

Implementation of Optical Genome Mapping into diagnostic workflows

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Leuven, 06-02-2026



Radboudumc
university medical center

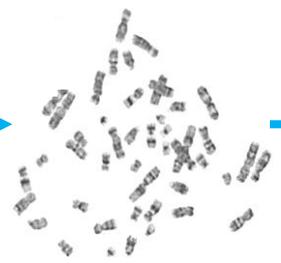


Patient sample

Karyotyping

Cell culture

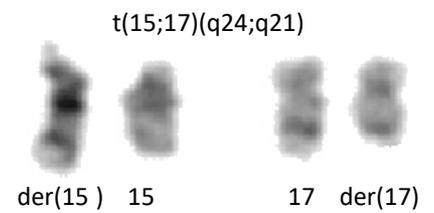
Banding of chromosomes



microscopic analysis



visual interpretation of chromosomes



OGM

DNA isolation

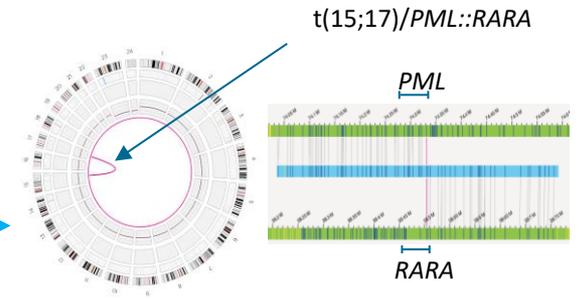


labeling of DNA molecules



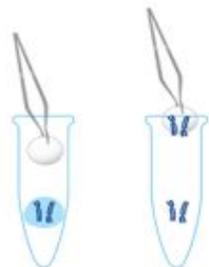
analysis van DNA molecules with Bionano Saphyr

@Bionano Genomics

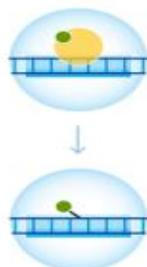


Interpretation of DNA molecules using software

OGM: How does it work?



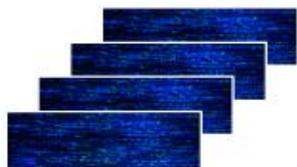
DNA isolation



DNA labeling



Linearization in nanochannels



Genome imaging



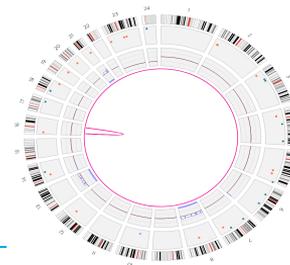
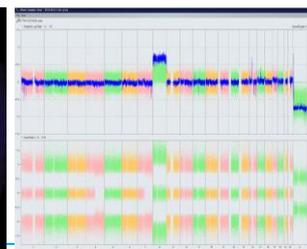
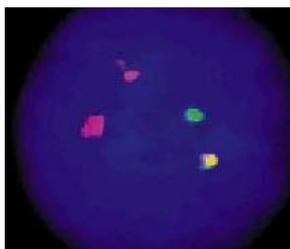
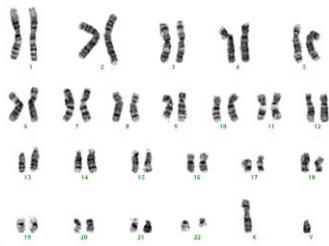
De novo assembly



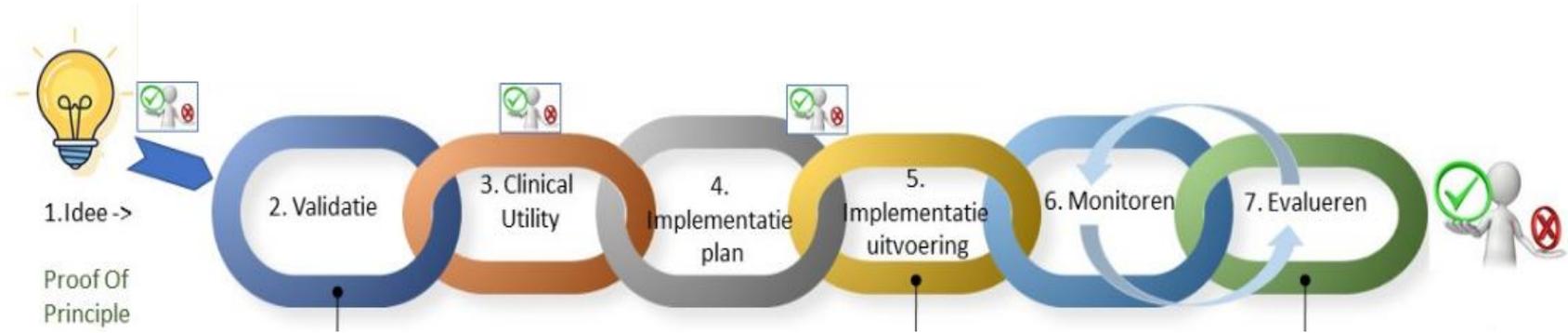
Structural variant calling

Cytogenetic diagnostics

	Karyotyping	FISH	array	OGM
Whole genome	✓	✗	✓	✓
Translocations	✓	✓	✗	✓
Deletions/ gains	✓	✓	✓	✓
resolution	low (5~10 Mb)	High	High (100 kb)	High (50 kb)
Detection limit	~10%	2% (SV) 10% (CNV)	5-10%	5% (SV) 10% (CNV)
Without cell culture	✗	✓	✓	✓



Implementation in diagnostics



Validation studies

Technical validation:

Comparison with previous findings

Hematological malignancies (n=52 samples):

- n = 52 samples
- 100% concordance for VAF > 10%



ARTICLE

Next-generation cytogenetics: Comprehensive assessment of 52 hematological malignancy genomes by optical genome mapping

Kornelia Neveling,^{1,2,6} Tuomo Mantere,^{1,3,4,6} Susan Vermeulen,¹ Michiel Oorsprong,¹ Ronald van Beek,¹ Ellen Kater-Baats,¹ Marc Pauper,¹ Guillaume van der Zande,¹ Dominique Smeets,¹ Daniel Olde Weghuis,¹ Marian J.P.L. Stevens-Kroef,¹ and Alexander Hoischen^{1,3,5,*}

Clinical validation:

Prospective study

Prospective (clinical utility) study

- n=50 AML samples
- 100% concordance for VAF > 5%



‘Next generation cytogenetics’: ‘optical genome mapping’ verbetert detectie van cytogenetische afwijkingen bij hematologische maligniteiten

Next generation cytogenetics: optical genome mapping improves detection of cytogenetic abnormalities in hematological malignancies

dr. M. Stevens-Kroef^{1,6}, drs. D. Olde Weghuis^{1,2,6}, dr. A. Hoischen^{3,6,7,8}, prof. dr. L.E.L.M. Vissers^{4,6,7}, dr. K. Neveling^{5,6,7}

Clinical validation

Abnormalities detected with SOC and OGM

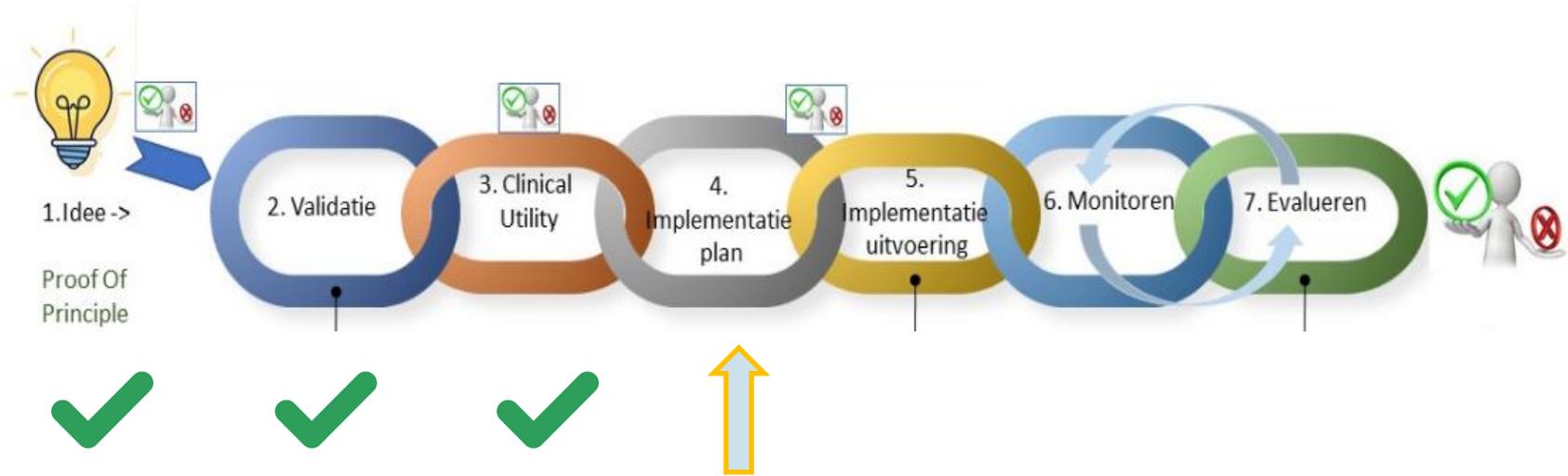
Patient ID	ELN2 Q22 en WHO2 Q22 t(15;17)(q24;q21) PML::RARA	t(8;21)(q22;q22) RUNX1::RARA	inv(16)(p13;q22) RUNX1::RUNX1T1	CBFB::MYH11 t(16;16)	GATA2, MECOM(EV1) t(3;3) MECOM::v	NUP98-rearranged	-5del(5q)	-7del(7q)	-11del(17p)	Complex X (23)	Andere frequente afwijkingen bij AML	deletion NF1	ETV6-rearranged or del(12p)	RUNX1-rearranged or del(21q)	KMT2A-PTD	del(20q)	+8	-Y	Andere afwijking	
6																				
8																				
12																				
14																				
16																				
18																				
19																				
20																				
22																				
23																				
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32																				
33																				
40																				
41																				
42																				
56																				
60																				
63																				
65																				
66																				

SOC en OGM concordant
 SOC afwijking niet aangetoond; OGM afwijking wel aangetoond
 SOC afwijking onduidelijk; OGM afwijking opghelderend

Other items relevant for diagnostics

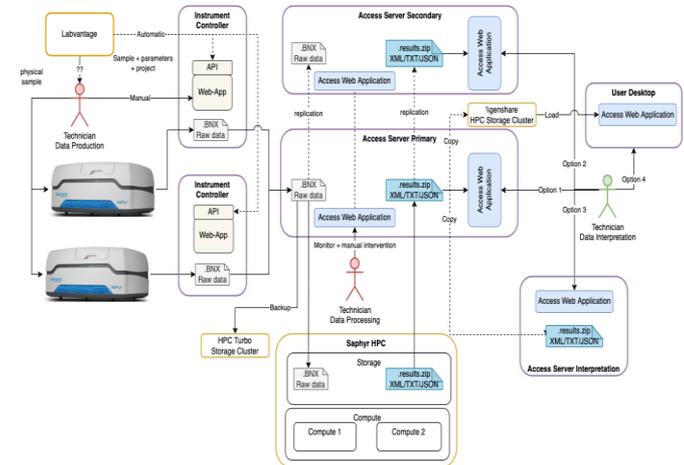
	SOC	OGM
Turnaround time	4-12 days	7-12 days
Current capacity	not applicable	12 pts a week run starts at Tuesday and Thursday
Success rate	75% (karyotyping)	90%
Diagnostic yield (clinical validation study)	38%	44%
Number of test / patient (clinical validation study)	2.4	1

Implementation in diagnostics



Items required for implementation OGM

- Laboratory redesign for equipment
- Data storage and server capacity
- Training employees
- Embedding in quality system (risk analyses, work instructions, application form, etc.)
- Informing and discussing with hematologists



items implemented in Radboud UMC for OGM

- Central sample reception for all hematological samples
- Process workflow in collaboration with Maastricht
- Laboratory process automation



Automation on LongStringVantage (StarV)

- DNA isolation and labeling
- 4-12 samples/run (24 samples/day)

Isolation	Run time
Sample 1-4	1.5h
Sample 5-8	2.5h
Sample 9-12	3.5h

Labeling	Run time
up to 12 samples	3.5h

- good QC for BM and heparine blood (and cell pellets)



Fully automated workflow

	Week 1					Week 2				
	mo	tue	we	thu	fri	mo	tue	we	thu	fri
HMW isolation										
Labeling / chip										
Data analysis										

Run 1

Run 2

The Saphyr and Stratys



2 Saphyr Systems (2024-2026)

Capacity per Saphyr: **6 samples***

Chips run with **3 samples**

Data collection: **24-65 hrs (3 samples)**

In diagnostics since: **1-10-2024**

Access 1.7.2 RVP



2 Stratys Systems (Q2 2026)

Capacity per Stratys: **12 samples**

Chips run **individually**

Data collection: **2-10 hrs (2 samples)**

In diagnostics: starting in **2026**

Access 1.8.3 GA-LAF (and RVP)

***12 samples per week**

OGM in diagnostics

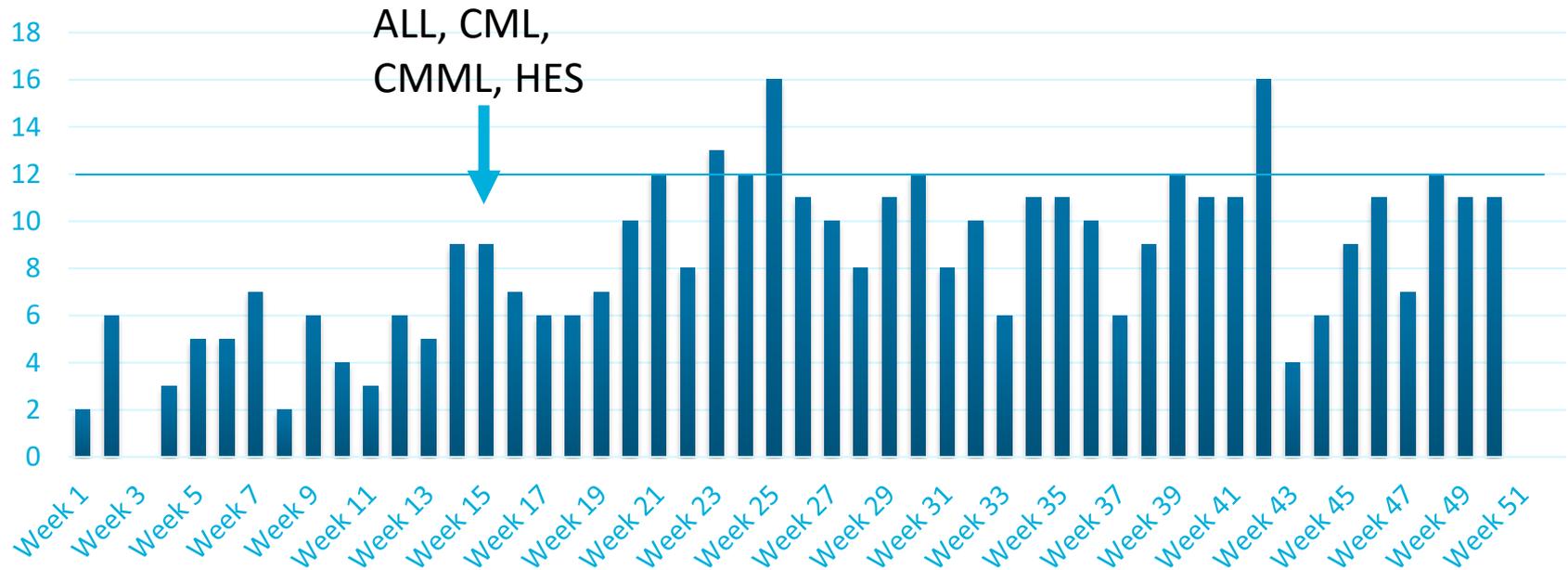
AML: 1 october 2024

MUMC Maastricht: 1 januari 2025

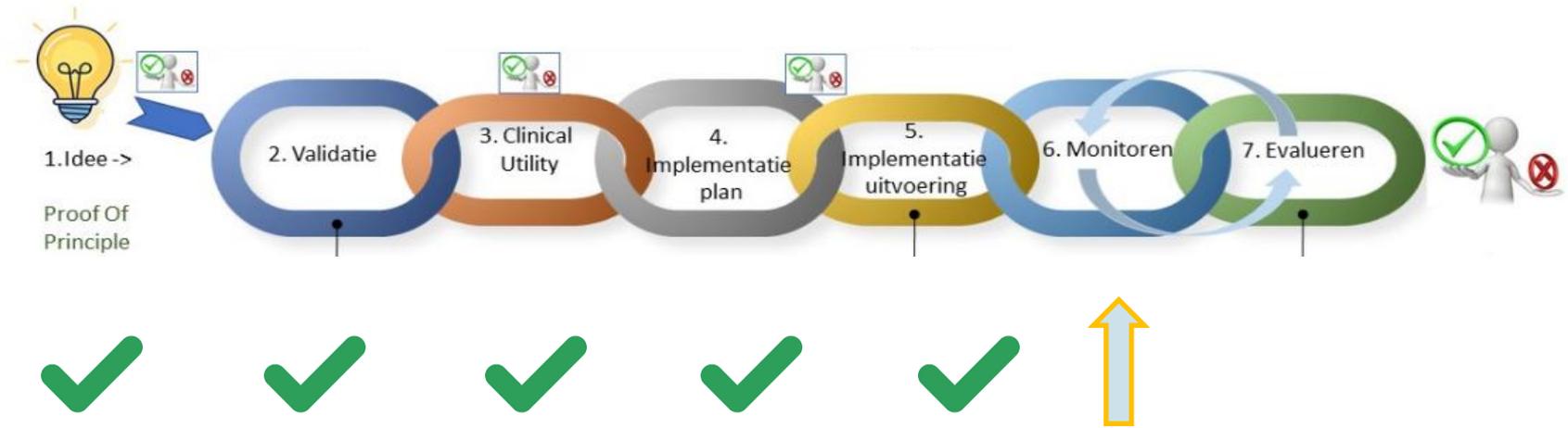
ALL, CML, CMML, HES: 1 april 2025

Other hematological malignancies: 2026

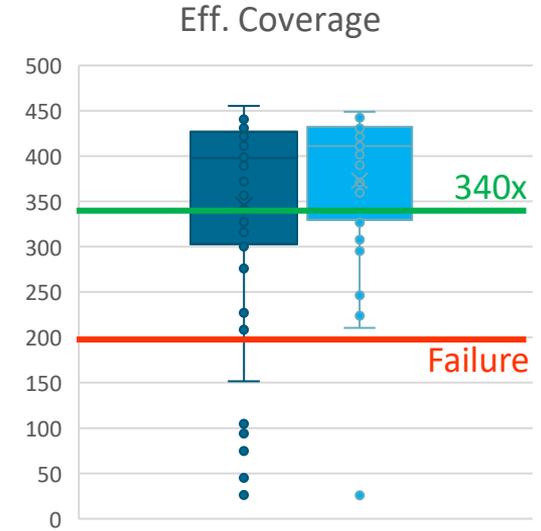
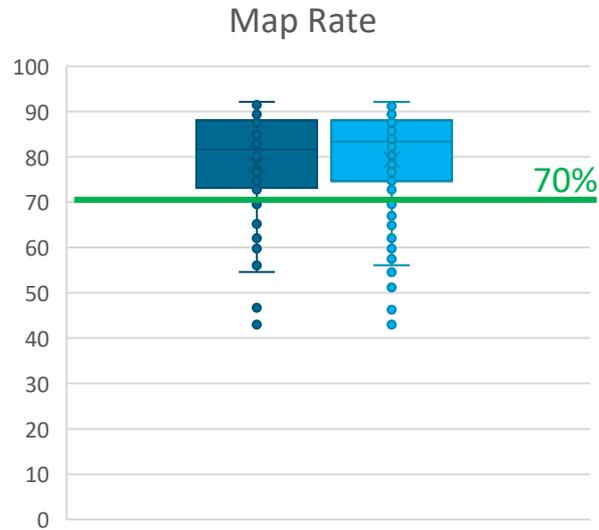
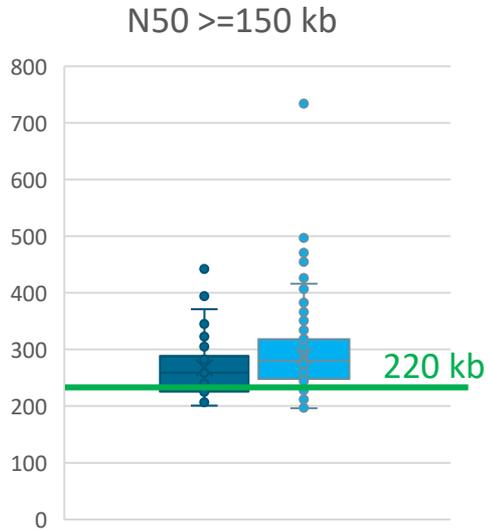
Number of samples for OGM (2025)



Monitor Phase



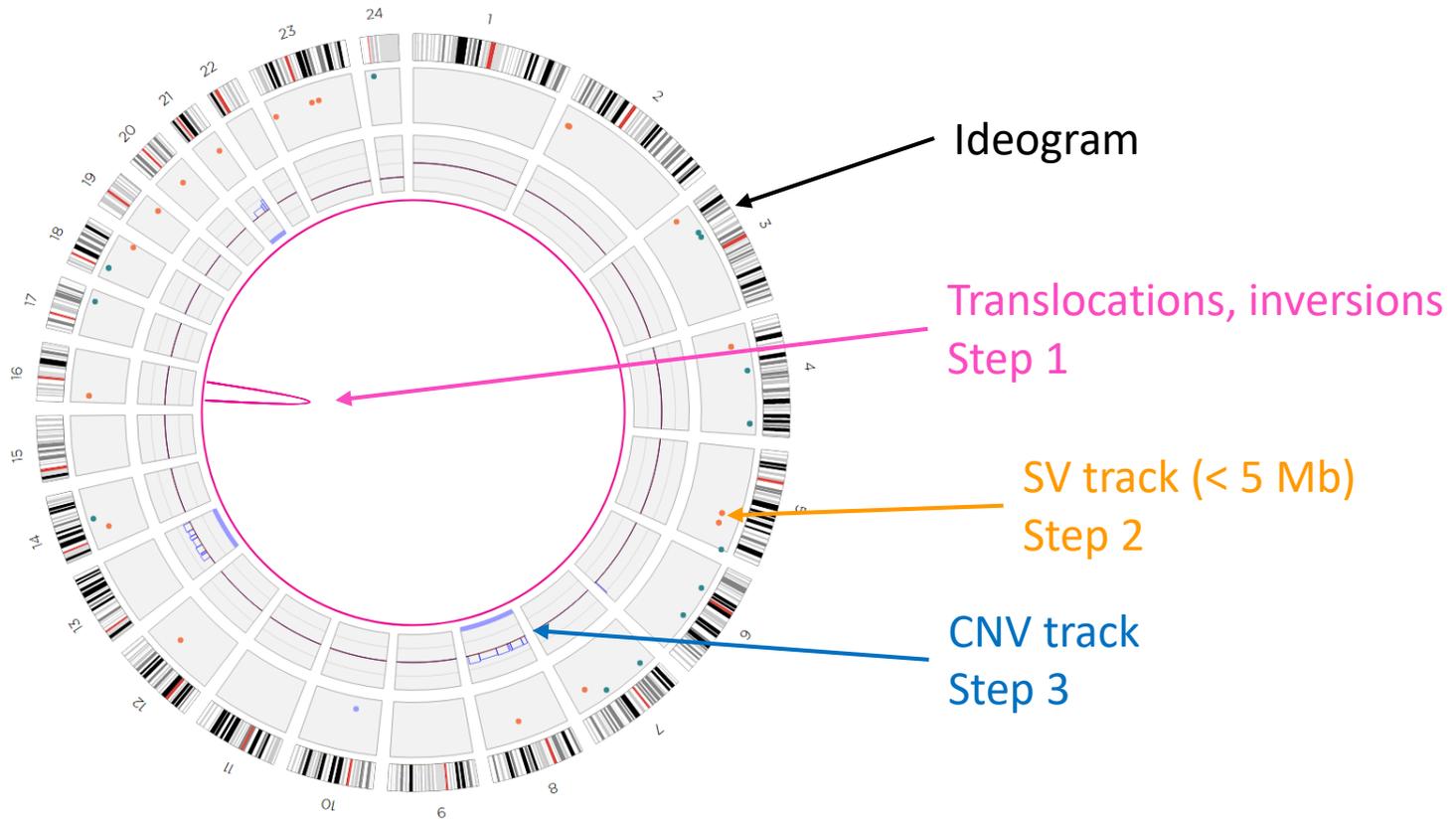
QC values



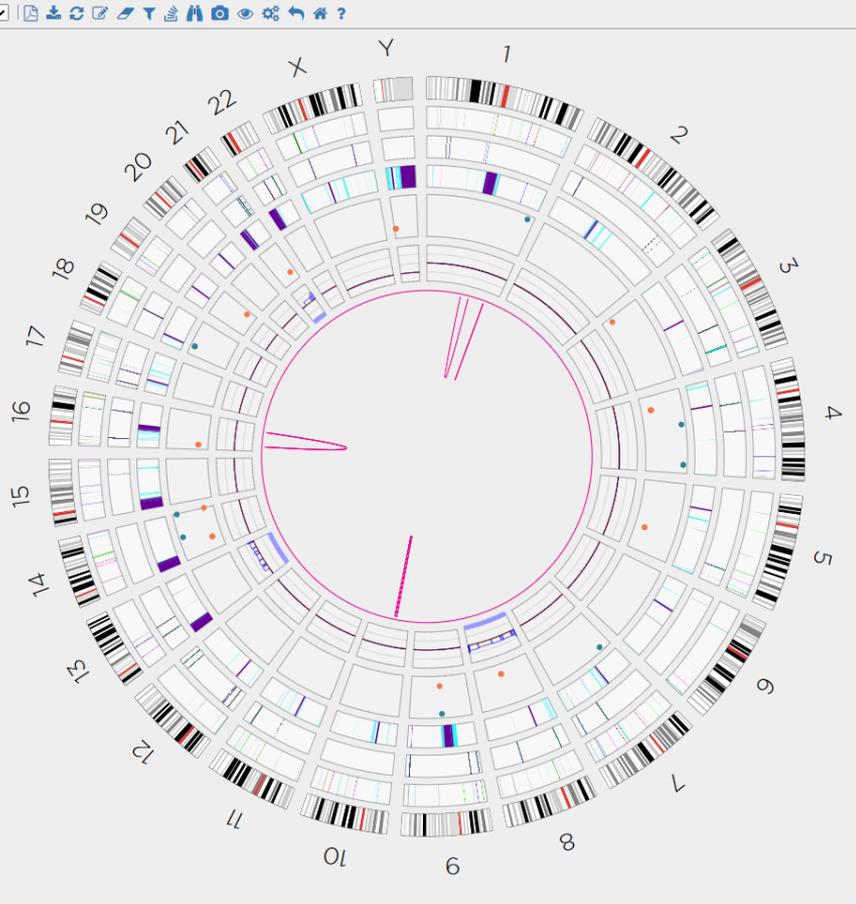
Results OGM (Radboudumc)

	2024	2025
Number of patients	49	239
Succesfull OGM result	43 (88%)	222 (93%)
Cases with cytogenetic abnormality	21 (49%)	99 (45%)
Cases with abn. only visible by OGM	6 (14%)	24 (11%)
turnaround time: average and range (days)	11.4 (8 – 17)	11.5 (6 – 17)
Number of cases with suboptimal QC (> 10%)	14 (33%)	42 (19%)

Analysis of OGM result: the Circos plot

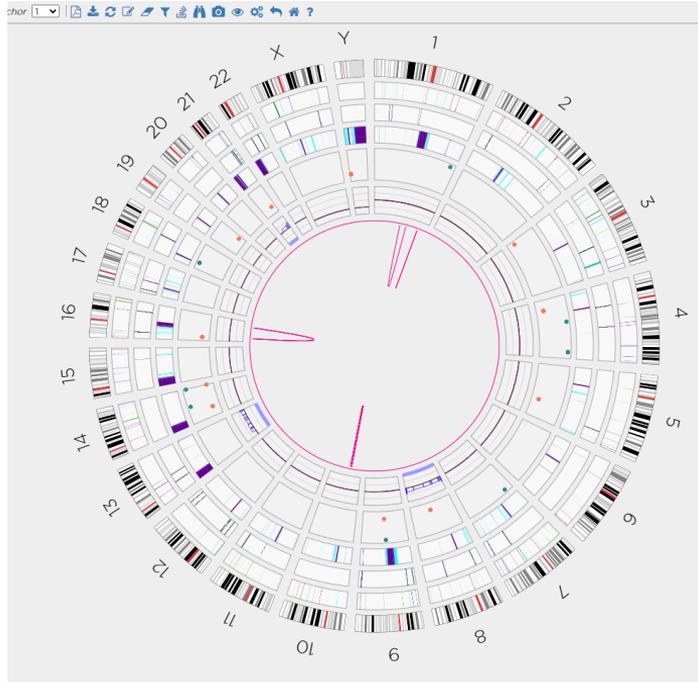


Patient 1: Analysis in 3 steps

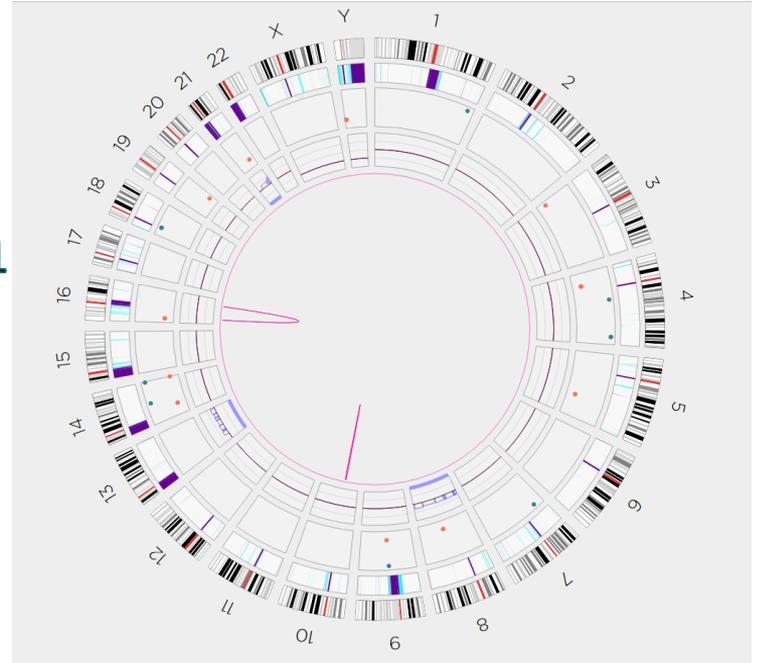


1. Analysis of intra- and inter-translocations (pink lines in circos plot)
2. Analysis of insertions, deletions, inversions, duplications (dots in circos plot) -> Reported only in case of overlap with myeloid gene
3. Analysis of aneuploidy (focussed on whole chromosome and/or aneuploidy extending to the telomeres)

Patient 1: false positive SV

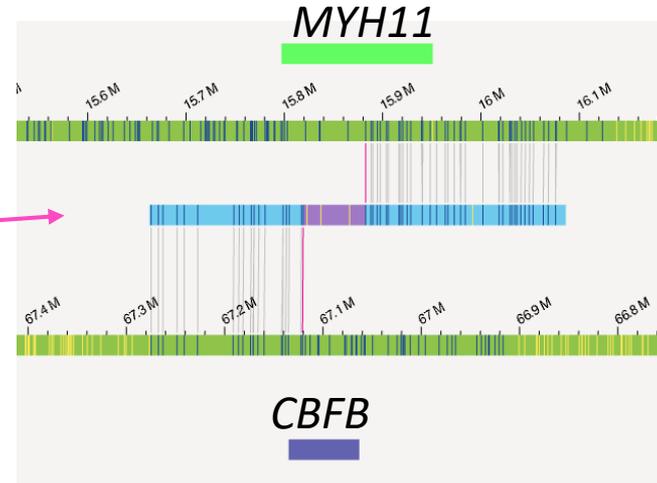
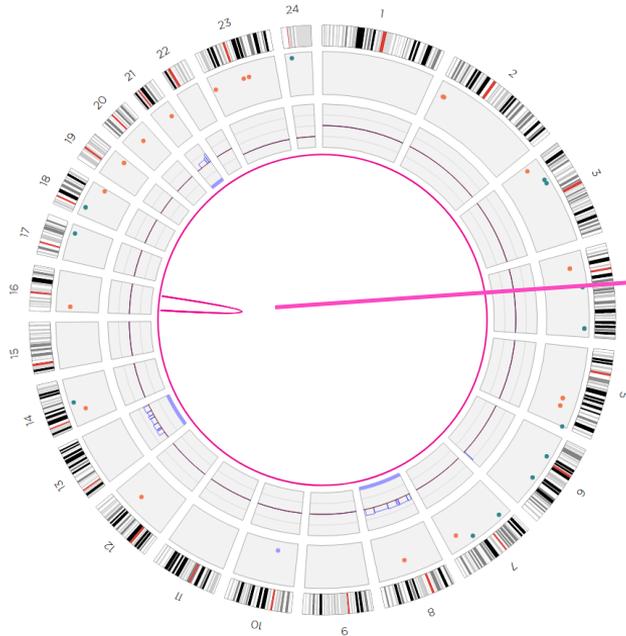


Filtering met rare variant Hg19DLE1 SV Mask



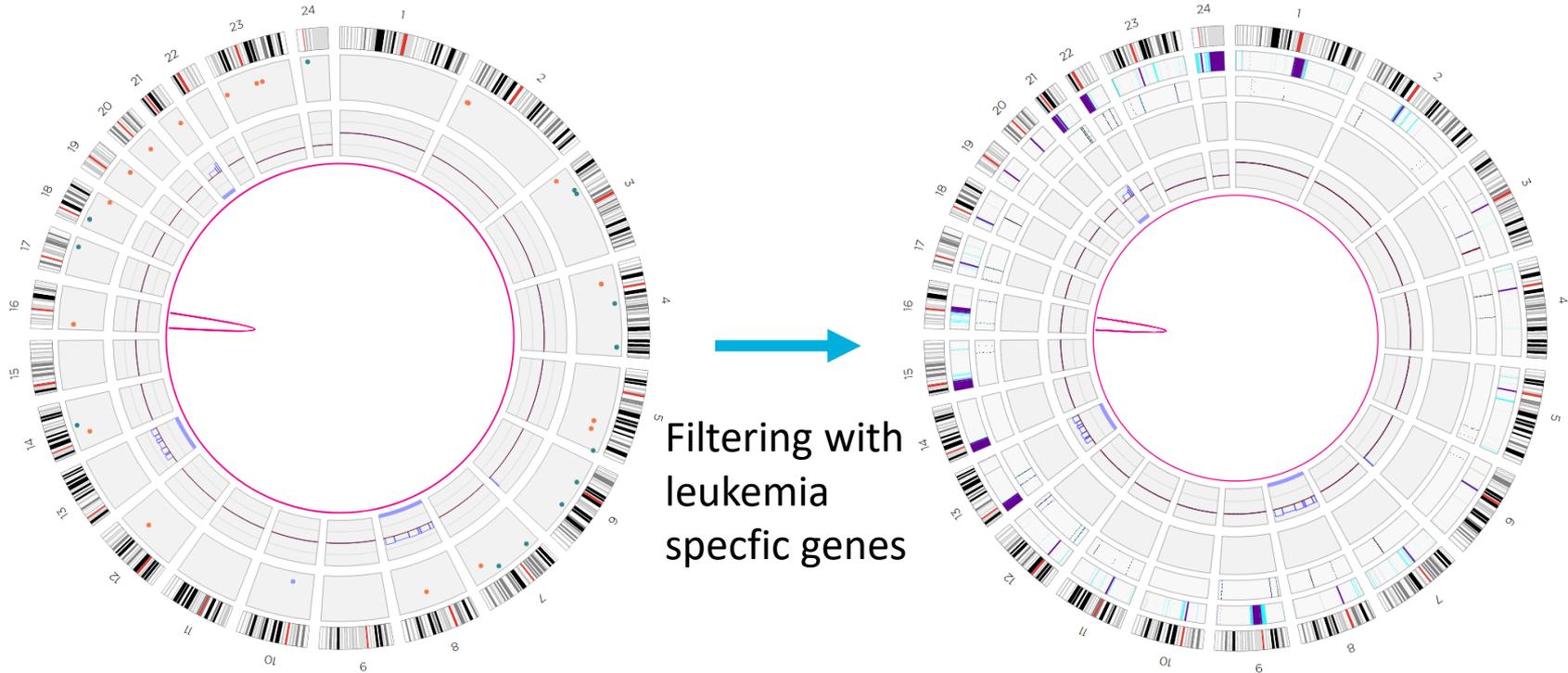
AML patient 1: Detail analysis with Genome Browser

Step 1: analysis of SV > 5 Mb (translocations, inversions, interstitial deletions)



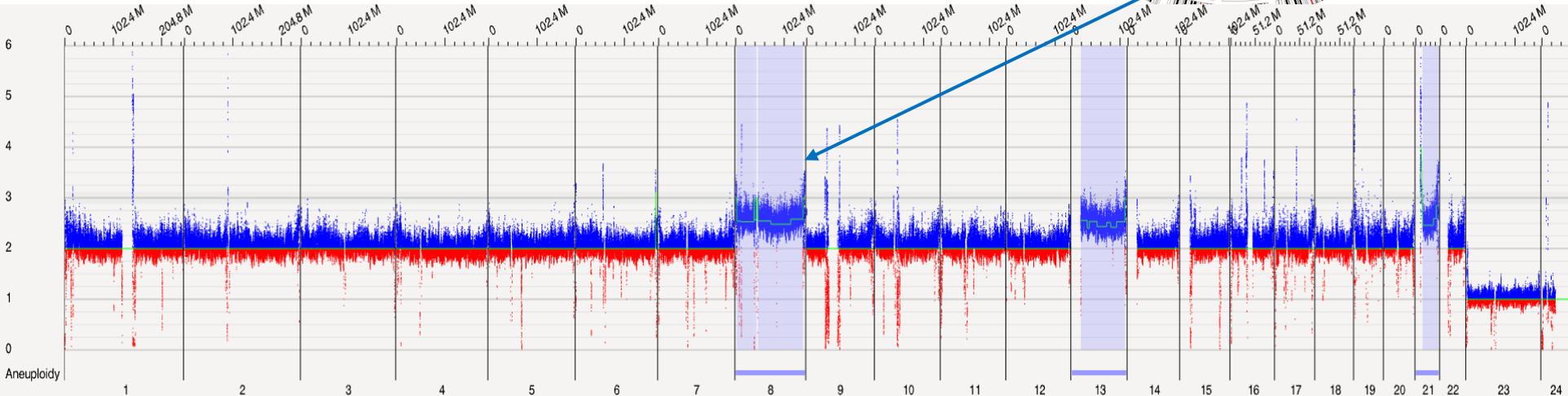
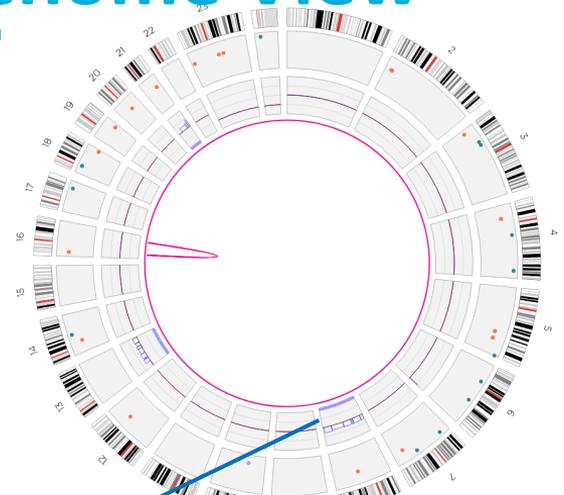
AML patient 1: Filtering for leukemia specific/cancer genes

Step 2: analysis of SV < 5 Mb (e.g. *KMT2A-PTD*, *TP53* loss)

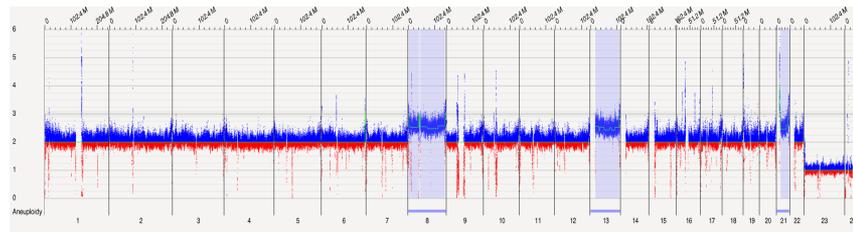
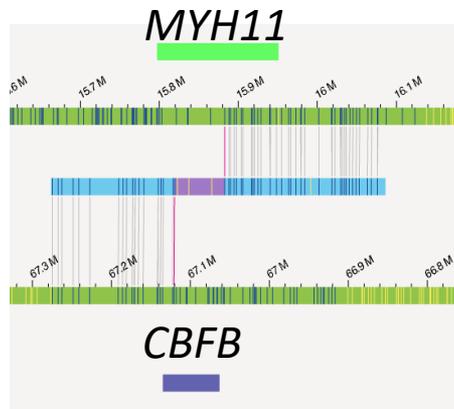
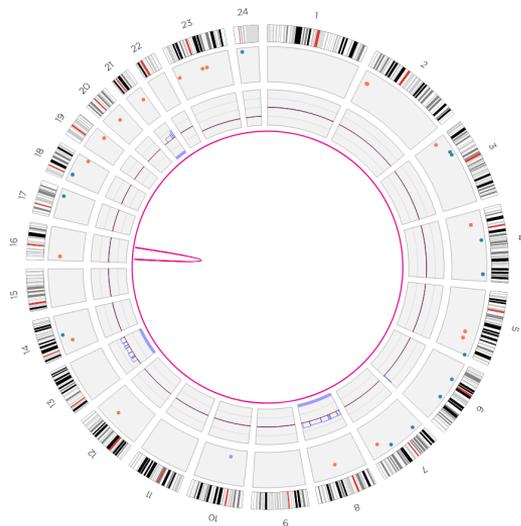


AML patient 1: Analysis with Genome View

Step 3: Analysis for whole chromosome (-arm) loss/gain
e.g. monosomy and trisomy



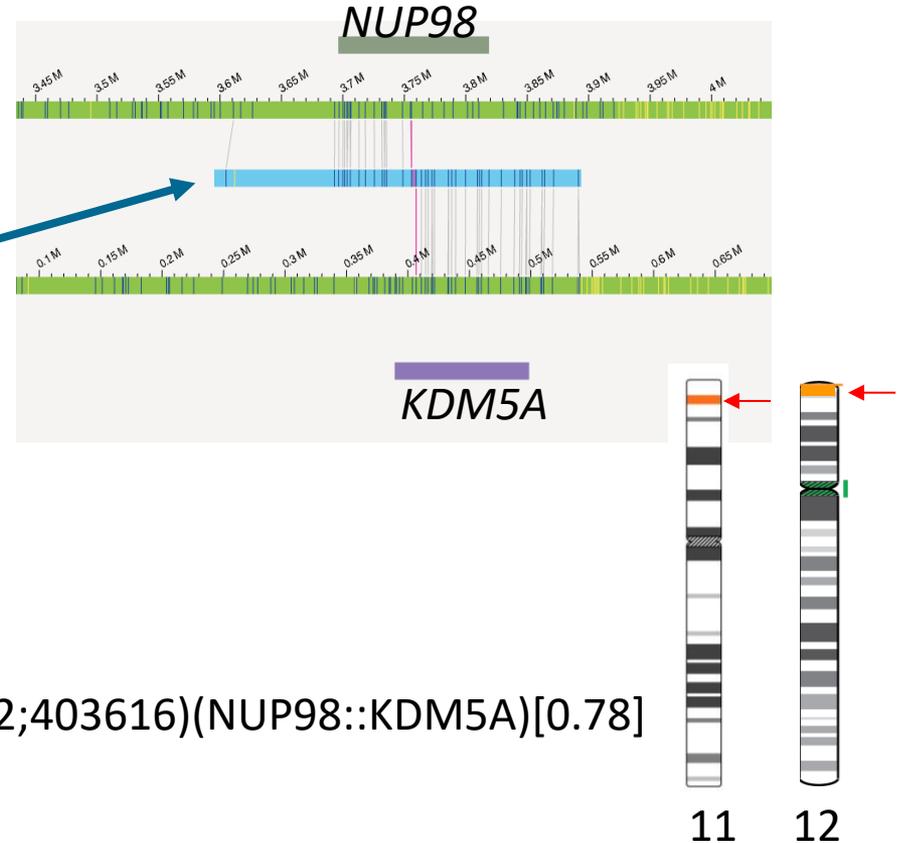
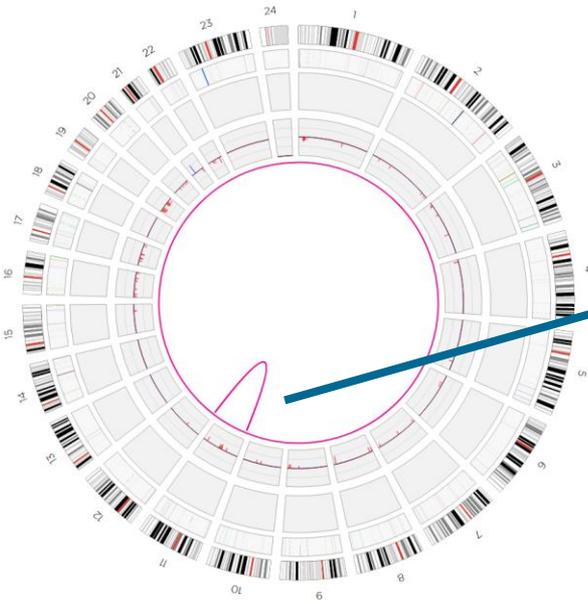
AML patient 1: result OGM



Reported result according to ISCN

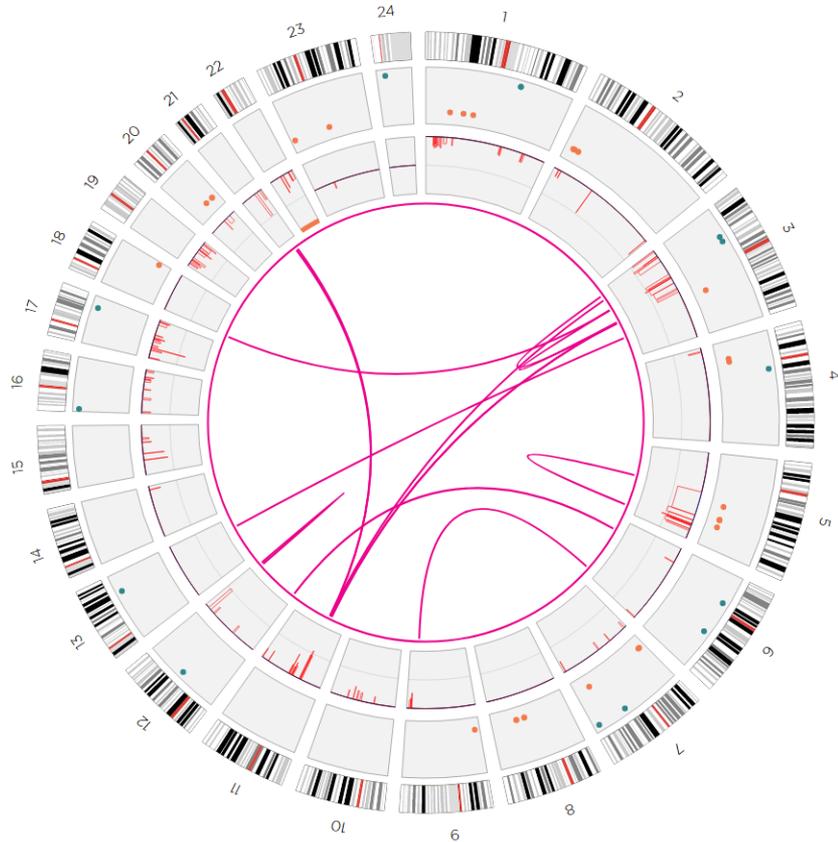
ogm[GRCh37] (8,13)x3[0.5],inv(16)(p13.11q22.1)(15803116_67118000)(CBFB::MYH11)[0.68], (21)x3[0.5]

Example 2: AML patient with 46,XX[20]

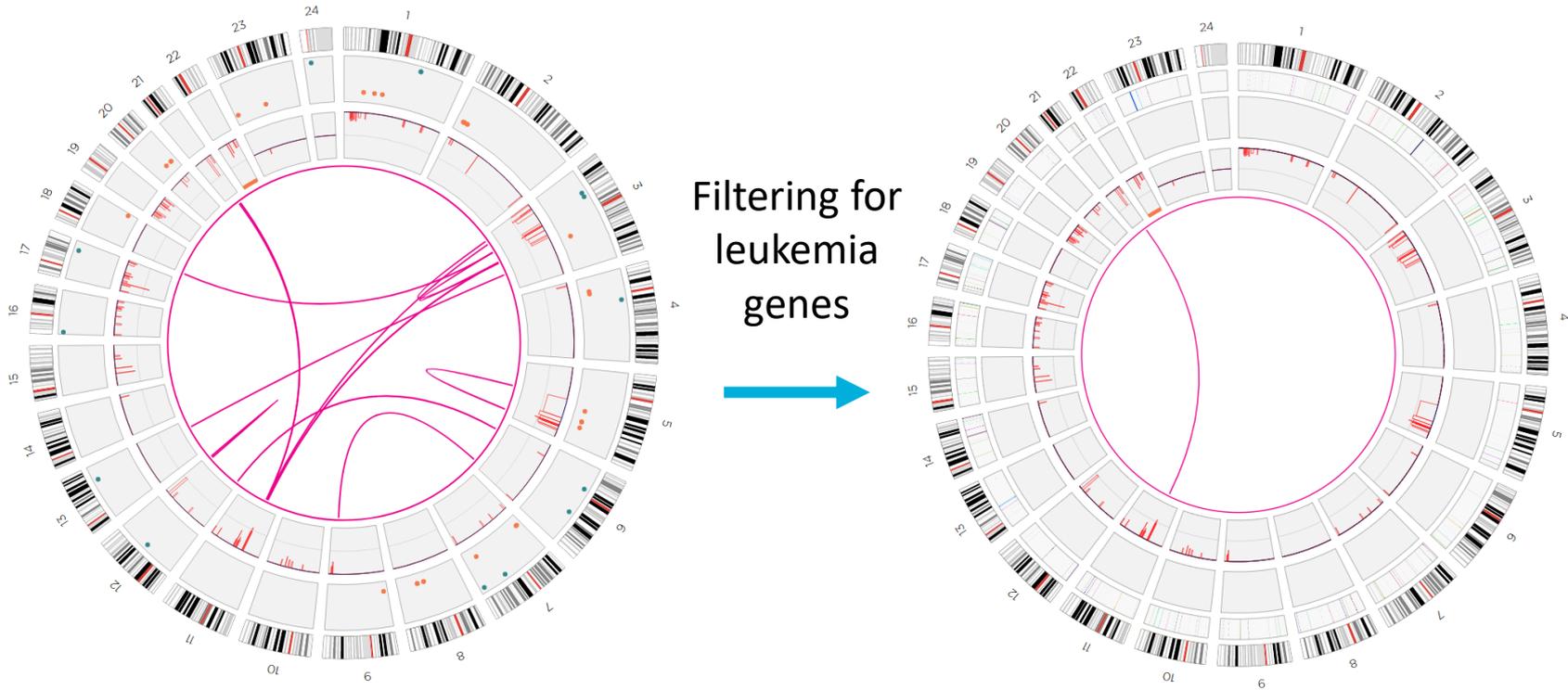


ogm[GRCh37] t(11;12)(p15.4;p13.33)(3755942;403616)(NUP98::KDM5A)[0.78]

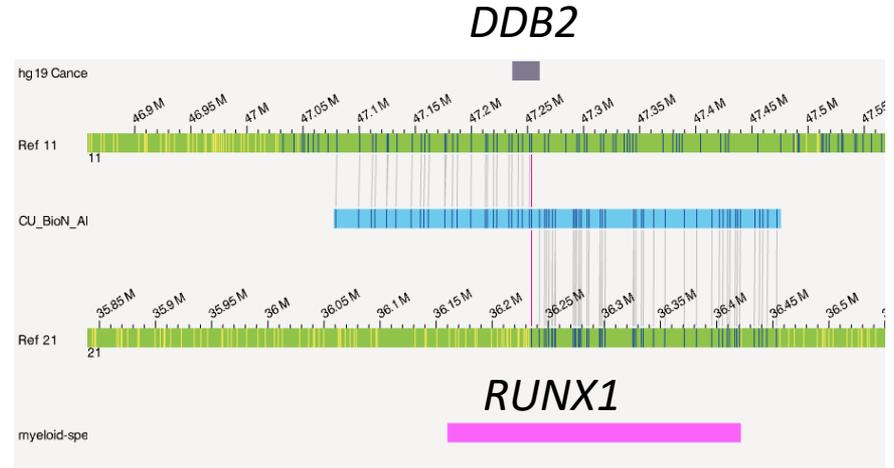
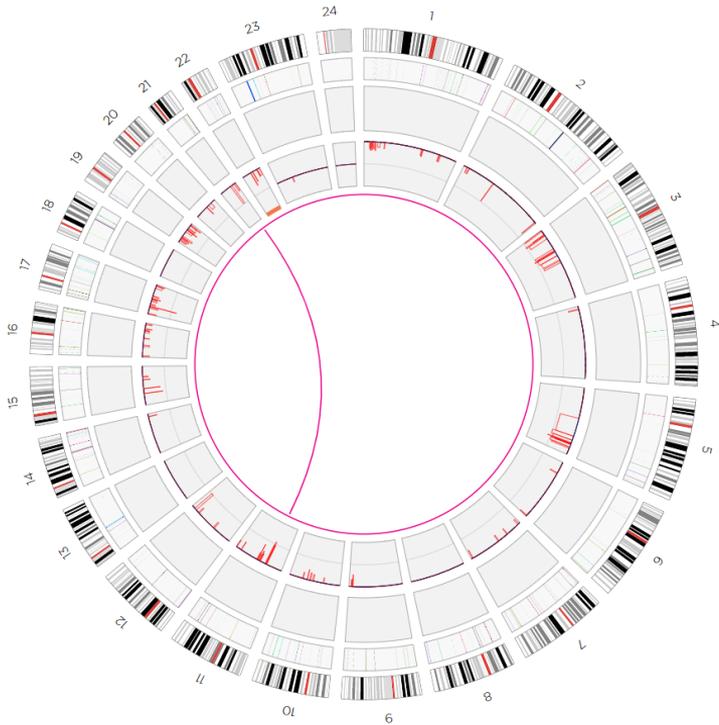
Example 3: AML patient with complex karyotype



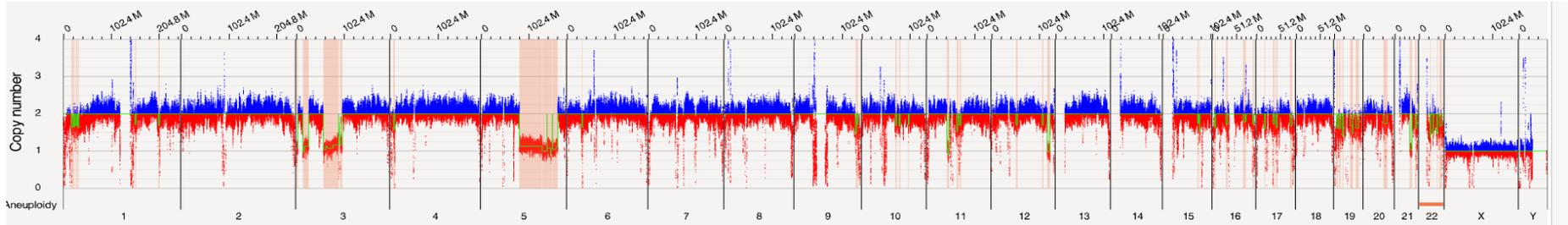
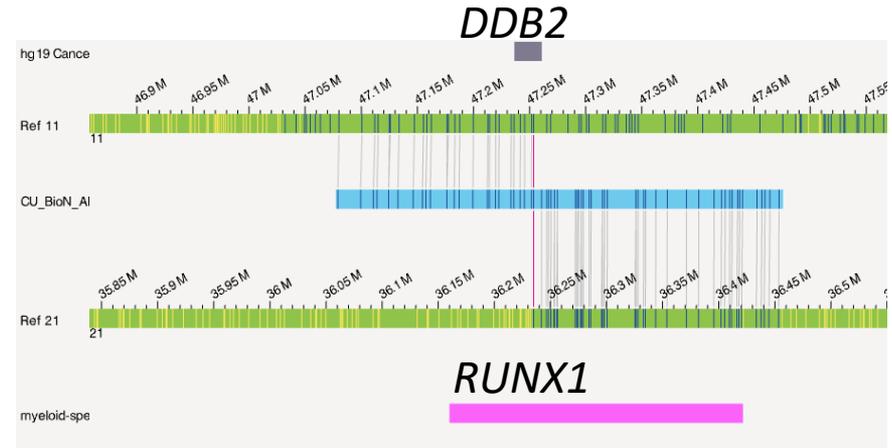
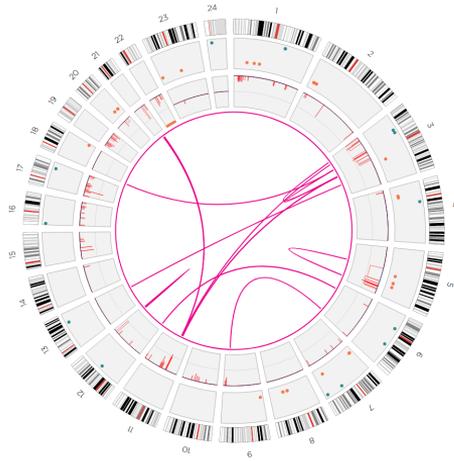
Example 3: AML patient with complex karyotype



Example 3: AML patient with complex karyotype

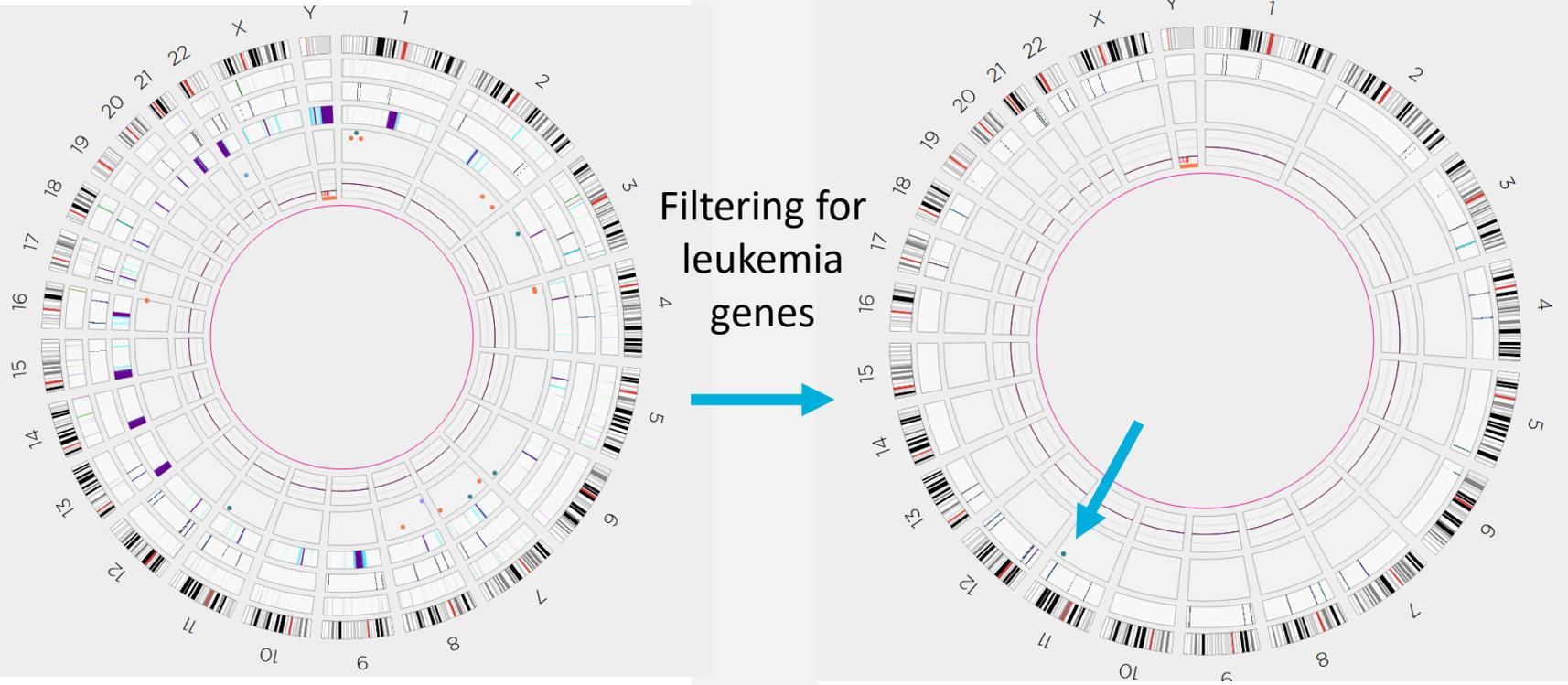


Example 3: AML patient with complex karyotype

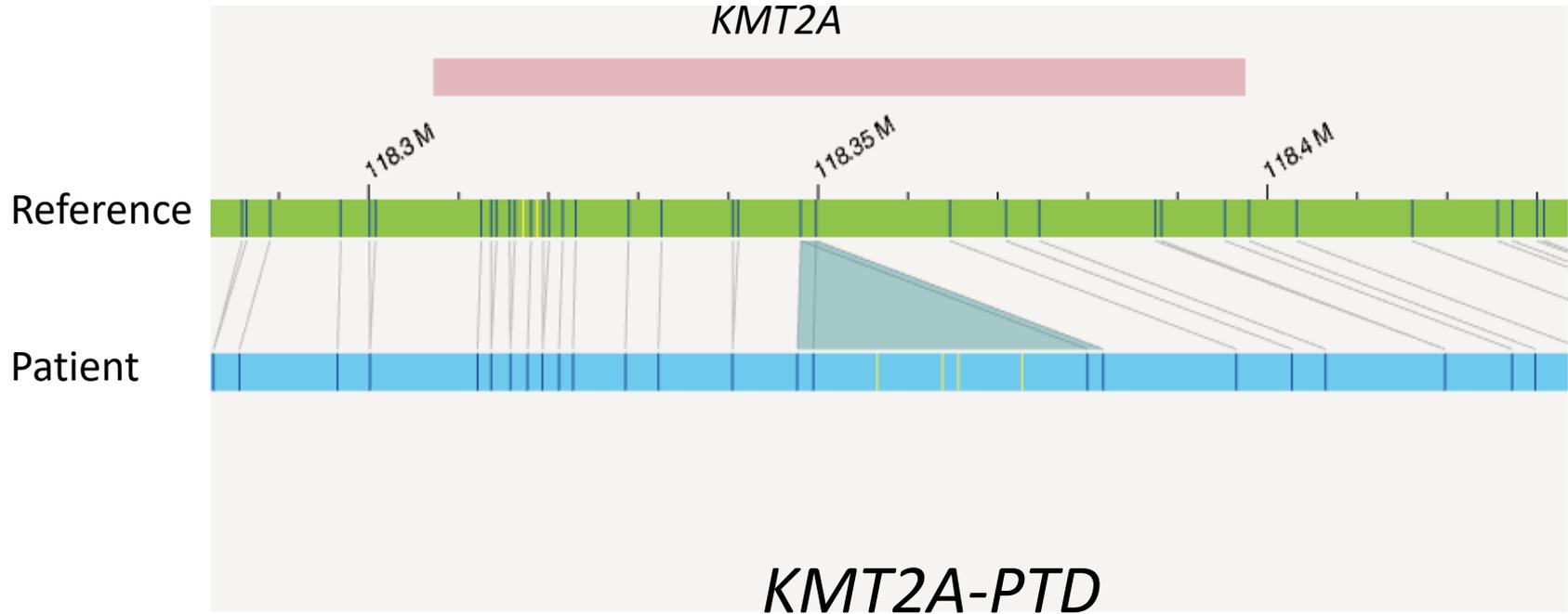


ogm[GRCh37] (3,6,9,11-13,18)cx,
del(5)(q14.2q34)(81632498_164107211)[0.9],
t(11;21)(p11.2;q22)(47253596;36235050)(DDB2::RUNX1)[0.8]

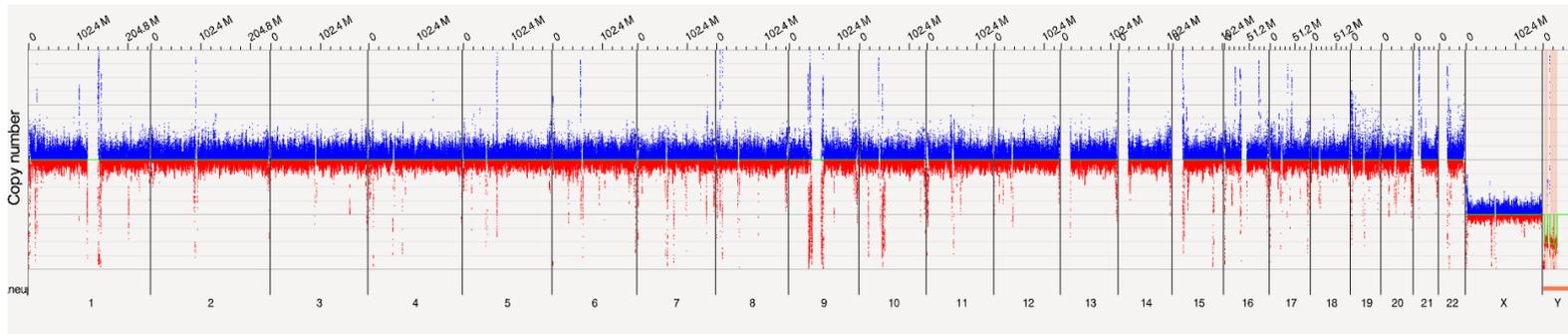
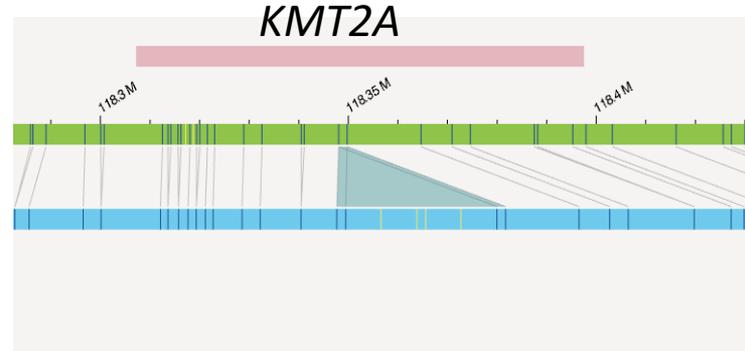
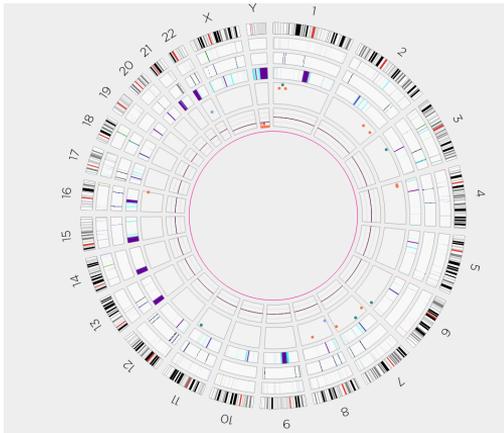
Example 4: AML patient with 45,X,-Y[8]/46,XY[12]



Example 4: AML patient with 45,X,-Y[8]/46,XY[12]



Example 4: AML patient with 45,X,-Y[8]/46,XY[12]



ogm[GRCh37] (Y)x0[0.5],dup(11)(q23.3q23.3)(118341120_118349783)[0.85]

Not detected by OGM

Not detected:

- Balanced whole arm translocation

Available in future:

- CNLOH (17p)
- Discrimination between hypo- and hyperdiploidy

THANKS to OGM Team

Technical labproces



Patient and data registration



Expertise OGM



Projectleaders



Data Interpretation and reporting



Software configuration



ICT



Data Interpretation





13th International workshop on Cancer Genetic & Cytogenetic Diagnostics

March 18 – 20, 2026

Nijmegen

