Features:

Variant Database
• Historical Database
• Pathogenicity Calling Information
• Pathogenicity Call Supporting Information
• Linkage to External Databases
• Automated Quality Control
• Accessibility
• User Management, Audit Trail, Access Control

Cool Tools
• Custom Report Builder
• Customer Web Portal
• Automated Informatics Pipeline
• Customizable Workflow Builder
• Sample Comparison
• Custom Filtering
• Artifact Flagging
• Process Quality Control
• Positive Control Verification
• Automatic BED file builder with regions of clinical significance

Developed in collaboration with Mayo Clinic
Developed in collaboration with the Laboratory Medicine, Information Technology and Health Science Research departments of Mayo Clinic, Geneticist Assistant NGS Interpretative Workbench is a unique tool for the management, control, visualization, functional interpretation and historical knowledge base of next generation sequencing Whole Exome data or Disease Panels targeted at specific genes for the purpose of identifying potentially pathogenic variants associated with specific conditions such as hereditary colon cancer and others.

Geneticist Assistant is compatible with data processed from all leading next generation sequencing platforms including Ion Torrent, Illumina and Roche platforms. The program accepts standardized BAM and VCF files, and includes information from the following sources:

**Functional Prediction information:**
- SIFT, PolyPhen-2, LRT, MutationTaster, FATHMM, CADD & MutationAssessor

**Disease association:**
- ClinVar, OMIM, CIViC & COSMIC*
- 1000 Genomes, Exome Variant Server, and ExAC
- phyloP, GERP++, phastCons & SiPhy

**Conservation scores:**
- phyloP, GERP++, phastCons & SiPhy

**Population frequencies:**
- 1000 Genomes, Exome Variant Server, and ExAC

Additionally, information from proprietary databases such as Alamut and LOVD (Leiden Open Variation Database) are easily accessible through embedded links. Information from other publicly available databases are easily imported into the workbench.

The new administration function provides a real-time tracking of current statuses; historical information; automated email notifications within a completely customizable workflow built to model your actual activities.

Unique tools include Custom Filtering, Patient Comparison, i.e. Trio Comparison, CAP Validation Assistance, automated BED file builder which automatically highlights areas of clinical significance, Positive Control Verification, and in conjunction with NextGENe software can form a completely automated informatics pipeline.

*Requires separate license

### Sources included:
- **Variant Interpretation:**
  - dbSNP
  - Exome Variant Server
- **Conservation Scores:**
  - phyloP
  - phastCons
  - GERP++
  - SiPhy
- **Functional Prediction:**
  - SIFT
  - PolyPhen-2
  - LRT
  - MutationTaster
  - MutationAssessor
  - FATHMM
  - CADD
- **Disease Association:**
  - COSMIC*
  - ClinVar & OMIM
  - CIViC
  - Alamut*
  - LOVD (Leiden Open Variation Database)

*Requires separate license

### Historical Database Development
Geneticist Assistant NGS Interpretative Workbench records variant pathogenicity determination on all found variants, eliminating time consuming duplication of researching the variant, thus speeding diagnosis while reducing costs. As the database is used the number of variants requiring pathogenicity calling is quickly reduced to a few novel variants.

Historical information on every found variant is recorded and available for instant recall. Additionally prior pathogenicity determination is logged by specific disease panel and globally for all disease panels. The variant review tab provides previously determined variant type, pathogenicity, variant frequency, HGVS Nomenclature, times observed, number of times observed in disease panel and panel group.

Use of the workbench will quickly reduce unnecessary pathogenicity research duplication, speeding diagnoses and reducing costs.

### Pathogenicity Calling Information
Geneticist Assistant NGS Interpretative Workbench provides Variant Interpretation, Functional Prediction, Conservation Scores and Disease Associations on each found variant from over 17 sources providing the information in a single view. Once a call has been made and confirmed, the research is stored in the database and applied to future recurrences of the variant either in the same disease panel or in any other panel, significantly reducing time and effort on future iterations of the variant in future analyses.

Geneticist Assistant Workbench provides a complete overview of information regarding variant pathogenicity in one detailed view. Prior samples which exhibited variant are also detailed.

### Sources included:
- **Variant Interpretation:**
  - dbSNP
  - Exome Variant Server
- **Conservation Scores:**
  - phyloP
  - phastCons
  - GERP++
  - SiPhy
- **Functional Prediction:**
  - SIFT
  - PolyPhen-2
  - LRT
  - MutationTaster
  - MutationAssessor
  - FATHMM
  - CADD
- **Disease Association:**
  - COSMIC*
  - ClinVar & OMIM
  - CIViC
  - Alamut*
  - LOVD (Leiden Open Variation Database)

*Requires separate license

### Population frequencies:
- 1000 Genomes
- Exome Variant Server
- ExAC

And others

*Requires separate license
Pathogenicity Call Supporting Information

Supporting information for a pathogenicity call is easily added to the database by a right mouse click in the variant tab. Data from any source such as dbSNP can be added for future recall.

Geneticist Assistant NGS Interpretative Workbench also includes a "mini web browser" which allows a user to search and link scientific information from any web source such as NCBI in support of the pathogenicity call which can be recalled at any time by authorized users. PubMed abstracts can be automatically downloaded into the workbench.

A simple right mouse click enters information and comments from multiple databases in support of pathogenicity call into Geneticist Assistant Interpretative Workbench.

Geneticist Assistant NGS Interpretative Workbench also includes a "mini web browser" which allows a user to search and link scientific information from any web source such as NCBI in support of the pathogenicity call which can be recalled at any time by authorized users. PubMed abstracts can be automatically downloaded into the workbench.

Linkage to External Databases

Retrieving further information from external proprietary tools such as Alamut, UCSC Genome Browser, or the LOVD database is a simple click away. (Alamut requires a license)

Alamut licensees can quickly retrieve information without error prone and tedious retyping by simply selecting variant of interest and clicking on the drop down menu.

Retrieving information from the LOVD database is a simple linked operation.

Automated Quality Control

Geneticist Assistant NGS Interpretative Workbench automatically monitors coverage depth, flagging regions to the base level that do not meet your pre-set requirements. The software will track over time the amplicon or regions' performance, providing feedback on the sequence performance, which may alert you to areas that require performance improvement.

Quality control requirements are easily set in the Quality Control tab, the software will then monitor the sequence performance to the base level, indicating regions of non-performance.

Quality data is presented for both the current sample and a complete history of analysis of all samples for a disease panel. Metrics provided include Minimum Coverage, Average Coverage, % Coverage Across Region and Pass/Fail Status of current run. Historical data includes average coverage of all runs, average percent coverage, absolute Pass/Fail counts, total samples for the region and passed percentage. Sequencing that often fails is easily reviewed, allowing user to determine and correct cause of sequencing failures.

Importantly, Geneticist Assistant NGS Interpretative Workbench, monitors areas of clinical significance providing a quick review of missed clinical variants as determined by the ClinVar database information.

Accessibility

Geneticist Assistant NGS Interpretative Workbench is comprised of a local installed database, either Linux or Windows®, and a client Windows program which provides the easy-to-use, graphical user interface. All data is stored locally, accessible only to authorized users. Off-site collaborators or sister facilities can securely (HTTPS security protocol) access the database via the internet.

1. Database and Client may reside on single computer
2. Geneticist Assistant can be accessed by any computer having client within institution network
3. Off-site collaborators or sister facilities can securely (HTTPS security protocol) access the database via the internet.
User Management, Audit Trail, Access Control

Geneticist Assistant NGS Interpretative database employs a customizable password system (such as an 8 character alpha-numeric password) to protect data integrity. Database records all log-in and log-off and all user activity by user, which can be recalled by administrative personnel. Access to various information contained in the database can be granted or limited by individuals, and groups. Geneticist Assistant NGS Interpretative Workbench records and tracks all changes and comments for future recall.

Geneticist Assistant Workbench employs a customizable password system (such as an 8 character alpha-numeric password) to gain access to the database.

Access to various information within Geneticist Assistant can be granted by individual and groups.

Geneticist Assistant Workbench records and tracks all changes and comments made to the database by users for future recall.

Customer Web Portal

Geneticist Assistant offer access to a customer web portal that can be used for tracking and managing tests ordered from referring institutions. The web portal is directly linked to the Geneticist Assistant database so that information regarding patients and sample submissions can be viewed in Geneticist Assistant and included in reports.

The web portal provides:
- Customizable interface
- Production and recognition of sample barcodes
- Secure encryption of patient information
- Patients and sample submissions linked directly with Geneticist Assistant
- Printing of packing slips for sample tracking

Patient Tracking

Patient information, including a patient ID, DOB, gender, relationships, and phenotype, can be imported to the Geneticist Assistant database. Each imported sample can then be assigned to a patient.

Compare Samples

Create a comparison of multiple samples to view differences in variant calls and/or variant frequencies. Output from different pipelines can be compared by importing VCF files from each pipeline and comparisons of family members, such as a trio comparison, can be created.

For family comparisons, specify the relationships and phenotypes for each patient to create a comparison based on a selected inheritance pattern.

Comparison results show variant coverage and allele frequency values for each patient to quickly identify differences and shared variants.
Custom Filtering Options

Variants lists, as well as any other data tables in Geneticist Assistant, can be filtered based on a combination of any data fields.

Drag and drop any data field to use for filtering. Multiple filters can be combined and the combined filter can be saved for later use.

Customizable Workflow Builder

Geneticist Assistant NGS Interpretative Workbench now includes a completely customizable workflow builder that enables you to model your physical NGS workflow. A workflow can then be designated for any cases entered in Geneticist Assistant.

Process Quality Control

Control Charting for real time and historic evaluation

Track run-to-run variability of control samples. Data is tracked for each individual target region. The data can be used to determine drift in the analytical quality both globally as well as for specific genes and target regions. In addition, the data can be used to easily determine changes between manufacturer reagent lots. The tabular format can easily be exported in csv format to create control charts and graphs.

Geneticist Assistant records variants in control samples allowing instant review and long term monitoring of process.

Positive Control Verification

Many users opt to incorporate a positive control, such as NIST Genome in a bottle, with each sequencing run. Geneticist Assistant captures the positive control data, permitting a quick review of the run’s efficacy and captures time-based data so that negative trends can be quickly observed and remedied.

Geneticist Assistant captures positive control data which is very useful in determining efficacy of sequencing run and for determining quality trending.
Import Existing Knowledge Base

For variants with previously determined pathogenicity, a VCF file can be imported to automatically update the pathogenicity for these variants in the Geneticist Assistant database.

Flag Artifacts

Geneticist Assistant NGS Interpretative Workbench allows users to flag variants that have been identified as artifacts and indicate the type of artifact, for example due to errors caused by chemistry or alignment. The variant can then automatically be flagged as an artifact when found in subsequent samples and can be easily filtered.

Automatic BED file builder

Geneticist Assistant includes the BED File Builder Tool which can be used to create custom BED files for any panel. Simply enter the name of each gene to be included, or load a text file with multiple genes, choose the desired transcript, indicate the type of regions to be included and optionally choose to include a set number of bases at either end of each region.

Complete Analysis Pipeline

In conjunction with NextGENe® software, Geneticist Assistant can be used in conjunction with NextGENe's AutoRun Tool to provide a seamless pipeline for analysis, review and database submission. NextGENe can be configured to automatically access and begin processing data from the sequencing platform, and to then export results to the Geneticist Assistant database. Geneticist Assistant can also be configured to automatically import data from other analysis packages through a simple script.

Recommended Hardware Requirements

Server:
- 2 cores
- 4 GB RAM
- 100 GB hard drive space available (solid state drive recommended)
- 64bit Linux (Ubuntu 12.04 or higher is recommended) or Windows Vista, 7, 8, 10 or Server 2003 through Server 2012 R2

Client:
- 2 cores
- 8 GB RAM
- 250 GB hard drive
- 64bit Windows Vista, 7, 8, Server 2003 through Server 2012 R2

For more information or to arrange a free webinar or trial of Geneticist Assistant NGS Interpretative Workbench please visit www.softgenetics.com or email: info@softgenetics.com