Chromosome Analysis Suite (ChAS) v4.2

New features and improvements

- Copy number segments can be listed in order of priority based on annotation overlap

- New links to external sources such as ClinGen, DECIPHER and gnomAD

- Additional annotation content visible in the ChAS Browser

- Notification when new annotation file(s), NetAffxGenomicAnnotation, is available for download

- Updated and customizable ISCN 2020 nomenclature

- Automatically run analysis on available cel files

- Updated ISCN LOH microarray nomenclature to include copy number state

- Updates to ClinVar Export which no longer require certain fields as mandatory

- Automatic naming of txt file exports, using the cychp file name, for the Segment and QC Tables

Changes and updates

- ChAS v4.2 does not support upgrades from ChAS v4.1 (or earlier). Before installing ChAS v4.2, you must use the Windows® **Add/Remove Program** feature to remove any previous version of ChAS. After the uninstall is complete, double-click on the ChAS v4.2 installer, then follow the installation prompts.

- While uninstalling ChAS v4.1 (or earlier), the installer automatically archives all previous ChAS library files into the following folder: C:\Affymetrix\ChAS\Library\Archived_ChAS_Lib_Files

- New library files for all CytoScan and OncoScan arrays are required for ChAS v4.2. After the installation/upgrade, you must download the latest library files within ChAS or copy the contents of the Analysis Files from the zip package(s) available on the website.

- New NetAffxGenomicAnnotation files are required to use Segment Prioritization in ChAS 4.2.

- The computer must be on the internet in order to receive notifications when updated NetAffxGenomicAnnotation files are available. NetAffxGenomicAnnotations are updated quarterly, if your computer is not on the internet, please contact Technical Support for update NetAffxGenomicAnnotation files.

- The ChAS 4.2 and ChAS 4.1 installers removed the installation of MSV. If you need MSV, please install RHAS 1.0.

- There is no longer a 'Database only' installer option for ChAS 4.1 or higher.

- ChAS Database Loader (CDL) is included in the ChAS Browser starting with ChAS 4.1. It is no longer a separate application.

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Recommended and minimum requirements

Table 1 Software

System Properties	Recommended System Requirements	Minimum System Requirements
Processor	3 GHz (or greater) Pentium Quad Core Processor	3 GHz (or greater) Pentium Dual Core Processor
64-bit Windows Operating System and Web Browser	Windows 10 Internet Explorer 11.0 (or above) or Windows Edge	Windows 10 Internet Explorer 11.0 (or above) or Windows Edge
Available Disk Space	250 GB HD + data storage	150 GB HD + data storage
Free Disk Space Required at Installation	$\geq$ 5 GB	$\geq$ 5 GB
RAM	16 GB	8 GB

Library file packages

Table 2 Available Library file packages

Array name	hg19	hg38
CytoScan HD	CytoScanHD_Array_Analysis_Files_NA33.r8.zip	CytoScanHD_Array_Analysis_Files_NA36.r5.zip
CytoScan 750K	CytoScan750K_Array_Analysis_Files_NA33.r8.zip	CytoScan750K_Array_Analysis_Files_NA36.r5.zip
CytoScan Optima	CytoScanOptima_Array_Analysis_Files_NA33.r8.zip	CytoScanOptima_Array_Analysis_Files_NA36.r5.zip
CytoScan XON	CytoScan_XON_Array_Analysis_files_hg19.r6.zip	CytoScan_XON_Array_Analysis_Files_hg38.r6.zip
OncoScan CNV Plus	OncoScan_Array_Analysis_Files_NA33.r8.zip	OncoScan_Array_Analysis_Files_NA36.r5.zip
OncoScan CNV	OncoScan_CNV_Analysis_Files_NA33.r6.zip	OncoScan_CNV_Analysis_Files_NA36.r5.zip
CytoScan HTCMA	CytoScan_HTCMA_96_ChAS_Files_hg19.r2.zip	CytoScan_HTCMA_96_ChAS_Files_hg38.r2.zip

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Known issues in v4.2

- More than 5GB of hard drive space is required for installation. The computer must be restarted after clearing space on the hard drive in order for the installer to recognize there is > 5GB

- If you are publishing data, merging data, or restoring/backing up a database, please do not interrupt the process. Let the database process complete, otherwise, the database will be unusable.

- If you are running the AutoCelAnalysis feature with folders on a server and lose internet connection, the "Retry" option sometimes does not work. To continue on, stop the application, restart ChAS, and relaunch the AutoCelAnalysis.

- When using the AutoCelAnalysis feature, it is a best practice to not use any spaces in the input, output and archive folders.

Known ChAS issues not addressed in v4.2

- It may take up to 30 minutes to remap a database containing ~150,000 segments.

- After a secure connection between ChAS Browser and ChAS Server is established, the message "*This site is not secure*" may appear upon opening the Database

- Tools page. If this message appears, refresh the window, then try again. Contact technical support for information on using a self-signed certificate when communicating with the ChAS DB.

- No message is displayed when exporting BAF to IGV for a CYCHP file (processed prior to ChAS v3.2) and therefore will not contain BAF information.

- In the Analysis Workflow, when exporting OncoScan CNV Plus somatic mutations, the start and stop column values are identical. This is different from the start and stop values in the Variants Table in ChAS in which they are offset by 1 bp.

- The message "*A connection attempt failed because the connected part did not properly respond after a period of time, or established connection failed because connected host has failed to respond*" may appear when you are connecting to a network drive. If this message appears, check your network connection or contact your IT department for assistance.

- Do not export or save your files to a root drive (example: C:\). Always use a sub- folder(s) (within the root drive) to store your exports or saved files (example: C:\ChAS\My_Exports).

- PDF exports are updated so that certain columns that can span multiple pages in tables are truncated into a single page. For example, when exporting the **Genes** column from the Segments Table (for a large segment), its cell may span several pages. The PDF writer truncates the information in that cell into a single page. If you want the full list of contents from that column, it is recommended that you export the Segments Table in 'Paragraph Style'.

- When restoring a database, make sure you do not query the database until the database restore is successfully completed.

- On Windows 10 systems, if you select the Database Tools and nothing is displayed, check that your user account control setting is set On.

- In some cases, .NET framework may not be installed on your system. If it is not, it must be installed manually.

- If creating a custom reference model file (specifically on Spanish and Chinese Windows operating systems), the computer must be rebooted in order to use these custom reference model file.

- An error message:
  The current type, Affymetrix.AnalaysisApplication.Infrastruction.IAnalysisDta, is an interface and cannot be constructed. Are you missing a type mapping? may appear after setting your input path. Click **OK** and continue. These paths will indeed be saved and the software will continue.

- An unexpected error message is displayed if the user selects **This PC** or **Network** to save an exported DOCX/PDF report. Make sure you save your report in a valid path location.

- If using Microsoft Edge, a message *Don't let this page create more messages* appears. The workaround for this is to close Microsoft Edge and re-login to the Database Tool page again.

- After installing and launching ChAS, an error message *ChAS database cannot be contacted. Server at "<server name>" did not respond* may appear. Click **OK** to acknowledge this message. To resolve this:

  a. Close ChAS, then right-click on the ChAS Desktop icon.

  b. From its right-click menu, select **Properties**.

  c. Select the **Compatibility** tab, then go to the Privilege Level section.

  d. Check the **Run this program as an administrator** check box, then click **OK**.

  e. Double-click on the ChAS Desktop icon to start ChAS again.

- Windows Server 2008 R2 Standard is supported, however, the installer will not complete on this Server's Enterprise edition.

- If a database has been opened for an extended period, the error code 500 may appear. If this error code appears, close, then relaunch ChAS.

- When submitting an analysis with special characters in the filename, the analysis will fail. Make sure only valid characters are used in your filename.

- When two users publish the same sample to the database, a warning message alerts the second user that the file already exists in the database. The user can choose to cancel or override the existing sample. There is no mechanism to revert to an older stat in this software version. In this case, a method to avoid unintentional re-analysis of the same sample/segment is recommended.

- The Analysis Workflow cannot create a CYCHP file if the file name contains a single quote ('), therefore do not use single (') in your ChAS filenames.

- In the Process Pipeline>Edits>Details> Log tab, Materially Modified Time and By values are not cleared out of their respective fields when you revert changes.

- Export of large amounts of data to TXT file from ChAS may contain quantities of characters in a single field that MS Excel cannot process. This is a limitation of Excel, but should be noted when exporting annotation columns with very large segments.

- Not all user-editable AED file fields can be edited from within the AED Editor. Some basic values (Start, Stop, Type) cannot be edited in the AED Editor table directly. You must use **View/Edit Annotation Properties...** for editing those particular fields in the annotation of interest.

- In rare cases, the chromosomal location for a particular OMIM gene or disease given on the OMIM site is different than the location in the ChAS browser that brought the user to that page. The Browser annotation track **OMIM** (which is impacted) is now called **Old OMIM**. The newer OMIM tracks **OMIM Genes** and **OMIM Phenotype Loci** are not known to be impacted by the issue described below. This is because a small number of these discrepancies (~3%) are the result of two bioinformatics issues.

  – First, OMIM provides a gene name field that is used to identify the RefSeq gene for the disease. In doing so, OMIM also provides alternative names and symbols in the same field. Unfortunately these alternative symbols often now refer to a different RefSeq gene than the primary symbol. As a result instead of mapping just the correct gene, the additional genes are mapped to other locations, producing links in the incorrect location in the ChAS browser.

– Second, OMIM does not provide mapping of the gene or region at the level of chromosomal coordinates. To get this information for use in the ChAS browser the RefSeq genes are aligned to the genome as part of the NetAffx process. Due to different parameter settings, filters, and builds of the genome some differences in locations are observed (Note, less than 1% of the genes map to a different Cytoband than is provided by OMIM).

Note: All OMIM data should be verified by linking out to the OMIM website (where the data's source was originally curated).

• In extremely rare cases, an OMIM gene or disease is not present in the OMIM track of the ChAS browser. This may be because OMIM data has been updated since NetAffx last downloaded data used to create the browser tracks. Always confirm any interpretations of data with the most current information available from the UCSC Browser or the OMIM database by linking out to these resources from within ChAS. Another possibility may be because the gene or region of interest maps to a special region of the genome that is not able to be displayed in the ChAS browser. Other instances why regions cannot be displayed in the ChAS browser are:

– When several genomic segments are known to be a part of a particular chromosome, but have not been formally assigned to a position on the genome.

– When four alternate haplotypes (for regions on Chromosome 5, 6, and 22) are not part of the reference build of the genome.