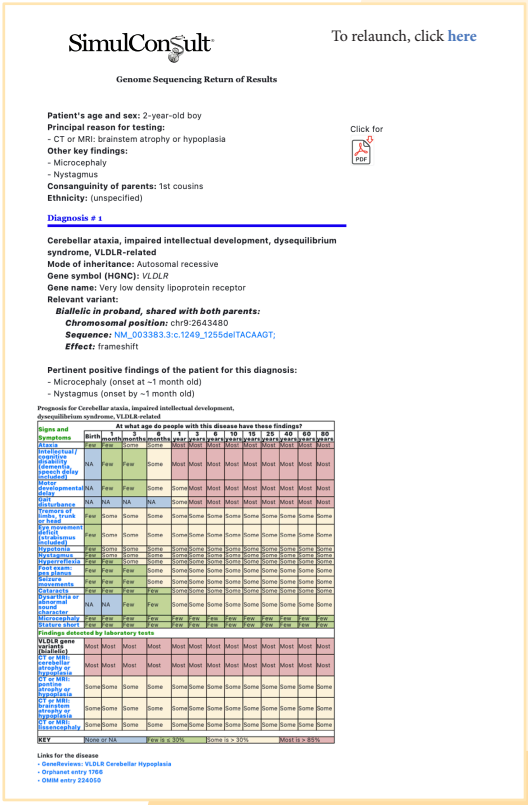
Genome-Phenome Dashboard

Clinician-centered genomic workflow

Analyze and interpret panels, exome and genome variant tables, and loss of heterozygosity in the full clinical context to rapidly identify causative genes and variants



SimulConsult

To relaunch, click here

Genome Sequencing Return of Results

Patient's age and sex: 2-year-old boy
Principal reason for testing:
- CT or MRI: brainstem atrophy or hypoplasia

Other key findings:
- Microcephaly
- Nystagmus

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

Click for PDF

Diagnosis # 1

Cerebellar ataxia, impaired intellectual development, dysequilibrium syndrome, VLDLR-related
Mode of inheritance: Autosomal recessive
Gene symbol (HGNC): *VLDLR*
Gene name: Very low density lipoprotein receptor
Relevant variant:
Biallelic in proband, shared with both parents:
Chromosomal position: chr9:2643480
Sequence: NM_003383.3:c.1249_1255delTACAAGT;
Effect: frameshift

Pertinent positive findings of the patient for this diagnosis:
- Microcephaly (onset at ~1 month old)
- Nystagmus (onset by ~1 month old)

Prognosis for Cerebellar ataxia, impaired intellectual development, dysequilibrium syndrome, VLDLR-related

Signs and Symptoms	At what age do people with this disease have these findings? Birth	1 month	3 months	6 months	1 year	2 years	4 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	Most
Intellectual/ cognitive impairment (dementia, speech delay included)	NA	Few	Few	Some	Most	Most	Most	Most	Most	Most	Most	Most	Most	Most
Developmental delay	NA	Few	Few	Some	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	Most
Incoordination of limbs, trunk or head	Few	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some
Eye movement deficit (gaze, nystagmus included)	Few	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some
Hypotonia	Few	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some
Nystagmus	Few	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some
Hyperreflexia	Few	Few	Few	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some
Fast saccadic eye movements	Few	Few	Few	Few	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some
Slow eye movements	Few	Few	Few	Few	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some
Cataracts	Few	Few	Few	Few	Few	Some	Some	Some	Some	Some	Some	Some	Some	Some
Dysarthria or abnormal speech character	NA	NA	Few	Few	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some
Microcephaly	Few	Few	Few	Few	Few	Few	Few	Few	Few	Few	Few	Few	Few	Few
Stature short	Few	Few	Few	Few	Few	Few	Few	Few	Few	Few	Few	Few	Few	Few
Findings detected by laboratory tests														
VLDLR gene variants (biallelic)	Most	Most	Most	Most	Most	Most	Most	Most	Most	Most	Most	Most	Most	Most
CT or MRI: cerebellar atrophy or hypoplasia	Most	Most	Most	Most	Most	Most	Most	Most	Most	Most	Most	Most	Most	Most
CT or MRI: brainstem atrophy or hypoplasia	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some
CT or MRI: cerebral atrophy or hypoplasia	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some
CT or MRI: ventriculomegaly	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some
KEY	None or NA				Few is ≤ 30%				Some is > 30%				Most is > 85%	

Links for the disease
- GeneReviews: VLDLR Cerebellar Hypoplasia
- Orphanet entry 1766
- OMIM entry 224050

Key Features

- Clinical correlation of patient findings and genomic results identifies the most pertinent causative genes from among described Mendelian disorders, highlighting the plausible causative variants in those genes
- Incidental ("seccondary") 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

Key Benefits

Fast. In under 5 seconds, identify the pertinent gene or genes and their associated 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. Enable re-analysis at every visit for the undiagnosed.

SimulConsult®
A Simultaneous Consult On Your Patient's Diagnosis

To subscribe, visit:
SimulConsult.com

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

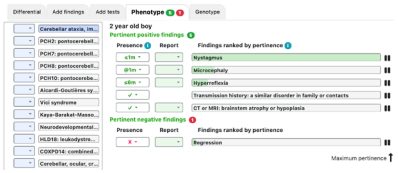
Most efficient if clinicians use SimulConsult anyway for diagnostic assistance

MD's staff uses simplified SimulConsult interface

Diagnoses hidden so labs can include it on their public websites

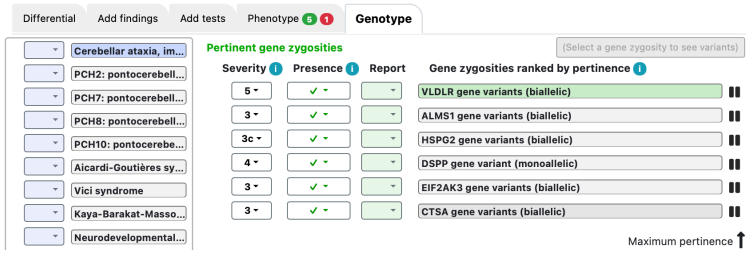
Phenome & Genome

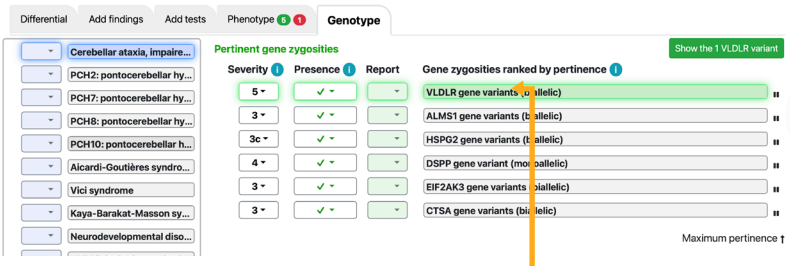
Patient Phenotype



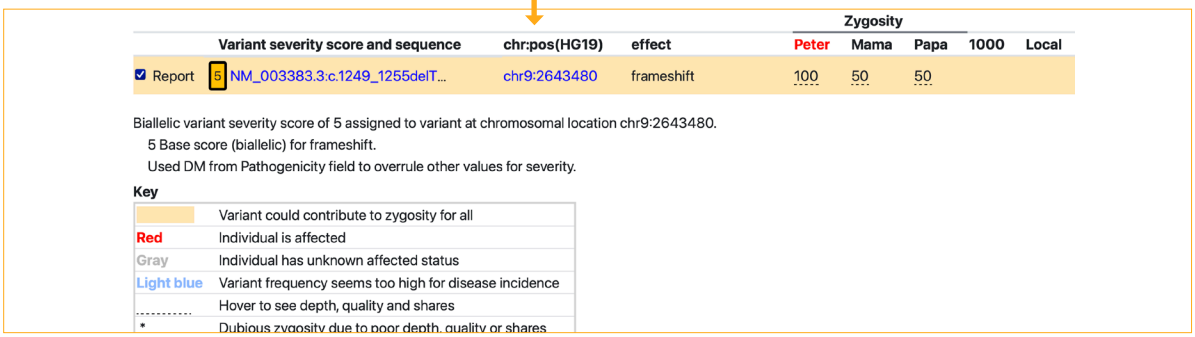
Annotated variant table

Genome-Phenome Analysis



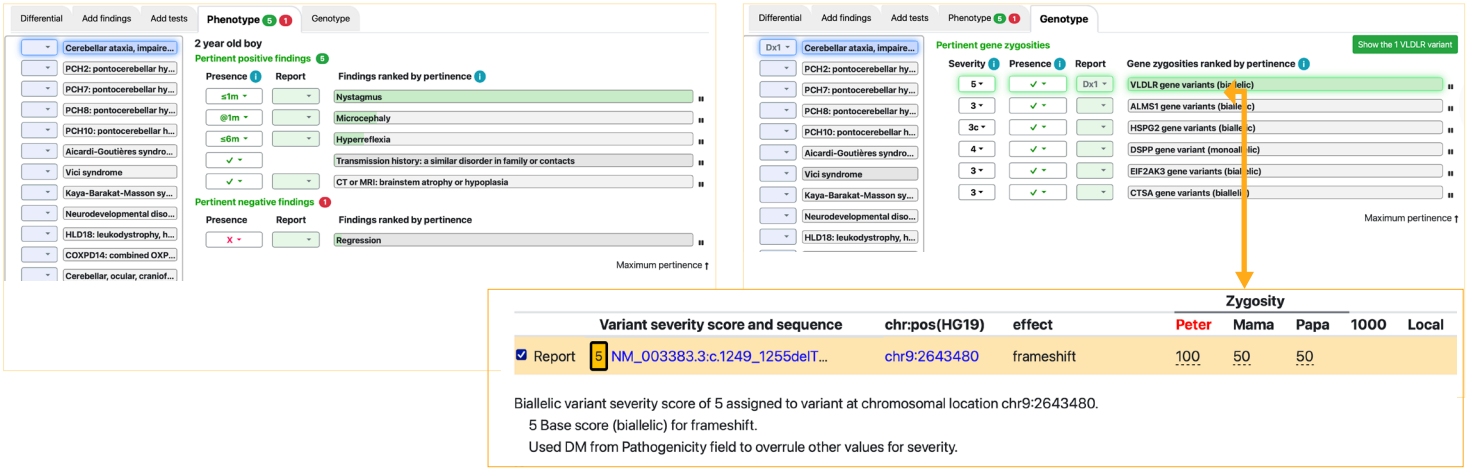


Pertinence measure for the gene (green shading), together with details about the relevant variants (orange shading below) and the factors underlying each gene severity score, allow for rapid interpretation.



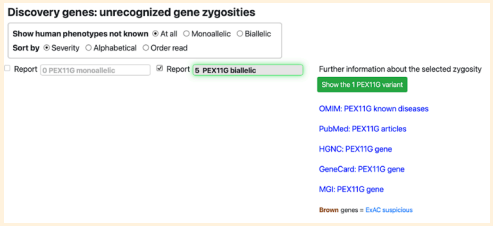
Genome Reporting Workflow

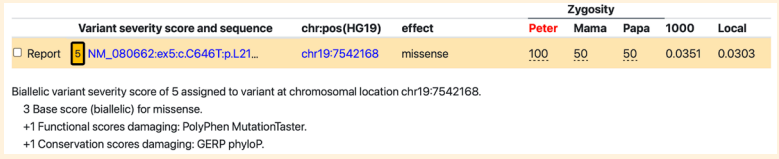
Phenome & Genome



Discovery (or incidental) 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"

Reason for testing:

CT or MRI: brainstem atrophy or hypoplasia (onset unknown)

Other findings:

Microcephaly (onset @1 mo)

Nystagmus (onset by 1 mo)

Diagnosis 1: Cerebellar ataxia, impaired intellectual development, dysequilibrium syndrome, VLDLR-related

VLDLR gene variants (biallelic)

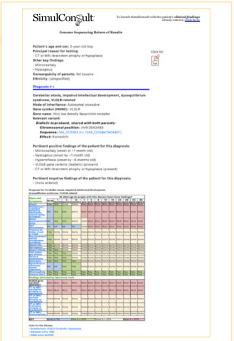
Severity 5 zygosity 100 at chr9:2643480 sequence NM_003383.3:c.1249_1255delTACAAGT;

Discovery gene candidate: PEX11G (biallelic)

Severity 5 zygosity 100 at chr19:7542168 sequence NM_080662:ex5:c.C646T:p.L216F;

No incidental diagnoses were selected

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.

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 Sequencing Return of Results

Patient's age and sex: 2-year-old boy
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- CT or MRI: brainstem atrophy or hypoplasia

Other key findings:
- Microcephaly
- Nystagmus

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

Click for PDF

Diagnosis # 1

Cerebellar ataxia, impaired intellectual development, dysequilibrium syndrome, VLDLR-related
Mode of inheritance: Autosomal recessive
Gene symbol (HGNC): *VLDLR*
Gene name: Very low density lipoprotein receptor
Relevant variant:
Biallelic in proband, shared with both parents:
Chromosomal position: chr9:2643480
Sequence: NM_003383.3:c.1249_1255delTACAAGT;
Effect: frameshift

Pertinent positive findings of the patient for this diagnosis:
- Microcephaly (onset at ~1 month old)
- Nystagmus (onset by ~1 month old)
- Hyperreflexia (onset by ~6 months old)
- VLDLR gene variants (biallelic) (present)
- CT or MRI: brainstem atrophy or hypoplasia (present)

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

Prognosis for Cerebellar ataxia, impaired intellectual development, dysequilibrium syndrome, VLDLR-related

Signs and Symptoms	At what age do people with this disease 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 / cognitive disability (dementia, speech delay included)	NA	Few	Few	Some	Most	Most	Most	Most	Most	Most	Most	Most	Most
Motor developmental delay	NA	Few	Few	Some	Some	Most	Most	Most	Most	Most	Most	Most	Most
Gait disturbance	NA	NA	NA	NA	Some	Most	Most	Most	Most	Most	Most	Most	Most
Tremors of limbs, trunk or head	Few	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some
Eye movement deficit (strabismus included)	Few	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some
Hypotonia	Few	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some
Nystagmus	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
Foot exam: pes planus	Few	Few	Few	Some	Some	Some	Some	Some	Some	Some	Some	Some	Some
Seizure movements	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
Microcephaly	Few	Few	Few	Few	Few	Few	Few	Few	Few	Few	Few	Few	Few
Stature short	Few	Few	Few	Few	Few	Few	Few	Few	Few	Few	Few	Few	Few
Findings detected by laboratory tests													
VLDLR gene variants (biallelic)	Most	Most	Most	Most	Most	Most	Most	Most	Most	Most	Most	Most	Most
CT or MRI: cerebellar atrophy or hypoplasia	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: brainstem 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
KEY	None or NA			Few is ≤ 30%			Some is > 30%				Most is > 85%		

Links for the disease
- GeneReviews: VLDLR Cerebellar Hypoplasia
- Orphanet entry 1766
- OMIM entry 224050

Discovery gene candidate

Discovery gene candidate: PEX11G (biallelic)

Relevant variant:
Biallelic in proband, shared with both parents:
Chromosomal position: chr19:7542168
Sequence: NM_080662:ex5:c.C646T:p.L216F;
Effect: missense

Clinician Resources: OMIM, PubMed and HGNC

Incidental ("secondary") findings

Incidental ("secondary") genes examined using Disease genes (ACMG v3.0), carrier genes, pharmacogenetic genes. Genes examined from Peter, Mama, Papa.

(No incidental ("secondary") genes called)

SimulConsult Analysis and Quality Parameters

Quality metrics for annotated variant table

Read 47 rows with 47 variant locations from file TinyTrio.tsv
Number of genomes analyzed: 3: Peter (male), Mama, Papa
RsID listed for 74% of variants
Proband monoallelic variants 87%
Proband variants overlapping with mother 64%
Proband variants overlapping with father 79%
De novo proband variants = 3 of 37 with severity score >1
Frequent de novo variants removed = 2 of 37 with severity score >1
Loss of heterozygosity variants = 0 of 37 with severity score >1

General settings for processing

- Frequency too common to consider: cutoff threshold: 0.1
- Frequency too common for incidental ("secondary") disease: cutoff threshold: 0.01
- Frequency too common for monoallelic: cutoff threshold to reduce variant severity by one: 0.01
- Frequencies: maximum of frequency columns 1 and 2
- Quality of call: cutoff threshold: 10.0
- Depth of read: cutoff threshold: 4
- De novo variants: add 1 to Variant Severity if fewer than: 20
- De novo variants: subtract 1 from Variant Severity if more than: 100
- De novo variants: subtract 2 from Variant Severity if more than: 1000
- Pathogenicity model: Loss of function

Report Features

- Clinical rationale for the diagnosis is clear
- Supports up to 4 diagnoses; the findings automatically group by diagnosis
- Prognosis table answers clinician and patient question "what should I expect"
- Contextual resource links for the provider and patient by diagnosis leverages 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.