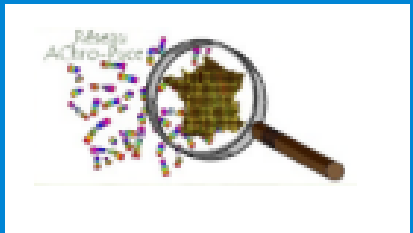
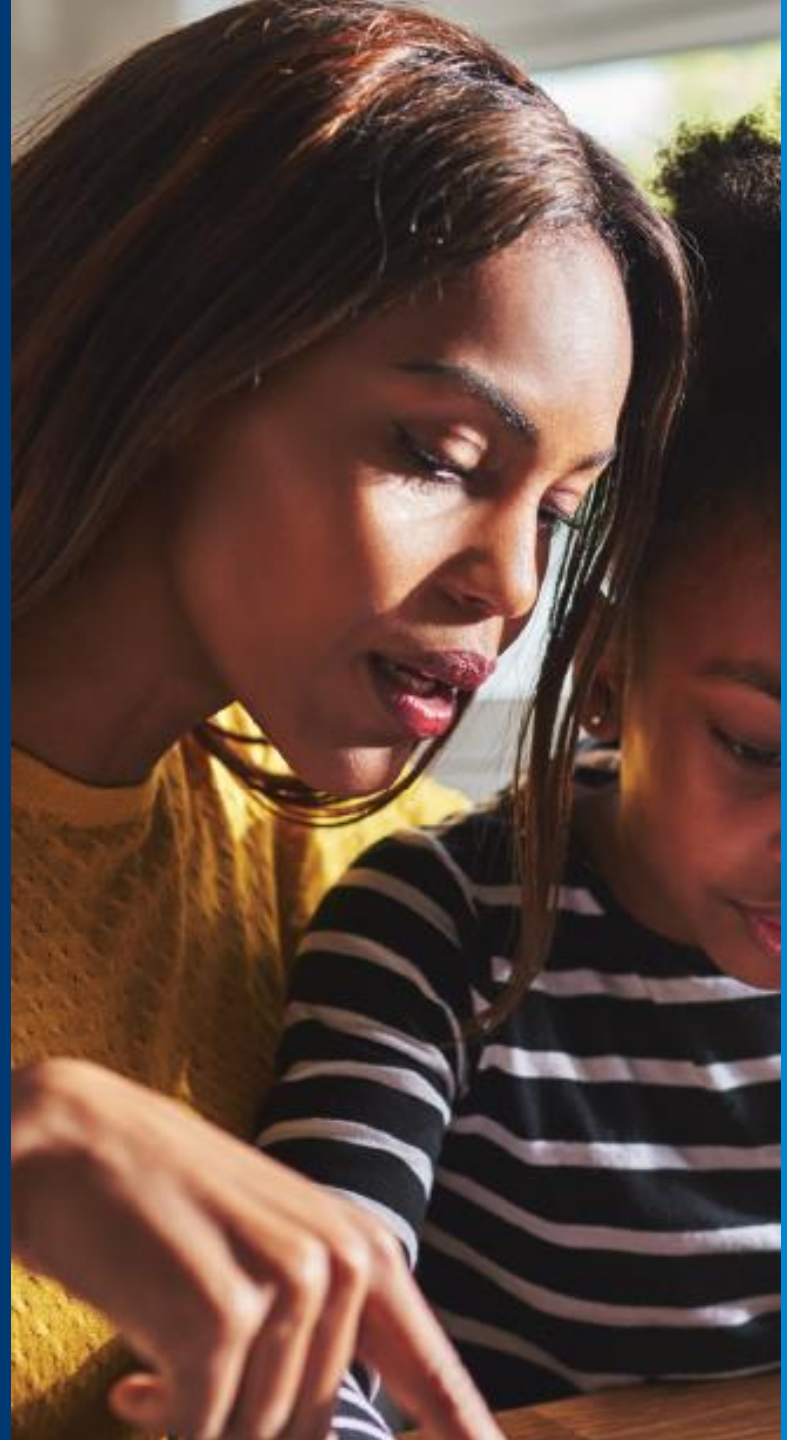
Mise en évidence des del/dup au niveau exonique par technique CGH array dans le cadre du pre et post natal en aval du NGS



Journée ACHRO-PUCE

Roubila Meziani, Ph.D
Manager des ventes France
Diagnostic and Genomics Group – Agilent
roubila.meziani@agilent.com



Agilent
Trusted Answers

PR7000-2403

NGS Results Validation Strategies by CMA differ based on Project Requirements

Towards Enabling Dedicated Project Solution

- Exon focused designs
- Full and easy access to design content
- Easy comparison of designs
- Full design creation flexibility

Catalogue Designs

- GenetiSure Cyto MicroArray

Exon centric array designs
180K CGH - 103 genes with single exon resolution

- GenetiSure PostNatal CGH+SNP 2x400K
- GenetiSure Cancer CGH+SNP 2x400K

Community & Published Designs

- Community Designs

Example: ACD FetalChip CGH+SNP 8x60K

- Published Designs
- Shared Designs (Consortium)

Custom Designs

- Highest density and resolution on market: Database of 29 Million probes available through SureDesign
- Probe design and probe scoring tools available in SureDesign
- Professional Design Service Team available

NGS Results Validation Strategies by CMA differ based on Project Requirements

Towards Enabling Dedicated Project Solution

- Exon focused designs
- Full and easy access to design content
- Easy comparison of designs
- Full design creation flexibility

Catalogue Designs

- GenetiSure Cyto MicroArray -3 designs

Exon centric array designs
180K CGH - 103 genes with single exon resolution

- GenetiSure PostNatal CGH+SNP 2x400K
- GenetiSure Cancer CGH+SNP 2x400K

Community & Published Designs

- Community Designs

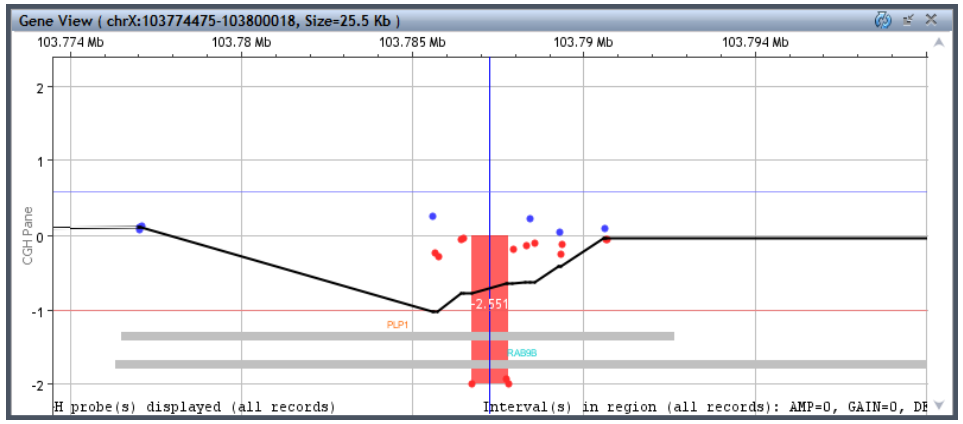
Example: ACD FetalChip CGH+SNP 8x60K

- Published Designs
- Shared Designs (Consortium)

Custom Designs

- Highest density and resolution on market: Database of 29 Million probes available through SureDesign
- Probe design and probe scoring tools available in SureDesign
- Professional Design Service Team available

GenetiSure Cyto Microarray

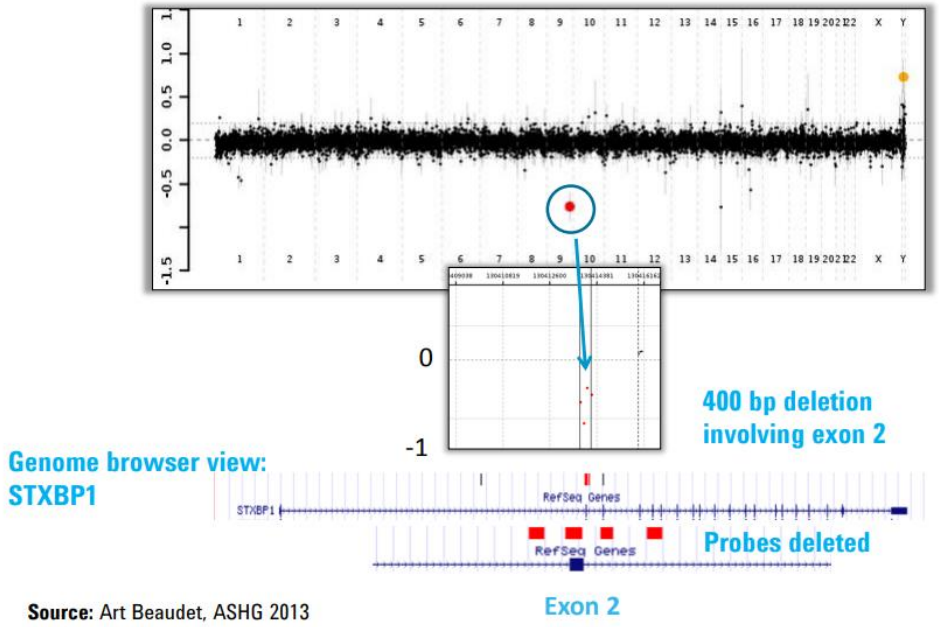


GSCMA – 180K CGH only design

CL Sample NA13434

CN Loss (~1kb, detected only with 3 probes)

Pathogenic deletion of parts of exons 3~4 and the intervening sequence in the PLP1 gene, ChrX q-arm



Genetisure Postnatal 2*400k CGH+SNP

GenetiSure Postnatal 2x400K CGH+SNP	CGH+SNP	078737	2x400K	8106

	GenetiSure Postnatal Research CGH+SNP 2x400K
Catalog part number	G5974A
Number of CGH probes	~ 300,000
Number of targeted CGH probes	~123,000
Median CGH probe spacing	~9.5 Kb overall, 20 Kb backbone
ClinGen/ISCA genes, exon coverage	~ 89% ≥3 probes/exon
Number of SNP probes	~103,000
Copy-neutral LOH resolution	~ 2.5–10 Mb

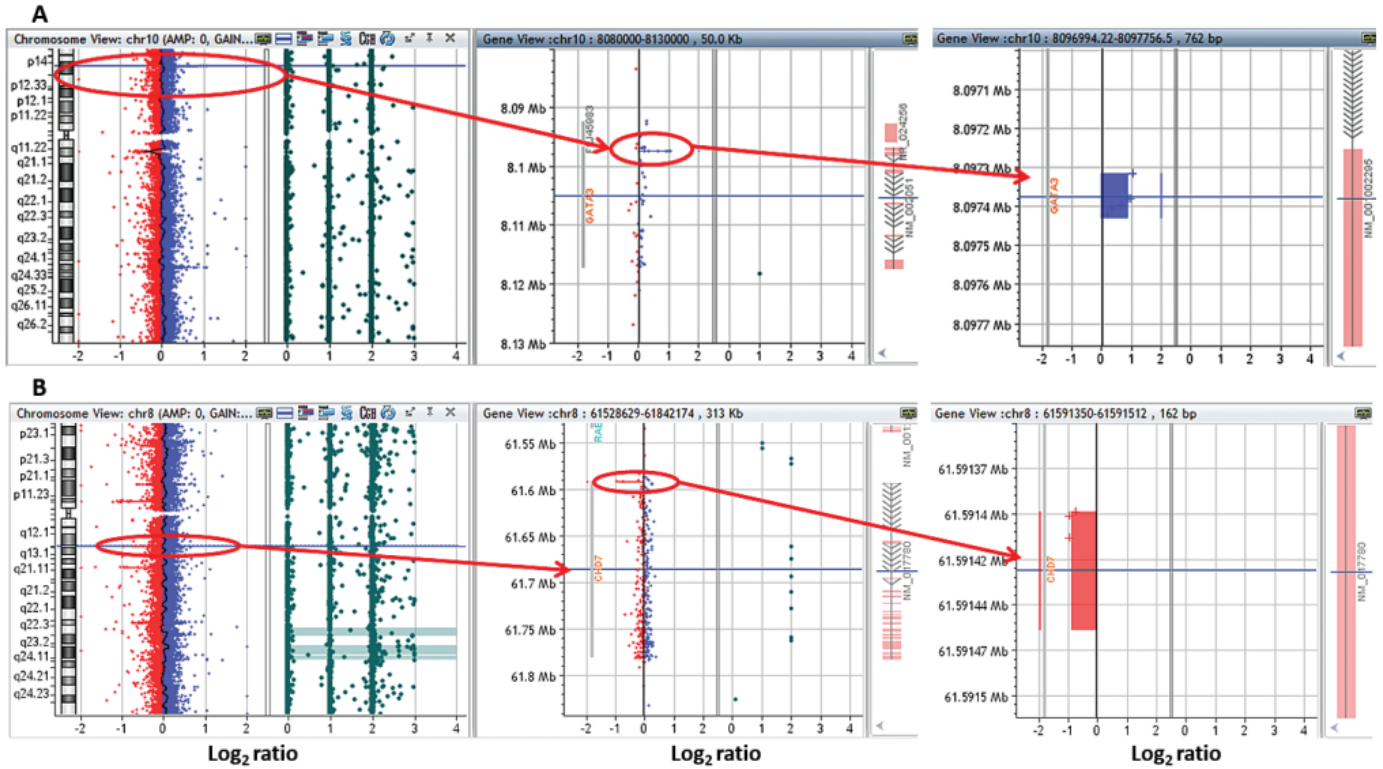


Figure 3. A) A small amplification (~120 bp, blue rectangular region) in a single exon (in pink on the right-hand vertical axis) in the GATA3 gene called using the GenetiSure Postnatal Research CGH+SNP array. B) A very small ~70 bp deletion was detected in a single exon of the CHD7 gene using the array. Views with increased magnification are shown in the middle and right-hand panels. In each case, the array provides increased gene focus, as shown by the presence of many more individual probes, indicated by the red and blue dots.

NGS Results Validation Strategies by CMA differ based on Project Requirements

Towards Enabling Dedicated Project Solution

- Exon focused designs
- Full and easy access to design content
- Easy comparison of designs
- Full design creation flexibility

Catalogue Designs

- GenetiSure Cyto MicroArray

Exon centric array designs
180K CGH - 103 genes with single exon resolution

- GenetiSure PostNatal CGH+SNP 2x400K
- GenetiSure Cancer CGH+SNP 2x400K

Community & Published Designs

- Community Designs

Example: ACD FetalChip CGH+SNP 8x60K

- Published Designs
- Shared Designs (Consortium)

Custom Designs

- Highest density and resolution on market: Database of 29 Million probes available through SureDesign
- Probe design and probe scoring tools available in SureDesign
- Professional Design Service Team available

Example of Published Designs

The custom CGH microarray (AMADID array design IDs: 031220/031221) used for CNV discovery was designed to have good power to detect **single exon CNVs by using 5 probes per exon**, as well as having a dense backbone of ~320k intronic and intergenic probes with a median probe spacing of 2kb. It is composed of **two 1 million probe Agilent arrays** and has been designed to target genes and ultra-conserved elements throughout the human genome.

The **custom exon-resolution CMA is expected to have the highest sensitivity because it targets most protein-coding exons with at least five probes**. These simulations suggested that if we assumed that two probes/baits are sufficient for reliable CNV detection then exon-resolution CMA would be expected to have **98% sensitivity for single exon CNVs**, whereas exome sequencing (which uses a single bait for most exons) would have 31% sensitivity, and the 180K and 60K CMA platforms would have 39% and 17% sensitivity, respectively. However, for CNVs which affect more than 3 exons, both exon-resolution CMA and ES-based CNV ascertainment would be expected to have 99% sensitivity, which exceeds by a wide margin the anticipated sensitivity of low resolution CMA (39% and 69%; Supplement S8a).

NGS Results Validation Strategies by CMA differ based on Project Requirements

Towards Enabling Dedicated Project Solution

- Exon focused designs
- Full and easy access to design content
- Easy comparison of designs
- Full design creation flexibility

Catalogue Designs

- GenetiSure Cyto MicroArray

Exon centric array designs
180K CGH - 103 genes with single exon resolution

- GenetiSure PostNatal CGH+SNP 2x400K
- GenetiSure Cancer CGH+SNP 2x400K

Community & Published Designs

- Community Designs

Example: ACD FetalChip CGH+SNP 8x60K

- Published Designs
- Shared Designs (Consortium)

Custom Designs

- Highest density and resolution on market: Database of 29 Million probes available through SureDesign
- Probe design and probe scoring tools available in SureDesign
- Professional Design Service Team available

Questions ?

roubila.meziani@agilent.com

MERCI