Release Notes

Agilent CytoGenomics v5.0.2

Product Number

G1662AA – "CytoGenomics Client 1 year named" license (including Feature Extraction). This license supports installation of one client and server (to host the CytoGenomics database) on one machine. For additional client only installations, which connect to the same database on the central server, additional copies of this license are needed

Overview

CytoGenomics is a cytogenetics research software tool designed to streamline your workflow for processing, analyzing and reporting of cytogenetic measurements. This includes copy number changes and copy neutral Loss of Heterozygosity and Uniparental Disomy data, generated with human samples on Agilent SurePrint G3 CGH-only and CGH+SNP microarray platforms. With CytoGenomics 5.0.1 we now offer an even more streamlined workflow with a highly sophisticated user interface.

CytoGenomics is designed to: (1) import raw TIFF images generated from the Agilent microarray scanner as well as some non-Agilent scanners and (2) run Feature Extraction and perform analysis using customizable workflows. Utilizing the built-in database, CytoGenomics allows the user to store and query samples and aberrations by classification information or location information. In addition, users can connect from aberration annotations to OMIM, DGV, and Entrez public databases to analyze sample aberrations. During sample review, multiple users can annotate, edit and classify aberrations with full record traceability and generate signed-off reports on processed samples.

CytoGenomics supports an enterprise server/client model for concurrent usage and collaboration. With strong analysis algorithms, data visualization, data management and reporting functionality, CytoGenomics software extends the Agilent microarray based product offerings into a complete cytogenetic clinical research solution.

Key new features (added in v5.0)

- Support for human genome build 38 (hg38), with continued support for hg17, hg18, and hg19.
- Increased database functionality that allows the server to store over 100,000 sample records with no impact on software performance.
- Expanded tools for displaying tracks in Triage View, including viewing tracks in different modes (dense, pack, squish), rearranging tracks by dragging and dropping, and displaying directions of genes and exons.
- Improved flexibility for assigning analysis methods, including the ability to assign different analysis methods to different arrays within a multipack in the Auto-Processing default settings.
- Tools for configuring custom sample attributes and exporting custom templates for sample attribute files (SAF).
- New process for bulk sign off of multiple sample records at the same time.
- Tools for saving your preferred Triage View layout to your profile and sharing saved layouts among CytoGenomics users on the same server.

- The ability to open up to 24 samples at a time in Triage View, greatly improving your ability to compare results across multiple samples.
- Support for display of the Triage View window across multiple monitors connected to your workstation.
- The ability to create custom user roles by selecting from a predefined set of user privileges.
- Expanded tools for viewing and comparing QC metric results across multiple runs or timelines for data trending purposes.
- Support for additional columns in a track BED file.
- Updated tracks bundled with the software.
- Ability to configure allocated application and workflow memory easily while in the application.
- Ability to save Single Cell reference as an external reference after the analysis is complete and evaluated.
- New QC report for the Single Cell reference pair (Male vs. Female or Female vs. Male) that allows users to evaluate their reference hybridization conditions closely.
- A new enhanced gridding feature used in the Feature Extraction (FE) protocols that come preloaded with Feature Extraction for CytoGenomics. The gridding enhancements were designed to improve automatic gridding in array images of lower quality, including those with non-linear features. Array images that may have previously received a "failed grid" error and require manual gridding can now be processed successfully using the enhanced algorithm. Note: If you have been using a previous version of CytoGenomics and want to start using the new FE protocols with enhanced gridding, Agilent recommends validating the new protocols before incorporating into your standard procedures.

Installation Instructions

New Installation

- Refer to the installation guide available at http://www.agilent.com/cs/library/usermanuals/public/GEN-MAN-G1662-90057.pdf

Note: Unlike previous CytoGenomics upgrades, installation of CytoGenomics 5.0.2 does not involve uninstalling the previous version of CytoGenomics, i.e., v3.0 or v4.0. Both versions can co-exist on the same machine. Once the data migration is complete and verified, you can uninstall the previous version manually.

Points to note regarding results generated in v5.0.2

- With the new gridding algorithm for FE integrated in 5.0, there may be some minor differences in some QC metric values and aberration calls between 4.0.x and 5.0 when the analysis includes feature extraction of a tiff image.
  To recreate the gridding algorithm used in 4.0.x, create a new protocol in Feature Extraction for CytoGenomics 5.0.2 with 'Use Enhanced Gridding' setting set to False. See the Feature Extraction for CytoGenomics 5.0 User Guide for instructions.
- In previous versions of FE, the Background Peak Shifting algorithm was only applied to Agilent arrays, and was not applied to non-Agilent arrays. This discrepancy has been fixed in FE for CytoGenomics 5.0.2. This fix might result in differences in the FE output file for non-Agilent arrays when compared to earlier versions of FE for CytoGenomics. These differences in the FE output file could further result in different QC metric results and aberration calls for the sample.
- The "Multisample" view for viewing workflow results was removed from CytoGenomics 5.0. CytoGenomics users are advised to use the Triage View to triage multiple samples (up to 24 at a time) with no restriction on the designs and analysis methods used among the samples being triaged.

- For CGH+SNP arrays, CytoGenomics 5.0 includes changes in how LOH intervals near the centromere are reported. In v4.0.3, LOH intervals were reported across p-q arm. In v5.0, this issue was corrected, resulting in either reporting the LOH interval as ending at the centromere or not reporting the interval at all if it does not cross the threshold.

Migrating data from the previous version of CytoGenomics

User can migrate their data from version 3.0 or 4.0 to version 5.0.2 using the new Migration Utility application. At the completion of installation of CytoGenomics 5.0.2, you are automatically prompted to launch the Migration Utility application, but you can choose to perform the migration at a later time. Please be aware, however, if you choose to migrate data at a later time, all newly processed samples in v5.0.2 will be lost and have to be reanalyzed again. The migration process copies the data from the previous version of the database into the new database structure.

Migration to v5.0.2 is supported from v3.0.x and v4.0.x. The process for migrating your data is described below.

Instructions for migrating from v3.0.x or v4.0.x (if not performed immediately after installation of v5.0.2

- Launch the 'MigrationUtility.exe' application from the client installation directory.
- Before proceeding with the migration, read the pre-requisites on the login screen carefully.
- Login with the installed user.
  Note: Installed user needs to have an enabled account with the administrator privileges on the old server to migrate the data.
- Enter the details for the old server.
- Click the "Start Migration" button.
- Confirm pre-requisites have been met to proceed with migration.

Migration from versions prior to v3.0

- First, upgrade the previous version (v1.0, 1.5, 2.0, 2.5, 2.7, or 2.9) to version 3.0 or 4.0 using CytoGenomics 3.0 installer or CytoGenomics 4.0 installer. Agilent Informatics Support team can provide that CytoGenomics installer upon request.
- Then, follow the steps specified in above section, *Instructions for migrating from v3.0.x or v4.0.x* .

Points to note regarding upgrading application from v5.0.0 or v5.0.1 to v5.0.2

Windows systems:

If you are using CytoGenomics 5.0.1 or 5.0.0 and want to upgrade to CytoGenomics 5.0.2, you only need to upgrade the CytoGenomics client application. You do not need to upgrade to the CytoGenomics server application or migrate data from the previous version to 5.0.2.

- Download Agilent CytoGenomics 5.0.2 from the Agilent website and check the system requirements.
- Double-click the Agilent CytoGenomics 5.0.2 application file that you downloaded from Agilent. The InstallAnywhere dialog box opens, then the installation wizard opens to the Introduction screen.
- Click Next.
- Click OK in the message box that notifies you to uninstall the client. The uninstaller for CytoGenomics 5.0.0 or 5.0.1 launches.
- Click Next in the uninstaller.
- Choose "Uninstall Specific Features" and click Next.
- Select Client and click Uninstall.

- Click Yes in the confirmation message box to confirm that you want to uninstall the CytoGenomics 5.0.0 or 5.0.1 client. At the completion of the uninstallation, the installation wizard for CytoGenomics 5.0.2 reopens.
- In the installation wizard, select Only Client on the Choose Install Set screen and click Next.
- Continue the installation wizard to finish the client installation for v5.0.2.

Macintosh systems:

The auto-uninstaller is not supported on Macintosh systems, which means you will need to first uninstall the CytoGenomics 5.0.0 or 5.0.1 client before launching the CytoGenomics 5.0.2 application file. The instructions for this process are below.

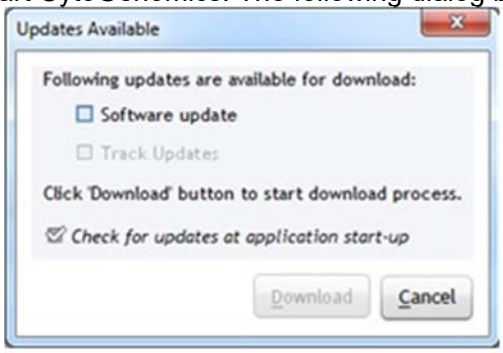
- Launch the uninstaller for Agilent CytoGenomics 5.0.0 or 5.0.1. Enter the credentials for the administrator.
- Click Next, then click Next again.
- Choose "Uninstall Specific Features" and click Next.
- Select Client and click Uninstall.
- Click Yes in the confirmation message box to confirm that you want to uninstall the CytoGenomics client. At the completion of the uninstallation, click Done to close the uninstaller.
- Download Agilent CytoGenomics 5.0.2 from the Agilent website and check the system requirements.
- Double-click the Agilent CytoGenomics 5.0.2 application file that you downloaded from Agilent. The InstallAnywhere dialog box opens, then the installation wizard opens to the Introduction screen.
- Click Next.
- Select "Only Client" and proceed with the installation of v5.0.2.

Upgrading from v5.0.1 via the Agilent cloud

Note: Cloud update to CytoGenomics 5.0.2 is only supported from CytoGenomics 5.0.1. If CytoGenomics 5.0.1 is installed on a machine that is behind a proxy server, make sure required proxy credentials are provided on the Admin > Partners > Set Proxy Settings screen.

To automatically download these software updates:

1. Restart CytoGenomics. The following dialog box automatically opens.



2. Mark the Software update check box in the Updates Available dialog box. This will enable the Download button.
3. Click Download. The Confirm message box opens asking you to confirm that you want to start downloading software update files.
4. Click OK to start the download process. A Progress Status message opens. The application is unavailable for use during the software update download.
5. Once the download is complete, a Download Successful message displays, and counts down from 5 seconds to close the application. Skip the countdown by clicking OK.
6. A dialog box indicates that the application has been updated. Click OK to launch CytoGenomics.

7. Upon logging in, a dialog box indicates that the Agilent CytoGenomics application was upgraded successfully. Click OK to continue.

Default and preloaded content

The hg19 version of the design file for the SurePrint G3 Human CGH Microarray 4X180K (022060) design is provided as part of CytoGenomics 5.0.2 installation.

Hg18 and hg19 version design files for the below listed commonly used designs can be downloaded from the CytoGenomics download page (https://www.agilent.com/en/download-agilent-cytogenomics-software):

- SurePrint G3 Human CGH+SNP Microarray 2X400K (028081)
- SurePrint G3 Human CGH+SNP ISCA Microarray 4X180K (029830)
- SurePrint G3 Cancer CGH+SNP Microarray 4x180K (030587), hg19 only
- SurePrint G3 Human CGH Microarray 4X180K (031748)
- SurePrint G3 Human CGH Microarray 2X105 (031750)
- SurePrint G3 Human CGH Microarray 8X60K (031746)
- SurePrint G3 Human CGH Microarray 4X180K (022060)
- SurePrint G3 Human CGH Microarray 8X60K (021924)
- SurePrint HD Human CGH Microarray 4X44K (014950)
- SurePrint HD Human CGH ISCA Microarray 4X44K (031747)

The following frequently used tracks are provided upon installation:

- Genes_hg17_Jan2018
- Genes_hg18_Jan2018
- Genes_hg19_Jan2018
- Genes_hg38_Jan2018
- Agilent_SureFISH_hg19_Nov2011
- Agilent_SureFISH_hg38_Jan2018
- Agilent_Female_CNV_Reference_hg19_Nov2011
- Agilent_Female_CNV_Reference_hg38_Jan2018
- Agilent_Male_CNV_Reference_hg19_Nov2011
- Agilent_Male_CNV_Reference_hg38_Jan2018
- CNV_DGV_hg18_May2016
- CNV_DGV_hg19_May2016
- CNV_DGV_hg38_May2016
- CpG_Island_hg18_Nov2011
- CpG_Island_hg19_Nov2011
- CpG_Island_hg38_Jan2018
- Cytoband_hg18_Nov2011
- Cytoband_hg19_Jan2018
- Cytoband_hg38_Jan2018
- miRNAs_hg18_Nov2011
- miRNAs_hg19_Nov2011
- miRNAs_hg38_Jan2018
- Multi_Transcripts_For_Genes_hg18_Jan2018
- Multi_Transcripts_For_Genes_hg19_Jan2018
- Multi_Transcripts_For_Genes_hg38_Jan2018
- OMIM_hg18_Jan2018
- OMIM_hg19_Jan2018
- OMIM_hg38_Jan2018
- Pseudo_Autosomal_Regions_hg18_Nov2011

- Pseudo_Autosomal_Regions_hg19_Nov2011
- Pseudo_Autosomal_Regions_hg38_Jan2018

Agilent recommended Feature Extraction protocols for CGH microarrays (CytoCGH_0500_1x_Nov17, CytoCGH_0500_2x_Nov17, CytoCGH_0500_4x_Nov17 and CytoCGH_0500_8x_Nov17, CytoCGH_0500_SingleCell_Nov17) and QC metric sets for CGH microarrays (CytoCGH_QCMT_1x_Nov17, CytoCGH_QCMT_2x_Nov17, CytoCGH_QCMT_4x_Nov17 and CytoCGH_QCMT_8x_Nov17,CytoCGH_QCMT_SingleCell_Nov17) are provided as default.

Agilent recommended CGH analysis settings (Default Analysis Method - CGH v2); CGH+SNP analysis settings (Default Analysis Method – CGH + SNP v2); Mosaic analysis settings (Mosaic Analysis Method) and Single cell analysis settings (Single Cell Small Aberration Analysis Method, Single Cell Long Low Aberration Analysis Method, and Single Cell Recommended Analysis method) are provided as default.

Agilent Feature Extraction for CytoGenomics

Overview

Agilent Feature Extraction (FE) for CytoGenomics is a component within CytoGenomics. FE performs TIFF image processing, background subtraction and normalization of microarray data. The user has the option of using this component as part of a CytoGenomics workflow or as a standalone tool.

System Requirements for Agilent CytoGenomics

Requirements for Windows systems

- Operating system: 64-bit Windows 7 Enterprise, 64-bit Windows 10 Enterprise or Professional, or Windows Server 2012 (Note: For all of these operating systems, the regional setting must be set to English)
- Programs: Any program that enables you to open PDF files (for example, Adobe Reader)
- Processor: > 2 GHz (> 3 GHz recommended)
- Working memory (RAM): 4 GB (8 GB recommended)
- Hard disk space: 500 GB
- Display Resolution 1280 x 768 or higher

Requirements for Macintosh systems

- Operating System: Macintosh OS Sierra or Macintosh OS X El Capitan
- Programs: Java 1.8 and any program that enables you to open PDF files (for example, Adobe Reader)
- Any program that enables you to open PDF files (for example, Adobe Reader)
- Processor: 3 GHz Intel Core 2 Duo CPU or better
- Working memory (RAM): 4 GB (8 GB recommended)
- Hard disk space: 40 GB (For analysis of large datasets, more space is required)
- Display resolution 1280 x 768 or higher

In an effort to improve the performance and overall user experience with CytoGenomics, as of version 4.0.3, CytoGenomics is no longer supported on 32-bit machines.

Issues Fixed in CytoGenomics 5.0.2

- Protocol settings in custom FE protocols may be overwritten with default settings during an extraction. (TT ID #284364)

- In some cases, when importing an analysis method from a previous version of CytoGenomics, the Genomic Region Filter parameter may not be correctly imported. (TT ID #285410)
- When exporting the table from the Sample Review Screen, the exported report may incorrectly display some values as empty or NA. (TT ID #283538)
- The link to the FE QC Report in the View Reports dialog box does not always work. (TT ID #283429)
- In Triage View and Legacy Triage windows, the tooltip that displays information on individual exons in a track is not functioning. (TT ID #285118)
- In the Legacy Triage window, re-sizing adjustments made in the Gene View revert to the default settings after closing and re-opening the window. (TT ID #284614)
- In the QC Metrics dialog box, the QC metric set selected in the drop-down list is not always the metric set that was used in the analysis. (TT ID# 284419)
- Data migration from v4.0 to v5.0 fails when the Score column of a track file contains invalid content. (TT ID #285122)
- In the Legacy Triage window, modifying the size of the data points from the View Preferences dialog box does not always work as expected. (TT ID #285432)
- When the Triage View is open for multiple samples, genotype reference files generated from the Secondary Analysis menu differ between CytoGenomics 4.0 and CytoGenomics 5.0. (TT ID #285556)
- Application fails to calculate SNP QC Metrics when the sample's design includes CGH probes on all chromosomes, but only includes SNP probes on a few chromosomes. (TT # 285874)

Known Issues for CytoGenomics 5.0.2

- Single Cell Triage View can take a long time to refresh after changes are made to the view preferences. (TT ID #279272)
- In Triage View, filtering the intervals of a track displayed in the Gene View does not work as expected when filter conditions include two of the same attributes. (TT ID #282443)
- In Triage View, the toolips used to identify dynamic tracks and aberrations tracks do not always close automatically. (TT ID #282526)
- In the Legacy Triage window, track names are not displayed when panning option is selected. (TT ID #282557)
- On some machines, the Postgres database fails to startup after installation. (TT ID #282641)
- Because Cartagenia BENCH Lab CNV does not support hg38 data, it fails to parse reports for hg38 samples uploaded through CytoGenomics. (TT # 285873)

Known issues for Feature Extraction for CytoGenomics 5.0.2

- Changing the color scale does not work while in grid mode. If the user attempts to change color scale from "All Channels" to either "Red Channel" or "Green Channel," the color scale does change. (TT ID #2309)
- In rare instances, the Switch to Configure Mode button is not enabled after the extraction is complete. The extraction must be closed and re-opened to enable the Config / Run Mode toggle button. (TT ID #2069)
- The grid template that is currently in use during an extraction can be removed, causing the extraction to fail. (TT ID #2042)
- Viewing the scan properties can cause the image to appear distorted. Minimizing followed by reopening the image is needed to correct the issue. (TT ID #1959)

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