13èmes ASSISES DE GÉNÉTIQUE HUMAINE ET MÉDICALE
CANNES, PALAIS DES FESTIVALS ET DES CONGRÈS
27-30 JANVIER 2026
www.assises-genetique.org
FFGH

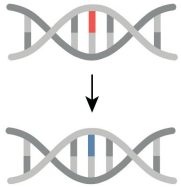
AURA GEN

BARACUDA

Priorisation et visualisation des disomies uniparentales et aneuploïdies en mosaïque

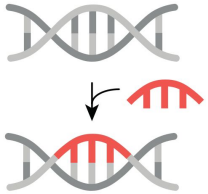
Virginie Bernard, Alexis Praga, Damien Sanlaville, Julien Thevenon

Génome short-read en trio à Auragen



2020

SNV, CNV, RoH

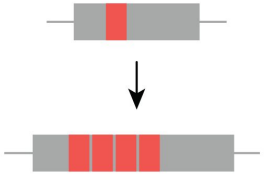


2021

Introniques profonds, SV, ploïdie

2022

CNV régions complexes, composites SNV+CNV



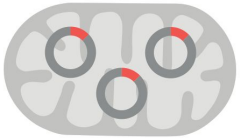
2023

Expansions nucléotidique

PhenoGenius

2024

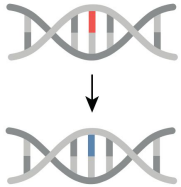
Priorisation v2

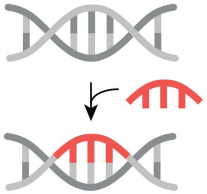


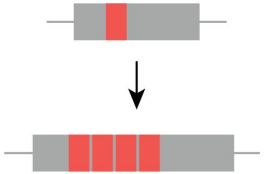
2025

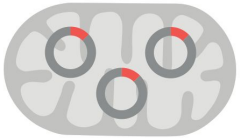
ADN mitochondrial, UTR

Génome short-read en trio à Auragen







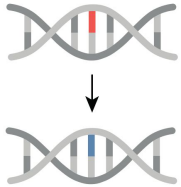


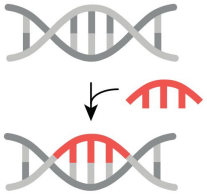
2020	2021	2022	2023	2024	2025
SNV, CNV, RoH	Introniques profonds, SV, ploïdie	CNV régions complexes, composites SNV+CNV	Expansions nucléotidique	Priorisation v2	ADN mitochondrial, UTR

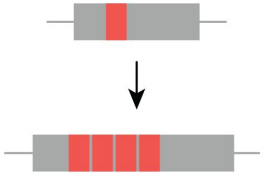
PhenoGenius

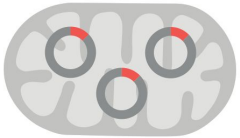
Quid des disomies ?

Génome short-read en trio à Auragen









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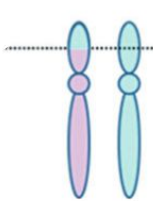
PhenoGenius

Quid des disomies ? … et en mosaïque ?

Disomies

Maternal heterodisomy

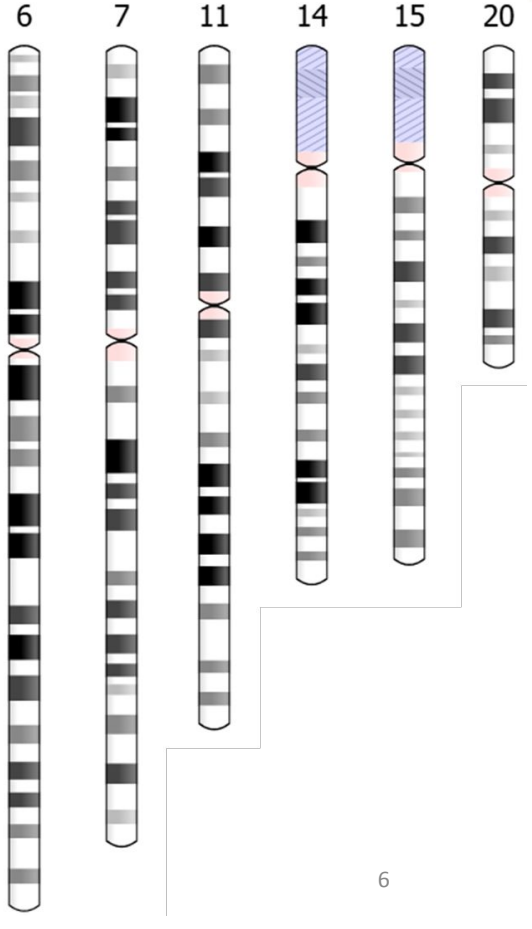
Paternal isodisomy



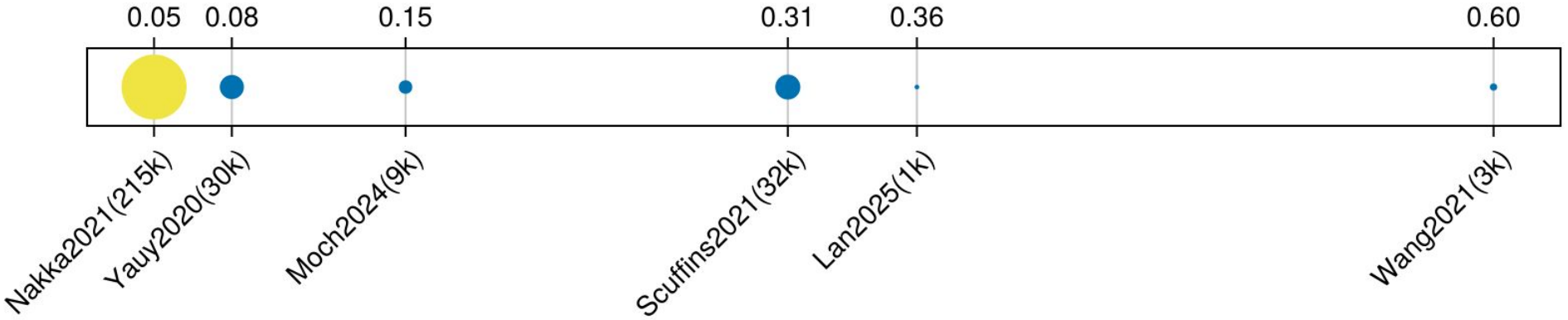
Resulting segmental uniparental disomy

Disomies

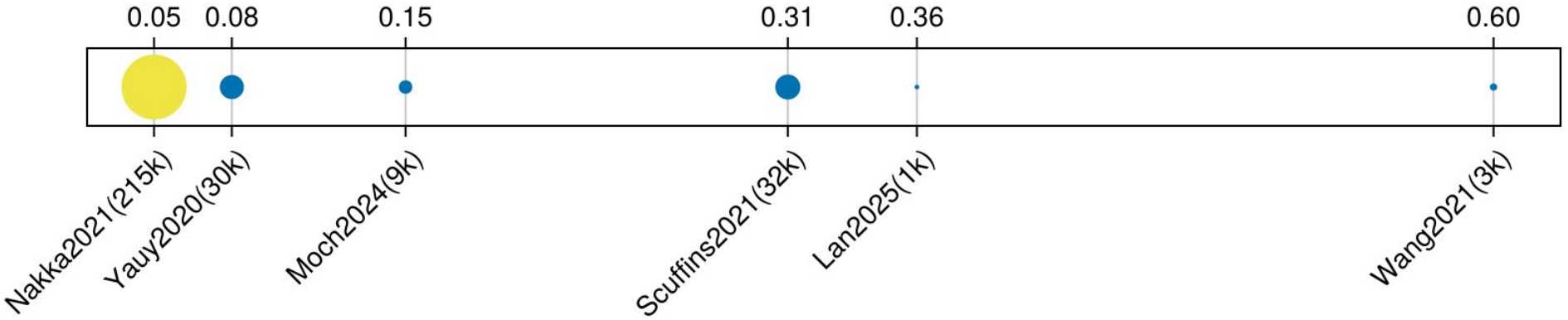
- Chromosomes 6, 7, 11, 14, 15, 20
- “Révélation” maladie récessive



Disomies en Next-Generation Sequencing

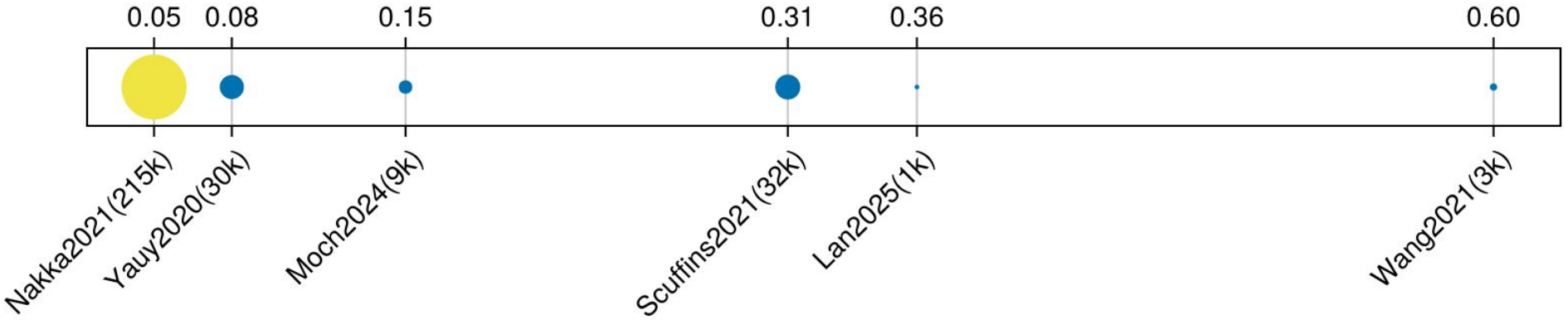


Disomies en Next-Generation Sequencing



Estimation pour notre cohorte : 5 à 71 disomies…

Disomies en Next-Generation Sequencing



Estimation pour notre cohorte : 5 à 71 disomies…
sans les mosaïques !

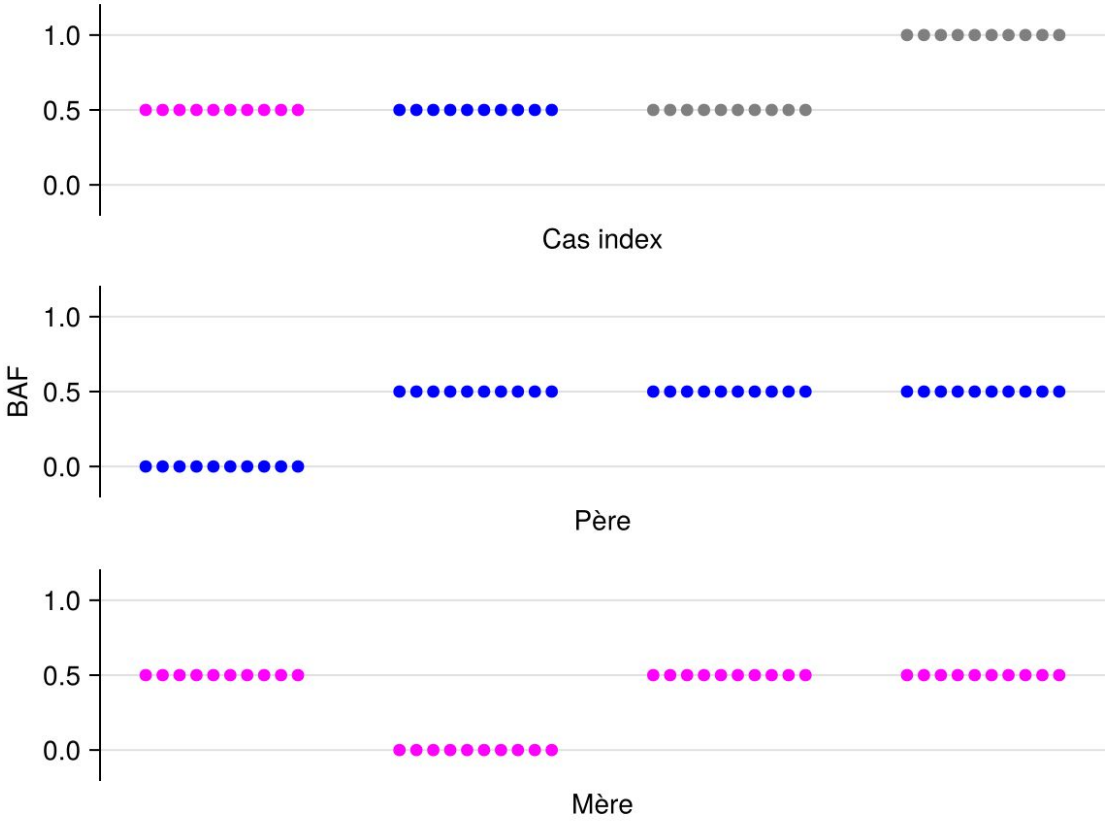
Apports

- Disomies et aneuploïdies en génome short-read trio
  - pré-sélection
  - nouvelles visualisations
- Hétérodisomies
- Mosaïques
- Première grande cohorte de disomies en génome
- En production depuis février 2025 (9.2)

1. **Méthodes**
2. **Dossiers d’intérêt**
3. **Résultat de la cohorte**

Méthode : sélection des dossiers

Prérequis :
ségrégation
de chaque variant
du cas index



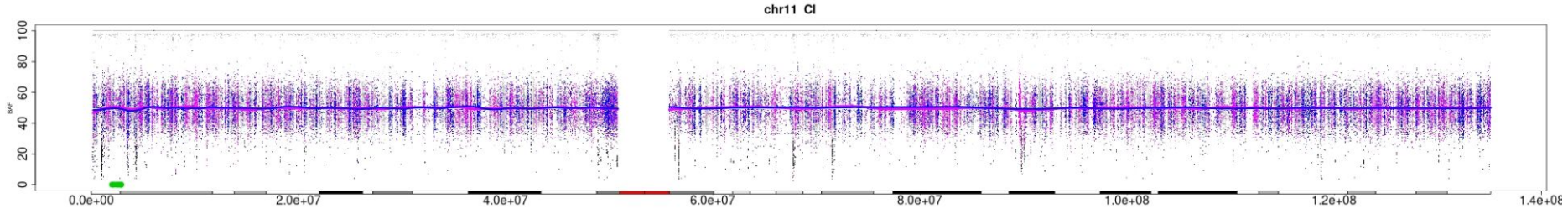
Méthode : sélection des dossiers

Principe : excès de variants hérités du père ou de la mère

Avertissement : Le profil de transmission des SNP parentaux est déséquilibré : 99.8% de SNP paternels sur le chr15. Cela pourrait évoquer une disomie uniparentale.
Consultez la section Autres.

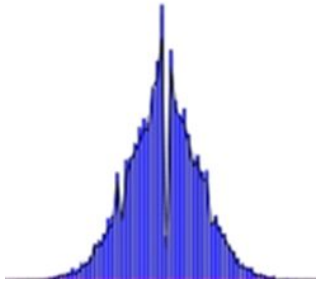
Méthode : visualisations

Dossier sans anomalies



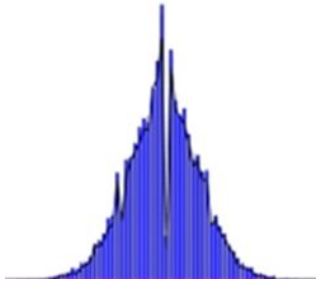
Méthode : visualisations

VAF variants paternels

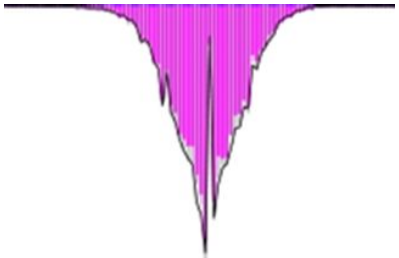


Méthode : visualisations

VAF variants paternels



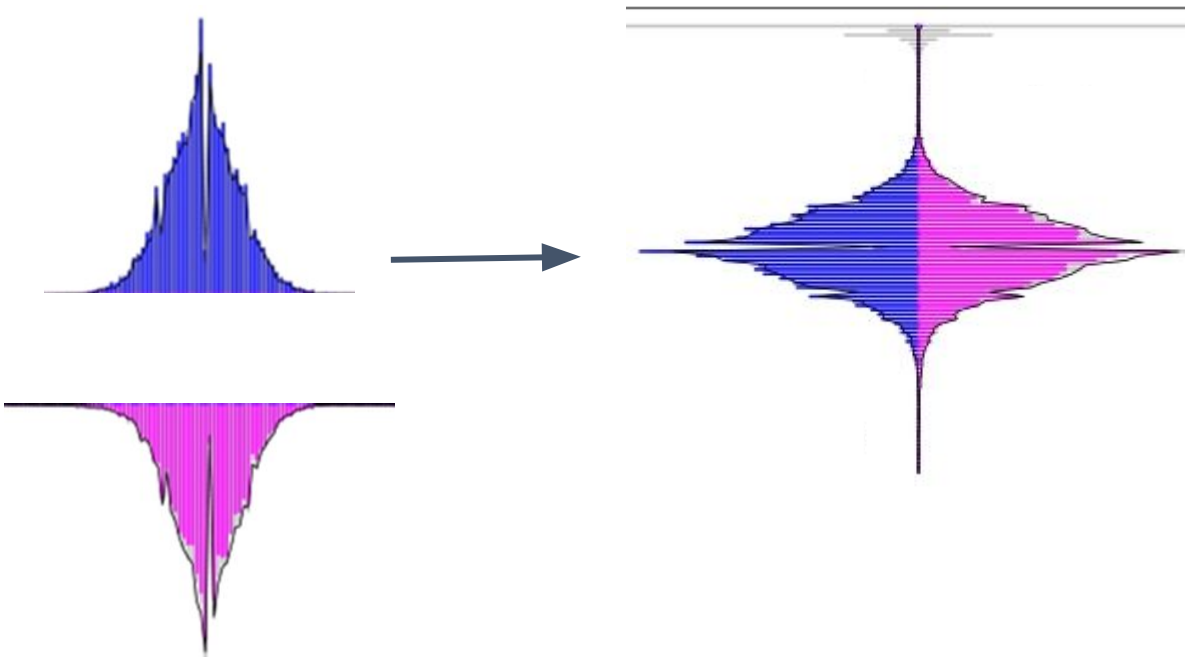
VAF
variants maternels



Méthode : visualisations

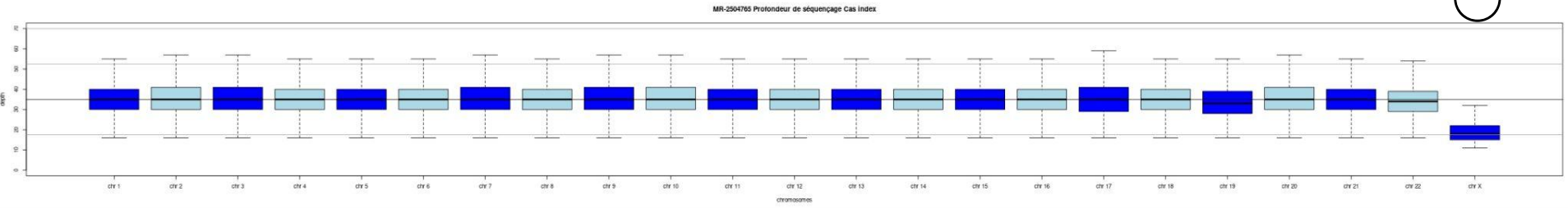
VAF variants paternels

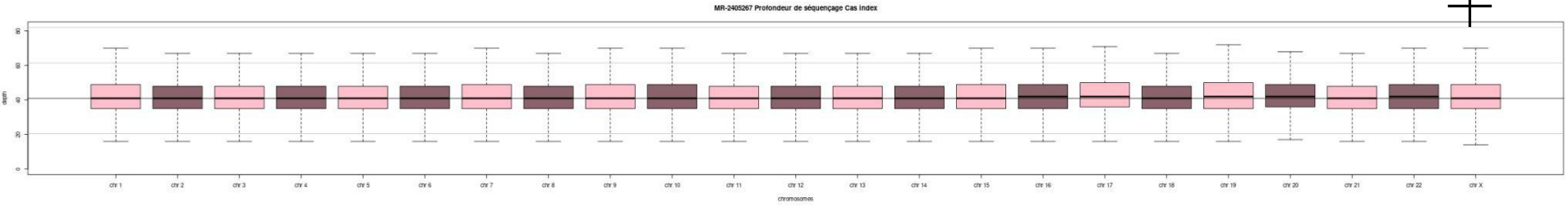
VAF
variants maternels



Méthode : visualisations (en cours)

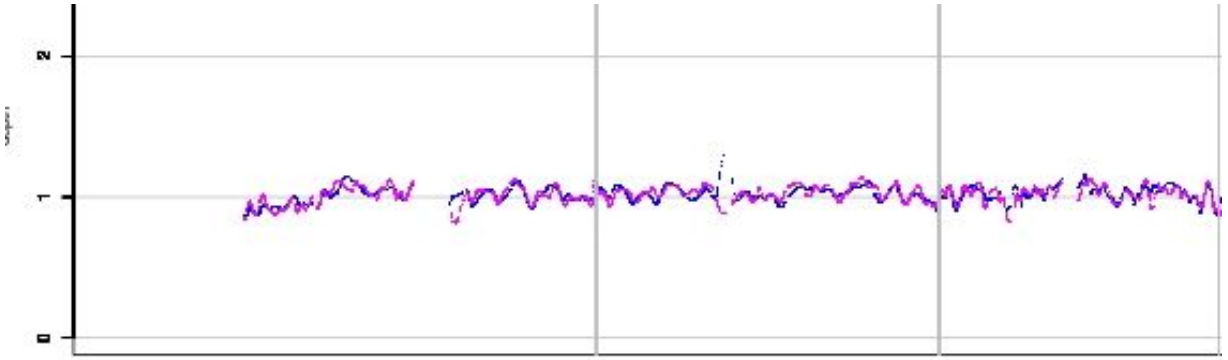
Profondeur par chromosome



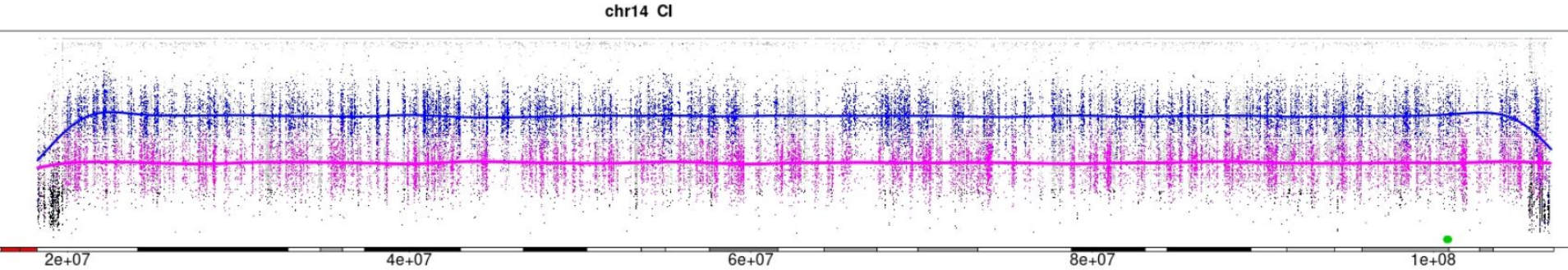


Méthode : visualisations (en cours)

Estimation du nombre de copies des variants de chaque parents



Validation : trisomie 14 en mosaïque



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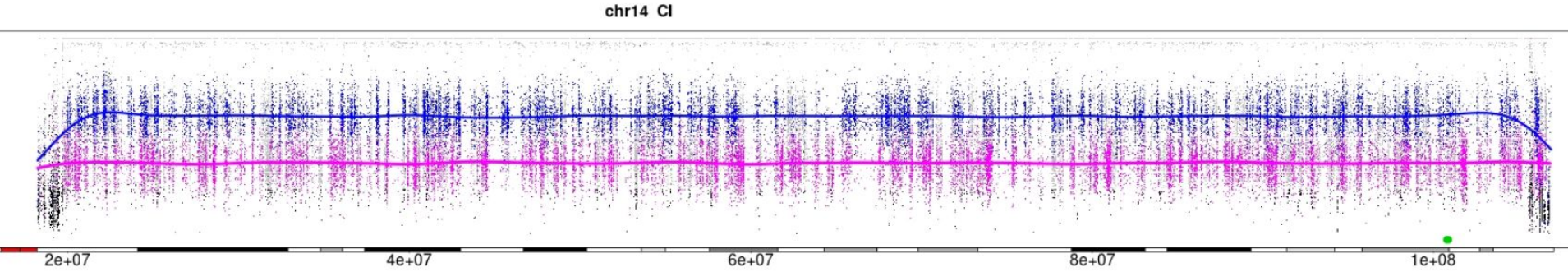
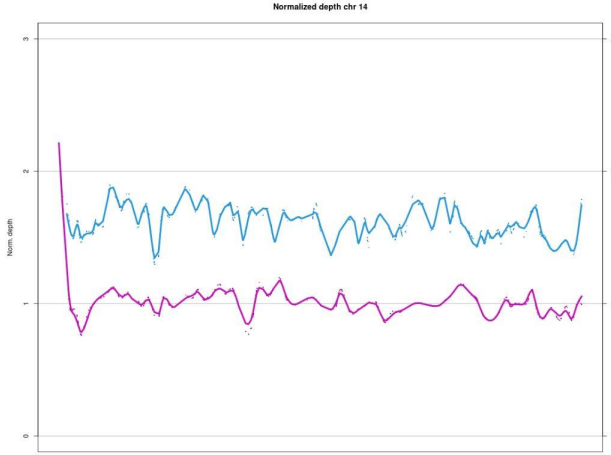
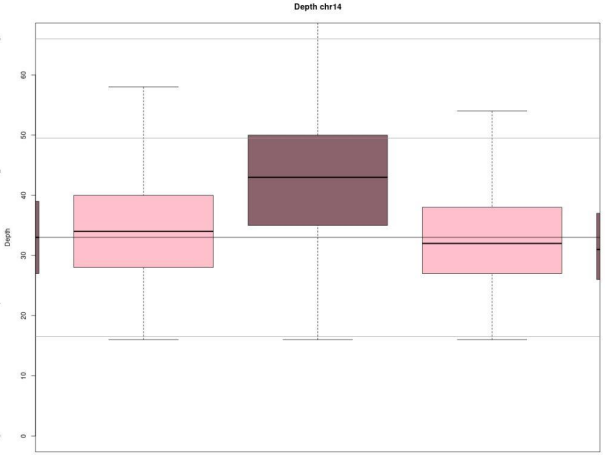
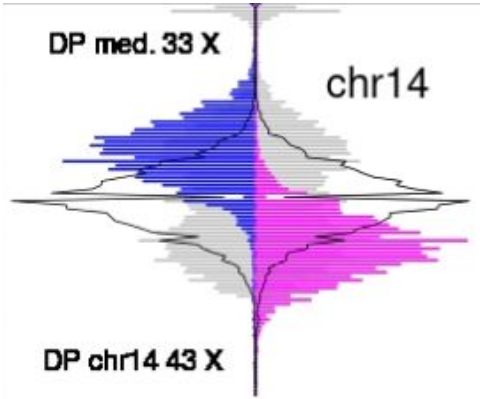
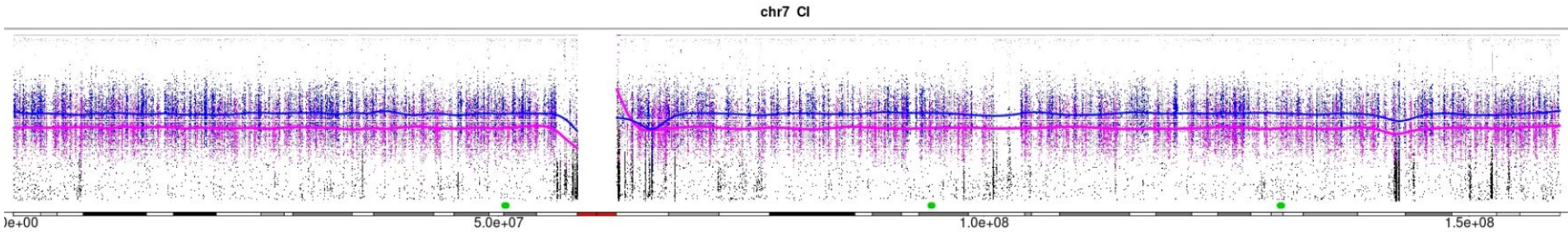




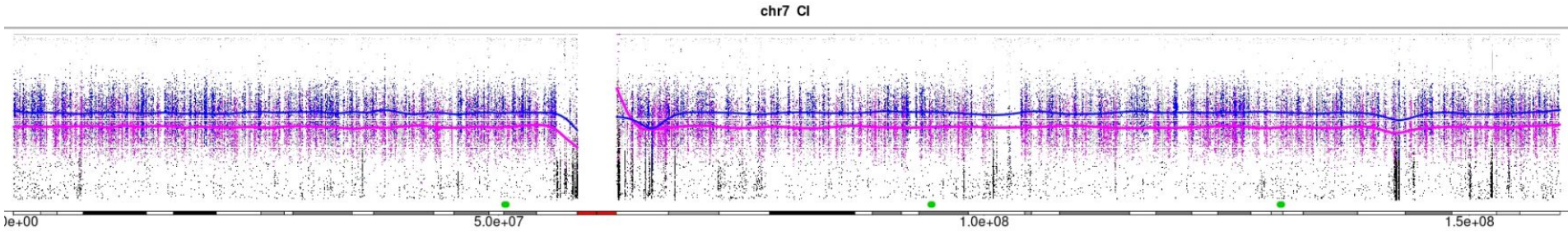


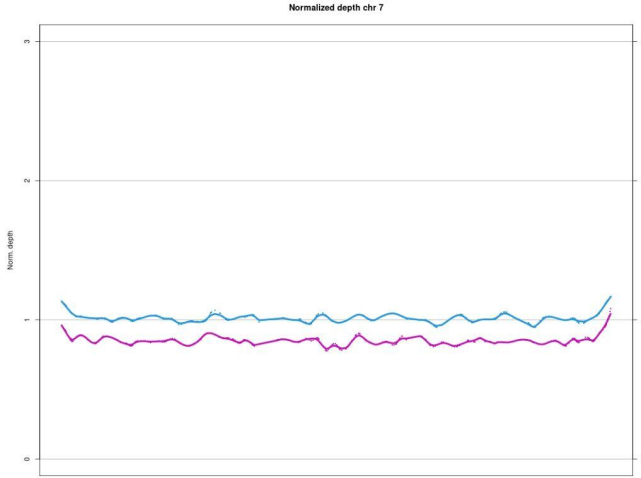


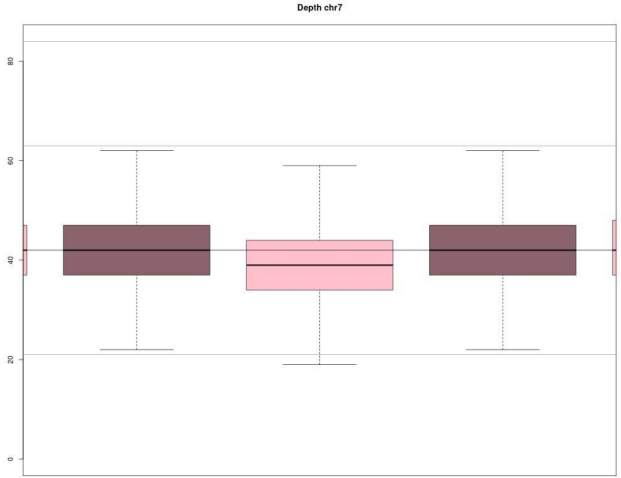
Validation : monosomie 7 en mosaïque

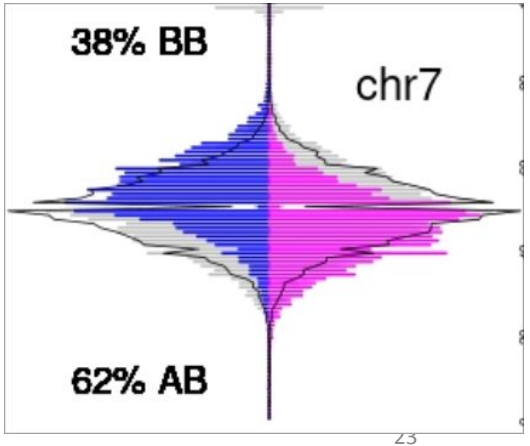


Validation : monosomie 7 en mosaïque

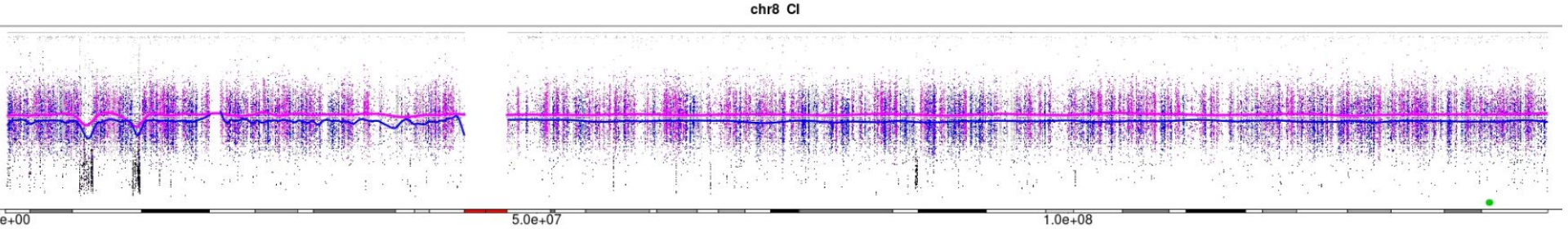


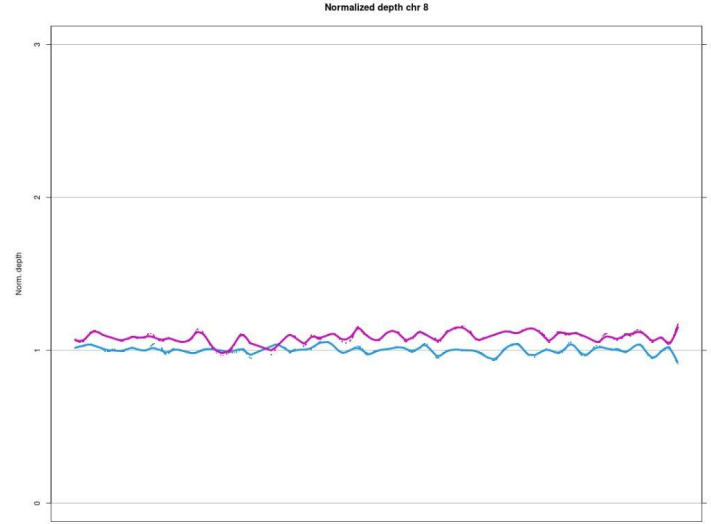


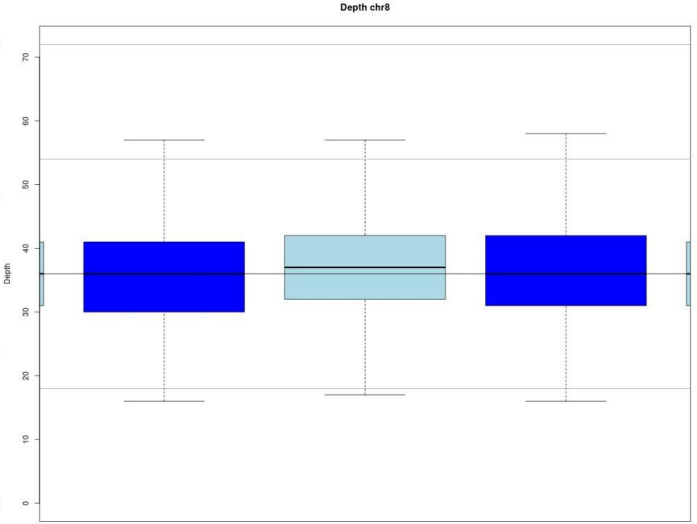


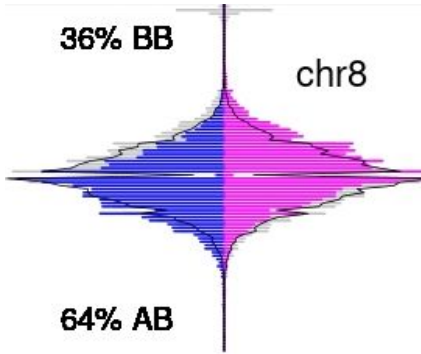


Validation : trisomie 8 faible

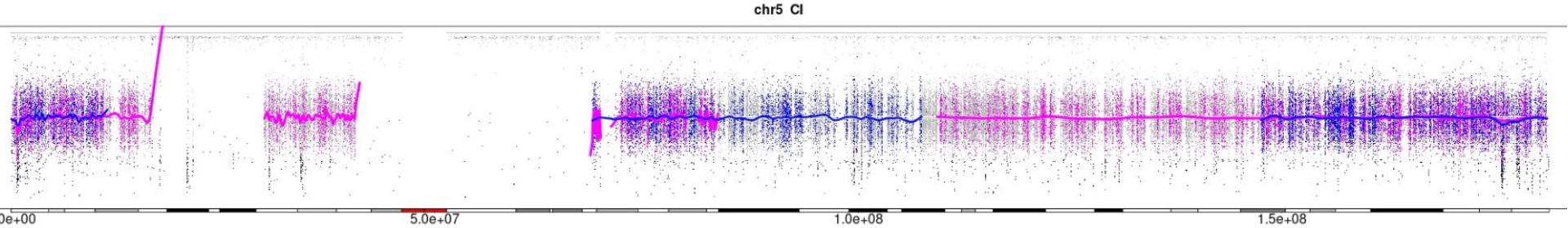


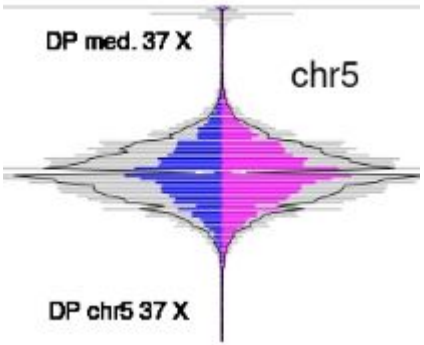


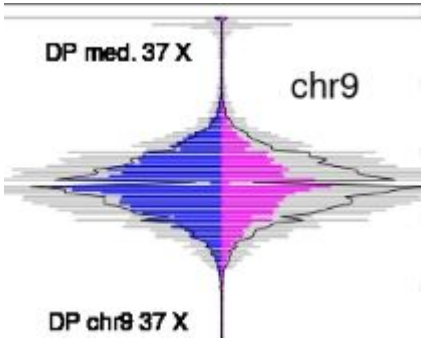


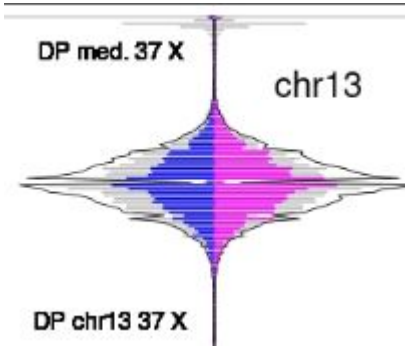


Attention à la consanguinité !



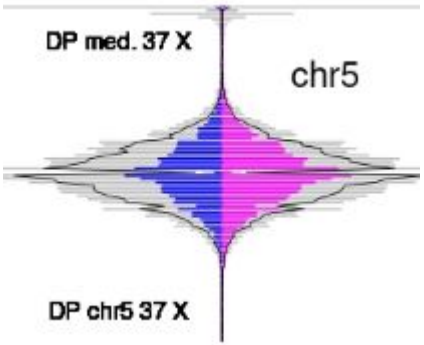


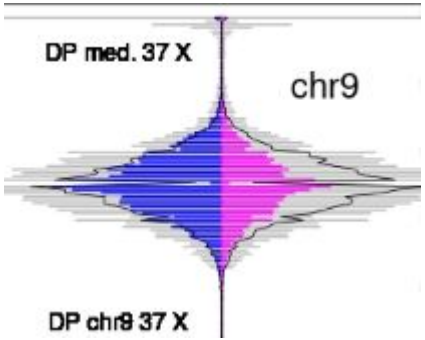


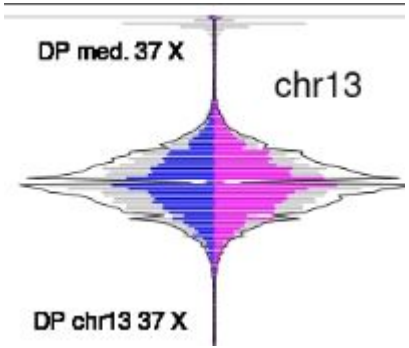


Attention à la consanguinité !

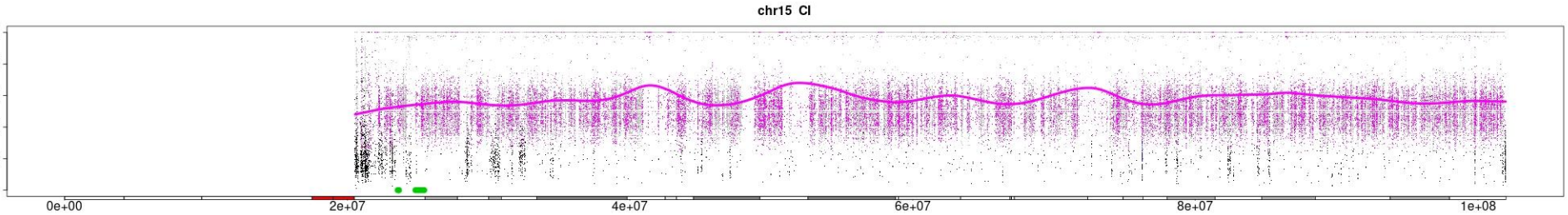
Régions d'homozygotie 225.99Mb (7.29% du génome)



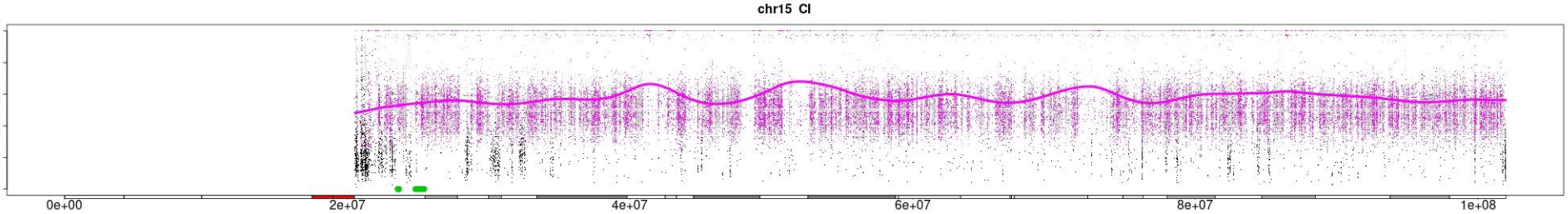


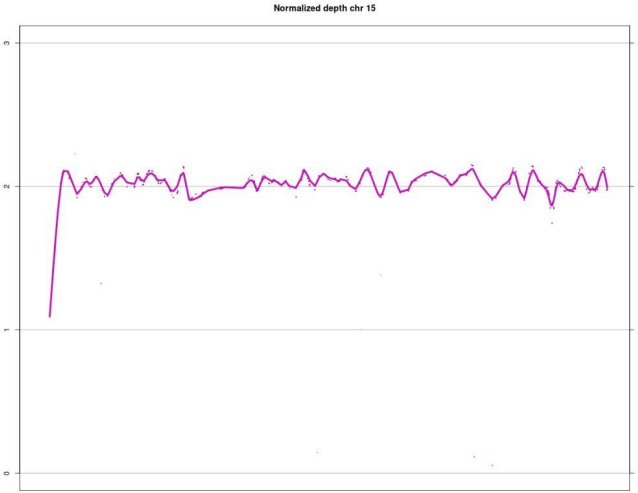


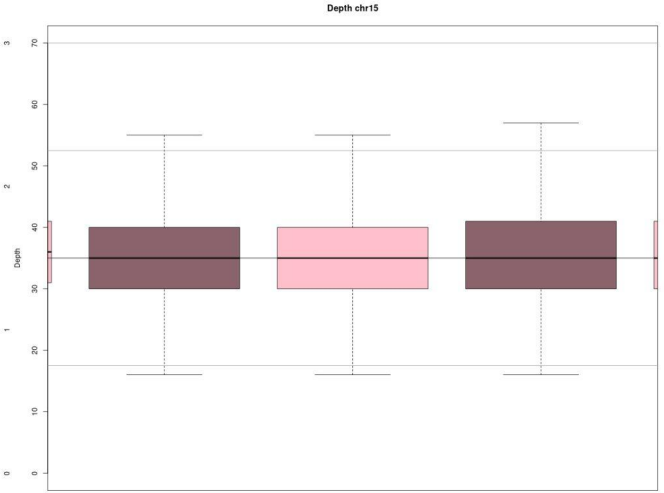
Nouveau diagnostic 1

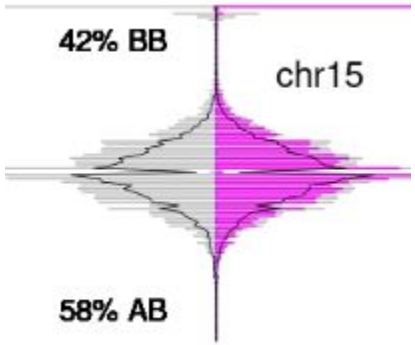


Nouveau diagnostic 1









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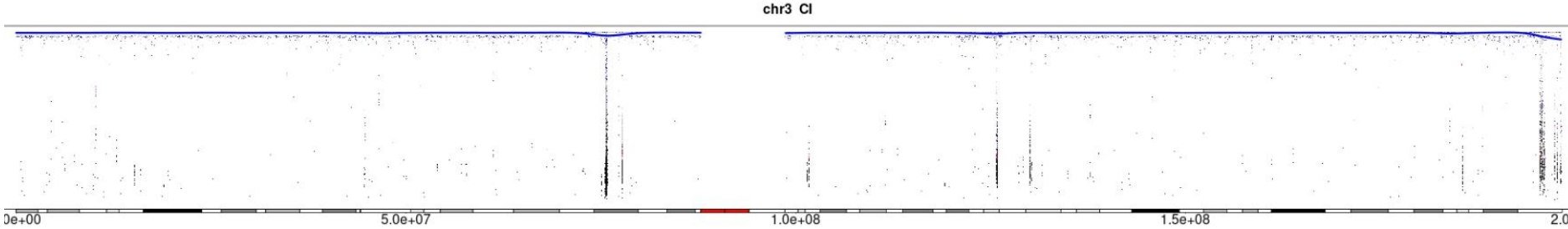
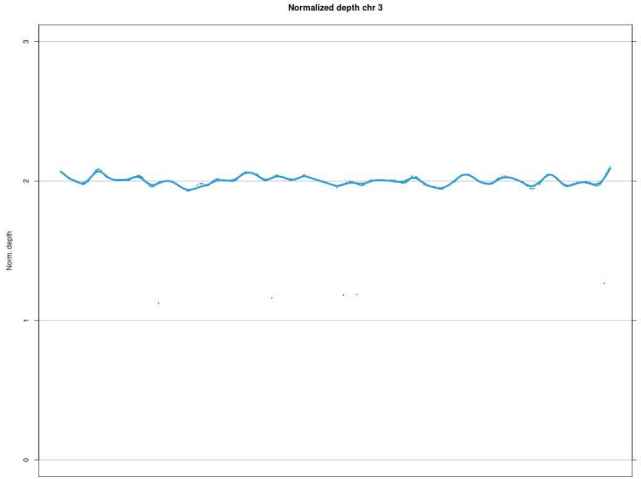
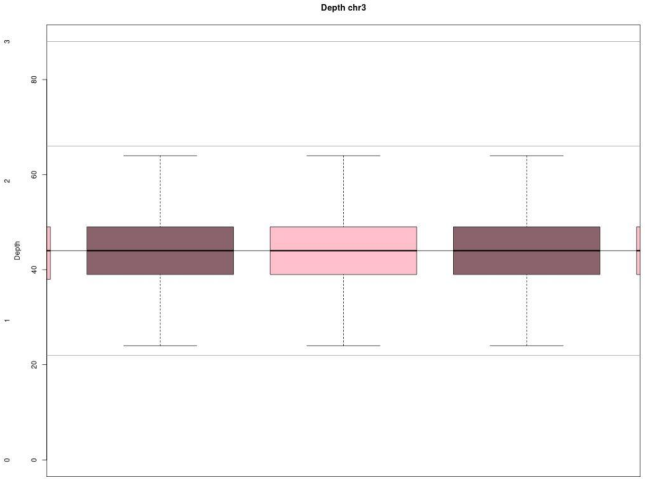
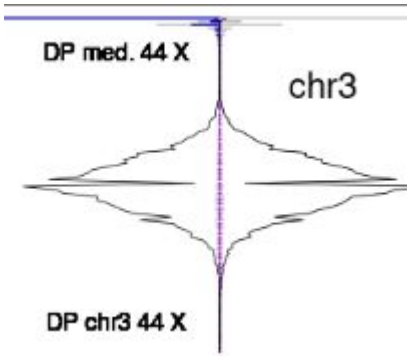
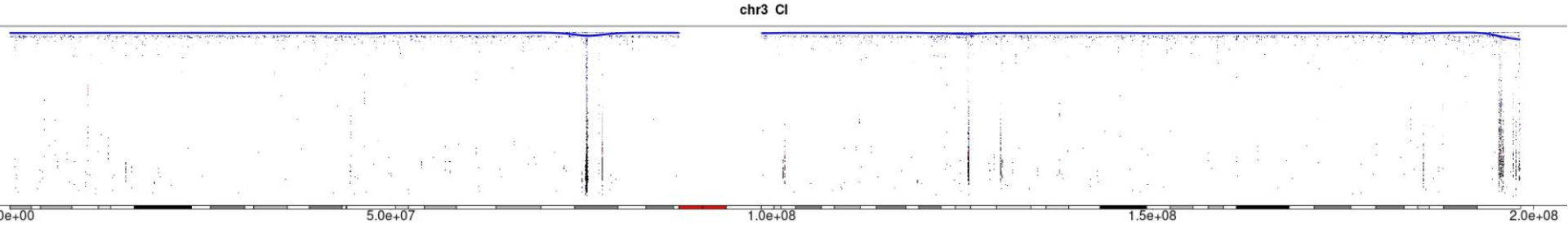




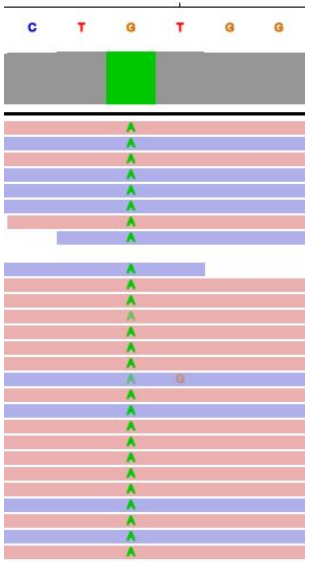




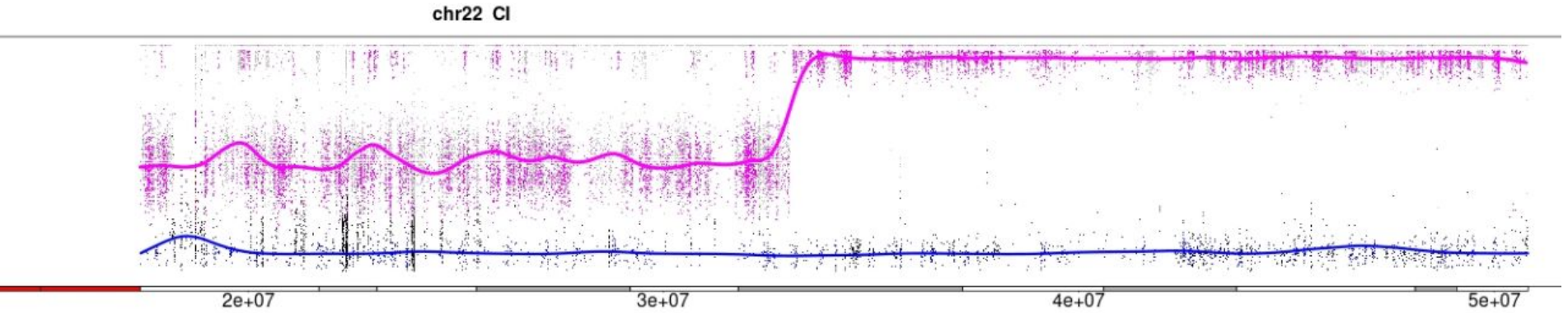
Nouveau diagnostic 2



Variant de *CREDL1* homozygote par disomie



Nouveau diagnostic 3



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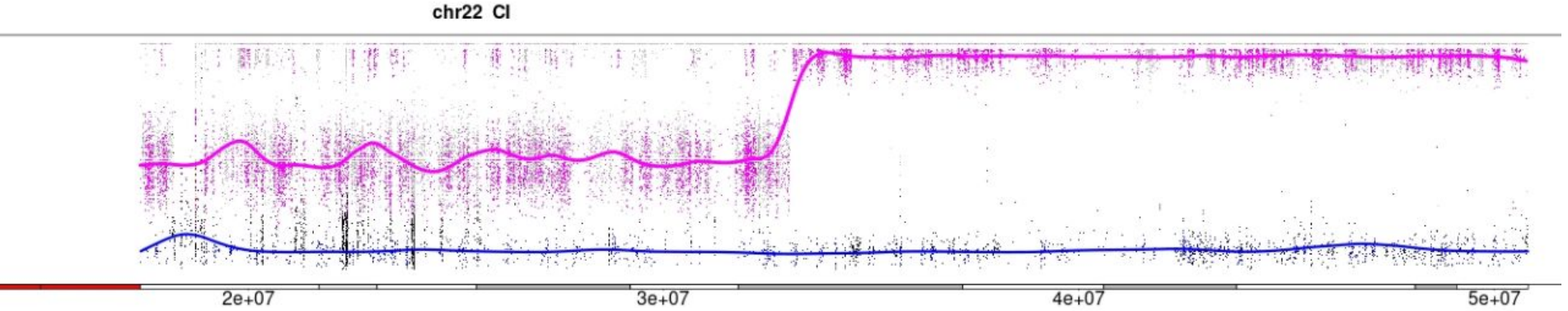
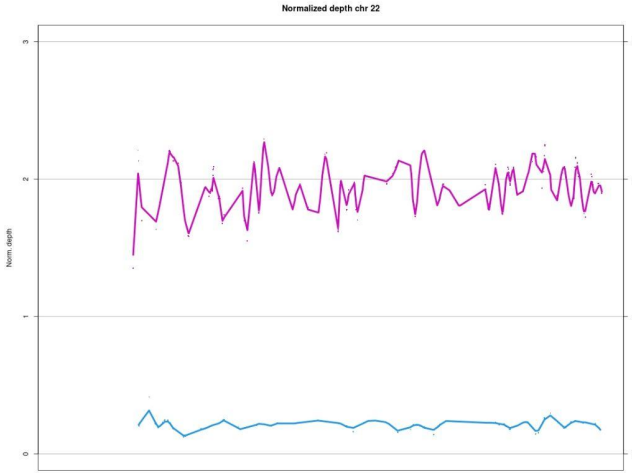
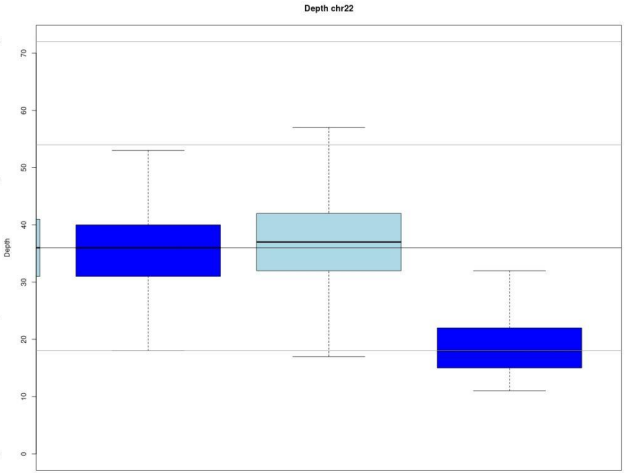
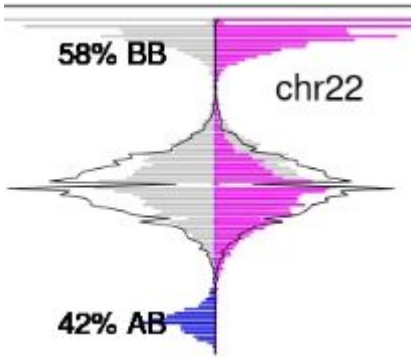
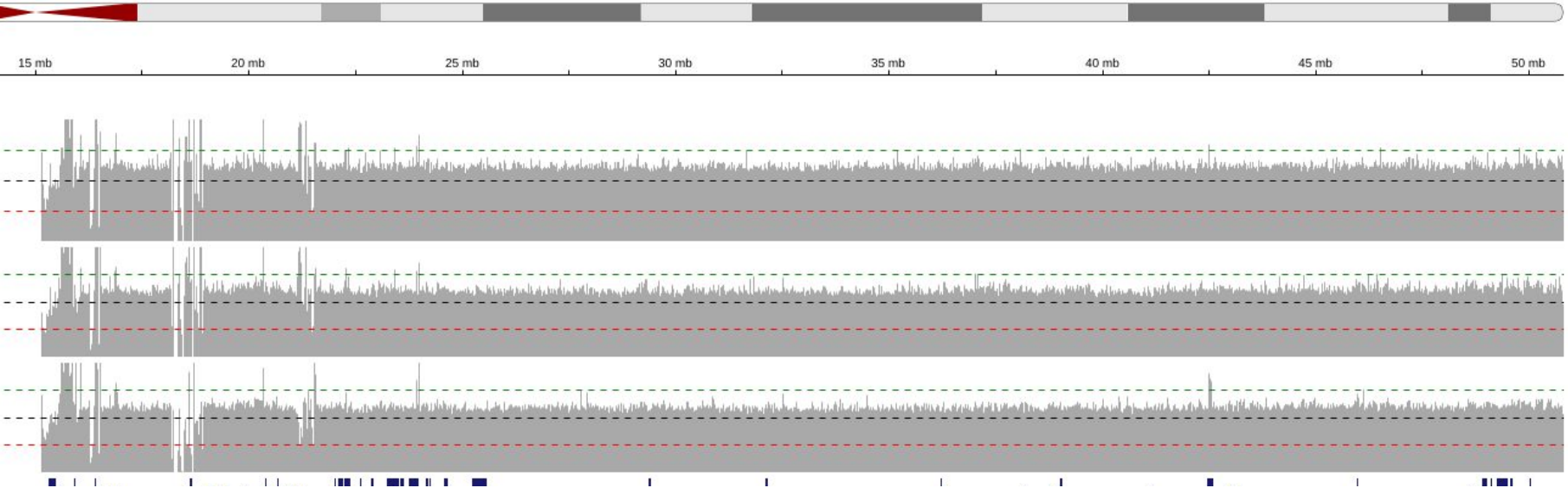








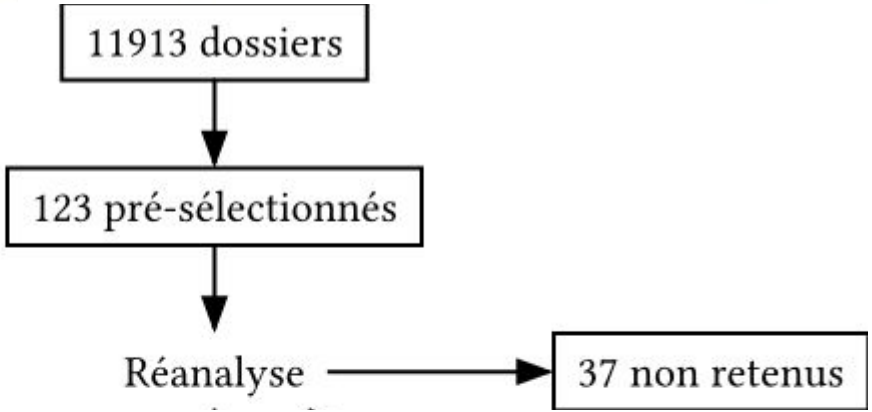
Nouveau diagnostic 3



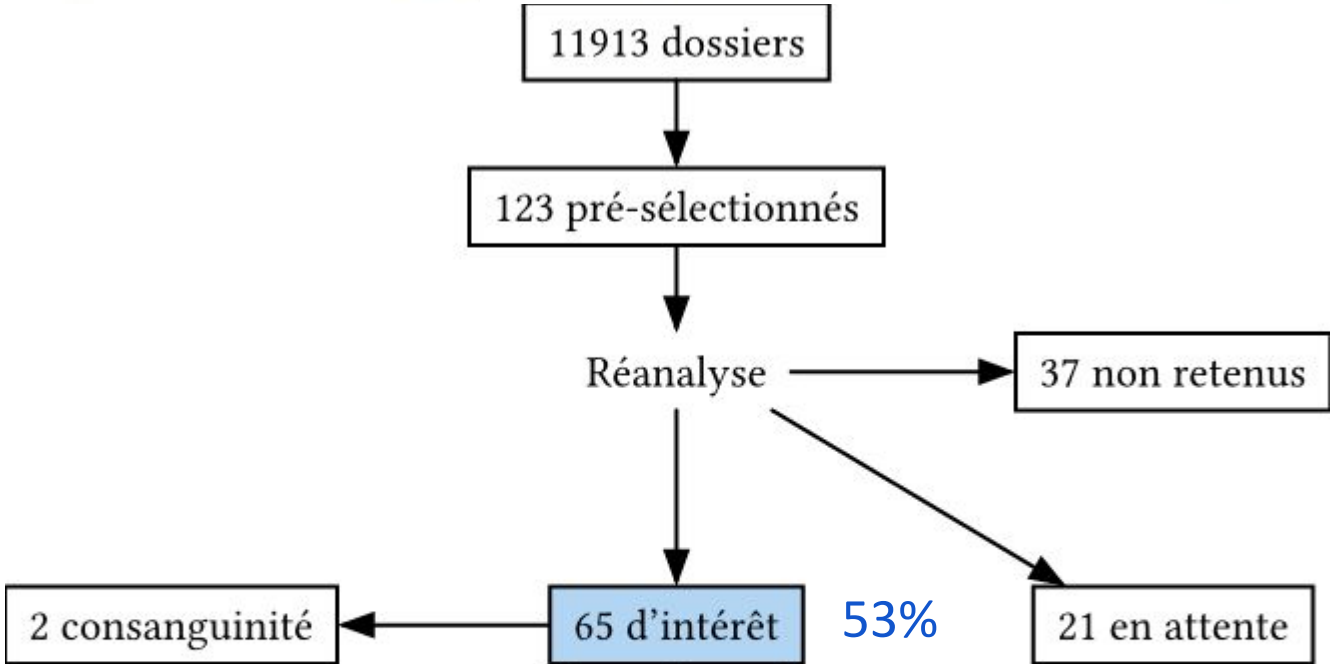
FISH :

- 12% foie (22qter + RP11-422p18)
- 17% poumon (22qter + cep14/22)

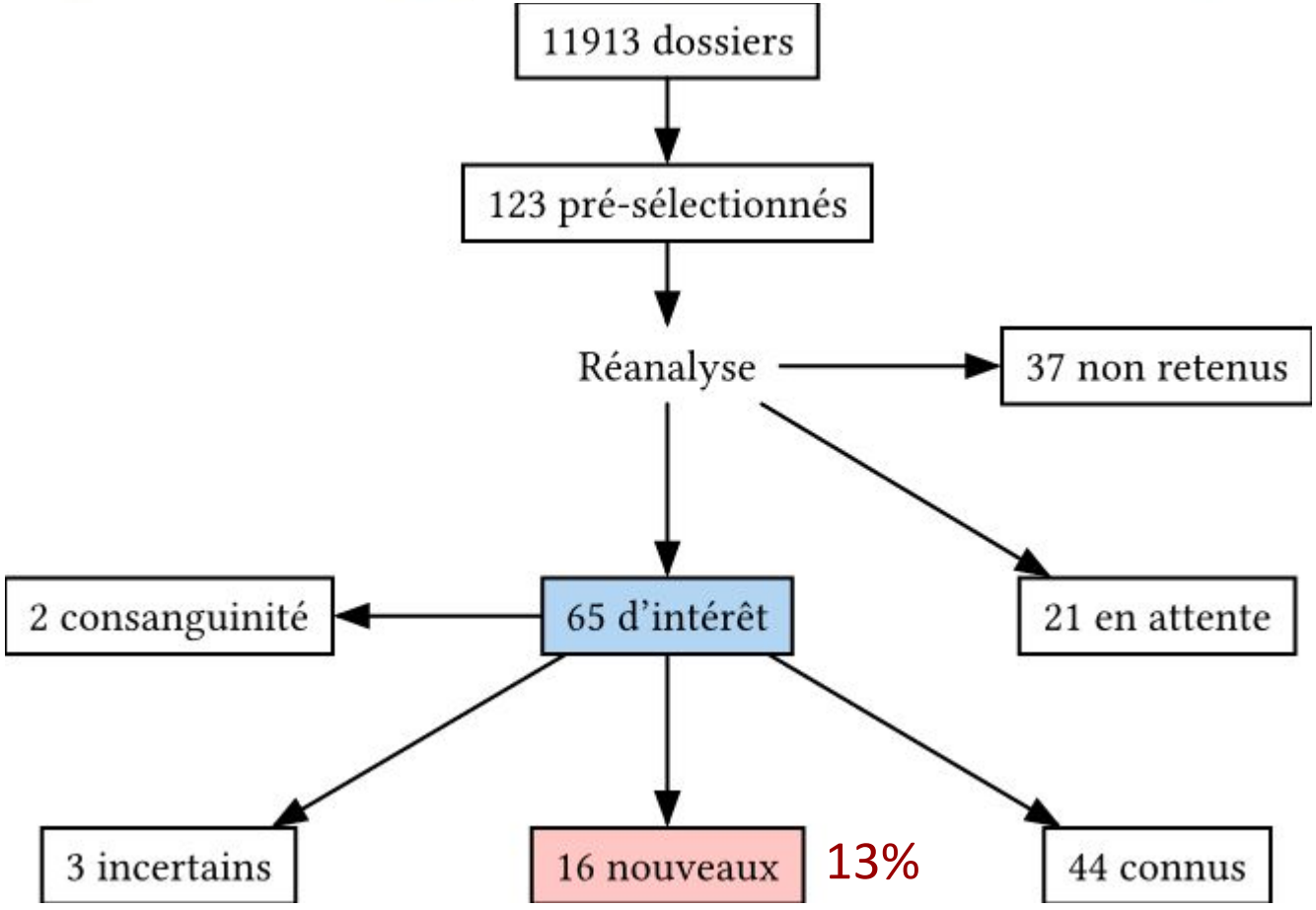
Résultats de la cohorte



Résultats de la cohorte



Résultats de la cohorte

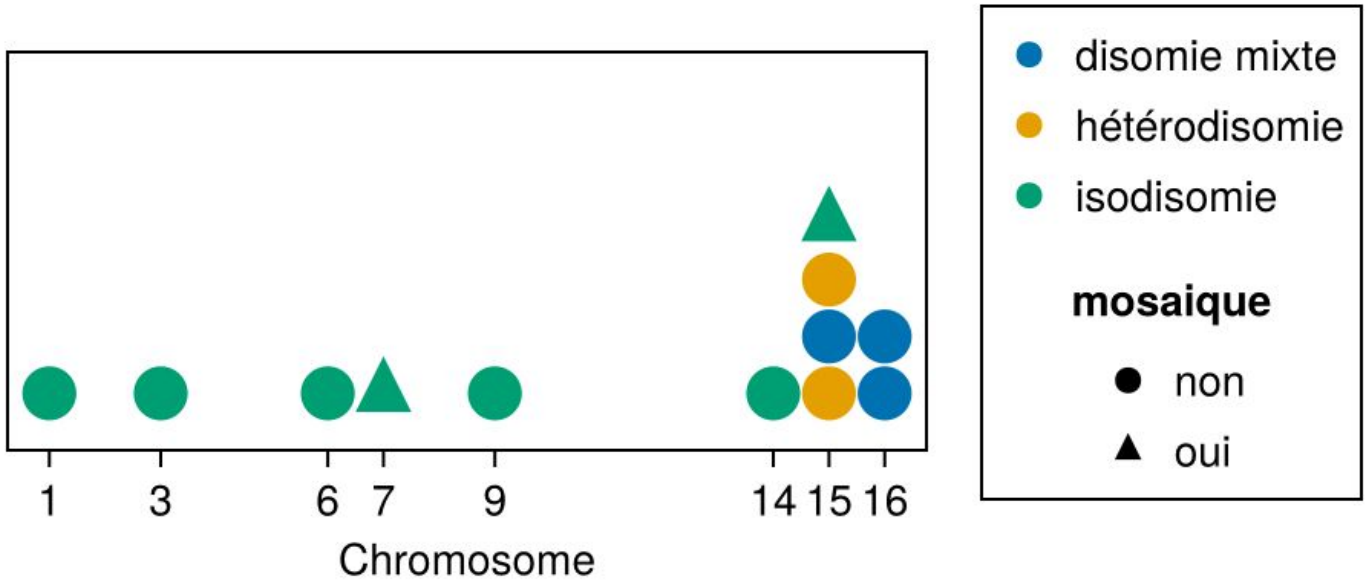


16 nouveaux diagnostics

CNV	gain 15q24.3q26.3 (24.6Mb)
SV	anneau du 13, inv dup del 2q
Aneuploïdie	trisomie 22 en mosaïque

Et 12 disomies !

12 nouvelles disomies



Take-home message

- 1ère grande cohorte de disomie en génome : 0.13% nouveaux diagnostics
- Pré-selection adaptée (13% de nouveaux diagnostics)
- Nouvelles visualisations pangénomiques
- Difficulté des mosaïques…

Discussion clinico-biologique !

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Discussion clinico-biologique !

Questions, suggestions… ? bioinfobio@chu-grenoble.fr

Merci !

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Tristan Celse

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Lucas Gauthier
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Marjorie Willems

Merci !

Merci !

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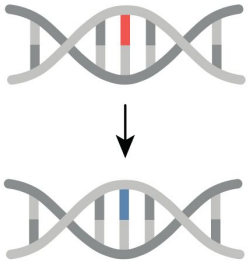
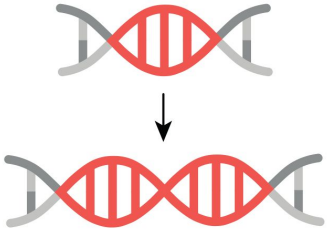
Anne Thomas
Frédéric Tran-Mau-Them
Nathalie Vacher
Alain Viari
Christine Vinciguerra
Anne-Christine Waymel

Génome short-read en trio à Auragen

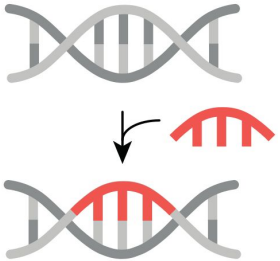
SNV



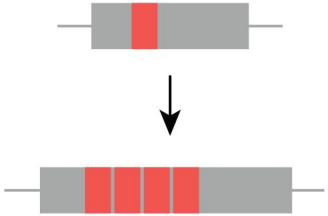
CNV



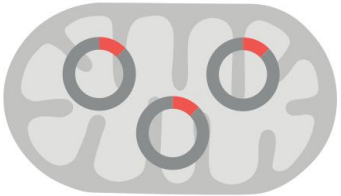
Variant de structure



Expansion de triplets



Mitochondrie



Et les disomies ?

French et al. 2022

Génome short-read en trio à Auragen

délétion SMN1 *de novo*

Variations ponctuelles et petites insertions délétions

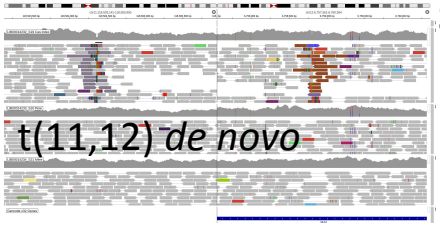
Les variations dans cette section ont été sélectionnées sur les critères **avec parent(s)**, *cf.* matériel et méthodes.

Code couleur allèle : De novo · Homozygote · Hérité du père · Hérité de la mère · Probablement hérité du père · Probablement hérité de la mère · Héritage non déterminé · Autre

Inter.	Gène Panels	Allèle & VAF Ségrégation familiale	HGVSg HGVSc Changement protéique	Fréquence GnomAD v3 Fréquence cohorte	Scores de prédiciton	ClinVar OMIM
	RNU4-2	0.43 Ségrégation familiale	chr12:g.120291839_120291840insA n.64_65insT e.1/1	— —	CADD — GERP++ — PPH2 — SpliceAI —	—

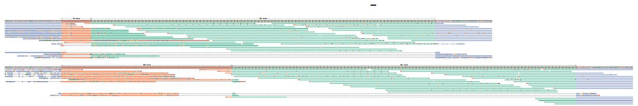
> 99.7% des P/LP priorisés

2020	2021	2022	2023	2024	2025
SNV (curagen), CNV, RoH, QC ciblé	**Introniques profonds, SV, ploïdie**	**Aurapport, CNV régions complexes, composites SNV+CNV, SeqOne**	**Expansions nucléotidique, phenogenius**	**CuragenV2, auramatcher**	**ADN mitochondrial, UTR, page d'accès personnalisée, littérature & aide CR**

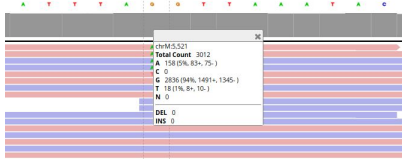


t(11,12) *de novo*

PhenoGenius



MitoDiag



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15000e CR MR/OC

Questions

Ok pour partage seqoia ?

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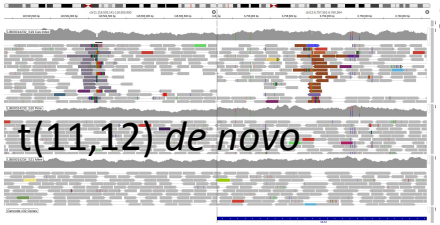
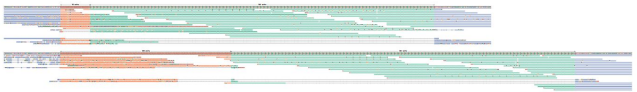
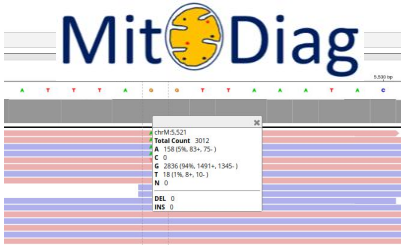


t(11,12) *de novo*

PhenoGenius



MitoDiag



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Quid des disomies?

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