MyScreen Application Note

For use with the Illumina® MiSeq™/ MiniSeq™

For Research Use Only (RUO)

<u>Manufacturer:</u>
**Developed by Gamidor Diagnostics Ltd. Manufactured by ©
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For Professional use only, for more information
https://gamidor.co.il/myscreen/

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Introduction

I.   Intended Use

The MyScreen Kit is used to detect and identify a panel of hundreds of different genetic diseases that are associated with various genetic disorders of the Israeli population. It is covering most of Israeli ethnic groups including: Jewish, Arabs, Bedouins, Christians, Druze.

The panel covers all Jewish ethnic groups including Ashkenazi and Non-Ashkenazi (Morocco, Libya, Algiers, Turkey, Bulgarian, Iraq, Iran, Egypt, Syria, Lebanon, Bukhara, Kurdistan, Yemenite etc.).

The panel list was designed with data collected from:

> ➢ The Department of Community Genetics at the Ministry of health - MOH (סל הבריאות)
> ➢ Israeli Society of Medical Genetics –ISMG (איגוד הגנטיקאיים)
> ➢ The Israeli National Genetic Database (Golden Helix)
> ➢ Pathogenic mutations described in Israeli populations with unknown prevalence that were gathered from several sources such as: medical geneticists, medical teams, publications and more.

Masking of any diseases from the panel is possible following MOH or ISMG request.

For Research Use Only. Preforming this test should be done by a professional lab technician who have been trained in NGS technologies and qualified by Illumina representative.

II.   Background

Israeli population comprised of many ethnic backgrounds. Different ethnic groups have a higher risk for specific disease-causing mutations than the general Israeli population. These diseases are inherited in an autosomal or x-linked recessive pattern.

The MyScreen assay is a targeted assay for a selected set of mutations per disease and per specific genes. The list of chosen diseases and selected mutations might be updated from time to time.

The detailed list of all mutations detected in this assay can be requested from: amichai@gamidor.com

Protocol User Guides

SureSelect $^{XT\ HS}$ and XT Low Input Enzymatic Fragmentation Kit. Agilent Technologies
https://www.agilent.com/cs/library/usermanuals/public/G9702-90050.pdf

SureSelect$^{XT\ HS}$ Target Enrichment System for Illumina Paired-End Multiplexed Sequencing Library. Agilent Technologies
Instructions for preparing samples using the Sureselect$^{XT\ HS}$ Target Enrichment System
https://www.agilent.com/cs/library/usermanuals/public/G9703-90000.pdf

MiSeq™ System Denature and Dilute Libraries Guide
This guide provides instructions for denaturing and diluting libraries after llibrary preparation and before sequencing on the MiSeq™. This guide also includes instructions for preparing a PhiX control.
https://support.illumina.com/content/dam/illumina-support/documents/documentation/system_documentation/miseq/miseq-denature-dilute-libraries-guide-15039740-10.pdf

MiniSeq™ System Denature and Dilute Libraries Guide
This guide contains instructions for denaturing and diluting libraries before sequencing on the MiniSeq™ System, and instructions for preparing a PhiX control.
https://support.illumina.com/content/dam/illumina-support/documents/documentation/system_documentation/miniseq/miniseq-denature-dilute-libraries-guide-1000000002697-00.pdf

Technical Assistance
Specialists from the Technical Assistance Center can help troubleshoot and resolve problems. Contact the Center via one of the following methods:

Phone:	052-2808772
Email:	amichai@gamidor.co.il

Precautions

• To prevent contamination of reagents by nucleases, always wear powder- free laboratory gloves and use dedicated solutions and pipettors with nuclease- free aerosol- resistant tips.

• Use best-practices to prevent PCR product contamination of samples throughout the workflow:
1. Assign separate pre-PCR and post- PCR work areas and use dedicated equipment, supplies, and reagents in each area. In particular, never use materials designated to post- PCR work areas for pre- PCR segments of the workflow.
2. Maintain clean work areas. Clean pre-PCR surfaces that pose the highest risk of contamination daily using a 10% bleach solution, or equivalent.
3. Always use dedicated pre-PCR pipettors with nuclease- free aerosol- resistant tips to pipette dedicated pre- PCR solutions.
4. Wear powder-free gloves. Use good laboratory hygiene, including changing gloves after contact with any potentially- contaminated surfaces.

• For each protocol step that requires removal of tube cap strips, reseal the tubes with a fresh strip of domed caps. Cap deformation may result from exposure of the cap strips to the heated lid of the thermal cycler and from other procedural steps. Reuse of strip caps can cause sample loss, sample contamination, or imprecision in sample temperatures during thermal cycler incubation steps.

• In general, follow Biosafety Level 1 (BL1) safety rules.

• Possible stopping points, where samples may be stored at –20°C, are marked in the protocol. Do not subject the samples to multiple freeze/thaw cycles.

References for Contamination Control:
Kwok, S. and Higuchi, R. (1989). Avoiding false positives with PCR. Nature (London) 339, 237.
Victor, T. et al. (1993). Laboratory experience and guidelines for avoiding false positive polymerase chain reaction results. Eur. J. Clin. Chem. Clin. Biochem. 31, 531.
Yap, E.P.H. et al. (1994). False-positives and contamination in PCR. In: PCR Technology: Current Innovations. Griffin, H.G. and Griffin, A.M., eds., CRC Press, Boca Raton, FL.

System and software guides from Illumina®

MiSeq™ System User Guide

This guide includes information about instrument components, MiSeq™ Control Software (MCS), and required consumables, and instructions for performing a sequencing run and maintaining the instrument.
https://support.illumina.com/content/dam/illumina-support/documents/documentation/system_documentation/miseq/miseq-system-guide-15027617-01.pdf

MiSeq™ Reporter Analysis Workflow Reference Guides

Each workflow reference guide contains an overview of the analysis workflow and descriptions of analysis output files. For information about the MiSeq™ Reporter interface and instructions for instructions for installing, using, and troubleshooting the software
https://emea.support.illumina.com/content/dam/illumina-support/documents/documentation/software_documentation/miseqreporter/miseq-reporter-enrichment-workflow-guide-15042315-01.pdf

MiniSeq™ System Guide

This guide contains an overview of instrument components and instructions for operating and maintaining the MiniSeq™ System
https://support.illumina.com/content/dam/illumina-support/documents/documentation/system_documentation/miseq/miseq-system-guide-15027617-01.pdf

Sequencing runs performance

1. When the Miseq™/Miniseq™ run ends copy the following files from output folder ***NAME OF RUN**\\ to SAV (Sequencing Analysis Viewer) analysis:
   - runinfo.xml file,
   - runparameters.xml file
   - InterOp folder

2. Download the Sequencing Analysis Viewer (SAV) software from this website: https://support.illumina.com/sequencing/sequencing_software/sequencing_analysis_viewer_sav/downloads.html

3. Install the SAV software on your computer and go over your run parameters by following the instructions in the user guide you can find in this link: https://support.illumina.com/sequencing/sequencing_software/sequencing_analysis_viewer_sav/documentation.html

4. For MiSeq™, you can find the recommended specifications regarding reads or cluster passing filter, cluster generation, sequencing and quality of the data in this link: https://www.illumina.com/systems/sequencing-platforms/miseq/specifications.html

   For MiniSeq™, you can find the recommended specifications regarding reads or cluster passing filter, cluster generation, sequencing and quality of the data in this link: https://www.illumina.com/systems/sequencing-platforms/miniseq/specifications.html

Analyzing the Data

A. Generating analysis files

1. Once the run and Illumina® analysis completed, copy (using Disk on Key) the following files for MyScreen analysis under the output run folder in
   - LRM (Local Run Manger) system in MiniSeq ***NAME OF RUN**\Alignment_1\xxx_xxx\:
     - *.bam
     - *.bai
     - aggregate.report.pdf - exists only in LRM system
   - MiSeq Reporter - Miseq ***NAME OF RUN*** \Data\Intensities\BaseCalls
   - *.bam
   - *.bai
   NAME OF RUN - for example 191216_M06216_0016_000000000-G4NJR
2. Save all those files in a new results library – COPY THE ***NAME OF RUN*** in your analysis computer (dedicated to MyScreen results).
3. Quality Control Step –
   Open "aggregate.report.pdf", on page 7 look at the "Coverage Summary" table and verify:
     - Mean Region Coverage Depth above 150 per sample
     - Uniformity of Coverage above 90% per sample
   If any of the above does not meet these thresholds you need to consider creating a new library for this sample. Rare analytic errors may occur that interfere with reporting.
4. In order to activate the MyScreen program analysis, double-click on the file named "MyScreen_Analysis_v#.bat".
     - A prompt interface will guide you to insert the ***NAME OF RUN***
     - Choose the run directory.
     - Please select "SamplesSheet.xlsx - sheet which defined the personal information of each sample (like ID, name, address and more) to create final report (PDF and WORD) for each sample.

The software will start process the genotyping+ CNV analysis (should takes around 10 min for sample) and will prompt a successful message:
"Genotyping Analysis Completed!"
CNV detection completed!
Word reports created
Converting reports to pdf...
Press any key to continue . . .

B. Viewing the result

A new library will be created under ***NAME OF RUN*** named MyScreen_Analysis_v#_RESULTS
1. The file "sample_summary_[DATE]" contains a summary of all the samples and their results (wild type or respective mutations from the current run).
   1.1. Each sample will be output as a result.
   1.2. If no mutations or problems were found it will be indicated as "No mutations identified (WT)"
   1.3. If genotyping/CNV mutations are found, the mutations will be detailed with its output parameters.

1.4. If problem/no-calls mutations are found, the mutations will be highlighted in yellow for problem. Every problem should be checked by the lab using IGV or other alternative method to verify the heterozygotes status.

2. All reports have been created in a directory named MyScreen_Analysis_v#_RESULTS in a folder named REPORTS.

   2.1. All reports named in the following format: [sample name]_[ID].docx/.pdf

   2.2. Only validated positives from our run will be appeared in the REPORTS.

   2.3. Positives indicated as Problems will be appeared as "Low Confidence" in the REPORTS

3. The file "db_statistics_[DATE]" containing ALL sample results obtained from ALL past runs performed (including the current run)   - this file can be used for statistics.

4. 'errors.log' file will be created in the main analysis output directory, if any variants failed to be detected in the analysis or any failed sample detected in the CNV analysis.

OPTIONAL - Other Libs in the MyScreen_Analysis_v#_RESULTS that can viewed:

A. Genotyping_results –

- Genotyping.xlsx – All information regarding the genotyping analysis, sheet separated to cases;   All, positiveResults, Non reported, gender.
- *Optional - VCF to load to the VariantStidio3.0 files

B. CNVs_results –

The following excel table and a text file (.tsv) are created, in addition to a LOG_files folder –

1. CNV-DECoN.xlsx – 3 sheets containing results made by DECoN CNV caller:

   I.   Calls – Contain list of CNV calls made by DECoN with the appropriate parameters associate to each call.
        Low coverage mutations or problematic Alternative Variant frequency variants will be displayed as "CNV-Problem".

   II. Failures_samples – If a sample did not pass minimum correlation threshold it will be listed in current sheet.

   III. Failures_exons – Listing gene exons that fail to pass minimum read coverage limit.

2. DECoN_results.tsv – Summary of CNV calls made by DECoN for each sample in the run. The following columns in the file are:

- Type – Deletion or Duplication in DMD only
- Custom.first and Custom.last – Exons deleted in gene
- Correlation – Sample correlation in sample set
- N.Comp – Number of samples compared with in the anlysis
- BF – Bayes Factor, statistical strength of evidence in favor of one theory among two competing theories. > 10 strong evidence, less than 10 = CNV-Problem (not reported)
- Info – If a sample did not pass quality control

3. LOG_files folder – Internal use

****

It is possible to run each step (Genotyping and CNV detection) separately.
For that, execute "MyScreen_Analysis_Genotyping.bat" followed by
"MyScreen_Analysis_CNV.bat".

- Type in the full path to the results folder when prompt

To execute "createReports.bat" please create a Reports with the following 3 input files –

A. samplesSheet.xlsx
B. positiveResults.tsv
C. DECoN_results.tsv

Double click on createReports.bat.

Type in the full path to the Reports folder in 1- A cmd window should appear with the report creation progress.

Please refer to section B to view the results.

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C.OPTIONAL - VariantStudio3.0

Basic recommended steps to view analyze and report data with VCF files

To view the data on the VariantStudio use Illumina® [VariantStudio User Guide](#)

Result viewing:
1. Open VariantStudio 3.0
2. Open MyScreenProject.VSProj under "C:\Gamidor\Appendix" (or from the recent menu option)
3. Load vcf files from the Home tab "Import VCF" or "Import Folder" under Genotyping_results/VS
4. VCF Import Option Window will be open, select "Variants in regions specified by BED file", browse the file under
   "C:\Gamidor\MyScreen_Analysis_v#\VariantStudioFiles\Bedfile_v#.bed"
5. Check "Load hom-ref positions"
6. Click OK
7. ManageSamples - From the Home tab, use commands on the Samples menu to import variant call files in VCF file format and manage samples in the project.
8. From the Home tab, select "View All Samples". It will show all samples in the project.
9. From the "Annotations and Classification" tab, click "Custom Annotation" in the menu to annotate variants, browse the file under
   "C:\Gamidor\MyScreen_Analysis_v#\VariantStudioFiles\Annotation_v#.txt"
10. From the "Annotations and Classification" tab, click "View Classification Database", browse the file under "C:\ Gamidor\MyScreen_Analysis_v#\VariantStudioFiles\Classification_v#.txt"
11. From the "Annotations and Classification" tab, click "Apply Classification from database" in the menu to classify the variants.

Result analysis:
To View WT or polymorphism variants, from the Home tab, apply filter by clicking the down arrow icon to expand a filter section, select "WT and POLYMORPHISM"

To View Gender variants, from the Home tab, apply filter by clicking the down arrow icon to expand a filter section, select "GENDER"

To view Failed, Low coverage mutations or problematic Alternative Variant frequency variants, read depth < 10 OR GQX< 15 (below 95%) OR Alt Var Freq > 10% and < 30%
from the Home tab, apply filter by clicking the down arrow icon to expand a filter section, select "PROBLEMS!"

To view all the CARRIER variants, HET calls or HOM mut
from the Home tab, apply filter by clicking the down arrow icon to expand a filter section, select "CARRIER"

To view all the NON-REPORTED variants, variants that not reported in the resukts but in the same postion of our mutations list.
from the Home tab, apply filter by clicking the down arrow icon to expand a filter section, select "CARRIER"

Result exporting:

To export text/csv file: VariantStudio provides tools for exporting to text files and graphical representations of data. From the Export menu in the Reports tab, select an option to "Filtered variants" data to a tab-separated values file. These text file formats are not application-specific and can be opened in any text editor.

To export all the CARRIER&PROBLEMS! variants, from the Home tab, apply filter by clicking the down arrow icon to expand a filter section, select "CARRIER&PROBLEMS!" and save as "positiveResults.tsv"

D. Viewing Raw Sequencing data using IGV.

1. Double click on IGV.bat to start the program.
2. Genomes are selected from the genome drop-down list on the upper-left of the IGV window. Choose hg19.
3. To load data from the file system: (The preferred file format for viewing alignments in IGV is the BAM format.) Load data files by browsing for files on the local file system.
4. Select File>Load from File. IGV displays the Select Files window.
5. Select one or more data files or sample information files, then click OK.
6. IGV will display a warning if the file is an un-indexed ASCII-format file over 50 MB. It is recommended that such files should be indexed or converted to the binary TDF format prior to loading (see section on igvtools). Meaning BAM and BAI files should be located in the same directory.
7. Use the search box to locate: A locus or a mutation (for example, chr5:90,339,000-90,349,000), A gene symbol or other feature identifier (e.g., DPYD or NM_10000000)
8. When searching features, IGV will accept partial matches. A mutation in a feature. IGV accepts 2 mutation formats: Amino acid mutation notation of this form:
9. KRAS:G12C - The above would look for a mutation in KRAS on the 12th amino acid, from Glycine to Cystine. * is stop codon
10. Nucleotide mutation of this form: KRAS:123A>T - The above would look for a mutation in KRAS from adenine to thymine at the 123rd base.
    For more details please use IGV user guide:
    http://software.broadinstitute.org/software/igv/book/export/html/6

E. Verifying a BIG DELETION using IGV:

1. Open the positive sample with at least 2 samples with similar mean coverage.
2. Use the search box to locate the big deletion boundaries (from the samples_summary,xls in the reports, for example, chr5:90,339,000-90,349,000)
3. You need to verify all the following
- There is no polymorphism or mutations in the deleted region, which could imply 2 alleles.
- Search the Break point region by reduction of the coverage region
- Look on parallel regions and verify that the number of reads in on average is half for the positive sample versus the controls ones
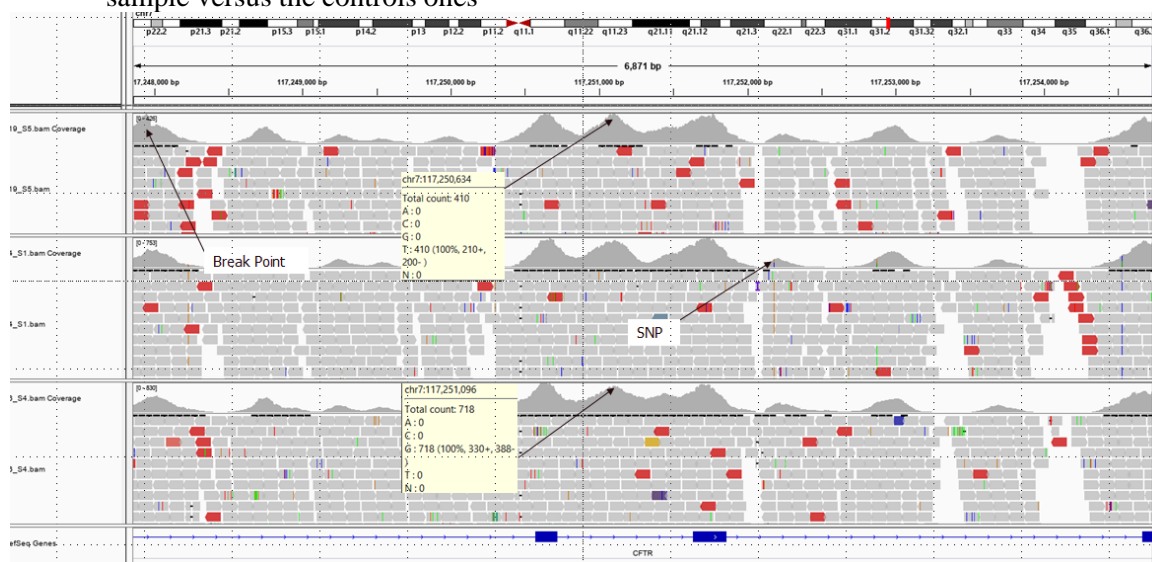
Appendix A: Software Installations Guides

A dedicated computer will be allocated for analysis.
The computer does not have to be connected to the Internet.
It is recommended that it will be connected to the MiSeq/MiniSeq tp transfer the results easily.

 - computing Requirements for the computer:

> ➢ ≥ 16 GB RAM
> ➢ ≥ 1 TB of disk space
> ➢ 64-bit quad core processor (2.8 GHz or higher) with the AVX instruction set (recommended) or Intel Core
> ➢ i7-210QE 2.10 GHz (or equivalent) processor with the AVX instruction set (minimum).
>   Display resolution of 1024 x 768 or higher

Software Requirements
> ➢ Windows 7 Pro 64-bit with Service Pack 1 (English-US) or Windows 10 (Personal Edition versions are not supported)
> ➢ Office 2016

F. Dependencies

- Python version 3: Main directory " C:\Users*USER*\AppData\Local\Programs\Python\Python38-32"
  DOWNLOAD here
- JAVA (JRE and JDK): Main directory "Java" lies in "C:\Program Files".
  DOWNLOAD JRE here
  DOWNLOAD JDK here
- Visual Studio 2017 version 15.9:
  DOWNLOAD Community version here
  It is **crucial** to select [.NET desktop development] when being asked what packages to additionally install.
- DOTNET (download ".NET Core SDK"): "C:\Program Files\dotnet\"
  DOWNLOAD here
- SAMTOOLS: Main directory "samtools" lies in "C:\Program Files".
  DOWNLOAD here
  Unzip the samtools.zip to "C:\Program Files".
- R version 3.1.2: Main directory "R" lies in "C:\Program Files".
  DOWNLOAD here
- Rtools32
  DOWNLOAD here

G.   Supplemental Software

- Illumina® Variant Studio v3:
  DOWNLOAD here
- Integrative Genomics Viewer (IGV):
  DOWNLOAD here

H.   Installation

I.   Download and accept all default install locations.
II. Copy all relevant files and programs to their respective locations:

Go to "This PC" -> right-click This PC on left toolbar -> "Properties" -> "Advanced system settings" -> "Environment Variables..."

Add the following environment variables to the "Path" variable in the "System variables" window:

- C:\Rtools\bin
- C:\Rtools\gcc-4.6.3\bin
- C:\Program Files\R\R-3.1.2\bin
- C:\Users*USER*\AppData\Local\Programs\Python\Python38-32
- C:\Users*USER* \AppData\Local\Programs\Python\Python38-32\Scripts
- C:\Program Files\Java\jre1.8.0_161\bin
- C:\Program Files\Java\jdk1.8.0_191\bin
- C:\Program Files\dotnet\
- C:\Program Files\samtools

- Rtools should be at top of list.
- Do not upgrade R and Rtools to a newer version
- If a newer version for JRE, JDK or Python was installed, update path accordingly.

III. Configure DECoN on the current machine:
Go to "C:\Gamidor\Appendix\DECoN-master\" and execute "setup.bat"

Illumina® VariantStudio v3 [Installation Guide](#)

IGV Installation Guide
To start IGV from using Java Web Start:
1. Go to the IGV downloads page: http://www.broadinstitute.org/igv/download.
2. When prompted, register or log in as requested. You must register to download IGV.
3. Click the launch icon. The browser displays the web start launch window.
4. Select Open with Java™ Web Start and click OK. If the system displays messages about trusting the application, confirm that you trust the application. Web Start downloads and starts IGV.

Appendix B: Appendix Directories

I. Genotyping

- Main directory containing permanent files "Genotyping" lies in "C:\Gamidor\Appendix".
- An additional directory containing the following version dependent files lies in "C:\Gamidor\MyScreen_Analysis_v#\Script\Genotyping":
    • Norm.RC.sort.txt
    • Norm.RC.sort.vcf
    • vcfParser.numpy.exe
    • vcfParser.numpy.py
    • vcfParser.numpy.spec

**** When running Genotyping.bat script and encountering error of "DLL not found" – you need to verify Visual Studio 2017 installation ([latest version of Visual Studio](#)). It is crucial to select [.NET desktop development] when being asked what packages to additionally install.

J. DECoN

- Main directory containing permanent files "DECoN-master" lies in "C:\Gamidor\Appendix":
  After installing R and Rtools run the "setup.bat" to configure DECoN on the system.
- An additional directory containing the following version dependent files lies in "C:\Gamidor\MyScreen_Analysis_v#\Script\DECoN":
    • targets.bed
    • targetsExon.txt
    • custom.txt
    • annotation.txt
    • outputHandler.py

K.   Patient Reports Creator

- BAT file "createReports.bat" lies in "C:\Gamidor\MyScreen_Analysis_v#\Script".
- Main directory "ReportCreator" lies in "C:\Gamidor\MyScreen_Analysis_v#\Script".
- The directory must contain the following files:
    • The main python program – ReportCreator.py
    • 4 template documents –
        ▪ template_norm.docx
        ▪ template_carrier.docx
        ▪ template_sick.docx
        ▪ template_carrier_and_sick.docx
    • One conversion table named VCFLocToMutationLoc.txt.
    • Constructor to pdf from word pdfCreator.ps1
- An additional file named "db_statistics-v2.xlsx" must be present in "C:\Gamidor\Appendix". This file keeps track of all runs performed since program installation.

Appendix C: Version Update Protocol

In order to correctly install a new version of MyScreen, the following steps must be taken:
1. Unzip the new version next to the current running version (in C:\Gamidor).
2. Move the entire current version folder into a folder named 'Old'.
3. In the following directory C:\Gamidor\MyScreen_Analysis_v#\Script\ReportCreator
4. Take the four template files from the relevant folder and copy them into the directory. The four template files should be 'template_carrier.docx', 'template_carrier_and_sick.docx', 'template_norm.docx' and 'template_sick.docx'.
5. *The files 'ReportCreator.py' and 'VCFLocToMutationLoc.txt' must NOT be changed.
6. The 'Appendix' folder should remain unchanged, unless specifically requested otherwise.

Appendix D: Legal Notices

L. Methods and Limitations

Targeted genotyping

Targeted DNA mutation analysis is used to simultaneously determine the genotype of hundreds variants associated with many diseases, these variants (mutations) can increase the likelihood of conceiving a pregnancy with a hereditary condition. Most of the conditions on the panel are inherited in an autosomal recessive manner, meaning that both parents have to carry a mutation in the same disease gene in order to be at risk of having an affected child. Due to varying modes of inheritance and disease severity, there are a few diseases on the panel that can be transmitted when only one parent is a carrier.

Sequencing

The SureSelectXT HS Reagent Kits and protocol are used to prepare indexed library samples with molecular barcodes prior to target enrichment to allow high- sensitivity next- generation sequencing (NGS) on the Illumina platform. These regions are sequenced to high coverage and the sequences are compared to standards and references of normal variation. Mutations may not be detected in areas of lower coverage.

Genotyping analysis and interpretation

Only the mutations regions are compared and are genotyped (using Illumina® Pisces software). The NGS technology test is highly reliable, with a >99% accuracy rate reported in the literature for targeted mutations. As with all medical screening tests, there is a chance of a false positive or false negative result. A "false positive" refers to the identification of a gene mutation that is not present. A "false negative" is the failure to recognize a mutation that indeed exists. Screening for the diseases on MyScreen panel may significantly reduce the likelihood of being a carrier but does not exclude the possibility of carrying another mutation within the genes of interest. The patient may still have a pathogenic variant that was not identified by this testing. Small insertions and deletions may not be as accurately determined as single nucleotide variants. Genes that have closely related pseudogenes are not well analyzed by this method.

Copy number analysis

Targeted large deletion and duplications analysis for several specific mutations is done by the DECoN software. Triplet repeats may not be detected.

*Fowler A, Mahamdallie S, Ruark E et al. **Accurate clinical detection of exon copy number variants in a targeted NGS panel using DECoN** [version 1; referees: 2 approved] Wellcome Open Research 2016, 1:20 (doi: 10.12688/wellcomeopenres.10069.1)*

SAM Tools provide various utilities for manipulating alignments in the SAM format, including sorting, merging, indexing and generating alignments in a per-position format.
Li H.*, Handsaker B.*, Wysoker A., Fennell T., Ruan J., Homer N., Marth G., Abecasis G., Durbin R. and 1000 Genome Project Data Processing Subgroup (2009) The Sequence alignment/map (SAM) format and SAMtools. Bioinformatics, 25, 2078-9. [PMID: 19505943]

Testing limitations

This test was developed and its performance characteristics determined by Gamidor Diagnostics Ltd (www.gamidor.com). It has not been cleared or approved by the FDA. Noteworthy, to date, the FDA does not require this test to go through premarket FDA review. Although molecular tests are highly accurate, it is a screening test only and not a diagnostic one. Rare analytic errors may occur that interfere with reporting. Sources of these errors include sample mix-up, trace contamination, bone marrow transplantation, blood transfusions and technical errors. The presence of additional variants nearby may interfere with mutation detection. The MyScreen test results must always be interpreted by a medical geneticist, genetic counselor or other qualified clinician in the context of clinical, familial and ancestral data. Genetic counseling is recommended to properly review and explain these results to the tested individual.

Research

Gamidor Diagnostics Ltd may use the aggregated and anonymous information provided by our users for internal research purposes.

Legal Agreement

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Any legal action or proceeding between Gamidor Diagnostics Ltd and you related to this agreement will be governed exclusively by the laws of the state of Israel. Any dispute, claim, or controversy in connection with or arising under the use of our Service or this agreement, its construction, existence, interpretation, validity, or any breach hereof which cannot be amicably settled between the parties, shall be finally and exclusively resolved by binding arbitration under the Rules of Arbitration of the Israeli Arbitration Association then prevailing.

Limited Product Warranty

Gamidor Diagnostics Ltd. warrants that this product will meet the specifications stated above. If any component of this product does not conform to these specifications Gamidor Diagnostics s Ltd. will at its sole discretion, as its sole and exclusive liability and as the users' sole and exclusive remedy, replace the product at no charge or refund the cost of the product; provided that notice of non-conformance is given to Gamidor Diagnostics Ltd.within sixty (30) days of receipt of the product.
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