Deciphering Chromosomes Cracking the code

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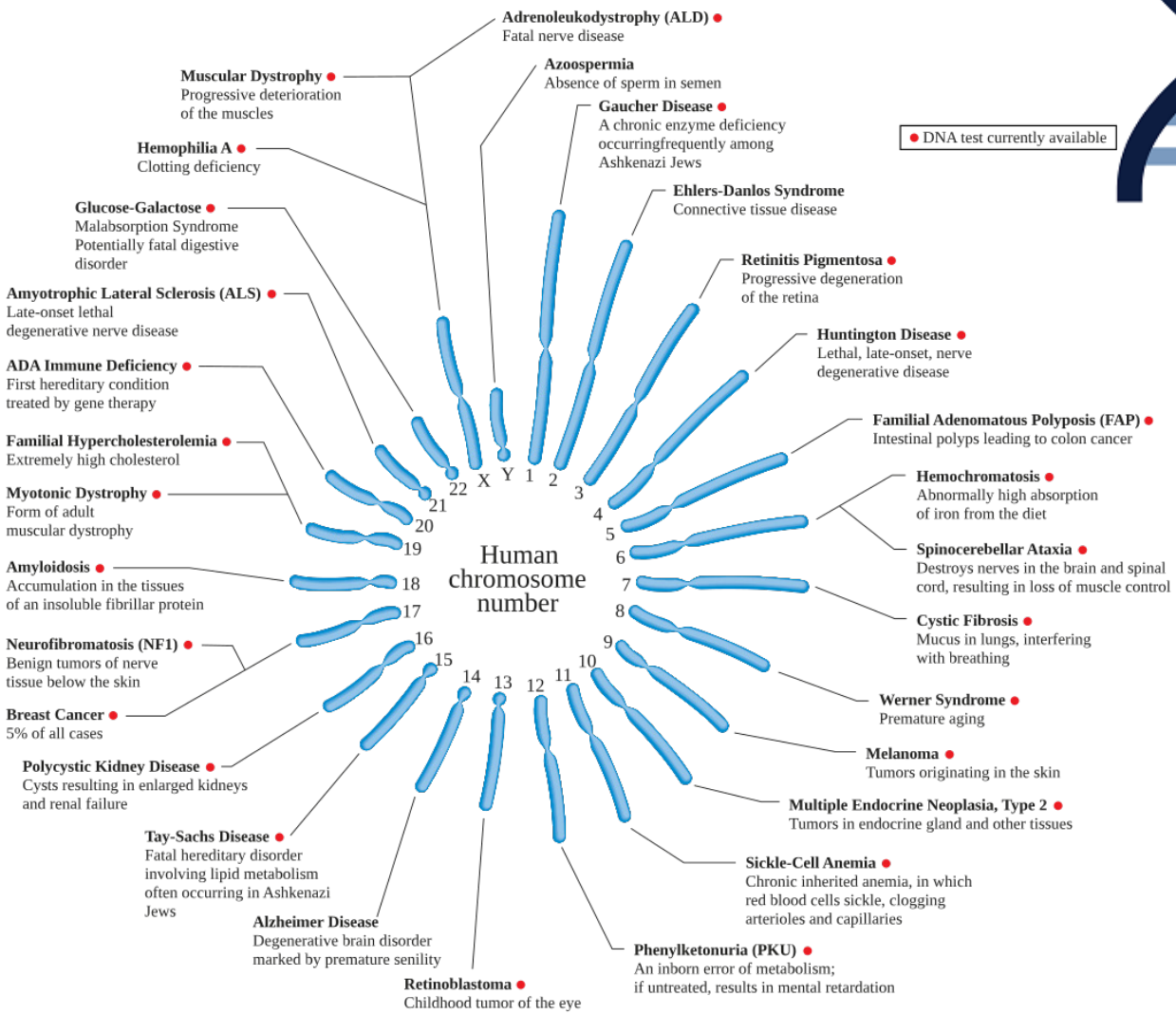
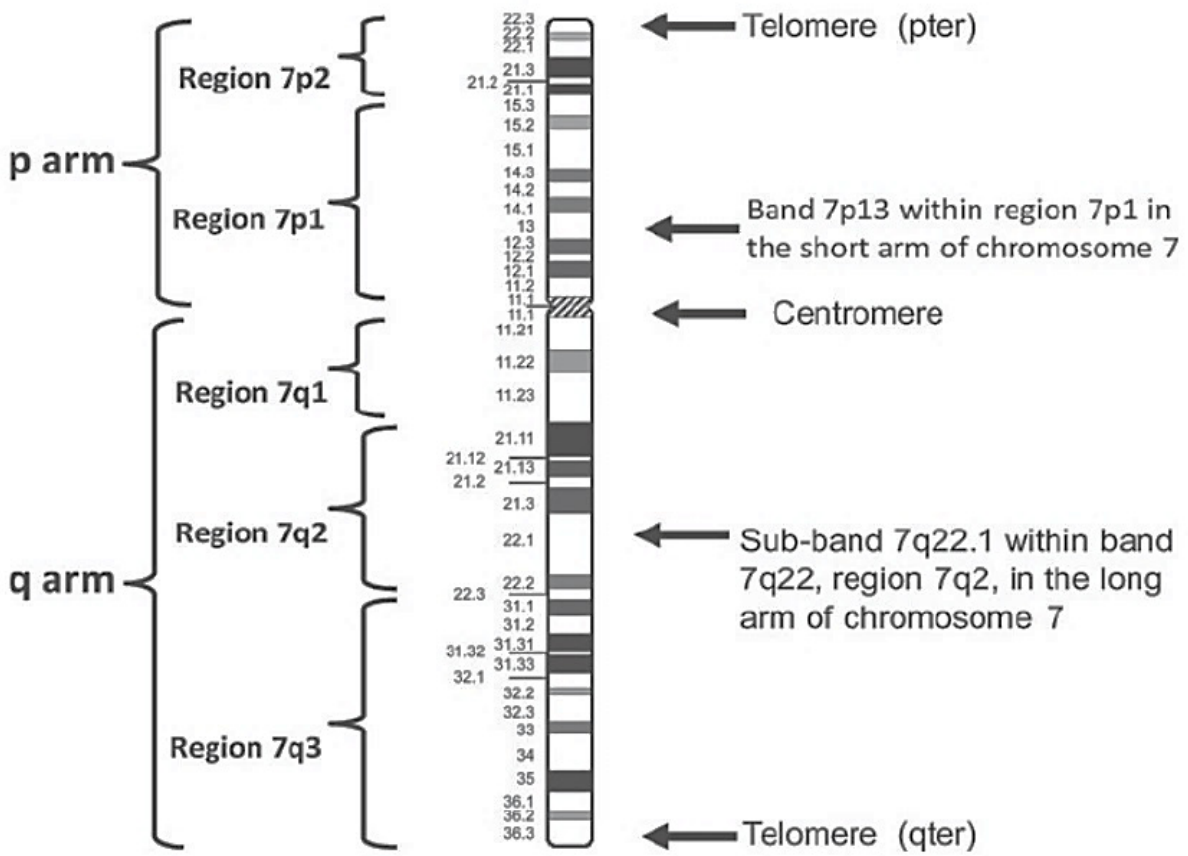
The importance of correctly reporting results.

- Diagnosis & prognosis
- Target specific factors that drive the cancer
- Statistical analysis



Anatomy of a Chromosome



Location of Genes

Gene	Location	Description
TP53	17p13.1	Regulation of cell division, acts as a tumor suppressor
IgVH	14q32.33	Involved in the production of antibodies by B cells.
Trisomy 12	+12	Extra copy of Chromosome 12; cellular adhesion and migration
ATM	11q22-q23	DNA repair and cell cycle control
CCND1	11q13	Regulates cell cycle t(11;14) is a more favorable prognosis
BCR:ABL	t(9;22)	Philadelphia chromosome
MYC	8q24.21	Cell cycle progression, apoptosis & cell transformation

Interpreting the code

- Standardization
- Nomenclature / ISCN description

ISCN Nomenclature

Symbols

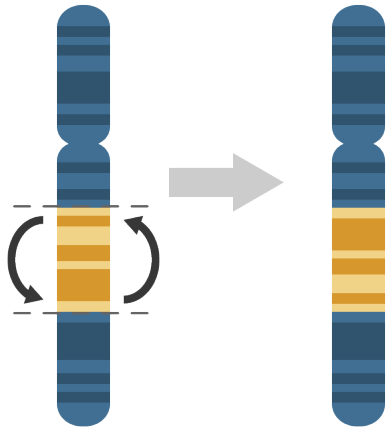
[ ]	# of cells in a line, or metaphases
:	Chromosomal break
::	Chromosomal break and reunion or fusion
,	Separates chromosome numbers & abnormalities
-	Loss
X	Multiple copies or number of copies
( )	Surround altered chromosomes or genes
+	Additional chromosome
;	Separates altered chromosome or break

Aberrations

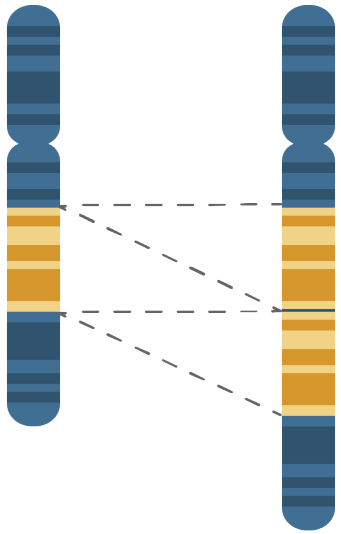
add	Additional material attached to chromosome
del	Deletion or loss of chromosome material
dup	Part of a chromosome is repeated
der	Rearrangement involve ≥ 2 chromosomes or by multiple aberrations.
dic	1 chromosome replaces 2 normal ones.
ins	Addition of material
inv	Part of chromosome inverted
rec	Recombinant, due to meiotic crossing over
t	Exchanged material between 2 chromosomes

Examples

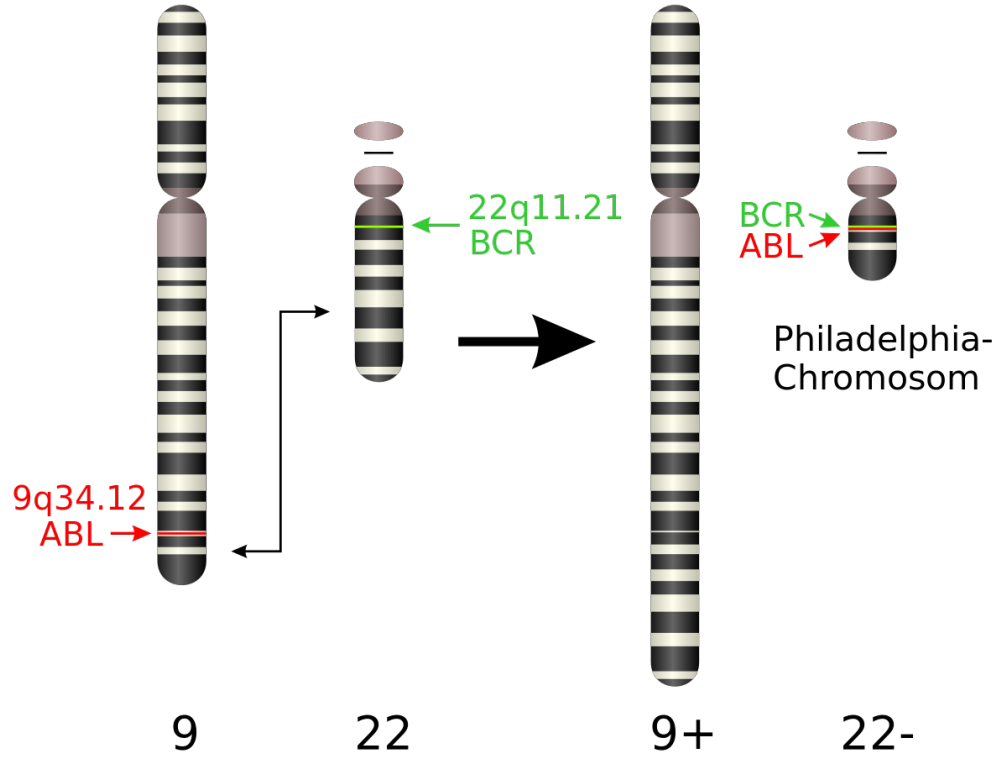
Inversion



Duplication



Translocation



S1925 CLL/SLL

Was cytogenetic analysis performed?	◯ Yes ◯ No
If yes, what was the date the specimen was collected?	☐☐ ☐☐☐ ☐☐☐☐
If yes, what was the type of specimen?	◯ Bone Marrow ◯ Peripheral Blood
If yes, what was the method?	◯ Karyotype From Stimulated Culture ◯ Karyotype From Unstimulated Culture
If yes, what was the number of total metaphases analyzed?	☐☐☐
If yes, what was the number of total abnormal cells?	☐☐☐
If yes, what was the karyotype ISCN description? *(Example 46, XY; 46, XX; etc)*	_____

"Peripheral blood lymphocytes were cultured and stimulated with PHA to induce mitosis"

"Unstimulated 24 – 48 hour culture of cells from peripheral blood"

S1925

Was cytogenetic analysis performed?	◯ Yes ◯ No
If yes, what was the date the specimen was collected?	☐☐ ☐☐☐ ☐☐☐☐
If yes, what was the type of specimen?	◯ Bone Marrow ◯ Peripheral Blood
If yes, what was the method?	◯ Karyotype From Stimulated Culture ◯ Karyotype From Unstimulated Culture
If yes, what was the number of total metaphases analyzed?	☐☐☐
If yes, what was the number of total abnormal cells?	☐☐☐
If yes, what was the karyotype ISCN description? *(Example 46, XY; 46, XX; etc)*	_____

Cells counted:	20
Band Level:	400
Cells Analyzed:	20
Cells karyotyped:	3

S1925

Was cytogenetic analysis performed?	◯ Yes ◯ No
If yes, what was the date the specimen was collected?	☐☐ ☐☐☐ ☐☐☐☐
If yes, what was the type of specimen?	◯ Bone Marrow ◯ Peripheral Blood
If yes, what was the method?	◯ Karyotype From Stimulated Culture ◯ Karyotype From Unstimulated Culture
If yes, what was the number of total metaphases analyzed?	☐☐☐
If yes, what was the number of total abnormal cells?	☐☐☐
If yes, what was the karyotype ISCN description? *(Example 46, XY; 46, XX; etc)*	_____

48, XY, +3, +5, del(5)(q13q14), t(8;14)(q24;32) [2]

S1925

nuc ish (D12Z3,MDM2)x3 [56/100], (TP53 x1,D17Z1x2)[44/100]

If yes, what was the FISH ISCN description? *(Example nuc ish 3q27(BCL6x2)[200]; etc)*	_____
If yes, was a del(17p) abnormality identified?	○ Yes ○ No
If yes, what was the total number of interphases/metaphase cells analyzed?	☐☐☐
If yes, of the total cells scored, what was the number of abnormal cells?	☐☐☐
If yes, was a del(13q) abnormality identified?	○ Yes ○ No
If yes, what was the total number of interphases/metaphase cells analyzed?	☐☐☐
If yes, of the total cells scored, what was the number of abnormal cells?	☐☐☐
If yes, was a trisomy 12 abnormality identified?	○ Yes ○ No
If yes, what was the total number of interphases/metaphase cells analyzed?	☐☐☐
If yes, of the total cells scored, what was the number of abnormal cells?	☐☐☐
If yes, was a del(11q) abnormality identified?	○ Yes ○ No
If yes, what was the total number of interphases/metaphase cells analyzed?	☐☐☐
If yes, of the total cells scored, what was the number of abnormal cells?	☐☐☐

Was TP53 mutational analysis testing performed? ○ Yes ○ No

If yes, what was the date the specimen was collected? ☐☐ ☐☐☐ ☐☐☐☐

If yes, what was the type of specimen? ○ Bone Marrow ○ Peripheral Blood

If yes, what was the result? ○ Mutated ○ Not Mutated

If mutated, what is the estimated level of the mutated clone(s)?
(Another term for this is variant allele frequency (VAF). Take this number from the genetic sequencing report for TP53 mutation, NOT the CLL FISH panel. The estimated level of TP53 mutated clone (or VAF) is different from % of del(17p) on the FISH report.)

☐☐☐.☐ %

If yes, which mutation was identified?
(Report in the format of this example:
TP53 (NM_000546.6) exon 5 p.Leu194Arg (c.581T>G)
- TP53=name of gene
- NM=TP53 normal status that the gene has been compared to—typically 000546.0, 000546.5 or 000546.6
- Exon=sometimes this is not listed on the report, ok to leave out
- p.=protein that is affected. In this example Leucine is changed to Arginine at the 194 locus. Sometimes the amino acid will be listed as a one letter abbreviation. If this is the case in this example would be listed as p.L194R.
- c.=DNA change and location that is noted.)

TP53(NM_000546.5) p.M2371 (c.711G>A)

Additional Details for Mutations

Gene	Protein Change	DNA Change	VAF%	Depth	Transcript
TP53	p.M237I	c.711G>A	19 %	15888	NM_000546.5

S1925

Was IgVH mutational analysis testing performed?	○ Yes ○ No
If yes, what was the date the specimen was collected?	☐☐ ☐☐☐ ☐☐☐☐
If yes, what was the type of specimen?	○ Bone Marrow ○ Peripheral Blood
If yes, what was the result?	○ Mutated ○ Not Mutated
Was Chromosome Genomic Array Testing (CGAT) or Chromosome Microarray performed?	○ Yes ○ No
If yes, what was the date the specimen was collected?	☐☐ ☐☐☐ ☐☐☐☐
If yes, what was the type of specimen?	○ Bone Marrow ○ Peripheral Blood
If yes, what was the result?	○ Normal ○ Abnormal
If abnormal, what was the result per ISCN2016? *(Example arr(1-22,X)x2; etc)*	_____
If abnormal, what was the estimated level of the abnormal clone(s)?	☐☐☐.☐ %

IGHV Mutation Analysis by Sequencing Non Mutated

S1925

Was IgVH mutational analysis testing performed?	○ Yes ○ No
If yes, what was the date the specimen was collected?	☐☐ ☐☐☐ ☐☐☐☐
If yes, what was the type of specimen?	○ Bone Marrow ○ Peripheral Blood
If yes, what was the result?	○ Mutated ○ Not Mutated
Was Chromosome Genomic Array Testing (CGAT) or Chromosome Microarray performed?	○ Yes ○ No
If yes, what was the date the specimen was collected?	☐☐ ☐☐☐ ☐☐☐☐
If yes, what was the type of specimen?	○ Bone Marrow ○ Peripheral Blood
If yes, what was the result?	○ Normal ○ Abnormal
If abnormal, what was the result per ISCN2016? *(Example arr(1-22,X)x2; etc)*	_____
If abnormal, what was the estimated level of the abnormal clone(s)?	☐10·0 %

arr[GRCh37]
8p23.2p11.22(3011099_38871615)x1[0.1],11q14.2q22.1(85754392_98901956)x3[0.1]

S1905 T-cell ALL

S1905 CYTOGENETICS LAB REPORT FORM

Patient Identifier | | | | | | | **Study Identifier** | S | 1 | 9 | 0 | 5 | **Registration Step** | 1 |

Patient Initials _____ (L, F M)

Page: Cytogenetics Lab Report

Instructions: **Registering Institution:** Please send this form along with the cytogenetics specimen to the cytogenetics lab of choice. When the results are received from the lab, submit the data from this form online and upload any available cytogenetics and FISH reports via MediData Rave (see Section 14.3).

Cytogenetics Lab: Please complete this form and submit along with the cytogenetics and FISH reports to the registering institution at the contact listed below.

Registering Institution Contact Name: _____

Email: _____

This form is completed at pretreatment and any time a bone marrow (or blood) exam including cytogenetics and/or FISH is performed. Date is in **DD MON YYYY** format. Explain any blank fields or blank dates in the **Comments** section.

S1905

Bone marrow		
Unstimulated short-term culture (24-72 hours)		1 0
Direct preparation (metaphases)		
Stimulated culture (metaphases)		
Mitogen type		
Other culture method		1 0
Culture method and duration	Overnight culture	

COMMENT: Ten metaphase cells were analyzed from the overnight culture and 10 metaphase cells were analyzed from the 72 hour unstimulated culture. Twenty cells analyzed showed a 46,XY karyotype, or had

S1905

Total number of metaphases	20
Total number of abnormal metaphases	19
Are results based on at least 400-band level for banded analysis?	☐ Yes ☒ No ☐ Unknown
Karyotype description	

Stemline: 47,XX,del(6)(q21q25),del(17)(p13.1),+19[4]
Sideline 1: 47,sl,del(4)(q21q31.3)[10]
Sideline 2: 47,sdl1,del(3)(p23p13)[5]

Banding Resolution	375 – 400
Metaphase Cells Counted	20
Analyzed	20
Karyogramed	8

S1905

Were FISH studies performed?	☒ Yes ☐ No ☐ Unknown
If Yes, FISH ISCN description	Nuc ish(D6z1,MYB)X3[21/200]

Abnormal FISH Results

nuc ish(D6Z1,MYB)x3[21/200]

FISH results: **POSITIVE for 3 signals for the D6Z1locus (pericentromeric region of chromosome 6) and the MYB locus (6q23) in 10.5% of cells**

Probe set: D6Z1 locus (pericentromeric region) and MYB locus (6q23) - In 21 of the 200 cells scored (10.5%), 3 signals were present for both probes. In the remaining cells a normal (or apparently random) probe signal pattern was noted.

Within Normal Limits

FISH Results

nuc ish(alpha sat4,alpha sat10,D17Z1)x2[500]

FISH results: **Negative for gain or loss of the pericentromeric regions of chromosomes 4, 10, or 17**

Probe set: Pericentromeric region of chromosome 4, 10, and 17 (alpha satellite DNA probes [for 17 this is locus D17Z1]) - A total of 500 interphase nuclei were scored. The probe signal values were not significantly different from negative controls.

S1905

If FISH studies were performed, enter all probes and abnormal signal patterns:

Probe 1: D6Z1locus6q23

Total number of interphase nuclei	200
Total number of abnormal interphases	21
Total number of metaphases	
Total number of abnormal metaphases	

nuc ish(D6Z1,MYB)x3[21/200]

FISH results: **POSITIVE for 3 signals for the D6Z1locus (pericentromeric region of chromosome 6) and the MYB locus (6q23) in 10.5% of cells**

Probe set: D6Z1 locus (pericentromeric region) and MYB locus (6q23) - In 21 of the 200 cells scored (10.5%), 3 signals were present for both probes. In the remaining cells a normal (or apparently random) probe signal pattern was noted

S1905

Abnormalities *(select all that apply)*	
del(1)(p32p32)	☐
t(1;14)(p32;q11)	☐
t(1;14)(p32;q11)	☐
Small insertion	☐
t(10;14)(q24;q11)	☐
t(7;10)(q34;q24)	☐
t(10;14)(q24;q11)	☐
t(5;14)(q35;q11)	☐
t(5;14)(q35;q32)	☐
inv(7)(p15;q34)	☐
t(10;11)(p13;q14)	☐
del(9)(q34;q34)	☐
inv(14)(q11;q13)	☐
T(14;20)(q11;p11)	☐

nuc ish(D6Z1,MYB)x3[21/200]

Probe set: D6Z1 locus (pericentromeric region) and MYB locus (6q23)

t(11;14)(p15;q11)	☐
t(11;14)(p13;q11)	☐
del(5)(q14;q14)	☐
t(7;19)(q34;p13)	☐
t(11;14)(p11;q32)	☐
dup(6) (q23;q23)	?
t(6;7)(q23;q34)	☐
Number of unrelated cytogenetic abnormalities	☐☐☐
Monosomy	☐ Yes ☐ No

46,XX,-13

nuc ish(D13Z1)X1

S2209 Multiple Myeloma

Was fluorescence in situ hybridization (FISH) performed and reviewed?	Yes
If yes, what was the date the specimen was collected?	06/07/2024
If yes, what was the type of specimen?	Bone Marrow
If yes, what plasma cell enrichment method was used?	CD-138 Enriched
If yes, was a del(17p) abnormality identified?	
If yes, was a t(14;16) abnormality identified?	
If yes, was a t(14;20) abnormality identified?	
If yes, was a 1q+ abnormality identified?	
If yes, was a t(4;14) abnormality identified?	

- ◯ CD-138 Enriched
- ◯ cIG-FISH
- ◯ None
- ◯ Unknown

Specimen Type: CD138+ cells enriched from bone marrow aspirate

S2209 Multiple Myeloma

Was fluorescence in situ hybridization (FISH) performed and reviewed?	Yes
If yes, what was the date the specimen was collected?	06/07/2024
If yes, what was the type of specimen?	Bone Marrow
If yes, what plasma cell enrichment method was used?	CD-138 Enriched
If yes, was a del(17p) abnormality identified?	
If yes, was a t(14;16) abnormality identified?	
If yes, was a t(14;20) abnormality identified?	
If yes, was a 1q+ abnormality identified?	
If yes, was a t(4;14) abnormality identified?	

del(17p) = TP53 loss
t(14,16) = MAF
t(14;20) = MAFB
t(4;14) = MMSET /MFGFR3
1q+ = MCL1 & CKS1B

1q+

amp(1q)
1(q21)
der(1;5)(q10;q10),
der(1;16)(q10;p10)

Faiman & Tariman; 2021, Wiedmeir-Nutor & Bergsagel; 2022, https://omim.org/entry/254500

S2114: Follicular B-cell Lymphoma

- ◯ Diffuse large B-Cell lymphoma (DLBCL) NOS
- ◯ DLBCL, Germinal-center B-cell type
- ◯ DLBCL, Activated B-cell type
- ◯ T-cell histiocyte-rich large B-cell lymphoma
- ◯ Primary cutaneous DLBCL, leg type
- ◯ Intravascular large B-cell lymphoma
- ◯ EBV$^+$ DLBCL, NOS
- ◯ DLBCL associated with chronic inflammation
- ◯ HHV8$^+$ DLBCL, NOS
- ◯ High-grade B-cell lymphoma with MYC and BCL2 and/or BCL6 rearrangements
- ◯ High-grade B-cell lymphoma, NOS
- ◯ Follicular lymphoma grade 3b
- ◯ Primary mediastinal (thymic) B-cell lymphoma

ISCN description:

- **MYC rearrangement**: t(8;14)(q24;q32)
- **BCL2 rearrangement**: t(14;18)(q32;q21)
- **BCL6 rearrangement**: t(3;14)(q27;q32)

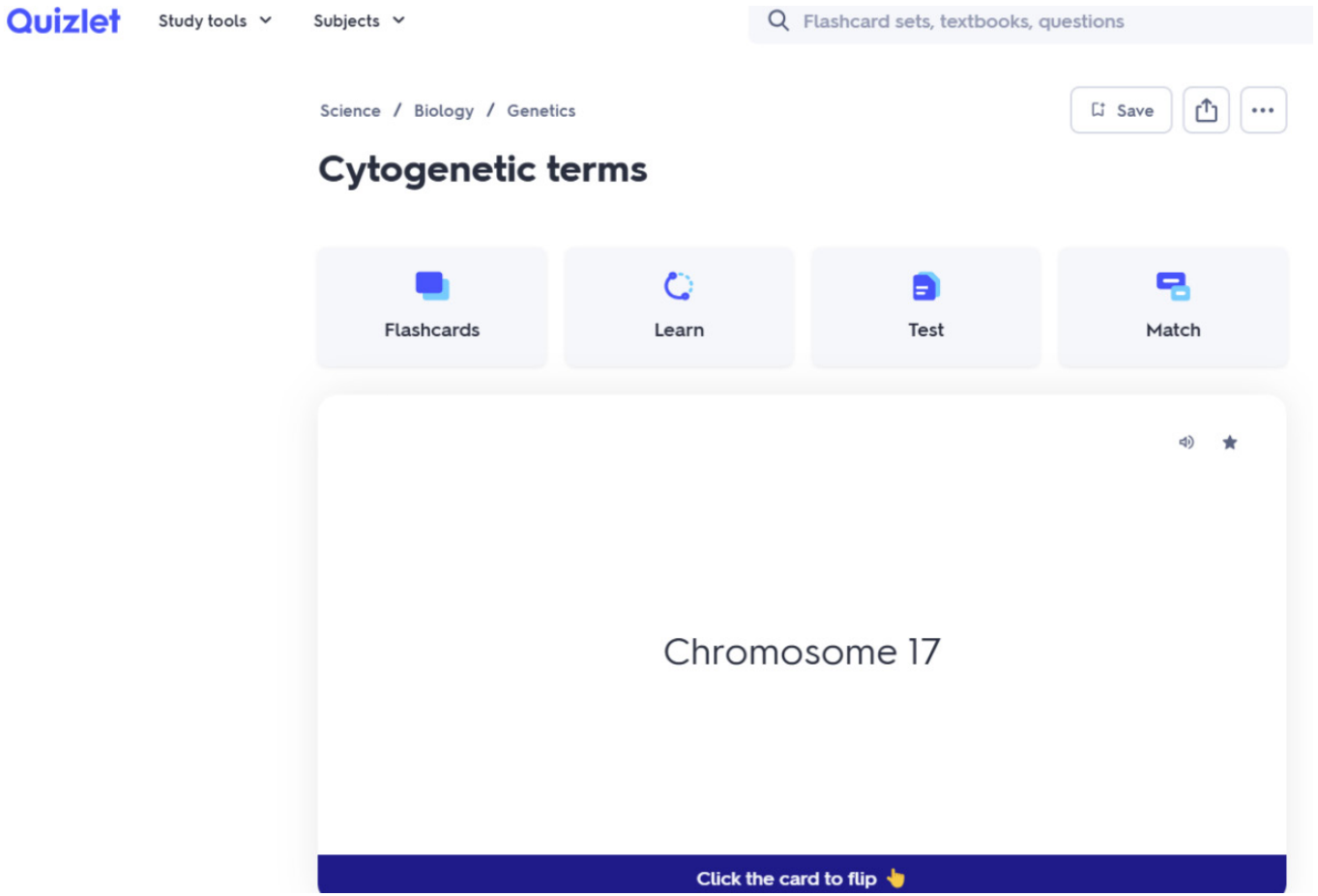
A case with both MYC and BCL2 rearrangements might be described as:

- **46,XX,t(8;14)(q24;q32),t(14;18)(q32;q21)**

And a case with MYC and BCL6 rearrangements might be described as:

- **46,XX,t(8;14)(q24;q32),t(3;14)(q27;q32)**

Quizlet


Quizlet
Study tools
Subjects
Flashcard sets, textbooks, questions
Science / Biology / Genetics
Save
Cytogenetic terms
Flashcards
Learn
Test
Match
Chromosome 17
Click the card to flip

Resources

- Genetic Testing Methods
  - https://www.jax.org/education-and-learning/clinical-and-continuing-education/ccep-non-cancer-resources/genetic-testing-methods
- Genetic and Precision Oncology Learning Library (ONS)
  - https://www.ons.org/genomics-and-precision-oncology-learning-library
- Gene Cards: https://www.genecards.org/
- NIH US National Library of Medicine – MedlinePlus
  - https://medlineplus.gov/genetics/
- Cancer Genomics Overview
  - https://www.cancer.gov/publications/pdq/information-summaries/genetics/overview-hp-pdq
- National Human Genome Research Institute
  - https://www.genome.gov/dna-day/15-ways/cancer-genomics
- Learn Genetics
  - https://learn.genetics.utah.edu/content/basics/
- Precision Medicine Advisors
  - https://precision-medicine-academy.thinkific.com/