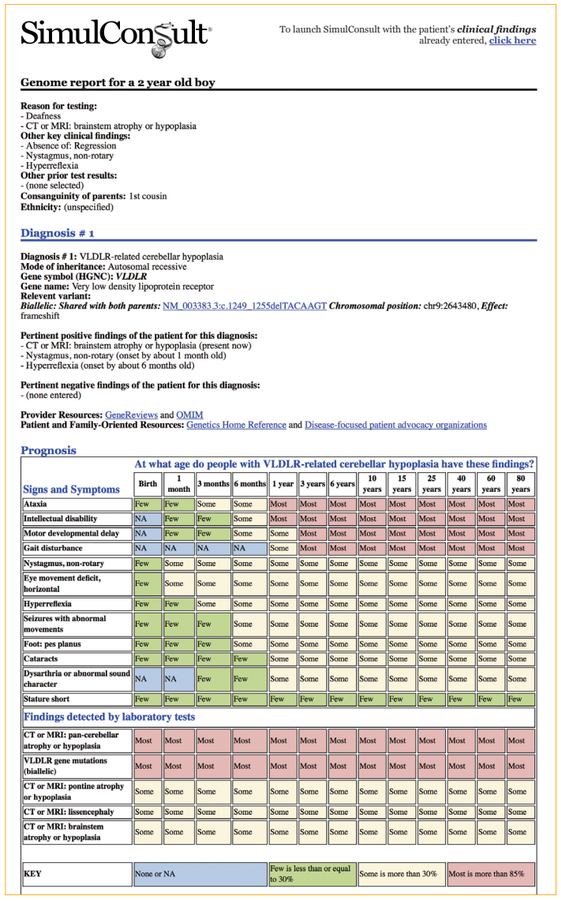
Genome-Phenome Report

Export report quickly and easily to lab's reporting platform using SimulConsult's API, or use cover letter with the default HTML output



SimulConsult®

To launch SimulConsult with the patient's ***clinical findings*** already entered, click here

Genome report for a 2 year old boy

Reason for testing:
- Deafness
- CT or MRI: brainstem atrophy or hypoplasia

Other key clinical findings:
- Absence of: Regression
- Nystagmus, non-rotary
- Hyperreflexia

Other prior test results:
- (none selected)

Consanguinity of parents: 1st cousin
Ethnicity: (unspecified)

Diagnosis # 1

Diagnosis # 1: VLDLR-related cerebellar hypoplasia
Mode of inheritance: Autosomal recessive
Gene symbol (HGNC): ***VLDLR***
Gene name: Very low density lipoprotein receptor
Relevent variant:
Biallelic: Shared with both parents: NM_003383.3:c.1249_1255delTACAAGT ***Chromosomal position:*** chr9:2643480, ***Effect:*** frameshift

Pertinent positive findings of the patient for this diagnosis:
- CT or MRI: brainstem atrophy or hypoplasia (present now)
- Nystagmus, non-rotary (onset by about 1 month old)
- Hyperreflexia (onset by about 6 months old)

Pertinent negative findings of the patient for this diagnosis:
- (none entered)

Provider Resources: GeneReviews and OMIM
Patient and Family-Oriented Resources: Genetics Home Reference and Disease-focused patient advocacy organizations

Prognosis

Signs and Symptoms	At what age do people with VLDLR-related cerebellar hypoplasia have these findings?												
	Birth	1 month	3 months	6 months	1 year	3 years	6 years	10 years	15 years	25 years	40 years	60 years	80 years
Ataxia	Few	Few	Some	Some	Most	Most	Most	Most	Most	Most	Most	Most	Most
Intellectual disability	NA	Few	Few	Some	Most	Most	Most	Most	Most	Most	Most	Most	Most
Motor developmental delay	NA	Few	Few	Some	Most	Most	Most	Most	Most	Most	Most	Most	Most
Gait disturbance	NA	NA	NA	NA	Some	Most	Most	Most	Most	Most	Most	Most	Most
Nystagmus, non-rotary	Few	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some
Eye movement deficit, horizontal	Few	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some
Hyperreflexia	Few	Few	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some
Seizures with abnormal movements	Few	Few	Few	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some
Foot: pes planus	Few	Few	Few	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some
Cataracts	Few	Few	Few	Few	Some	Some	Some	Some	Some	Some	Some	Some	Some
Dysarthria or abnormal sound character	NA	NA	Few	Few	Some	Some	Some	Some	Some	Some	Some	Some	Some
Stature short	Few	Few	Few	Few	Few	Few	Few	Few	Few	Few	Few	Few	Few
Findings detected by laboratory tests													
CT or MRI: pan-cerebellar atrophy or hypoplasia	Most	Most	Most	Most	Most	Most	Most	Most	Most	Most	Most	Most	Most
VLDLR gene mutations (biallelic)	Most	Most	Most	Most	Most	Most	Most	Most	Most	Most	Most	Most	Most
CT or MRI: pontine atrophy or hypoplasia	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some
CT or MRI: lissencephaly	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some
CT or MRI: brainstem atrophy or hypoplasia	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some
KEY	None or NA				Few is less than or equal to 30%			Some is more than 30%				Most is more than 85%	

Diagnosis # 2

Diagnosis # 2: GJB2-related deafness, AR, nonsyndromic
Mode of inheritance: Autosomal recessive
Gene symbol (HGNC): ***GJB2***
Gene name: gap junction protein, beta 2, 26kDa; DFNB1, DFNA3, connexin 26
Relevent variant:
Biallelic: Shared with both parents: NM_004004.5:c.229T>C ***Chromosomal position:*** chr13:20763492, ***Effect:*** missense

Pertinent positive findings of the patient for this diagnosis:
- Deafness (onset at about birth)

Pertinent negative findings of the patient for this diagnosis:
- (none entered)

Provider Resources: GeneReviews and OMIM
Patient and Family-Oriented Resources: Genetics Home Reference and Disease-focused patient advocacy organizations

Prognosis

Signs and Symptoms	At what age do people with GJB2-related deafness, AR, nonsyndromic have these findings?												
	Birth	1 month	3 months	6 months	1 year	3 years	6 years	10 years	15 years	25 years	40 years	60 years	80 years
Deafness	Some	Some	Most	Most	Most	Most	Most	Most	Most	Most	Most	Most	Most
Vertigo, significant	Few	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some
Findings detected by laboratory tests													
GJB2 gene mutations (biallelic)	Most	Most	Most	Most	Most	Most	Most	Most	Most	Most	Most	Most	Most
ABR abnormal	Some	Some	Most	Most	Most	Most	Most	Most	Most	Most	Most	Most	Most
GJB2 gene deletion (monoallelic)	Few	Few	Few	Few	Few	Few	Few	Few	Few	Few	Few	Few	Few
GJB2 gene mutation (monoallelic)	Few	Few	Few	Few	Few	Few	Few	Few	Few	Few	Few	Few	Few
GJB2 gene deletions (biallelic)	Few	Few	Few	Few	Few	Few	Few	Few	Few	Few	Few	Few	Few
KEY	None or NA				Few is less than or equal to 30%			Some is more than 30%				Most is more than 85%	

Incidental findings

Incidental genes examined using Geisinger ACMG superset (76), carrier genes, pharmacogenetic genes. Genes examined from P, M, F.

Incidental gene for P: GBA gene mutation (monoallelic)
Gene name: Glucosidase, beta, acid; glucosylceramidase
Incidental gene type: Carrier
Relevant variant:
Monoallelic: Apparently de novo: NM_001005741:ex9:c.G1093A:p.E365K ***Chromosomal position:*** chr1:155206167, ***Effect:*** missense

Provider Resources: OMIM
Patient and Family-Oriented Resources: Genetics Home Reference and Disease-focused patient advocacy organizations

SimulConsult Analysis and Quality Parameters

Quality metrics for annotated variant table

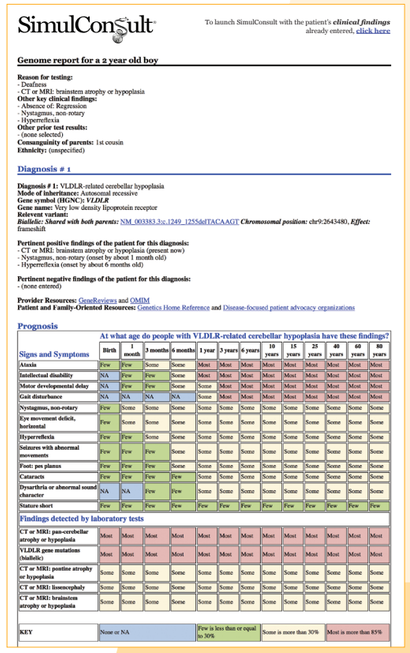
- Rows read: 48
- Variants read (can be more than one per row): 48
- Number of genomes analyzed: 3: P, M, F
- P: variants consistent with phenotypic sex provided
- M: variants consistent with phenotypic sex provided
- F: variants consistent with phenotypic sex provided
- RsID for variants: 75%
- Monoallelic variants in proband: 85%
- Proband variants matching mother: 65%
- Proband variants matching father: 79%
- De novo mutations: 3 of 43 with severity score > zero (typical exomes have < 5 de novo variants if family aware variant calling was used)
- Loss of heterozygosity: 0 of 43 with severity score > zero

Report Features

- **Clinical rationale** for the diagnosis is clear
- **Supports up to two diagnoses**; the findings automatically group by diagnosis
- **Prognosis table** answers the clinician and patient question "what should I expect"
- **Contextual resource links** for the clinician and patient by diagnosis leverage the time the provider and patient spend together
- **Structured terms** (ICD 10, SNOMED, IMO® lexical ID) are available automatically via a partnership with Intelligent Medical Objects®, including patient-friendly terms for various medical concepts and HPO terms available for findings. (*Orphanet available soon*)

Genome-Phenome Analyzer

Analyze and interpret panel, exome and genome variant tables in the full clinical context to rapidly identify causative genes and variants



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Key Features

- **Clinical correlation** of patient findings and genomic results identifies the most pertinent genes from among >6,100 described disorders, highlighting those most plausible as causative variants
- **Incidental findings** with options of gene lists and individuals to report
- **Discovery gene list** for genes with phenotypes not yet described in the literature
- **Genome Report workflow** enables fast selection of diagnoses, genes and variants and export to reporting platform, including a Prognosis Table© to answer the question "what should I expect"
- **Complete coverage** of known Mendelian disorders and many CNV disorders

Key Benefits

Fast. In under 5 seconds, identify the pertinent **gene or genes and their variants** that could be causative in the patient, identified in a way that is hypothesis-independent as to mode of inheritance, number of genes involved and key clinical findings. Workflow allows clinical interpretation and reporting to be done in just a few minutes.

Accurate. Uses gene pertinence, a measure of confidence in the diagnosis. The top gene in confirmed diagnosis typically has >99% pertinence. (PMID 25156663, open access)

Cost effective. Reduce the need to do trios to diagnose known diseases. Make good use of scarce time of experts on clinical interpretation

SimulConsult®
A Simultaneous Consult On Your Patient's Diagnosis

To set up a trial and order
genome@simulconsult.com
857-205-2914 *(mobile)*
617-879-1670 *(office)*

Analysis Workflow

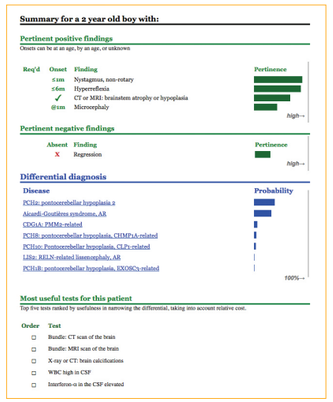
MD orders test
Findings can be collected in 1 of 3 ways

Lab staff uses SimulConsult
Collects findings from MD staff or notes

MD uses SimulConsult
Most efficient if clinicians use SimulConsult anyway for diagnostic assistance

MD's staff uses simplified SimulConsult interface
Diagnoses hidden so labs can include it on their public websites

Phenome & Genome



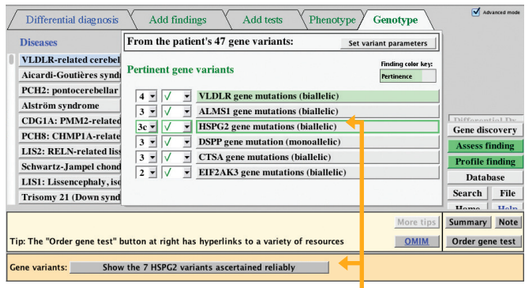
Annotated variant table

Lab generated

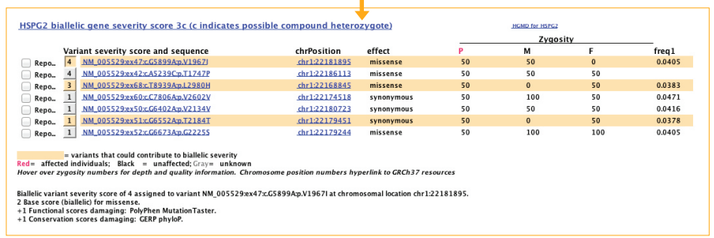
All information stays on user's computer

Customization options available for processing and reporting

Genome-Phenome Analysis

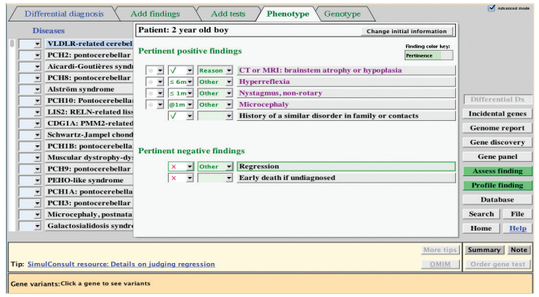


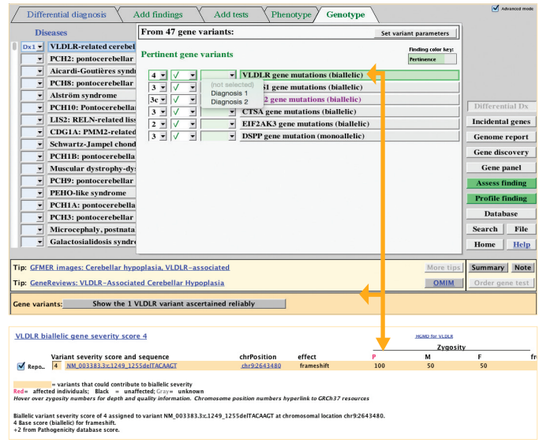
Pertinence measure for the gene (green shading), together with details about the relevant variants (orange shading below) and the factors underlying each gene severity score, allow for rapid interpretation



Genome Reporting Workflow

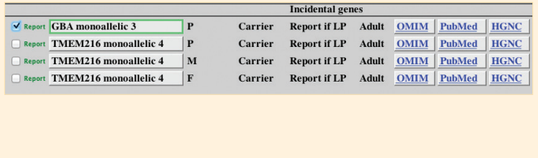
Phenome & Genome

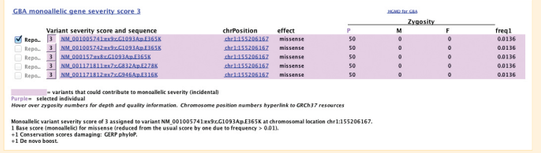




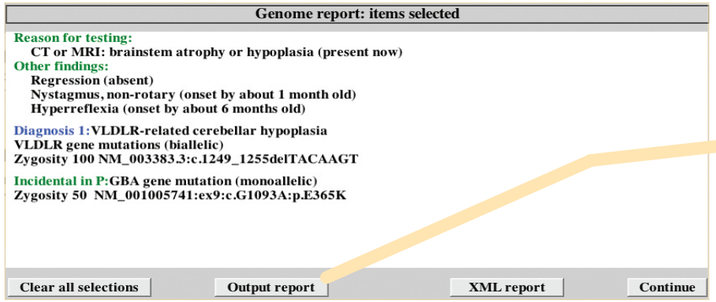
Incidental (or discovery) genes

Interpreter sets preferences for genes to report (ACMG or more), who to examine (proband, trio...), whether only to report childhood onset and for whom to report results



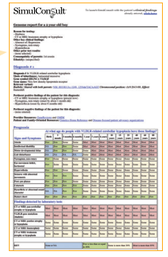


Confirm the output in the report "cart" and export Genome Report



Genome Report "cart"

See report on next page



Export to SimulConsult's standard Genome-Phenome Report (shown on next page) or xml API to lab's reporting platform. Prognosis information about the disease in each diagnosis helps the provider and patient know what to expect and informs care.