Agilent CytoGenomics 1.5
Streamlining your cytogenetic workflow

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Agilent CytoGenomics 1.5

Take home message

Agilent CytoGenomics software is a workflow based easy to use analysis tool for CGH and CGH+SNP analysis to detect CNC, LOH and UPD
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Constitutional and cancer sample analysis

CGH analysis to detect CNCs:

- Constitutional samples
- Cancer samples: Liquid, Solid, FFPE, up to 10% mosaicism can be detected

SNP analysis to detect LOH/UPD and confirm CGH data:

- Constitutional samples only, no cancer samples and no mosaic detection

* Next version of CytoGenomics software will support SNP analysis for hematological cancer samples with ability to detect as low as 20% clonal fraction

Not approved for use in diagnostic procedures
CytoGenomics is designed for the cytogenetics researcher who needs a simple streamlined software solution for cytogenetic analysis of human samples.

Agilent Genomic Workbench (AGW, previously DNA analytics) is designed for many aspects of DNA research of both human and non-human samples and for the researcher who needs the ability of on the fly tweaking of all aspects of his (cytogenetics) workflow and who is not interested in a simple streamlined solution.
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Result of the cytogenetic analysis: Cyto Report

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**Sample Information**

Array ID: 252983010002_1_1
Global Display Name: US23502418_252983010002_S01_CGH_1010_Aug 10_1_1
Green Sample: European Male (NA12891_v1)
Red Sample: NA09208
Polarity: 1
DerivativeOfLogRatioSTD: 0.197981

**Amp/Del Intervals Table**

<table>
<thead>
<tr>
<th>Location</th>
<th>Size</th>
<th>Cytoband</th>
<th>#Probes</th>
<th>Amp/Del</th>
<th>P-value</th>
<th>Annotations</th>
</tr>
</thead>
</table>
| chr17:24457-5501054 | 6,876,598 | p13.3 - p13.2 | 340     | -0.865466 | 0.008500 | DOC3B, RPH3AL, C7orf97, FAM101B, VPS33, FAM57A, SEM11A, ELPL2P, GLC34, RMT1L, NON, TIMM32, ABR, BHLHA9, TUSC5, YWHAE, CRK, MYO1C, INPP5K, LOC103036951, PITPNA, SLC43A2, SCARF1, RILP, PRPF8...

**LOH Intervals Table**

<table>
<thead>
<tr>
<th>Location</th>
<th>#Probes</th>
<th>LOH Score</th>
<th>Annotations</th>
</tr>
</thead>
</table>
| chr17:22083-5503091 | 84      | 0.035000 | RH3AL, C7orf97, FAM101B, VPS33, FAM57A, SEM11A, ELPL2P, GLC34, RMT1L, NON, TIMM32, ABR, BHLHA9, TUSC5, YWHAE, CRK, MYO1C, INPP5K, LOC103036951, PITPNA, SLC43A2, SCARF1, RILP, PRPF8, TUCD2...

**Analysis Settings**

- Aberration Algorithm: ADM-2
- Threshold: 6.0
- Window Size: 2Kb
- Bin Size: 10
- SNP Copy Number: ON
- LOH: ON
- Fuzzy Zero: OFF
- Combine Replicates (Intra): ON (Array)
- Aberration Filters: minProbes = 3 AND minAvgAbsLogRatio = 0.25 AND maxAberrations = 100000 AND percentPenetration = 0
- Design Level Filters: NONE
- Metric Set Filters: NONE

Design: 029830_20100521
GC Correction: ON
Centralization: ON
SNP CN Confidence Level: 0.95
LOH Threshold: 6.0
Nesting Level: OFF
Genome: hg19
Feature Level Filters: glsSaturated = true OR risSatisfied = true OR glsFeatureUniqR = true OR risFeatNonUnique = true
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Value Proposition

- Streamlining the Cytogenetic data analysis workflow for CNC (copy number changes) and/or cnLOH / UPD detection of samples processed on Agilent SurePrint G3 CGH and CGH+SNP Microarrays.

To enable the Cytogenetic Researcher to analyze a normal CGH (or CGH+SNP) sample in less than 5 minutes, including report generation.
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Streamlined data analysis for Cytogenetic research labs

- Simple and quick workflow for data analysis
- Convenient input and output support allowing for integration with LIMS

Sample info, export from LIMS

Run data analysis

Laboratory LIMS

Cyto report, upload to LIMS

Triage & sign off

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Workflow setup and user roles

- Initial set up: Configuring the Workflow

1. Configure analysis method
2. Configure CytoReport
3. Configure Workflow

- Day to day usage:
  - Technician (manual) / Auto-processing
    1. Upload TIFF images (or FE files)
    2. Map array to sample attributes
    3. Engage configured workflow to run FE (TIFF only) and analysis
  - Scientist
    1. Triage the sample and sign off
    2. Generate the CytoReport

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Powerful algorithms for calling CNC, LOH and UPD

Feature Extraction

Log$_2$ ratio of intensities to call CNCs
No. of uncut alleles to call LOH/UPD

CGH probes
Copy Number Changes

SNP probes
LOH/UPD

ADM-1
Amp/Del calling

ADM-2

SNP CN & LOH
LOH calling
Genotype SNPs using restriction digestion (Alu/Rsa)

We measure the copy number of one allele at each SNP site relative to a known reference

Regions of LOH are located by finding genomic regions with a statistically significant scarcity of heterozygous call

~5-10 Mb LOH/UPD resolution across the entire genome
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Example 1: Consanguineous Sample
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Example 2: Sample with one copy deletion on chr9 p-arm
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Sample Triage – Access to external databases

Preloaded track: DGV-CNV

Link out from aberrations and associated genes to external Databases: UCSC, DGV, OMIM, Entrez

View and compare aberrations in DGV and UCSC genome browser
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Sample Triage – Using CytoGenomics Database

Auto updated tracks based on aberration classification in CytoGenomics Database

Right click on ‘Classification’ allows query for overlapping aberrations in CytoGenomics database: results will be shown as new track along the gene view

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Sample Triage – Sample and Aberration annotation

Add notes to sample
Add notes to aberrations
Suppress aberrations
Classify aberrations
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Multi Sample View

Comparing 2 or more samples side by side
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Additional features

- Workflow Automation Mode for automatic processing of TIFF images and report generation.
- Data upload to ISCA DB via Cartagenia bench.

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System specs

- Client/server system with database (multiple users can access database at the same time).
- Runs on PC (XP, Windows 7).
- Runs on Mac (OS X Leopard and OS X Snow Leopard).
- Supported on both 32 and 64 bit machines.
- Minimum of 4GB of memory needed for 32 bit (8GB for 64 bit).
- Feature extraction is integrated component of CytoGenomics software.

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