Genomic discovery

A patient walks into hospital.

The doctors says:

"We were expecting you.

"Yesterday we diagnosed your illness and have prepared your treatment plan."

“Why is it this way?”

~~“Because we say so”~~

Our doctor is an expert knowledge curator.

Provide medical diagnosis
that is evidence-based.

How can I trust medicine
from an algorithm ?

Video clip: 1992 “Computers can not replace AT&T switchboard operators.”

A patient has a severe illness.

The doctor can provide a treatment.

How can the doctor be sure ?

The doctor states the facts :

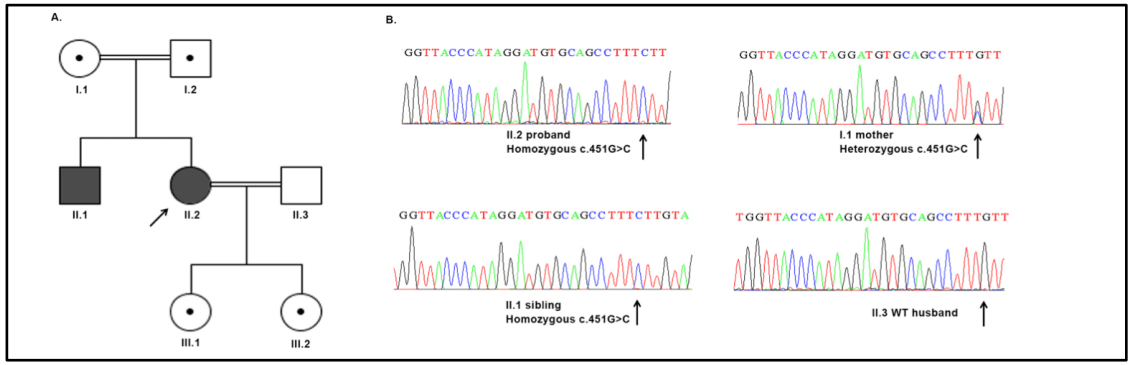
We can explain your illness.

Due to a variant in your DNA,
your immune systems is often overactive.

This causes inflammation and pain.

We know the mechanism because of
existing scientific evidence.

We can explain your illness.



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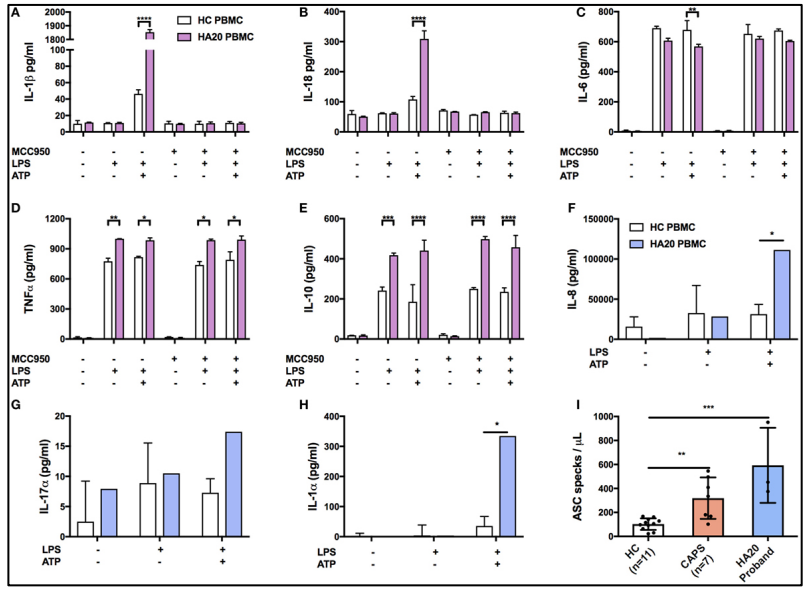

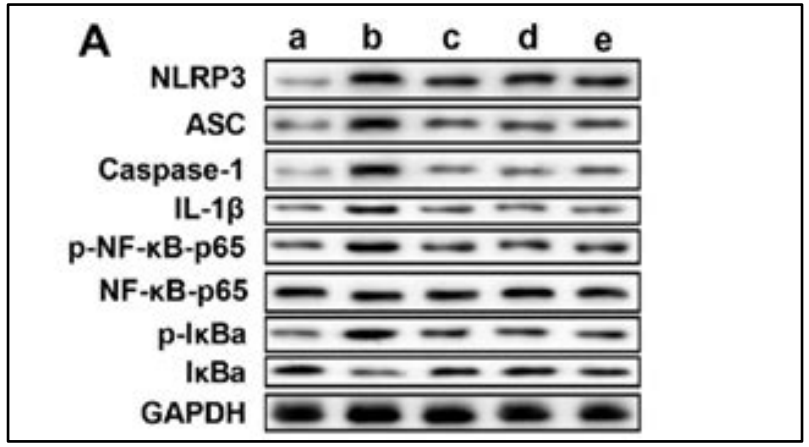

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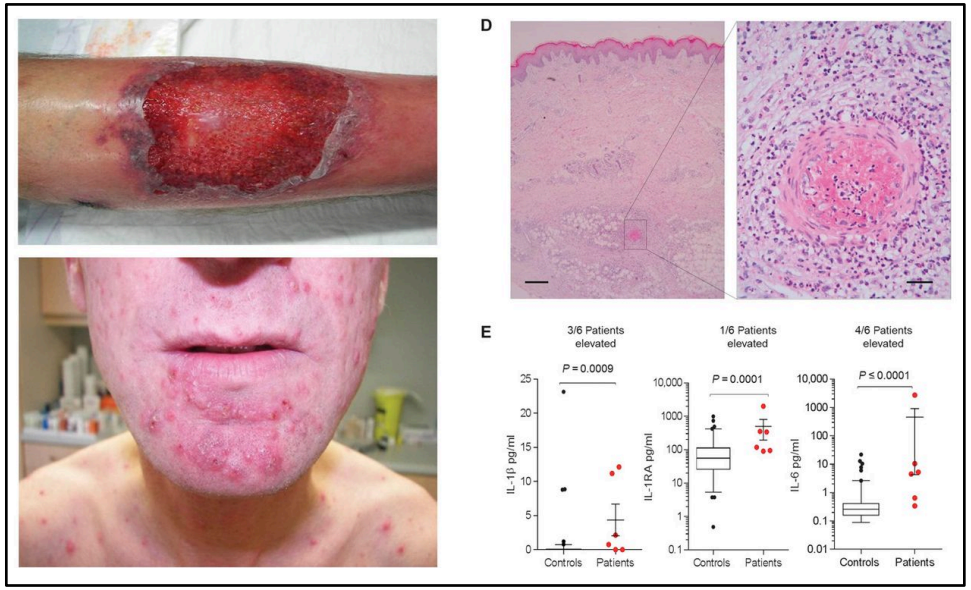

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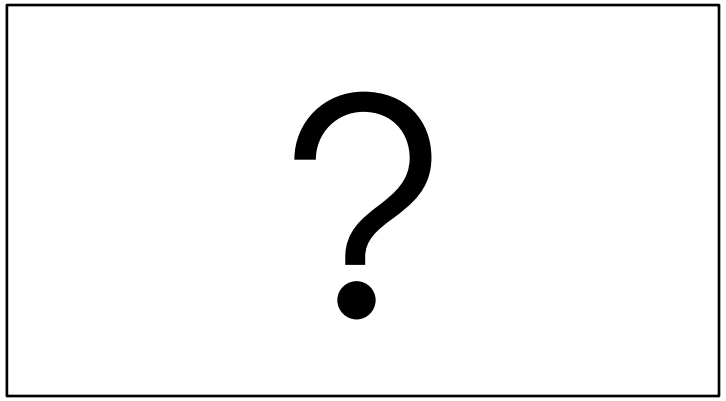


Evidence builder

- Controls intricate analysis protocols.
- Generates actionable diagnosis.
- Folds down into a *simple*, *single*, *concise* report.

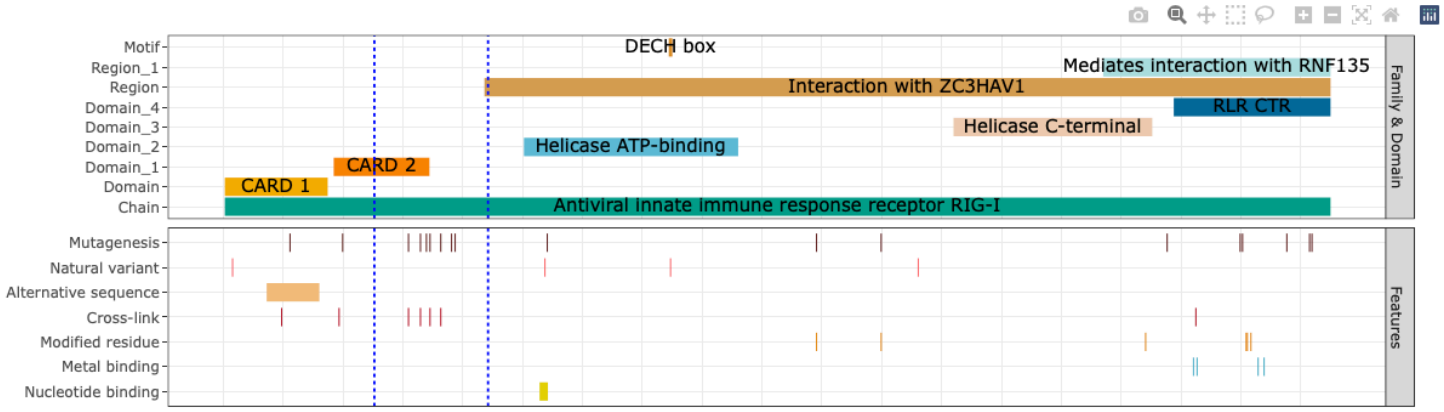
Protocol

Evidence source

Simple report

Search

SYMBOL	Consequence	IMPACT	HGVSc	HGVSp	CANONICAL	MAX_AF	MAX_AF_POPS	gnomAD_exomes_non_topmed_POPMAX_AF	gnomAD_genomes_POPM_AF
DDX58	missense_variant	MODERATE	ENST00000379883.3:c.662N>G	ENSP00000369213.2:p.Asn221Ser	YES	0.0004539	AA	8.972790e-06	4.825090e-
DDX58	missense_variant	MODERATE	ENST00000379883.3:c.377N>G	ENSP00000369213.2:p.Asp126Gly	YES	0.0001462	gnomAD_AMR	1.467310e-04	2.939450e-

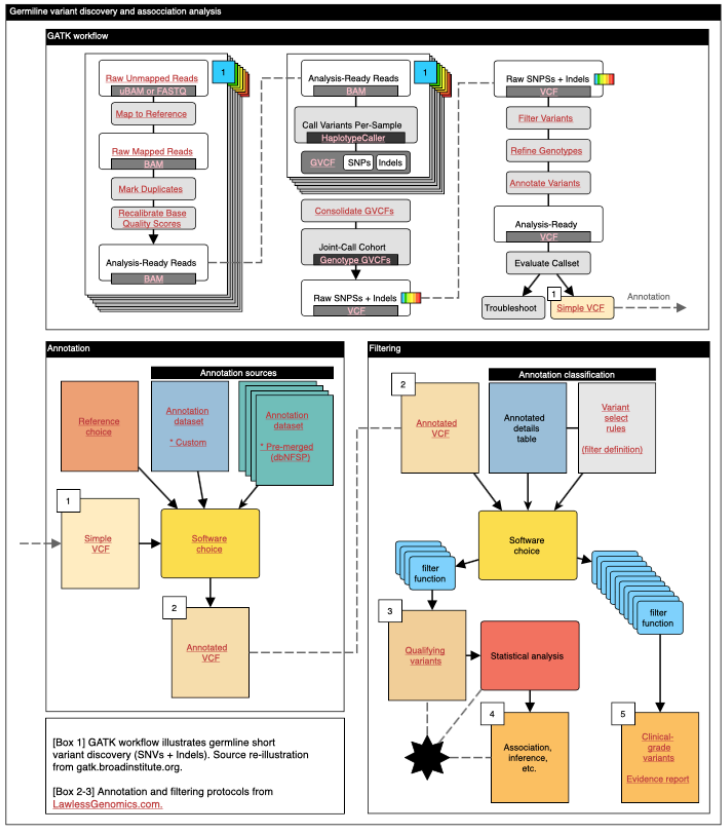


Protocol

Was the correct method used ?

How was it done ?

What does each step do ?

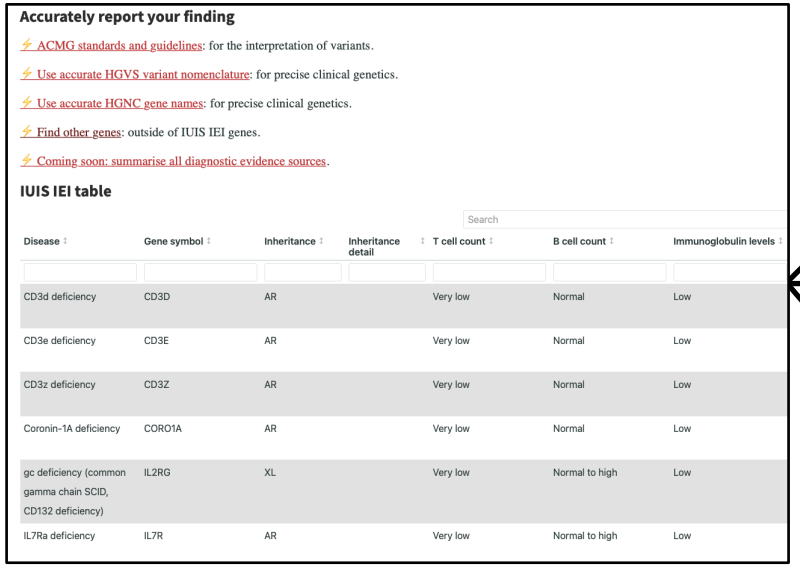


[Link: example protocol page]

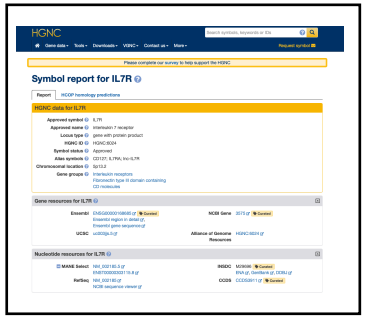
Evidence source

Analysis browser.

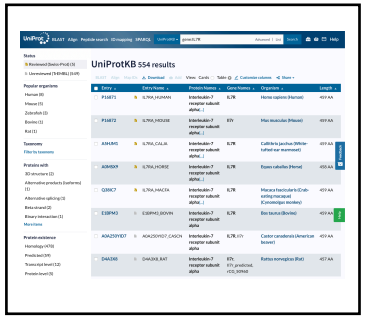
Query report to access evidence sources.



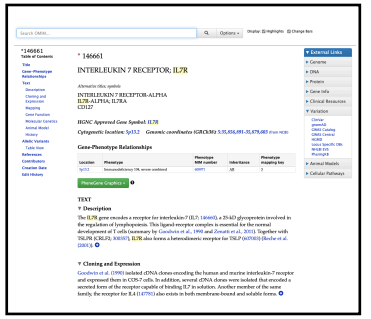
HGNC



UniProt

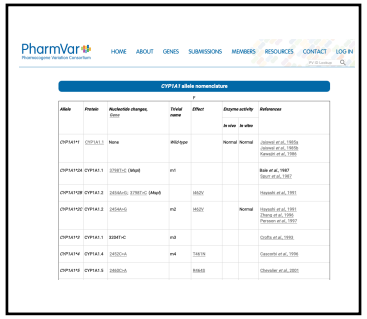


OMIM

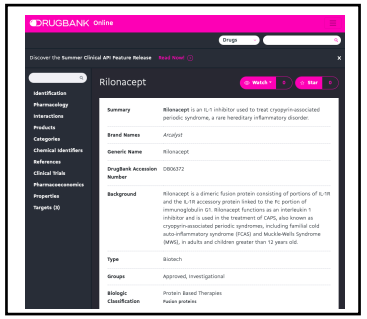


GnomAD

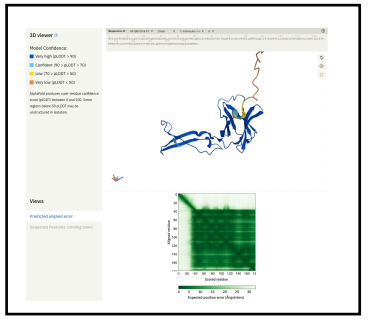
PharmVar



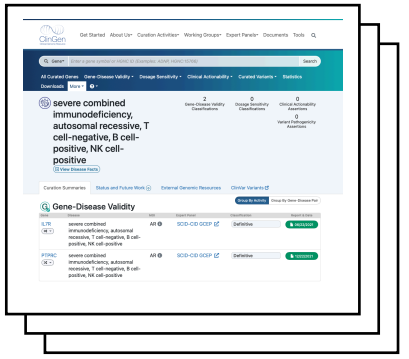
DrugBank



Alpha fold



ClinGen



many more

[Link: example evidence page]

When you have an efficient tool
you open new doors.

Clinical diagnosis is a
simple application example.

Every step

For every genetics-based application,
there are key critical factors:

1. Accurate application of protocols.
2. Easy protocol substitution.
3. Ensure that all relevant evidence has been assessed.
4. Summarize actionable results.
5. Provide a chain of custody for analysis and interpretation.

Every step

- Drug development and regulation
- Genomic-based discovery
- Genomic medicine

Every field

- Pharmaceutical industry
- Personalised medicine
- Biomedical sciences

Examples in use

Personalized medicine

Science Translational Medicine. Familial autoinflammation with neutrophilic dermatosis reveals a regulatory mechanism of pyrin activation. 10.1126/scitranslmed.aaf1471 *S.L. Masters, et al*.

Frontiers in Immunology. A case of AOSD caused by a novel splicing mutation in TNFAIP3 successfully treated with tocilizumab. 10.3389/fimmu.2018.01527 *D. Lawless, et al*.

Blood. Germline TET2 Loss-Of-Function Causes Childhood Immunodeficiency and Lymphoma. 10.1182/blood.2020005844 *J. Spegarova, and D. Lawless, et a*l.

JACI-D-22-00926 (in-press) Prevalence of CFTR variants in PID patients with bronchiectasis - an important modifying co-factor. *D. Lawless, et al*.

Viral epidemiology

medRxiv. Viral genetic determinants of prolonged respiratory syncytial virus infection among infants in a healthy term birth cohort. 10.1101/2022.06.22.22276752 *D. Lawless, et al*.

Pharmacogenomic discovery pipeline

Pharmacogenomics for personal medicine — x8 EPFL MSc projects (2019-2022) for Health 2030 initiative.

Who would take a prototype today ?

Personalized medicine

Swiss Personalized Health Network
Health 2030, Swiss Hospitals

Clinical genetics

Blueprint Genetics, US
Dante labs, Italy
Sophia genetics, Swsiss, US
BGI, China
Genomics England, UK

Pharma

Novartis, Roche, Genentech, J&J, etc.