Erasmus MC
Universitair Medisch Centrum Rotterdam

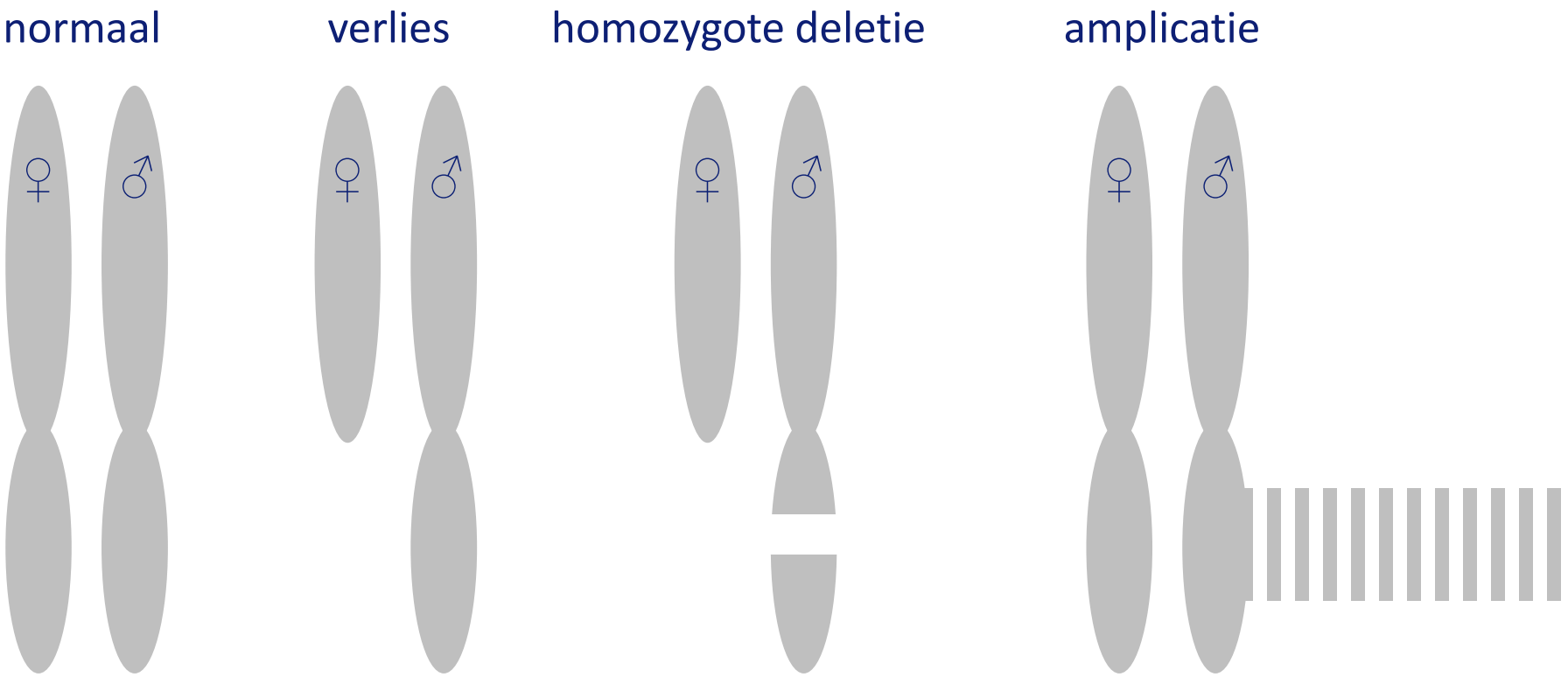
Kanker Instituut

CNV detectie mbv NGS

Ina Geurts-Giele, KMBPio
afdeling Pathologie
Erasmus MC, Rotterdam

Deelnemersbijeenkomst SKML sectie Pathologie
26-05-2016

Typen grote chromosomale afwijkingen



Methodes van diagnostische detectie van CNV

- FISH – fluorescentie in situ hybridisatie
- MLPA – multiplex ligation-dependent probe amplification
- Microsatelliet analyse

- Nieuw (binnen diagnostiek setting): SNP analyse

Single nucleotide polymorphisms (SNPs)

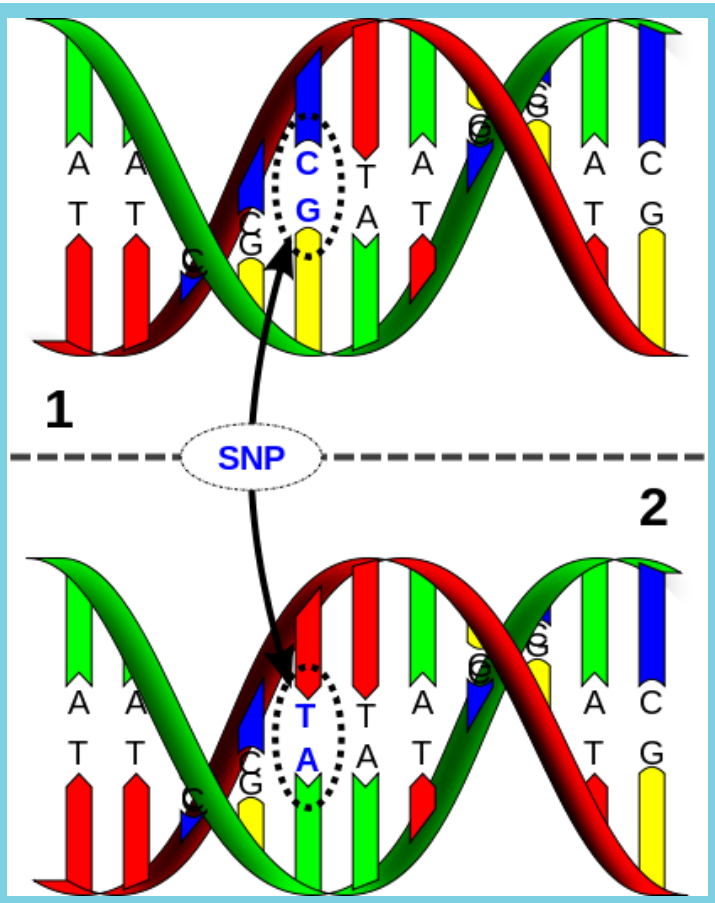
Natuurlijk voorkomende variaties die betrekking hebben op één basenpaar

Allel 1

AAGC**C**TAGCAC
TTCG**G**ATCGTG

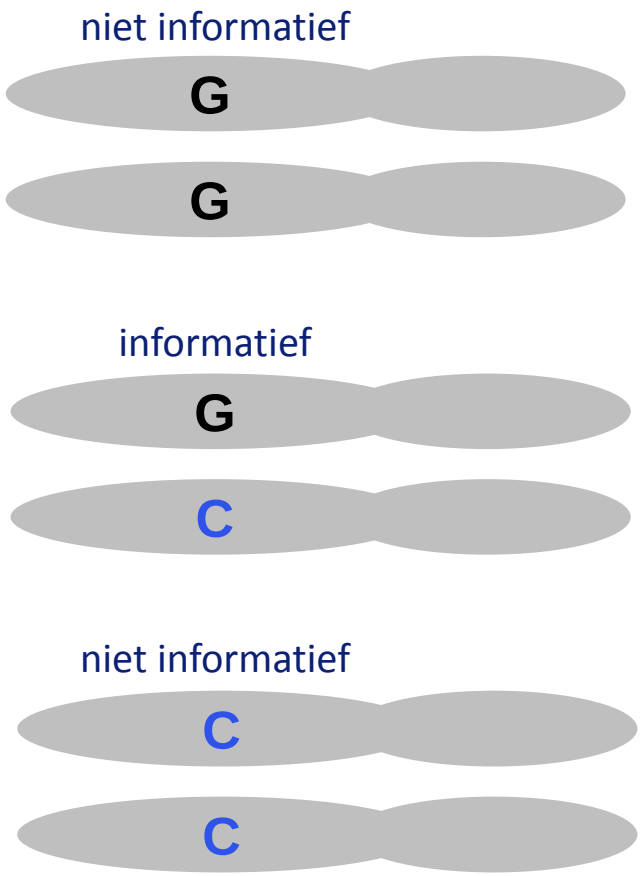
Allel 2

AAGC**T**TAGCAC
TTCG**A**ATCGTG



CNV analyse mbv SNPs

- Selectie hoog polymorfe SNPs in regio van interesse (bv chromosoom 1p en 19q)
- Sequencen SNPs mbv NGS analyse
- Berekenen van percentage variante allel (B-allel of minor allel frequentie)



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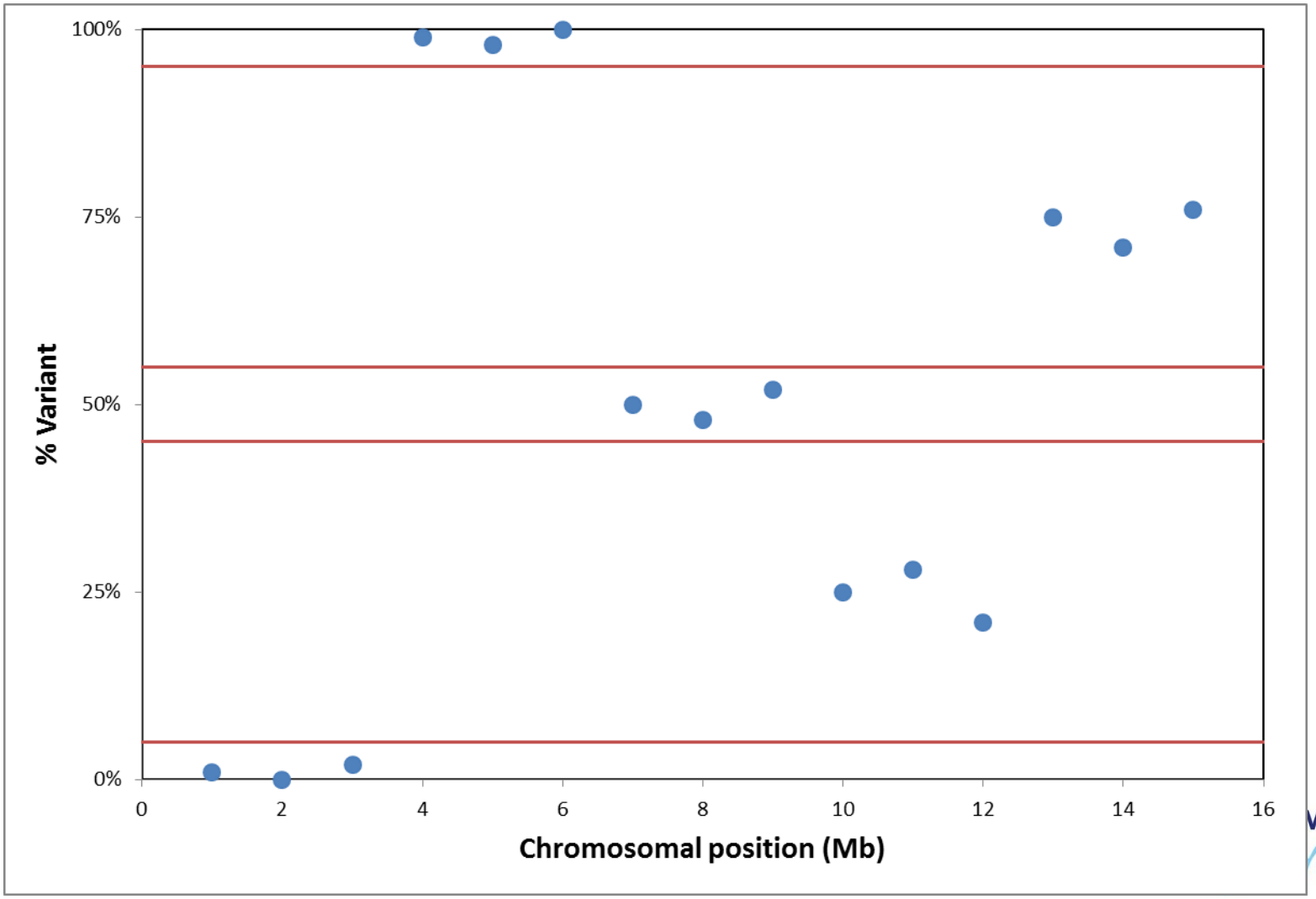
CNV analyse mbv SNPs



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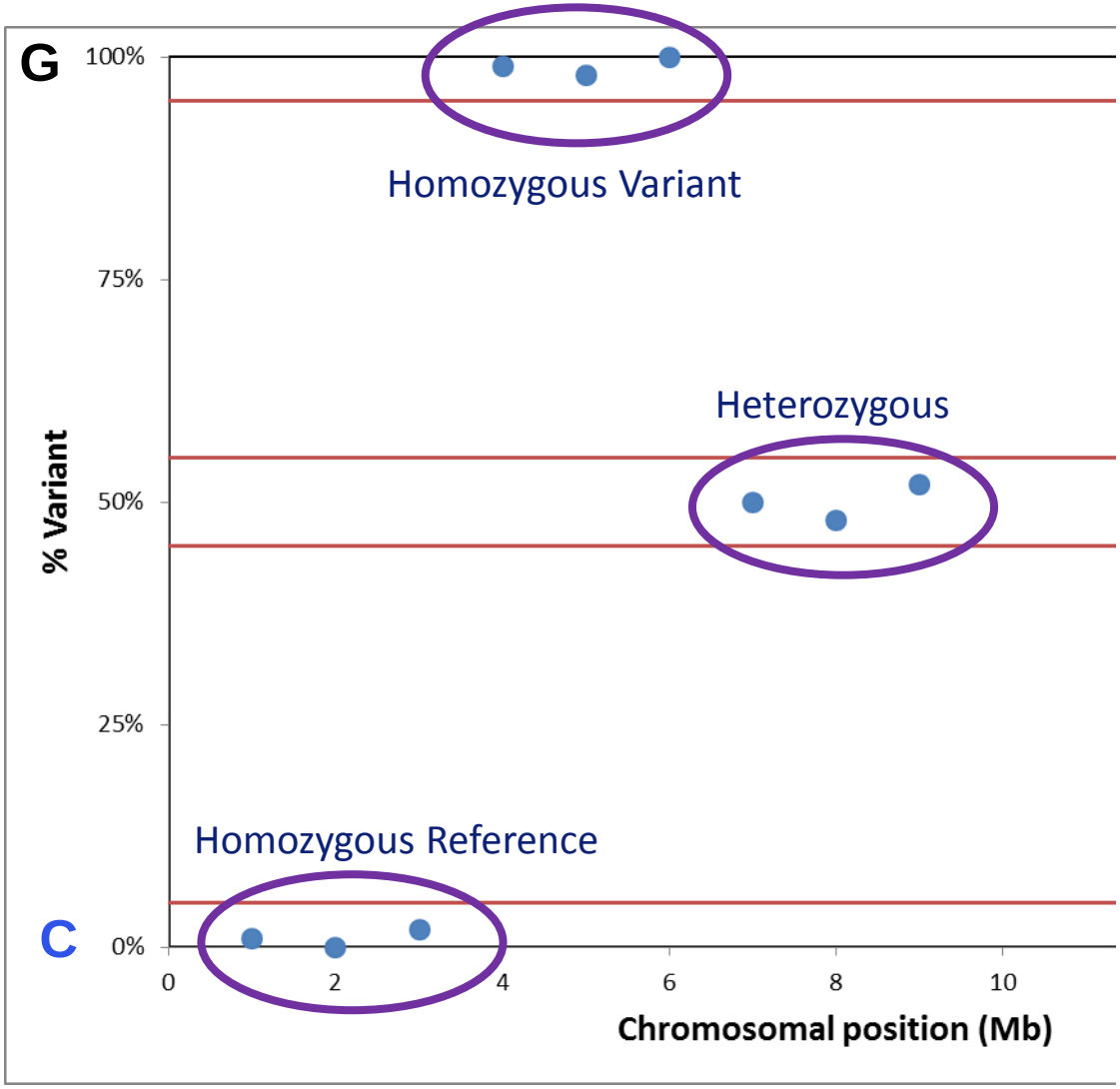
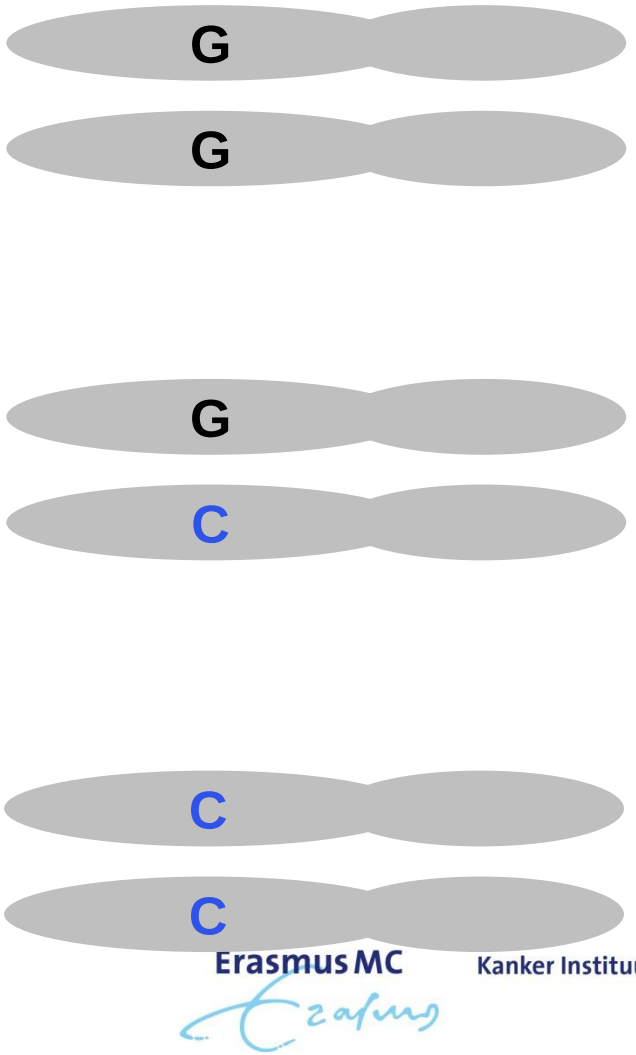
CNV analyse mbv SNPs





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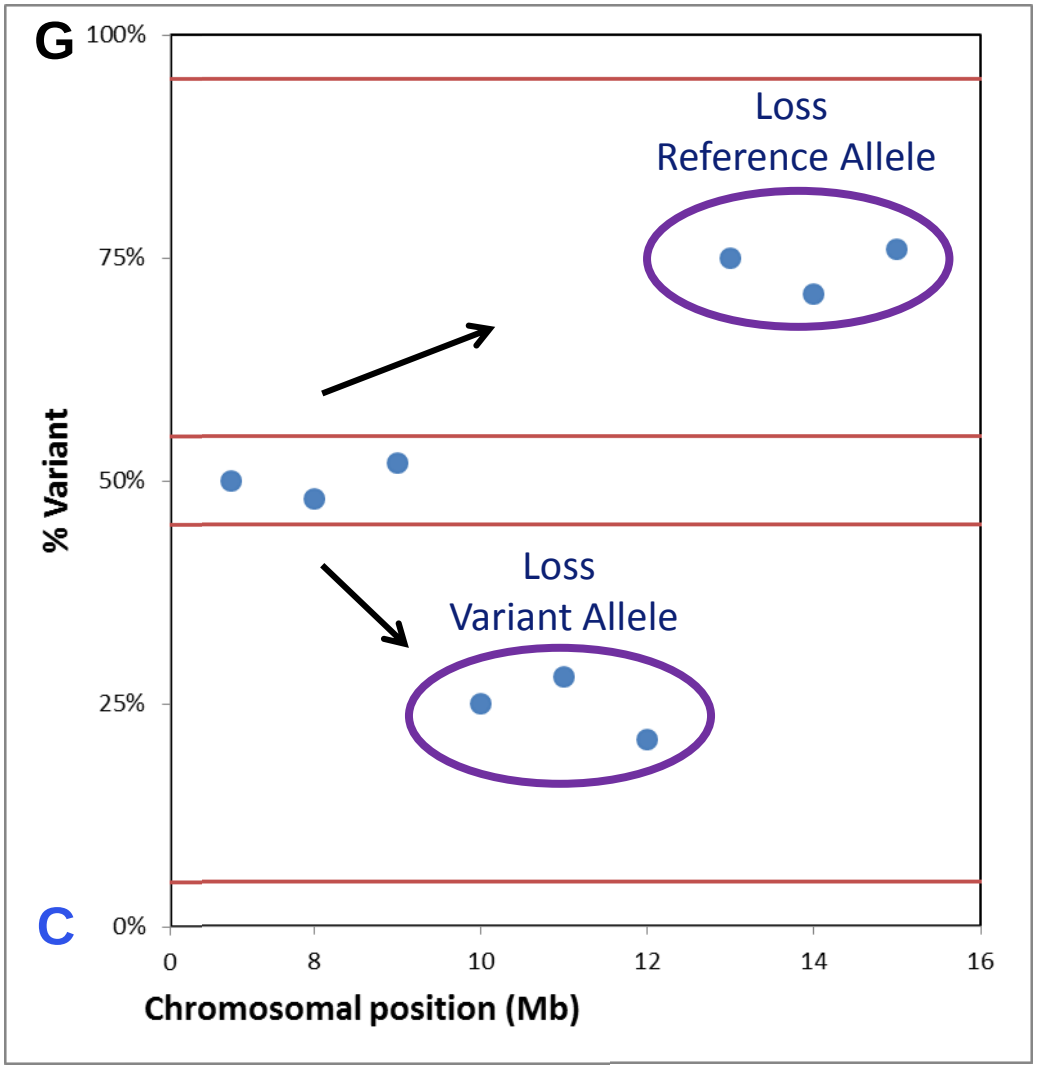
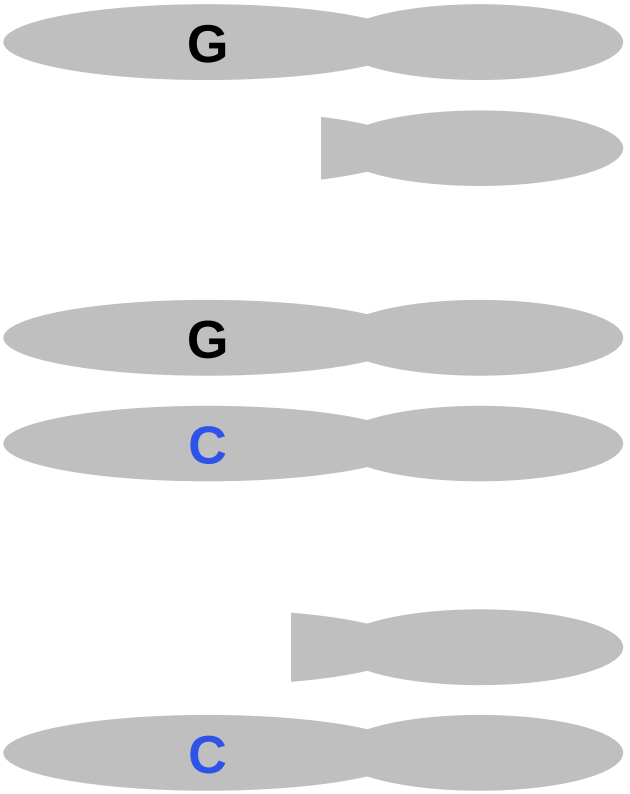
CNV analyse mbv SNPs





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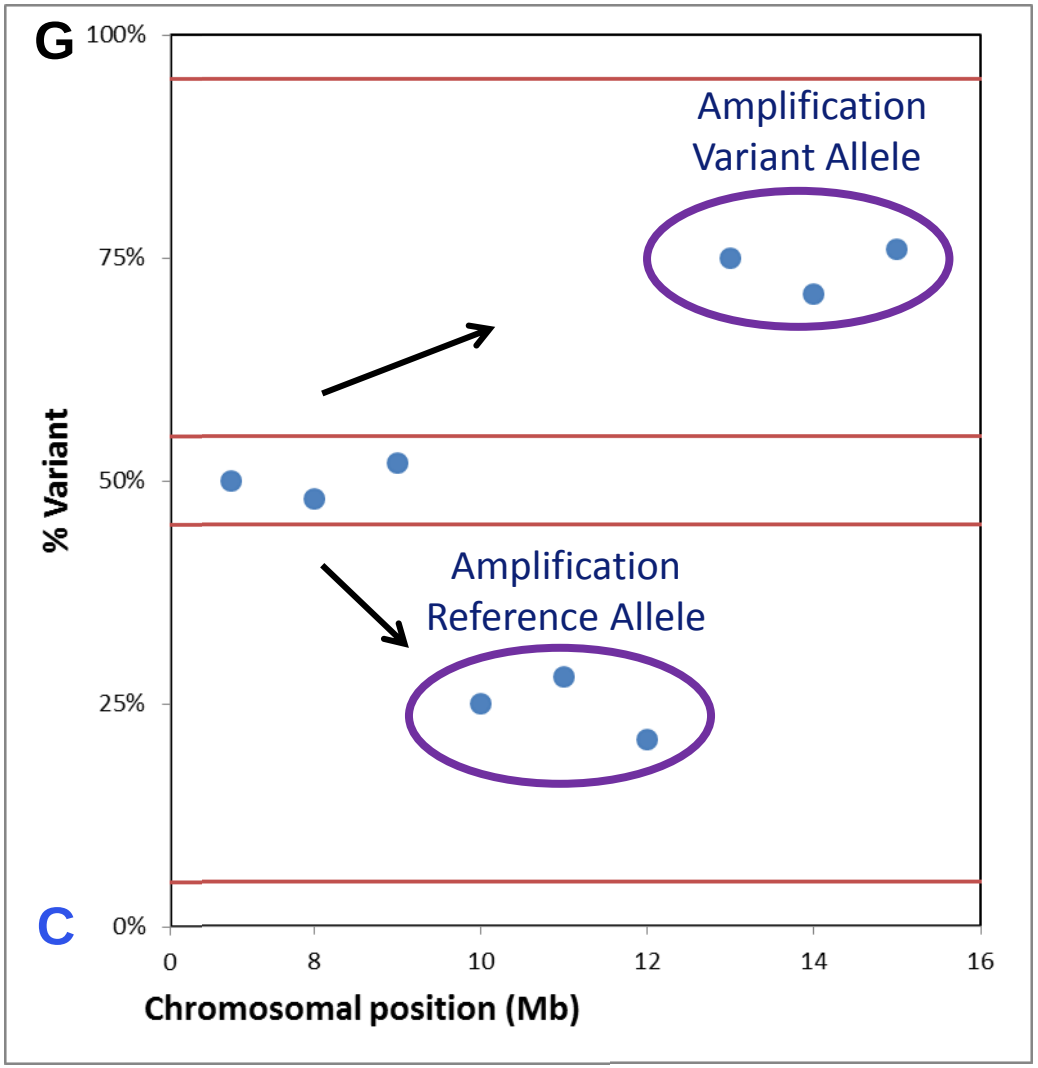
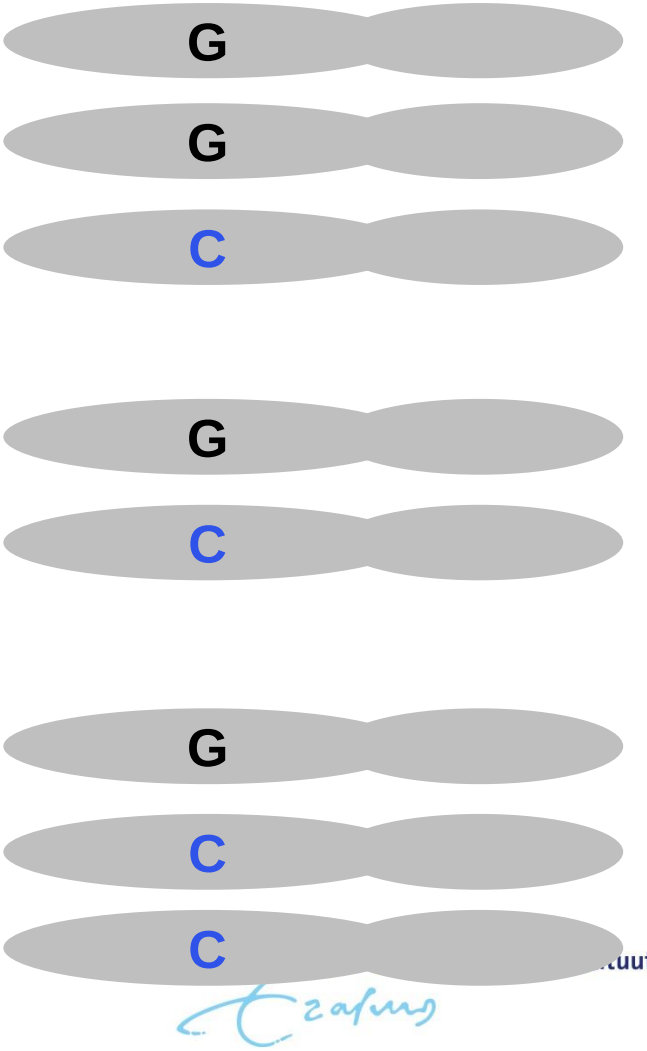
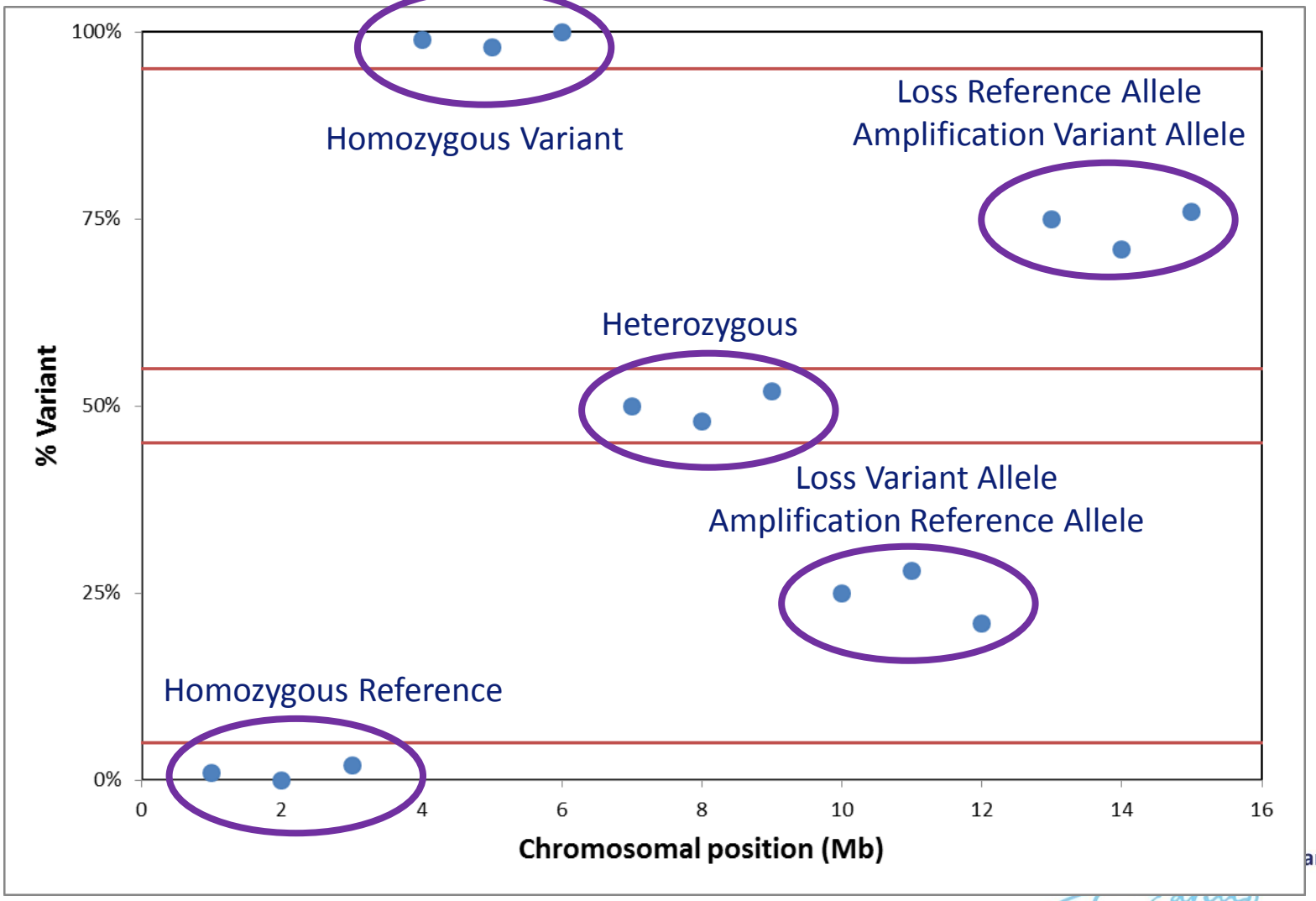
CNV analyse mbv SNPs

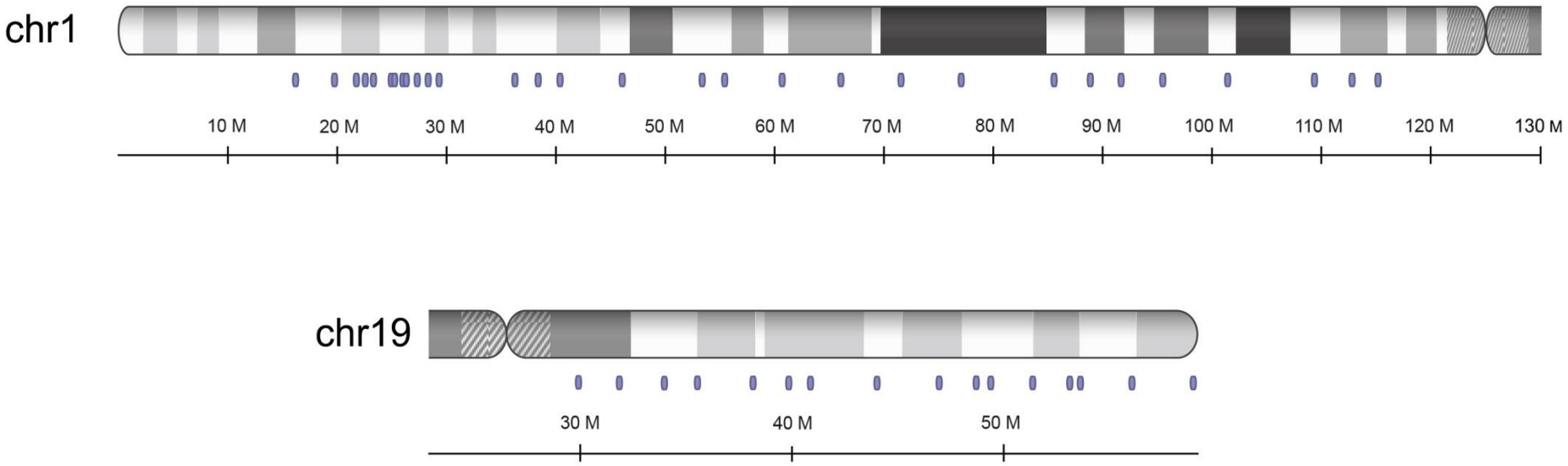




CNV analyse mbv SNPs



Verdeling SNPs over chromosoom 1p en 19q



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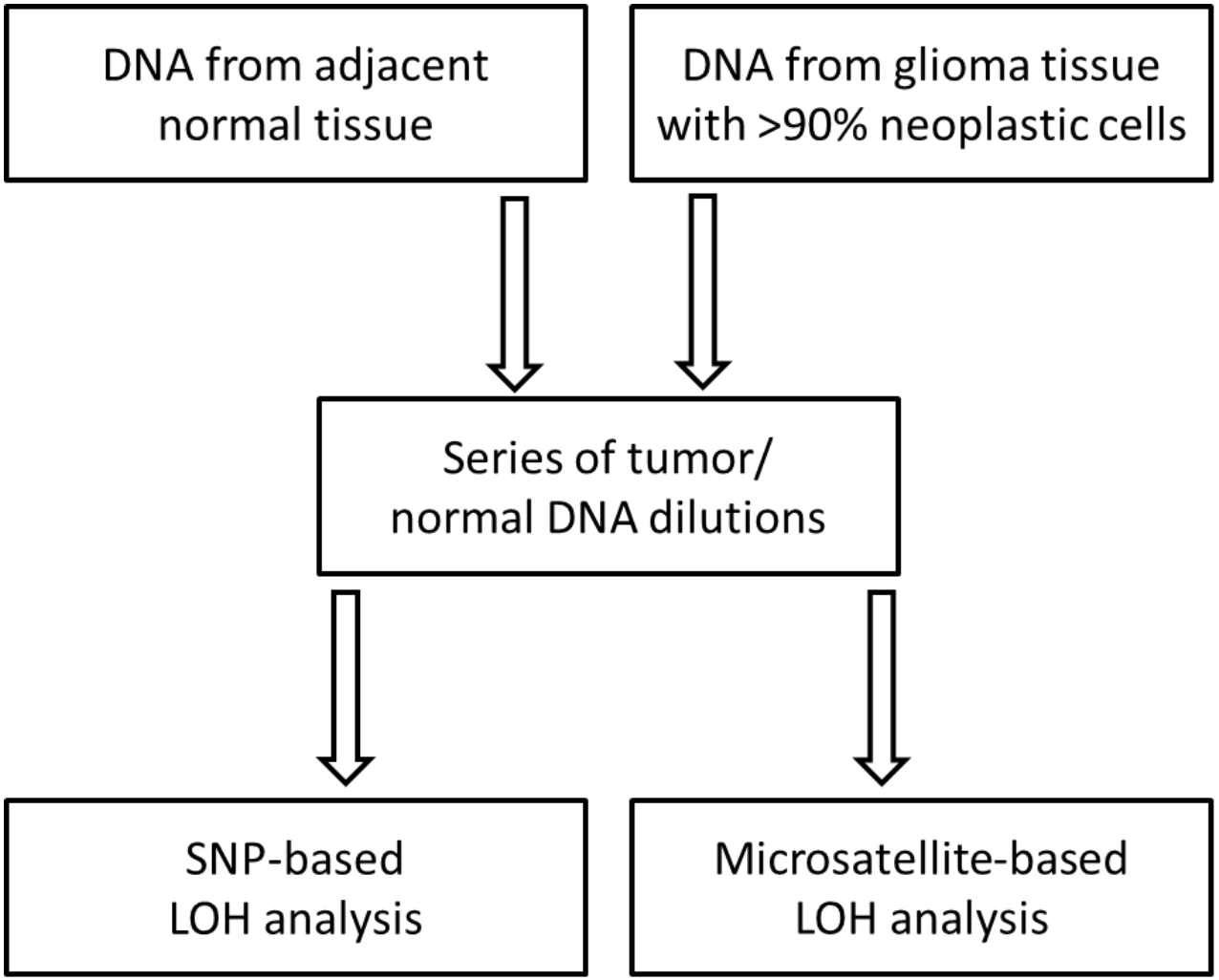
Gevoeligheid SNP vs microsatelliet LOH analyse



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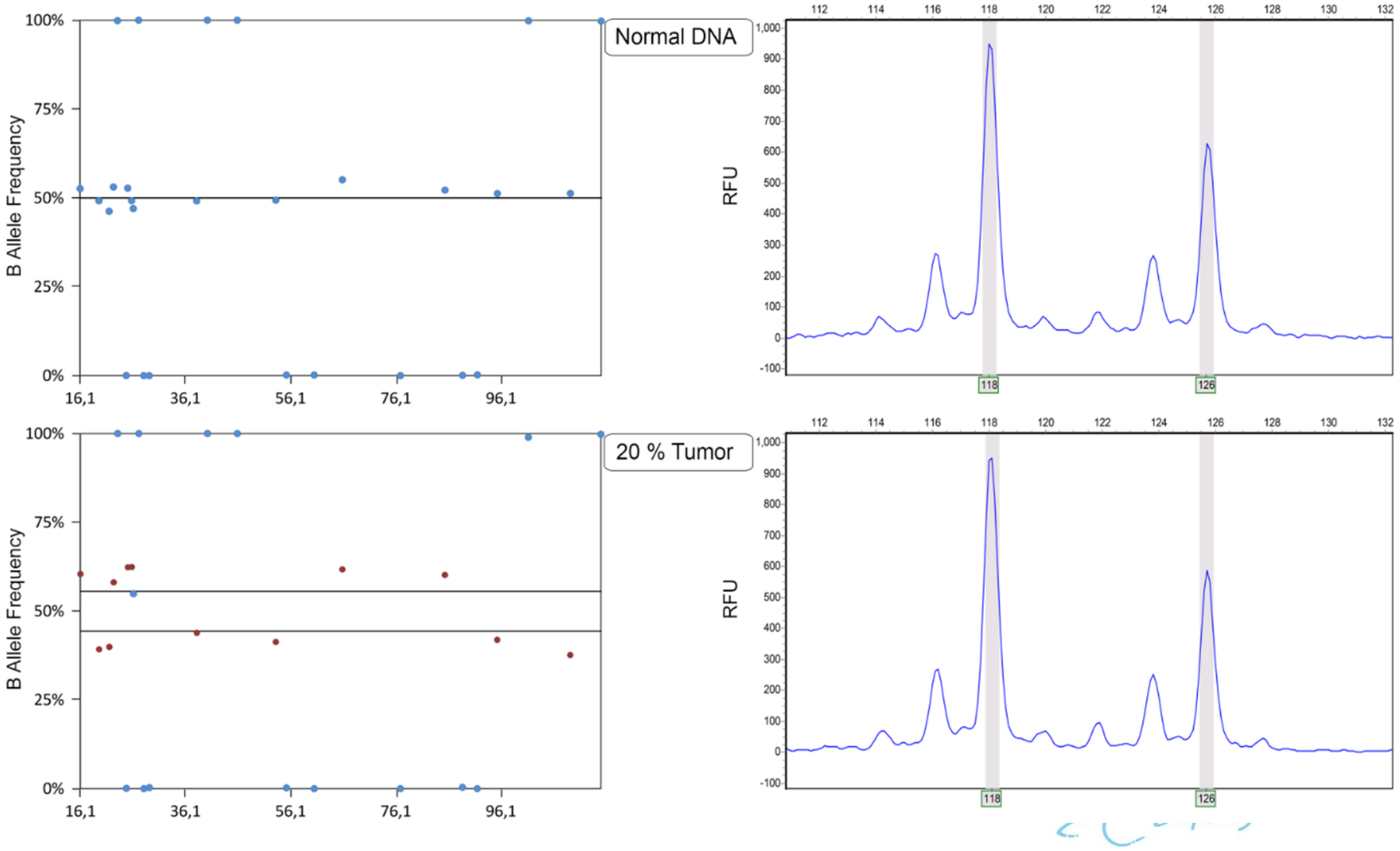
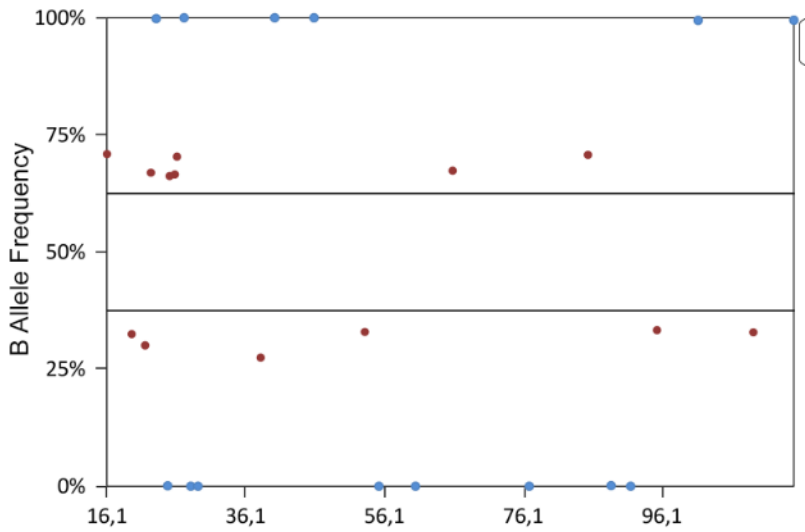
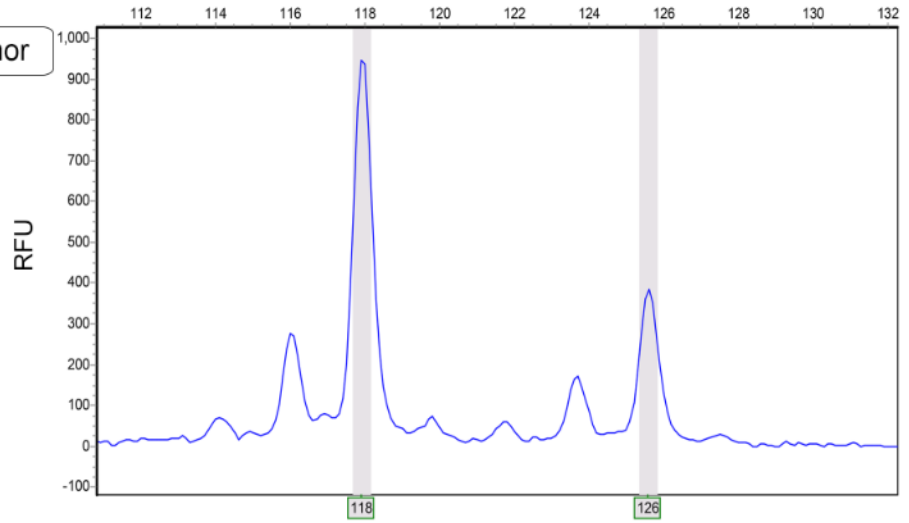
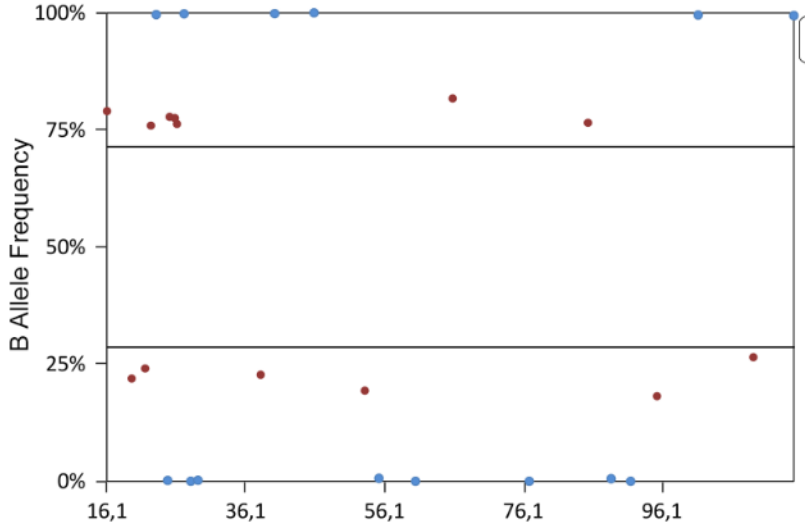


Gevoeligheid SNP vs microsatelliet LOH analyse

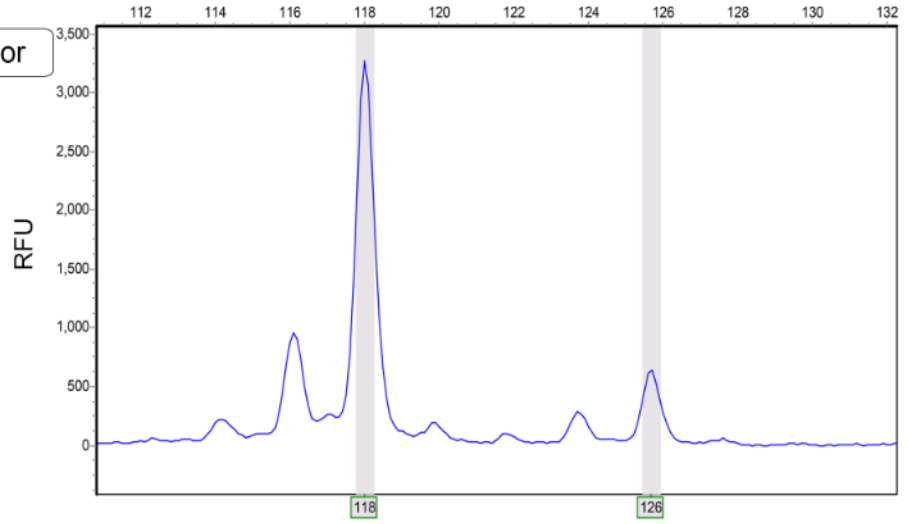


40 % Tumor

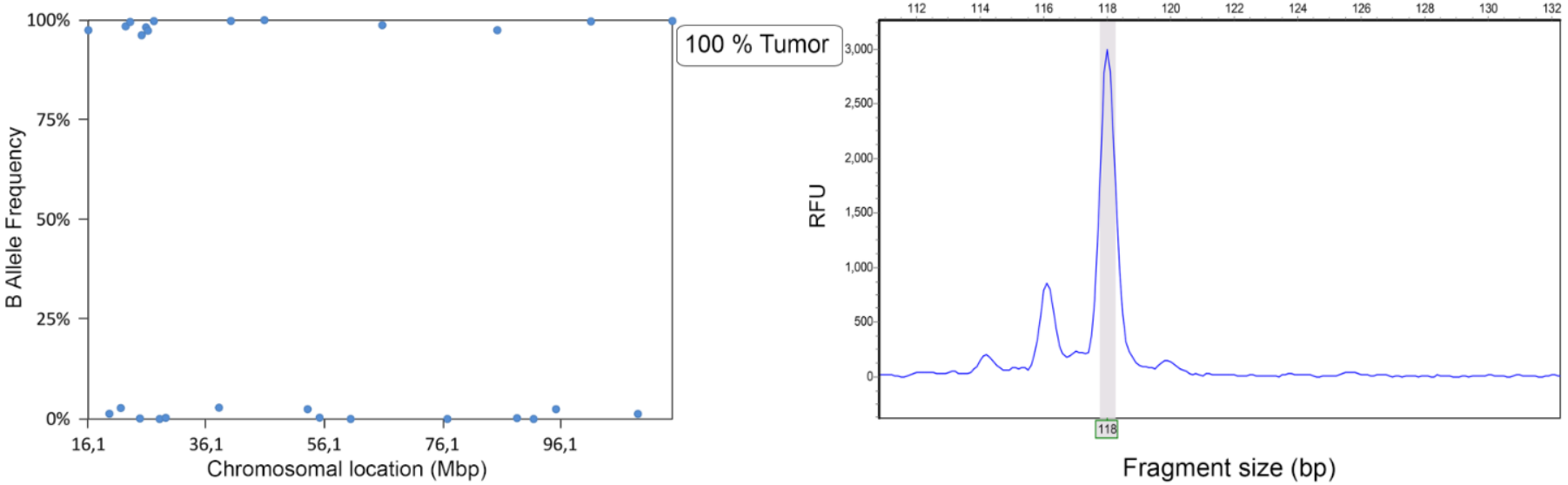




60 % Tumor



Gevoeligheid SNP vs microsatelliet LOH analyse



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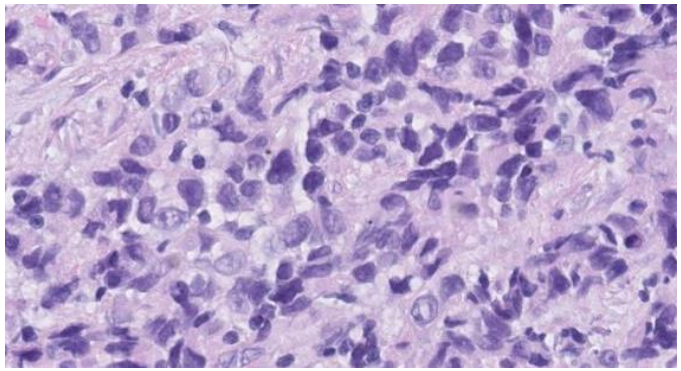
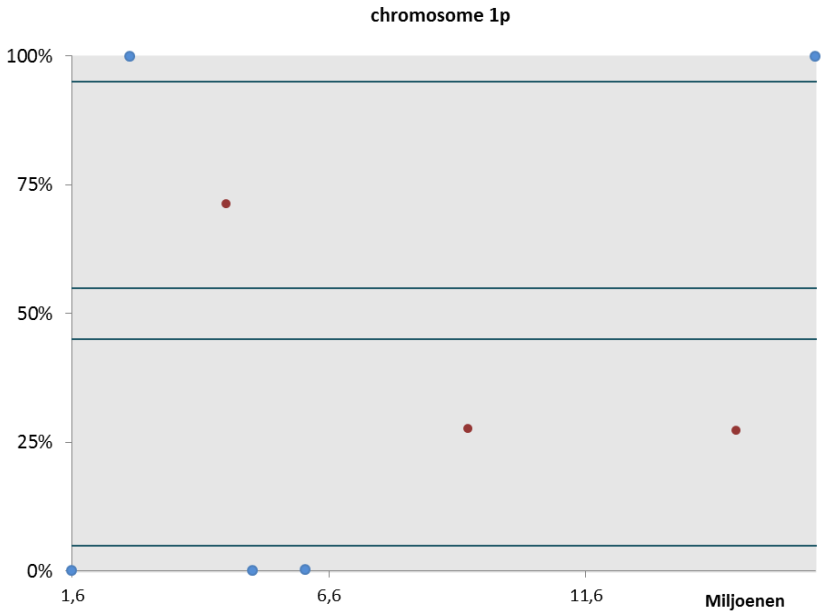
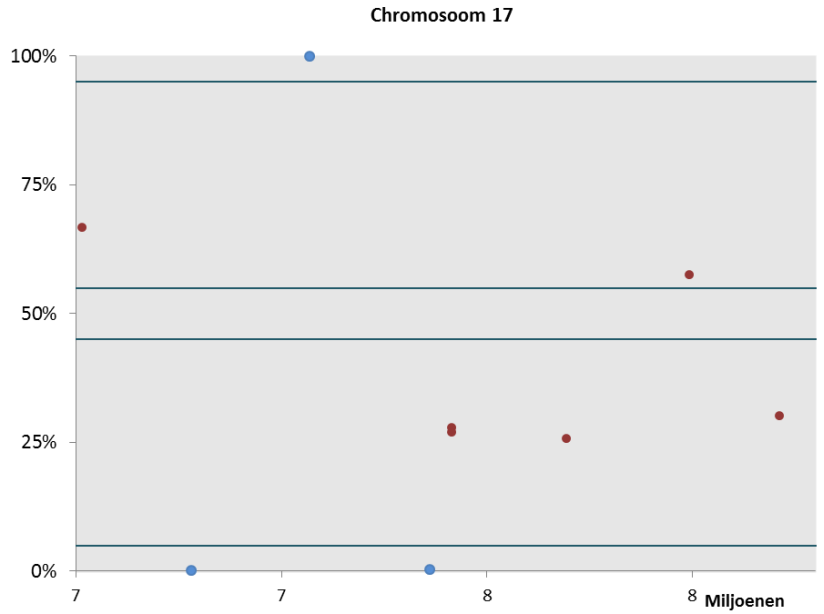
Mutatie analyse longpanel ivm therapiekeuze



Adenocarcinoom long
Percentage neoplastische cellen: 40%
Geen mutaties gevonden met NGS





-> Afwijking past bij ongeveer 60% neoplastische cellen

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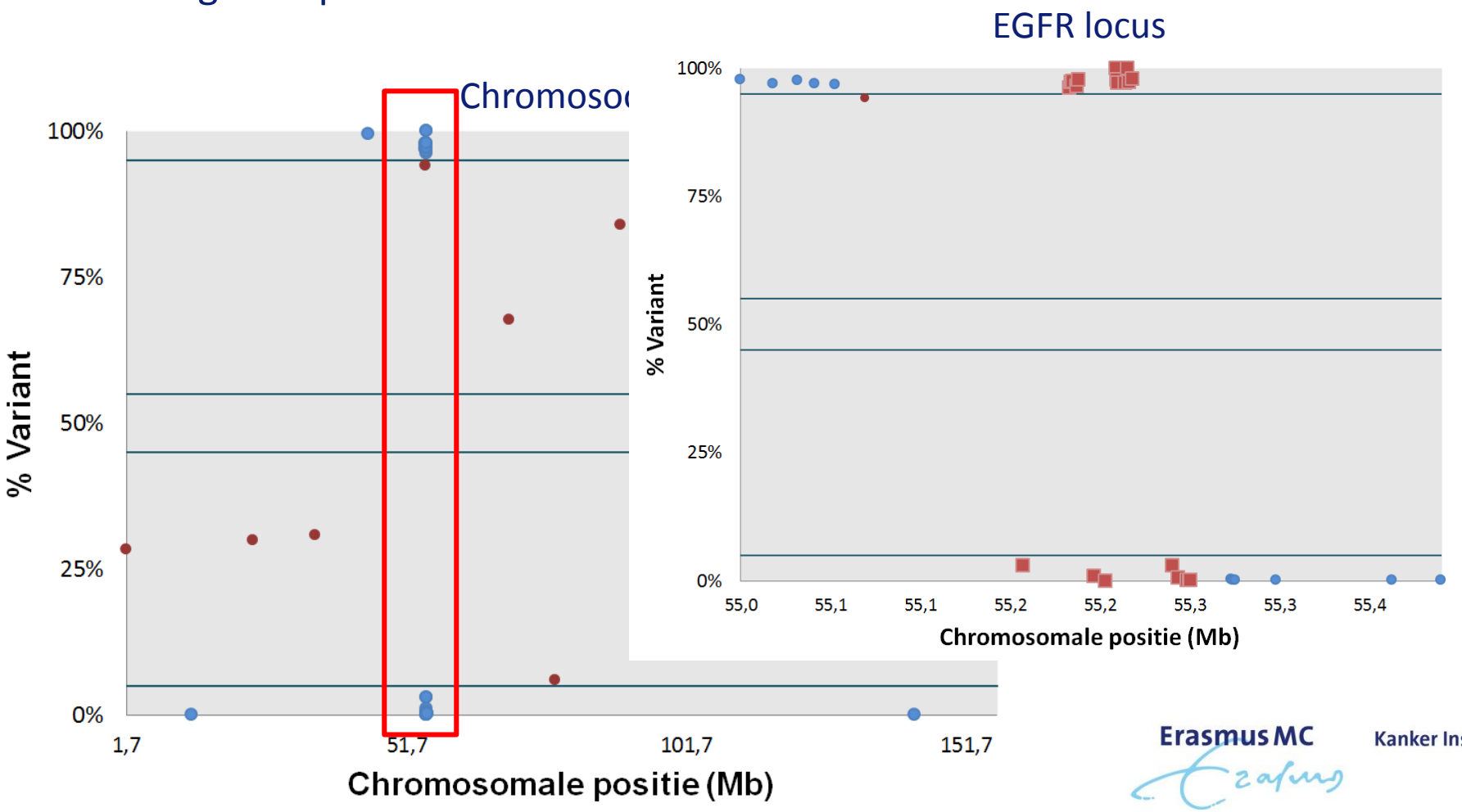
Glioblastoom

Moleculaire analyse ivm therapiekeuze/differentiaal diagnostiek
Percentage neoplastische cellen: 80%



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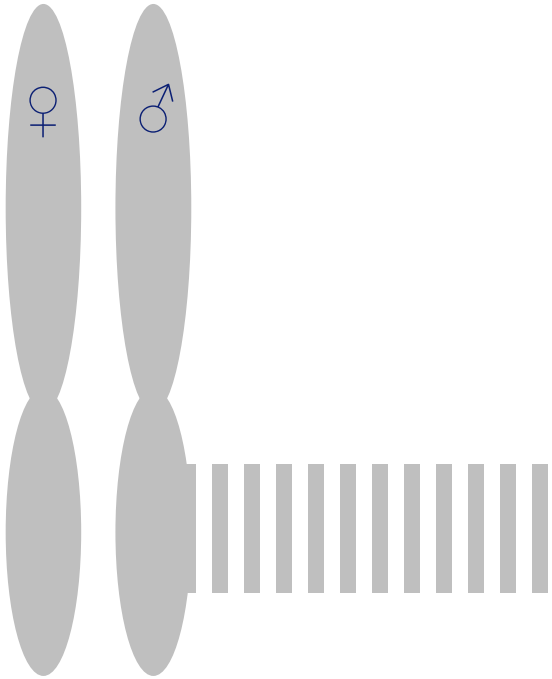
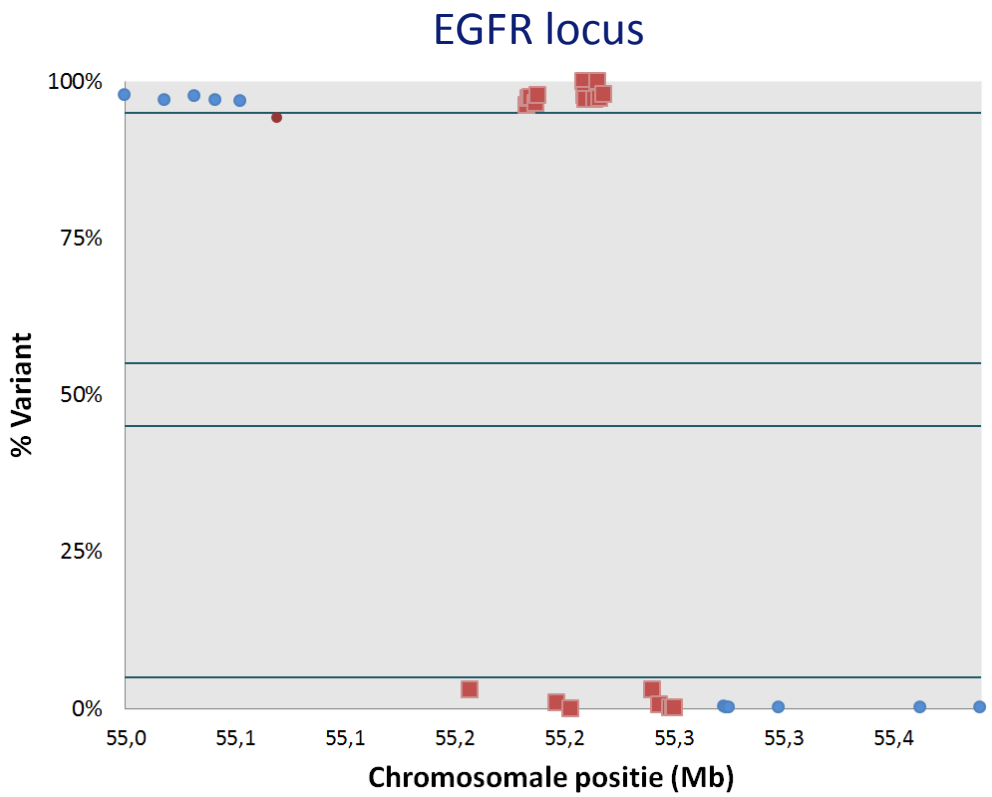
Glioblastoom





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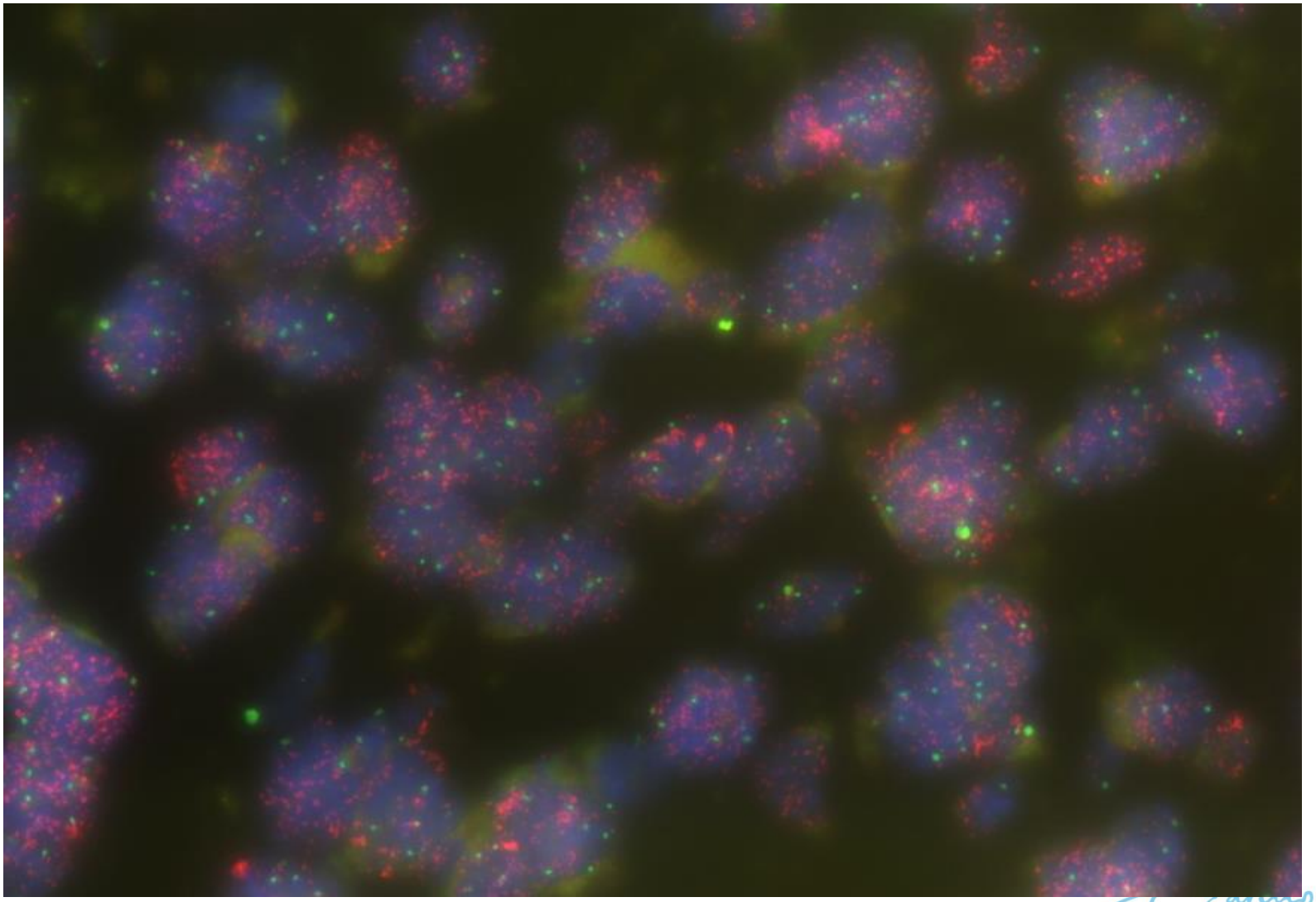
Glioblastoom



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Conclusies

- SNP analyse is een gevoelige methode voor detectie van grote chromosomale afwijkingen in routine FFPE weefsels
- Normaal referentieweefsel is niet nodig
- De analyse kan worden uitgevoerd op kleine hoeveelheden DNA (3-10 ng)
- Goed te combineren met mutatie analyse

Dankwoord

Moleculaire diagnostiek Erasmus MC Rotterdam

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