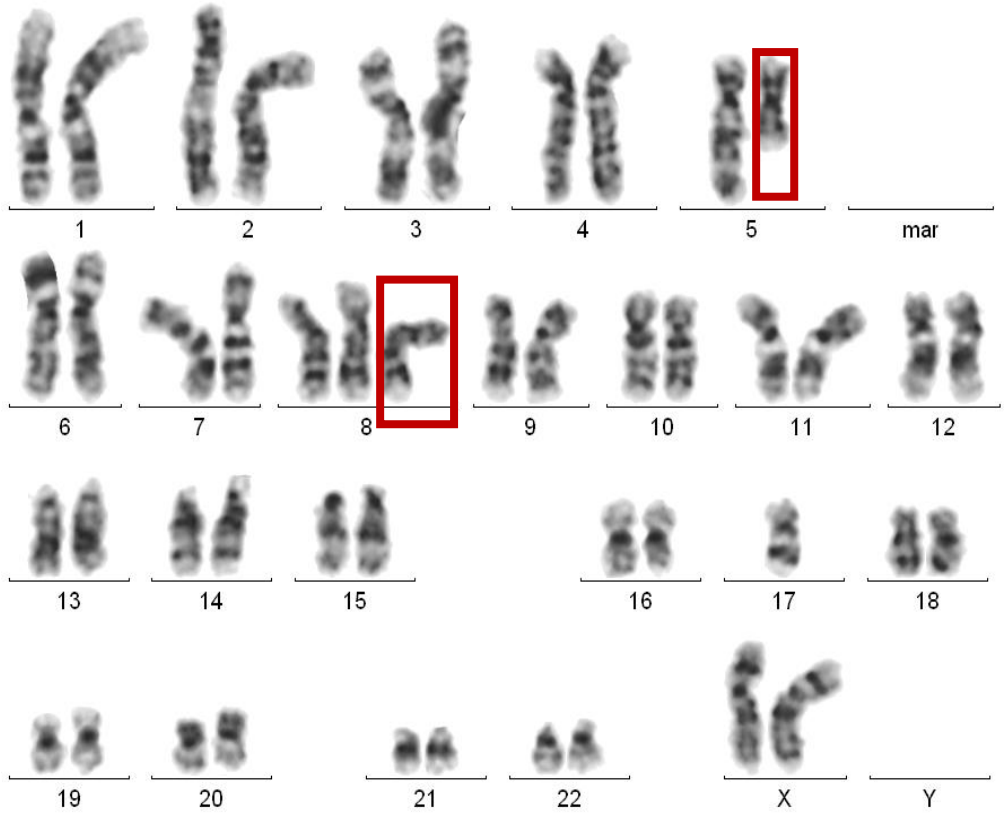


Should we test separately for the iAMP21?- Triple FISH strategy for B-ALL

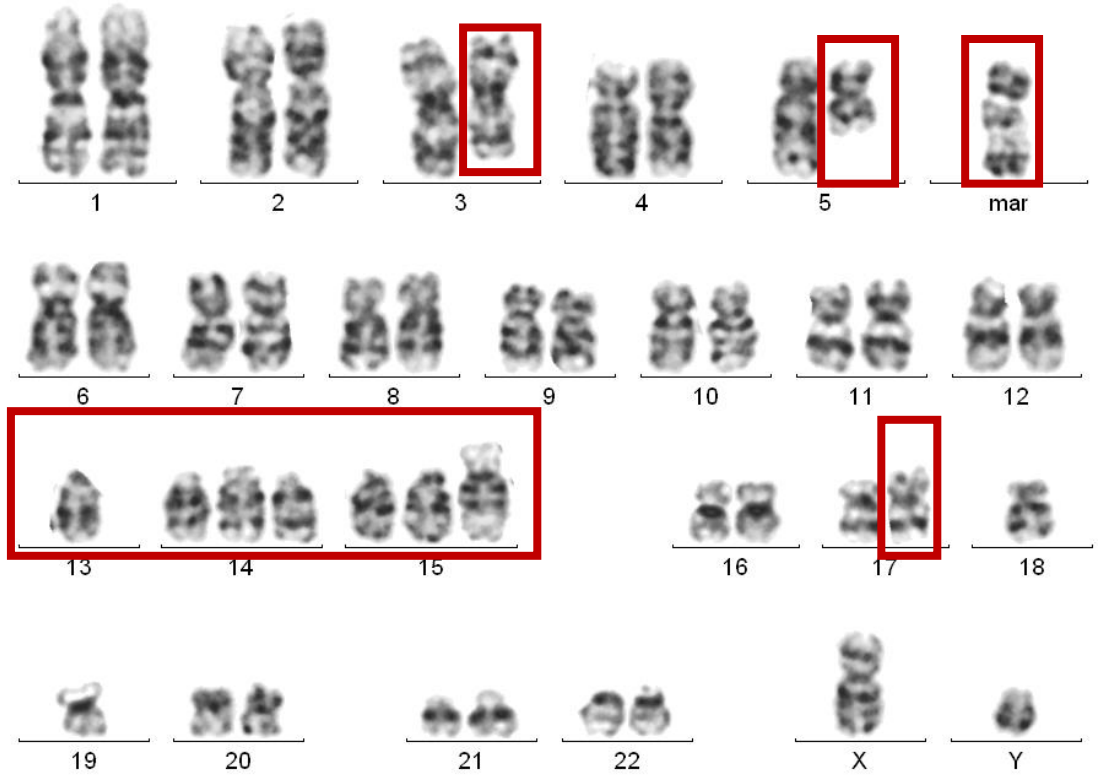


Pediatr Blood Cancer. 2018;e27366

Monosomal and complex karyotypes in myeloid neoplasms



46,XX,del(5)(q13q33),+8,-17



46,XY,del(3)(q?),del(5)(q13q33),+8,-13,+14,+15,add(17)(p?),
-18,-19,+mar

Monosomal karyotype : Loss of 2 autosomes/ 1 autosome+ 1 structural abnormality

Complex karyotype : 3 or more abnormalities

Why should we test for chromosomal abnormalities?

To establish the specific diagnosis

To estimate prognosis, based on the presence of a recurring abnormality, appearance of new karyotypic abnormalities, or the existence of clonal heterogeneity/evolution, which often signal a change in the pace of the disease, usually to a more aggressive course

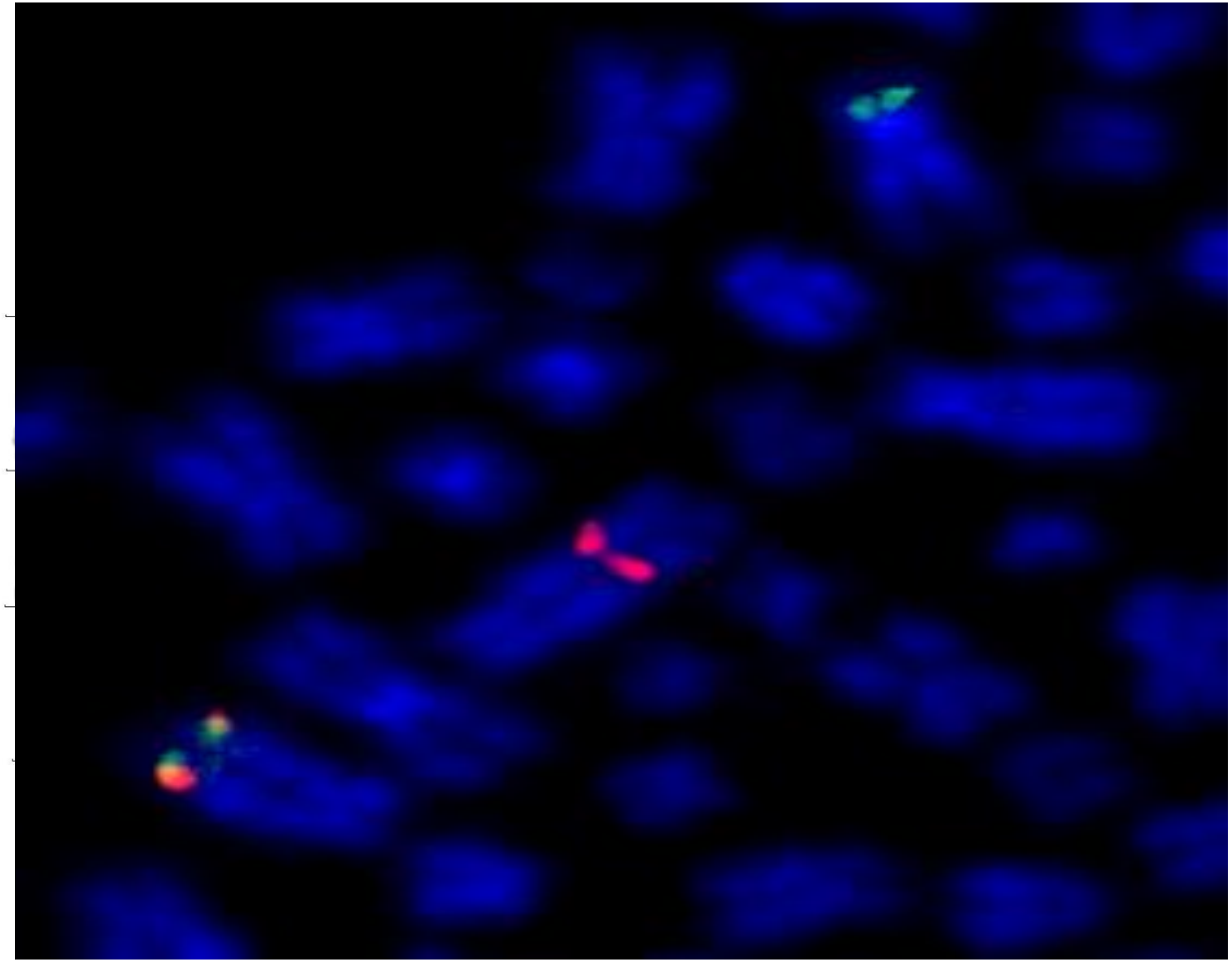
To help in the planning of treatment, since some chromosomal changes predict for response (or nonresponse) to specific therapies, or to inform the selection of a targeted therapy

To distinguish between benign reactive lymphoid or myeloid hyperplasia and a monoclonal malignant proliferation

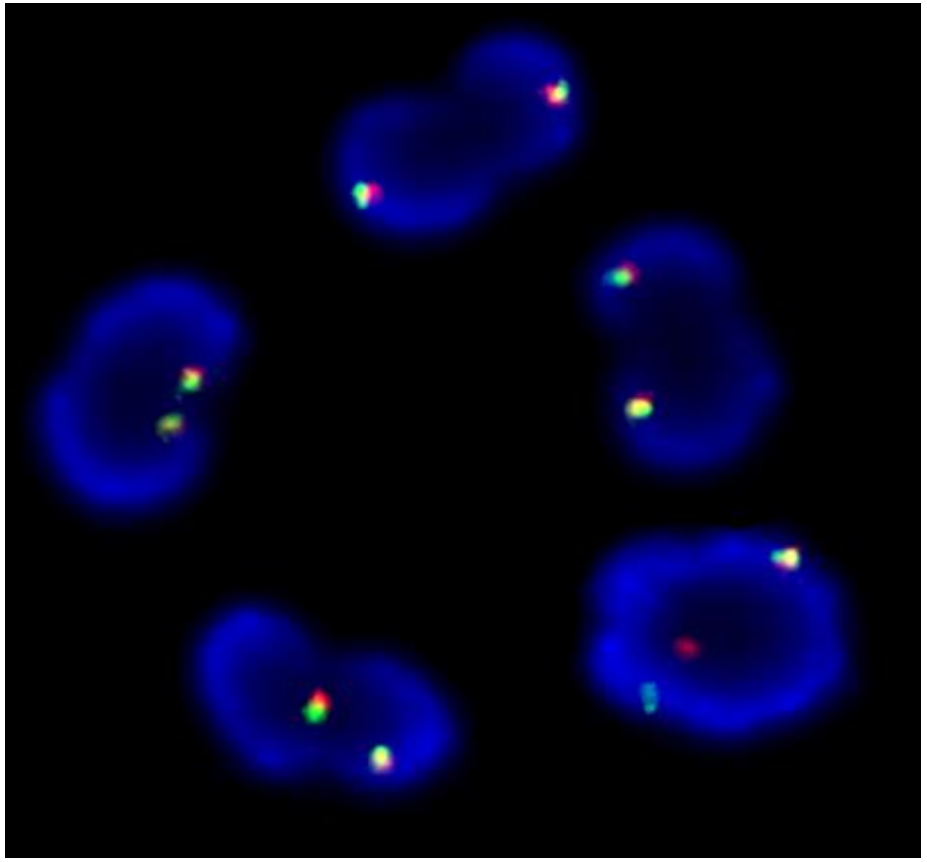
1year/Female
Clinical diagnosis: ? MDS with peripheral eosinophilia
Aspirate :Cellular marrow with myeloid hyperplasia, moderate eosinophilia, reduced megakaryocytes and no abnormal cells.
Trephine :Cellular marrow with trilineage hematopoiesis, moderate eosinophilia, adequate megakaryocytes and mild diffuse lymphocytosis
Total WBC : 51600/cu.mm
Platelet :130000/cu.mm
Hb :11.6 g/dL
DC :Neutrophils:33, Lymphocytes:20, Monocytes:7, Eosinophils:38, Basophils:02

PDGFRβ rearrangement confirmed by FISH analysis

46,XX,t(1;5)(q21;q32)

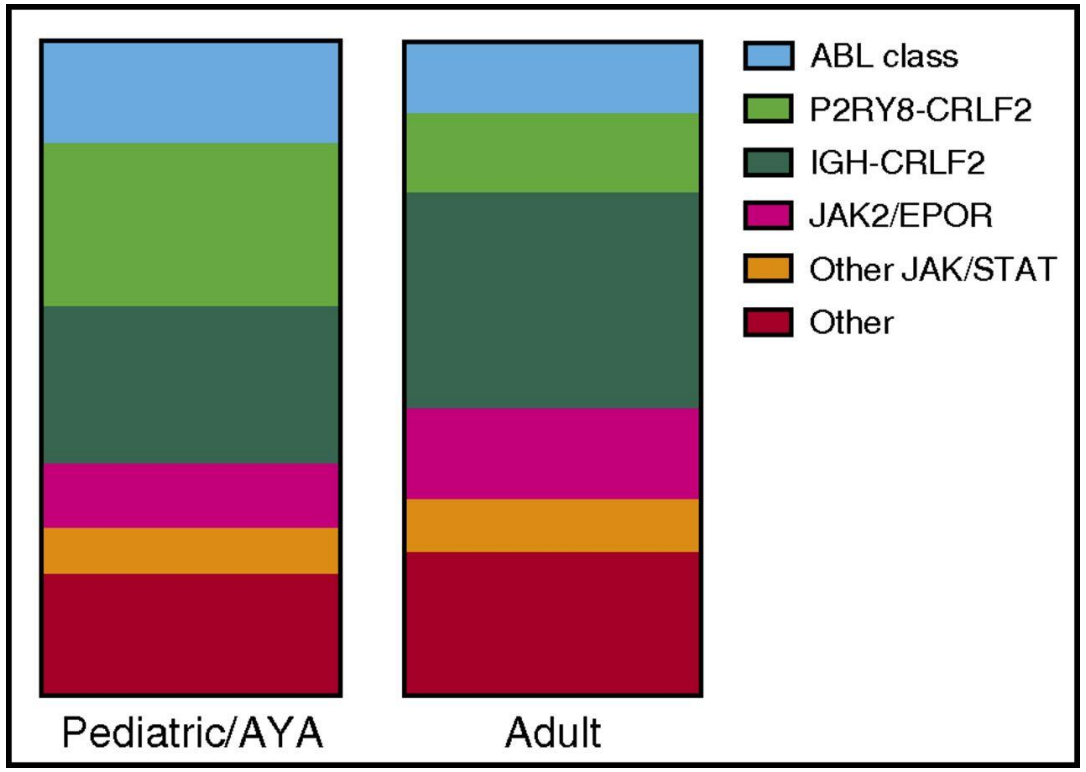


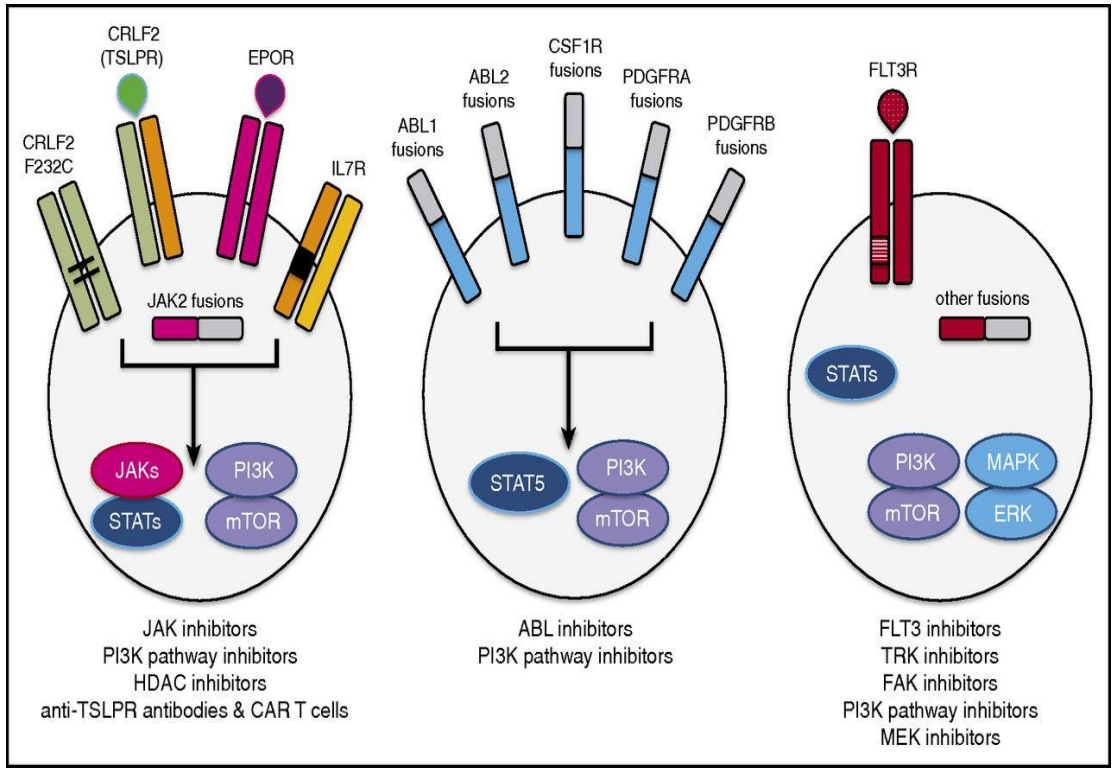
Post treatment with Imatinib- PDGFRβ FISH



Interphase FISH analysis shows 2 fusions (normal chromosomes 5) in the majority of cells analysed.

Philadelphia-like B-ALL



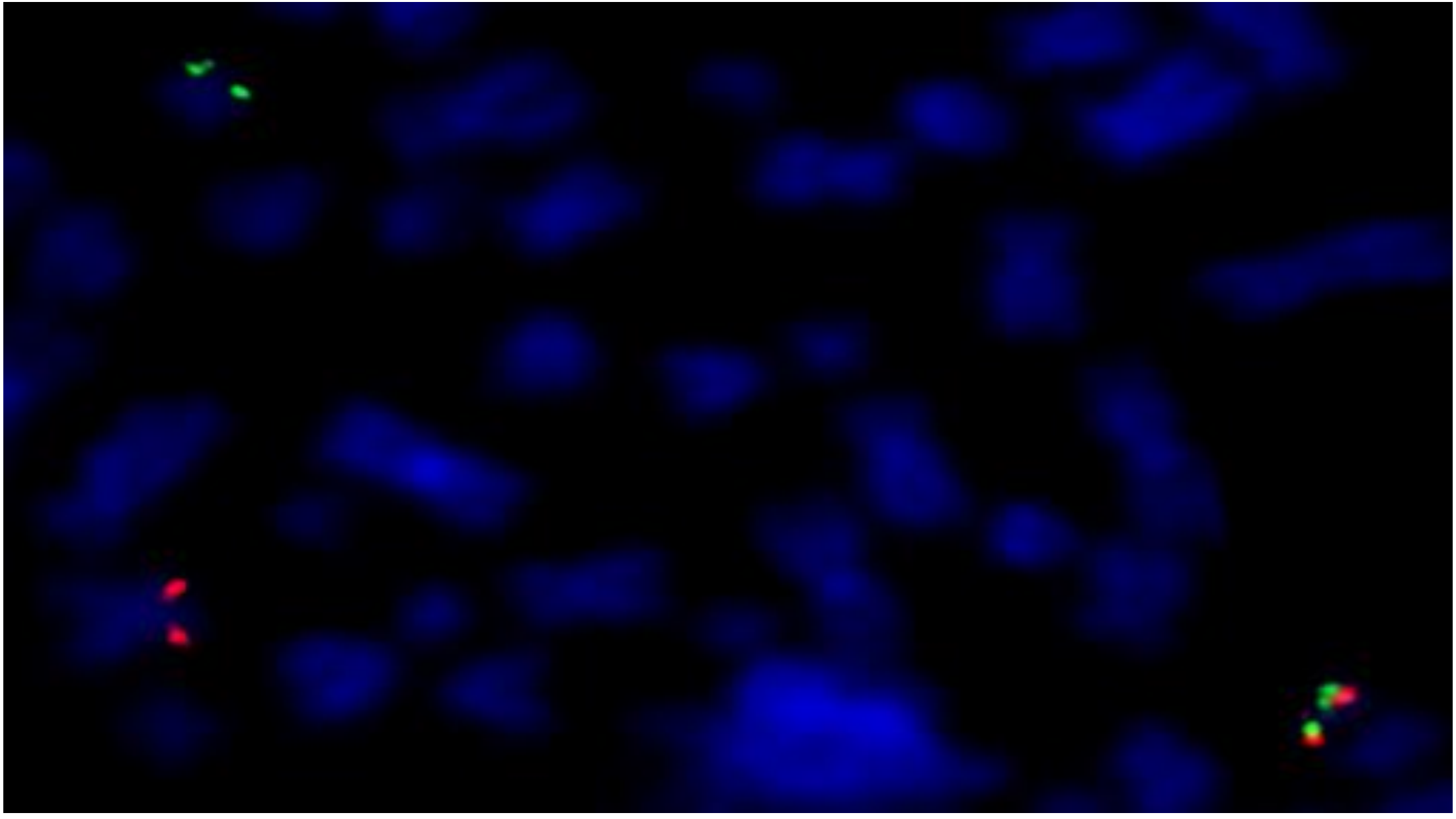


Sarah K. Tasian,Mignon L. Loh,Stephen P. Hunger, Philadelphia chromosome–like acute lymphoblastic leukemia, Blood, 2017

JAK2 rearrangement in B-ALL

40-year-old male, evaluated for fatigue and fever. WBC 144900 with 70% blasts. Diagnosed as B cell ALL. Treated with GMALL protocol. Poor steroid response on day 8. End-induction MRD bulk positive

JAK2 rearrangement in B-ALL

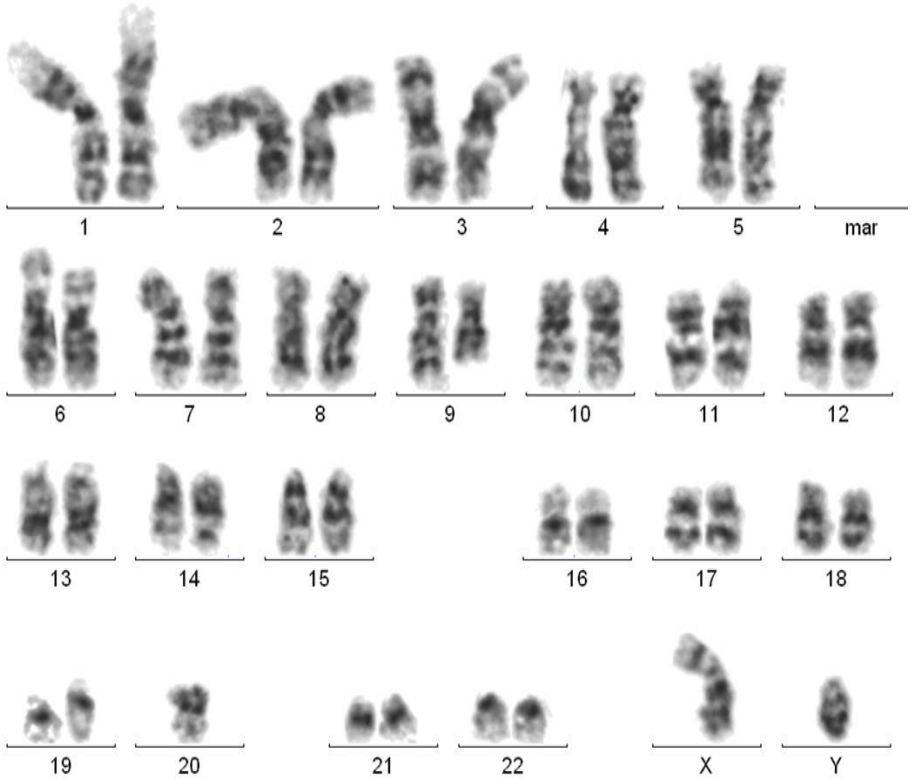


Chromosome paint to identify an abnormality with Ph-like B ALL gene expression

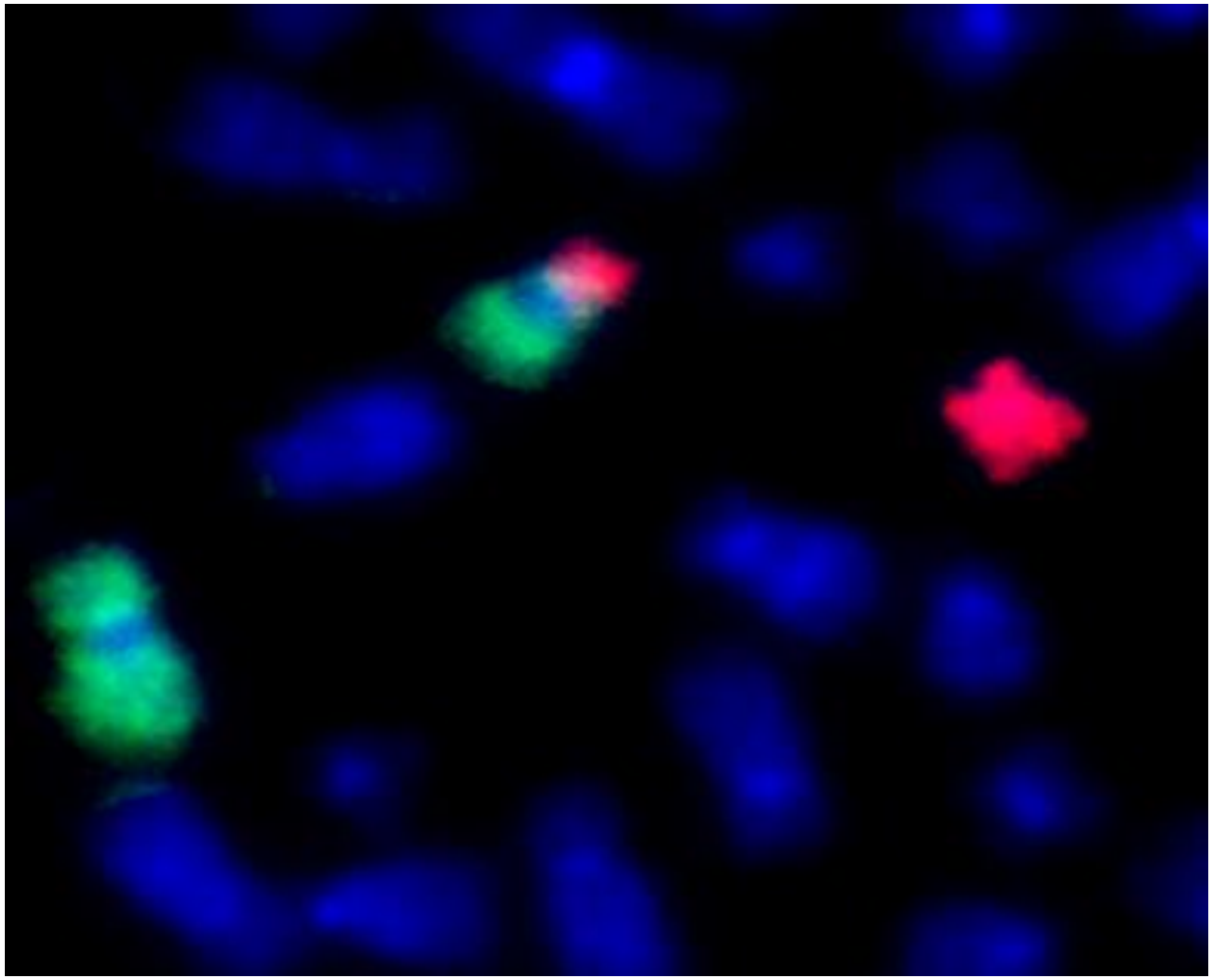
5 year old boy presented with fever and fatigue. Noted to have lymphadenopathy and hepatosplenomegaly. Investigations revealed anemia, thrombocytopenia with WBC count of 56000 per cu.mm and 95% blasts.

Aspirate : Acute leukemia (95% blasts)
Trephine : Acute leukemia
IPT : Consistent with B-ALL with aberrant CD7

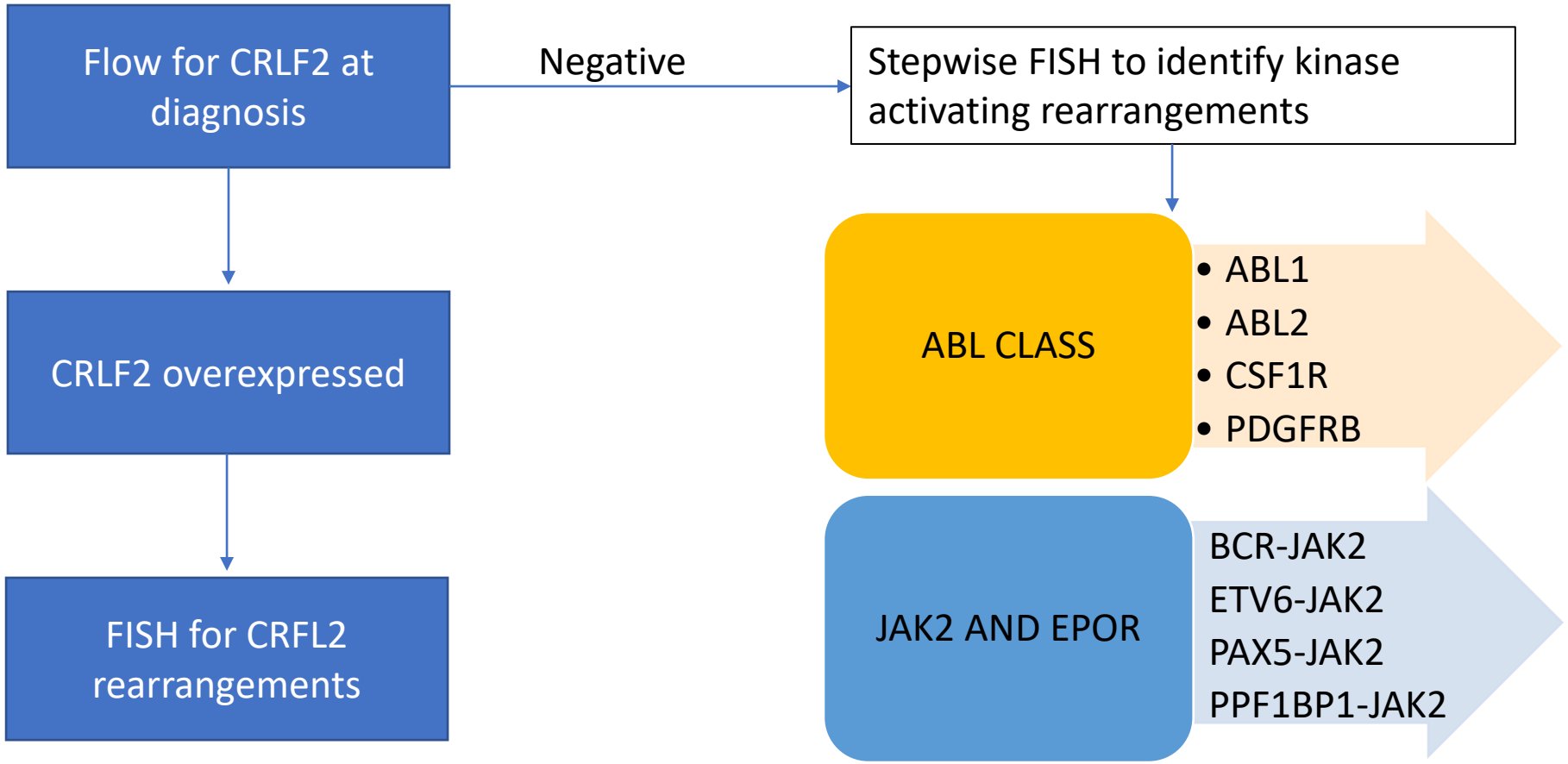
Chromosome paint to identify an abnormality with Ph-like B ALL gene expression



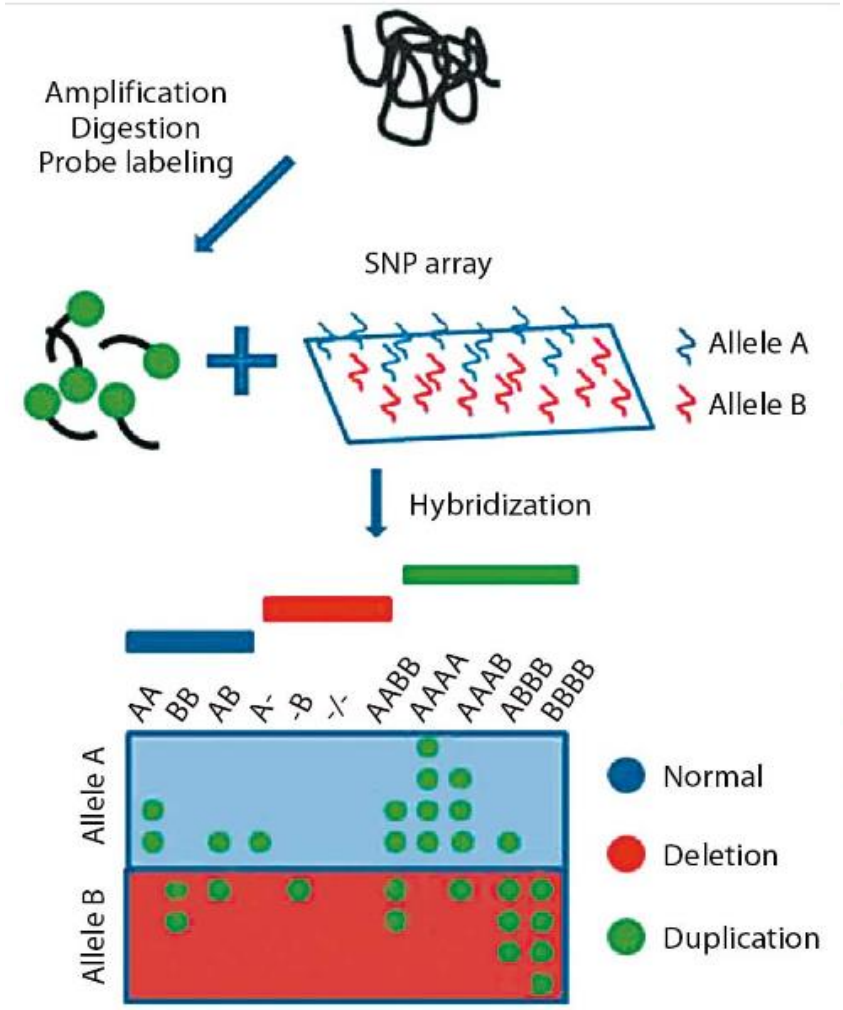
45,XY,dic(9;20)(p11;q11)

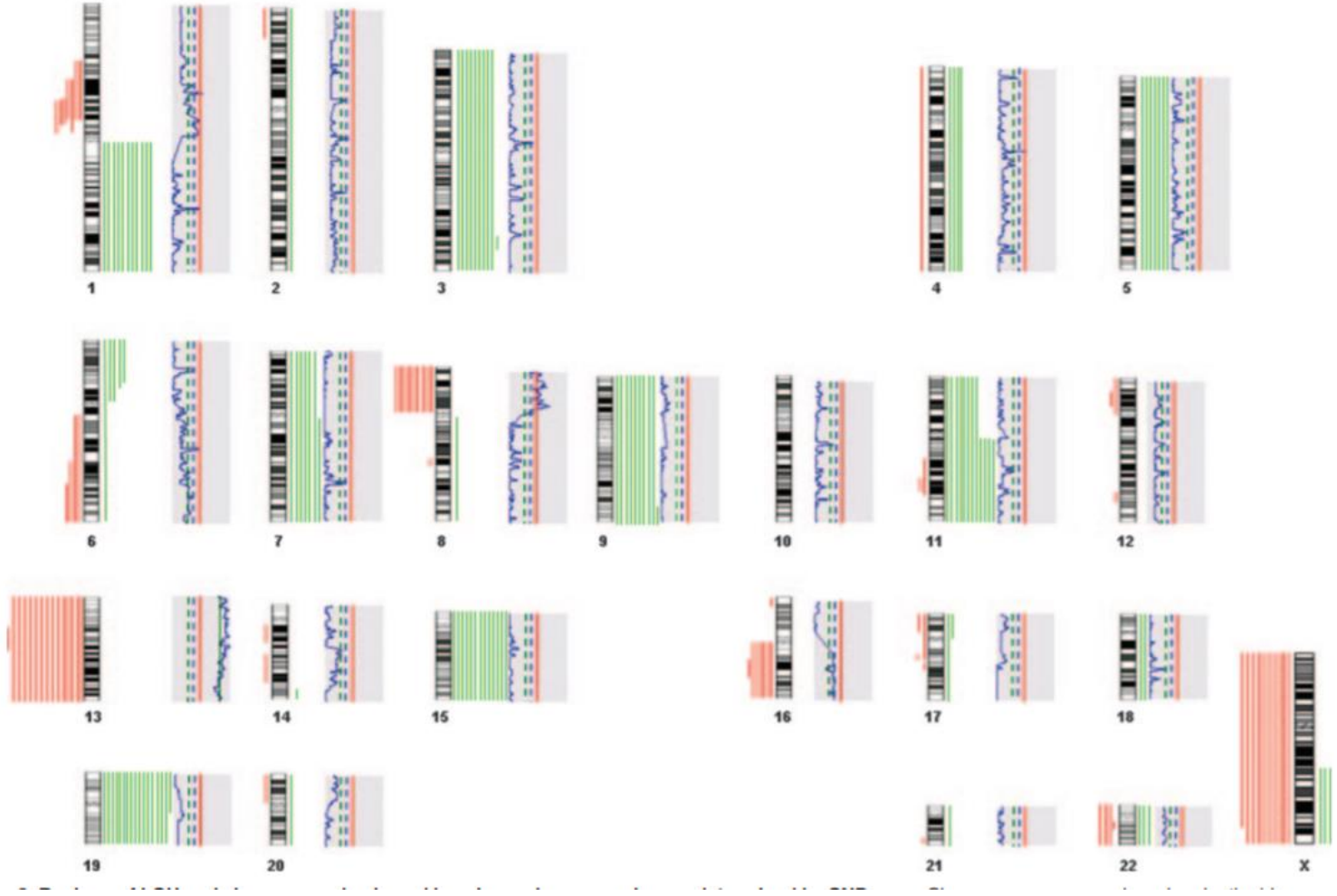


Algorithm for evaluation of Ph-like ALL



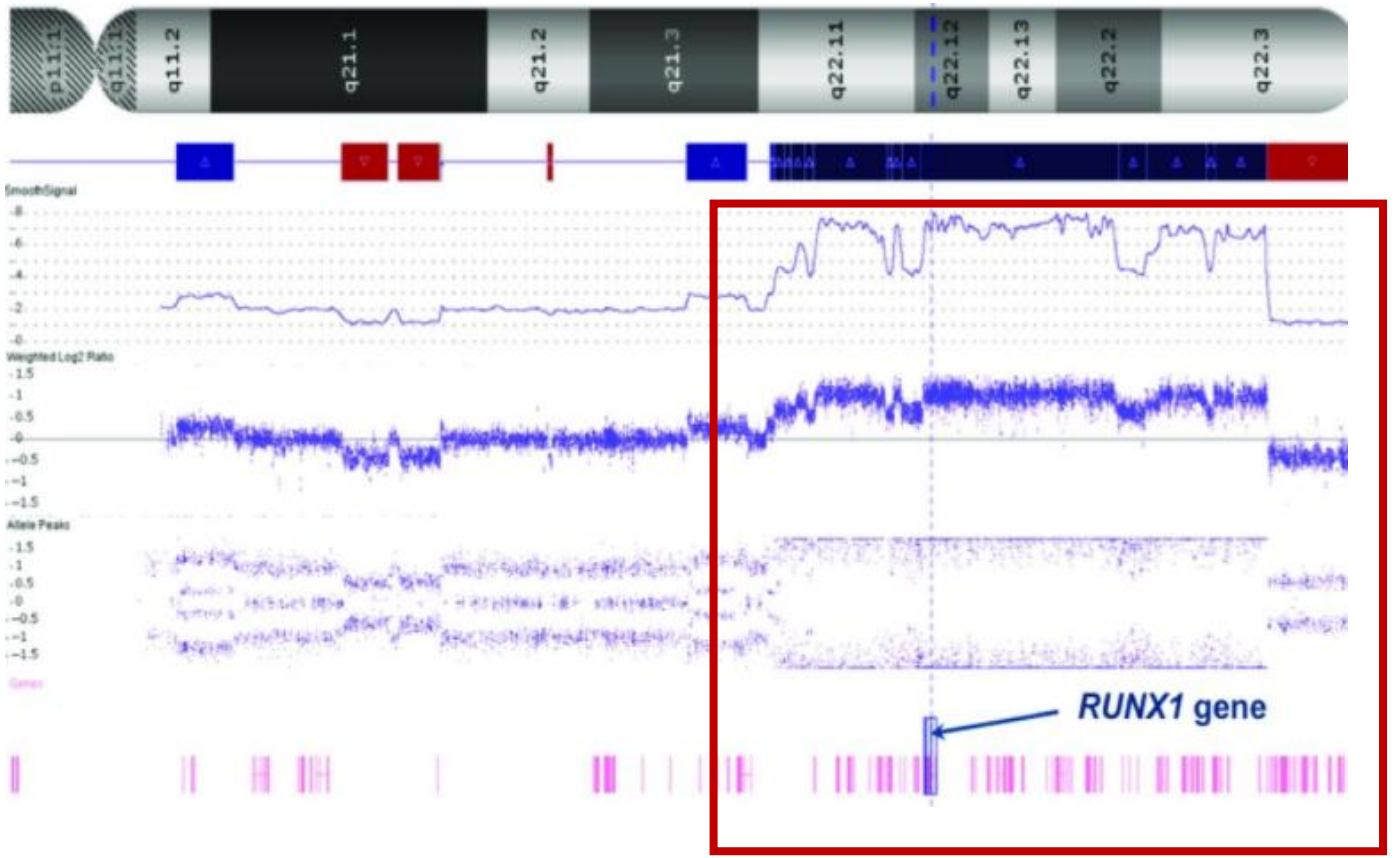
SNP arrays in haematologic malignancies





BLOOD, 1 SEPTEMBER 2006 VOLUME 108, NUMBER 5

SNP arrays in haematologic malignancies



Can detect: Gains and losses of genomic material
Cannot detect : balanced translocation

Molecular Cytogenetics, 10.1186/s13039-016-0294-0, **9**, 1, (2016)

The cytogenetics team at CMC,Vellore

Clinical faculty , Nursing staff ,Flow cytometry and Molecular labs

Thank you