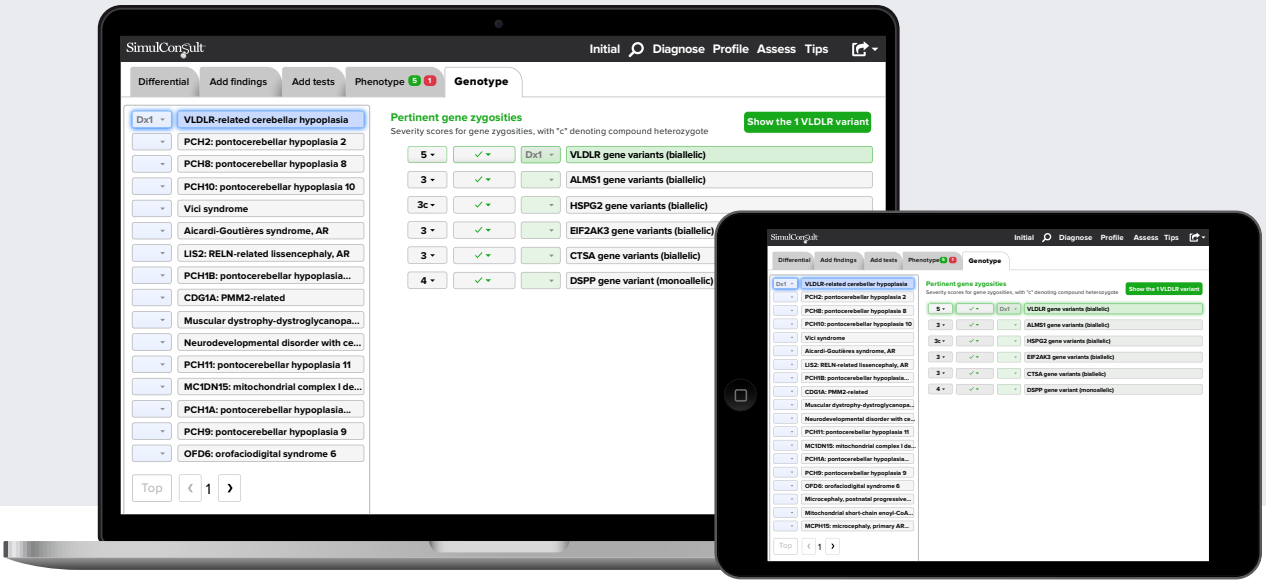
Genome-Phenome Analyzer

Genome Interpretation plus Gene Discovery with SimulConsult



Empowers you to quickly make diagnoses from genomic results in the clinical context!

Coverage

Covers all chromosomal abnormalities and genes with germline changes convincingly associated with human disease and their clinical and lab findings, as well as non-genetic diseases in their differential diagnosis.

Clear logic

You assess the rationale of the fit between your patient and the disease. It achieves “explainable artificial intelligence” using a human-curated database, it is not a black box.

Platform

Access the software on your computer or tablet.

Focused on your patient

Use your patient’s genomic variant table and their clinical information to focus on the pertienent genes. Then get suggestions on useful clinical findings to check and tests to order.

Accurate and cost effective

Top gene in confirmed diagnosis often has >99% pertinence. Can identify multiple genetic diagnoses simultaneously, such as in cases of consanguinity.

Fast

Import variants in seconds and rapidly interpret them in the full clinical context. Quickly prioritize discovery genes, if relevant, and regularly reanalyze undiagnosed and consanguinous patients.

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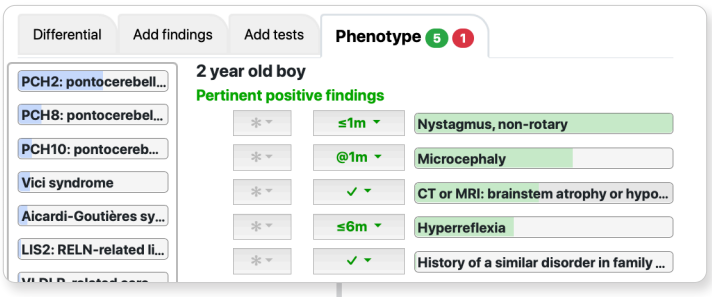
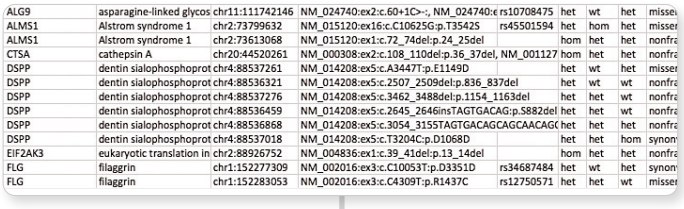
Getting to the diagnosis

Phenome + Genome



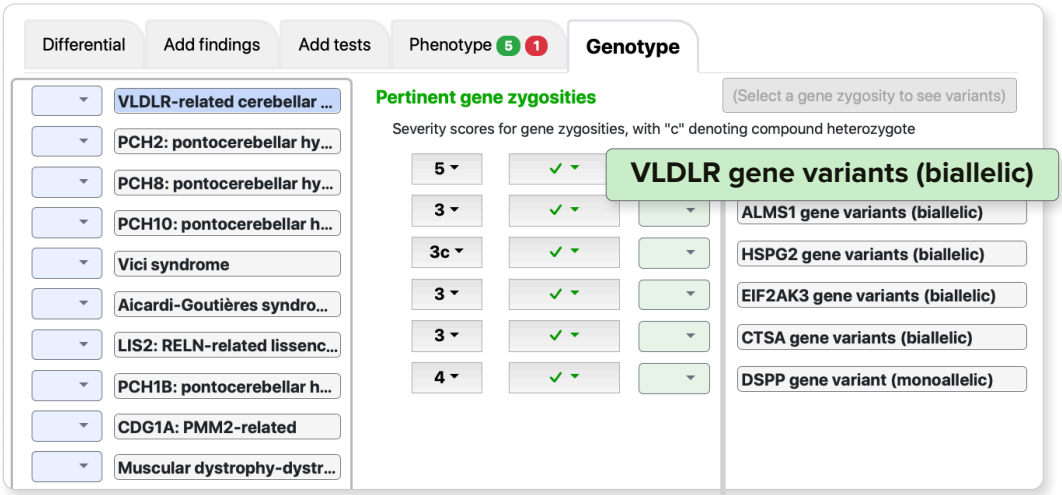
Annotated Variant Table (Lab-generated)

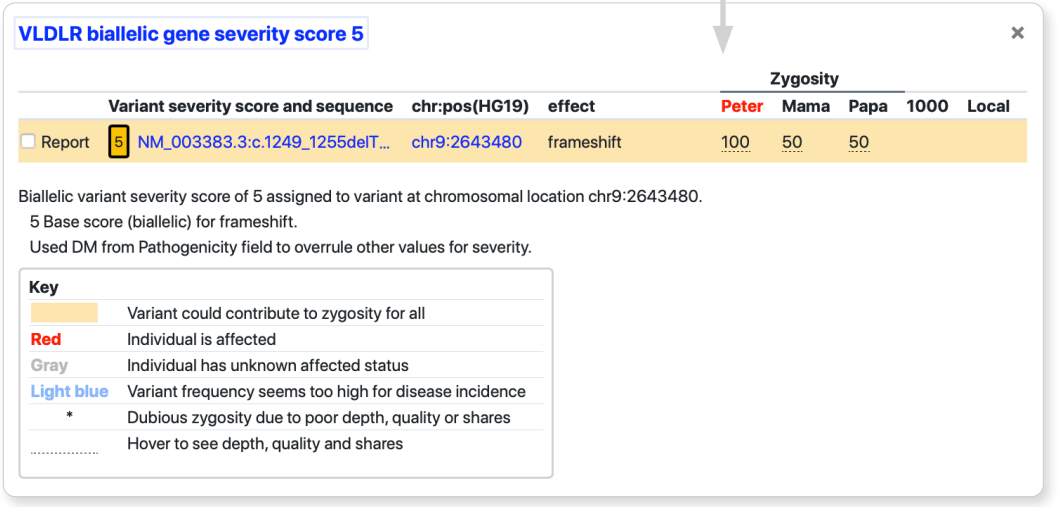


ALG9	asparagine-linked glycos	chr11:111742146	NM_024740:ex2:c.60+1C>-, NM_024740:e	rs10708475	het	wt	het	misse
ALMS1	Alstrom syndrome 1	chr2:73799632	NM_015120:ex16:c.C10625G:p.T3542S	rs45501594	het	hom	het	misse
ALMS1	Alstrom syndrome 1	chr2:73613068	NM_015120:ex1:c.72_74del:p.24_25del		hom	het	het	nonfra
CTSA	cathepsin A	chr20:44520261	NM_000308:ex2:c.108_110del:p.36_37del, NM_001127		hom	het	het	nonfra
DSPP	dentin sialophosphoprot	chr4:88537261	NM_014208:ex5:c.A3447T:p.E1149D		het	wt	het	misse
DSPP	dentin sialophosphoprot	chr4:88536321	NM_014208:ex5:c.2507_2509del:p.836_837del		het	wt	wt	nonfra
DSPP	dentin sialophosphoprot	chr4:88537276	NM_014208:ex5:c.3462_3488del:p.1154_1163del		het	het	wt	nonfra
DSPP	dentin sialophosphoprot	chr4:88536459	NM_014208:ex5:c.2645_2646insTAGTGACAG:p.S882del		het	het	wt	nonfra
DSPP	dentin sialophosphoprot	chr4:88536868	NM_014208:ex5:c.3054_3155TAGTGACAGCAGCAACAG(		het	het	het	nonfra
DSPP	dentin sialophosphoprot	chr4:88537018	NM_014208:ex5:c.T3204C:p.D1068D		het	het	hom	synon
EIF2AK3	eukaryotic translation in	chr2:88926752	NM_004836:ex1:c.39_41del:p.13_14del		hom	het	het	nonfra
FLG	filaggrin	chr1:152277309	NM_002016:ex3:c.C10053T:p.D3351D	rs34687484	het	wt	het	synon
FLG	filaggrin	chr1:152283053	NM_002016:ex3:c.C4309T:p.R1437C	rs12750571	het	het	wt	misse

Specify the pertinent clinical information

Import the annotated variants



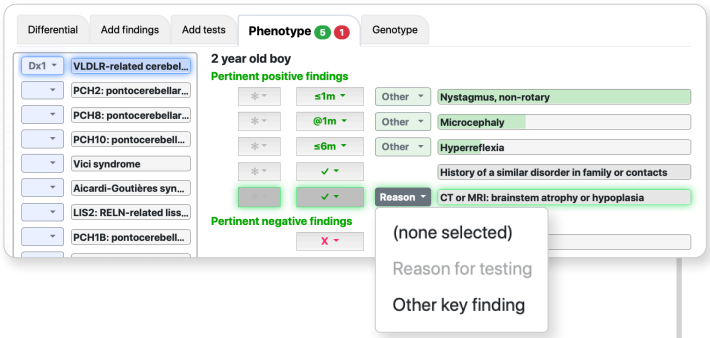


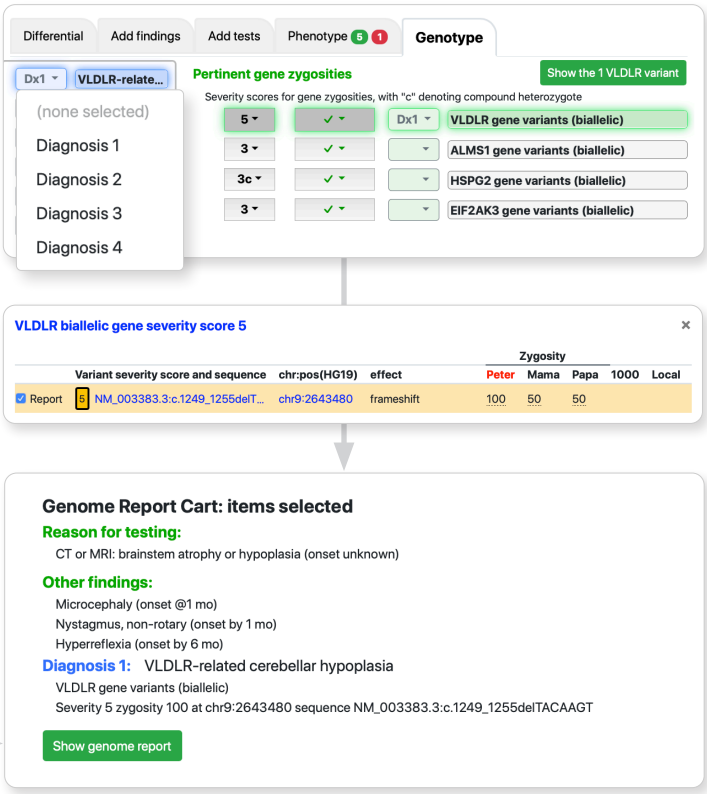
The clinical correlation of patient findings and genomic results:

- **Ranks** genes by pertinence to the clinical presentation rather than severity
- **Identifies** the most pertinent causative genes from among described human disorders (shown in green shading)
- **Highlights** variants that may be causative in those genes and which variants are implausibly frequent given the known disease incidence
- **Identifies** further useful clinical or lab findings to make the diagnosis

Automated reporting

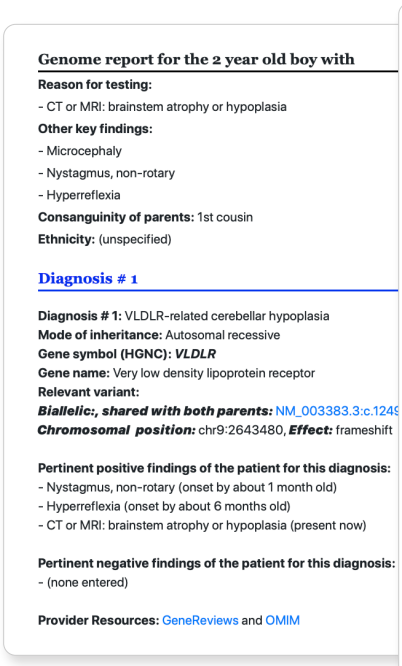
Phenome + Genome





Automated reporting.
You generate the report after you:

- **Select the disease**, gene and variant by diagnosis (supports up to 4 diagnoses in a patient)
- **Assign findings** to be a "reason for testing" or "other key finding"
- **Confirm selection** in "cart"



Genome report for the 2 year old boy with

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

Other key findings:
- Microcephaly
- Nystagmus, non-rotary
- Hyperreflexia

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

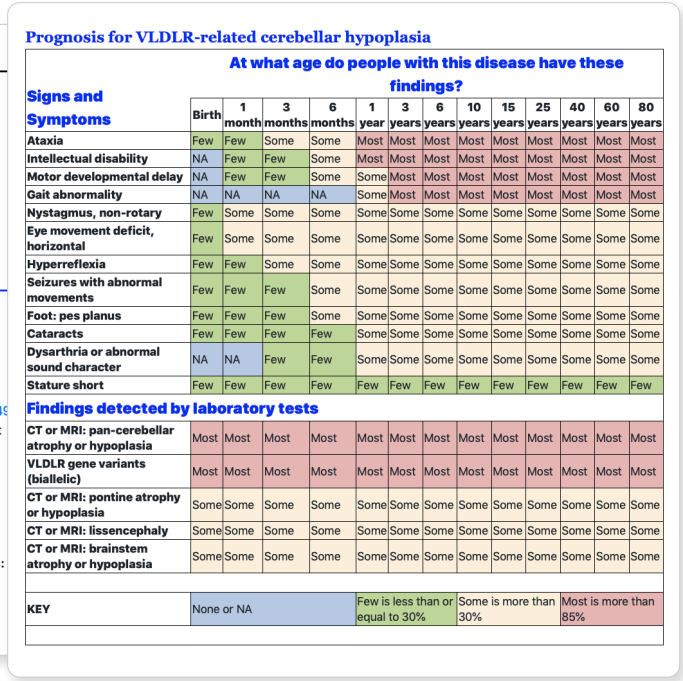
Diagnosis # 1

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

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

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

Provider Resources: GeneReviews and OMIM



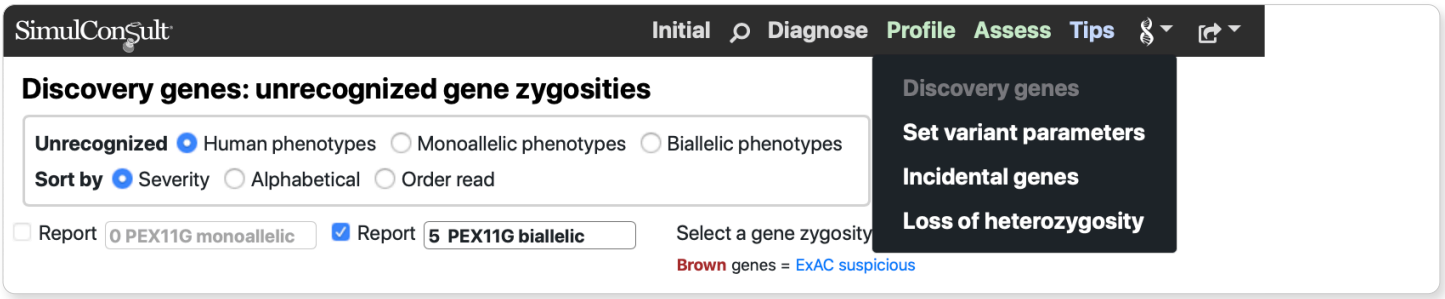
Prognosis for VLDLR-related cerebellar hypoplasia

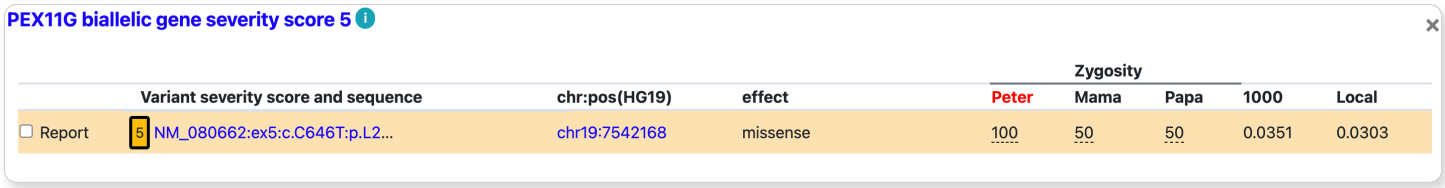
Signs and Symptoms	At what age do people with this disease have these findings?												
	Birth	1 month	3 months	6 months	1 year	3 years	6 years	10 years	15 years	25 years	40 years	60 years	80 years
Ataxia	Few	Few	Some	Some	Most	Most	Most	Most	Most	Most	Most	Most	Most
Intellectual disability	NA	Few	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 abnormality	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 variants (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

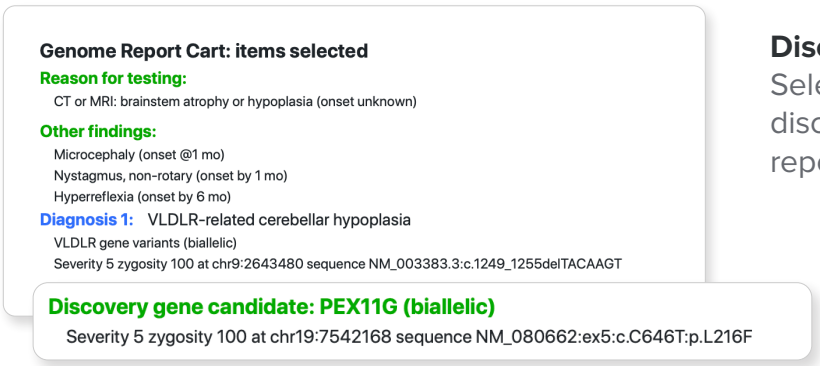
KEY	None or NA	Few is less than or equal to 30%	Some is more than 30%	Most is more than 85%

PCORI-funded research has shown the report to be well liked by patient families and referring physicians, especially the **Prognosis Table**, which allows you to quickly answer their question "With this diagnosis, what should I expect?"

Prioritizing discovery genes using clinical context & family history

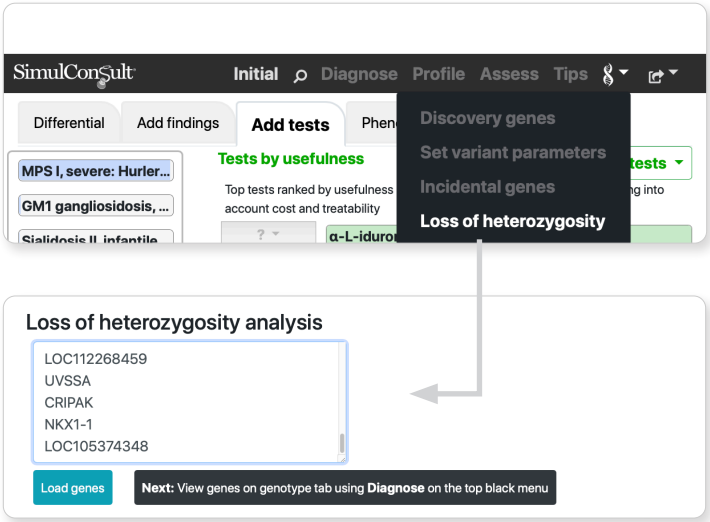






Discovery section of report
Selection of the variant adds discovery section to the "cart" and report

Loss of heterozygosity analysis



Use results from a microarray about loss of heterozygosity

- **Select Loss of heterozygosity.** Find "Loss of heterozygosity" under DNA menu
- **Input gene list.** Convert the regions where loss of heterozygosity was found (e.g., chr4 801509 1503857), to a list of genes. Paste in gene list and "Load genes"
- **Review genes.** The green shading will indicate the gene zygosities most pertinent to your patient. Then you can use suggestions of useful clinical or lab findings to distinguish among the diseases in the differential diagnosis

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