



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.

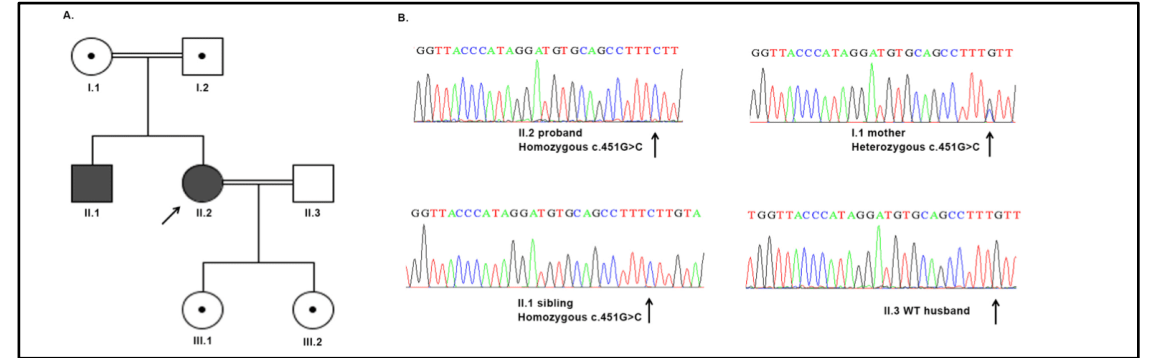
We know the mechanism because of  
existing scientific evidence.

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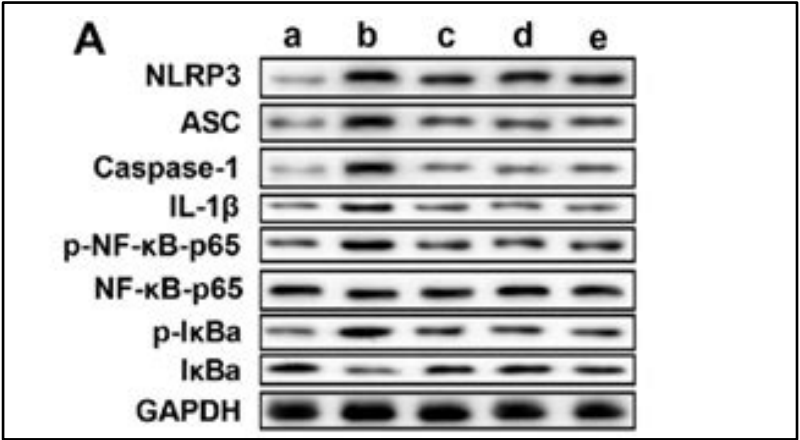
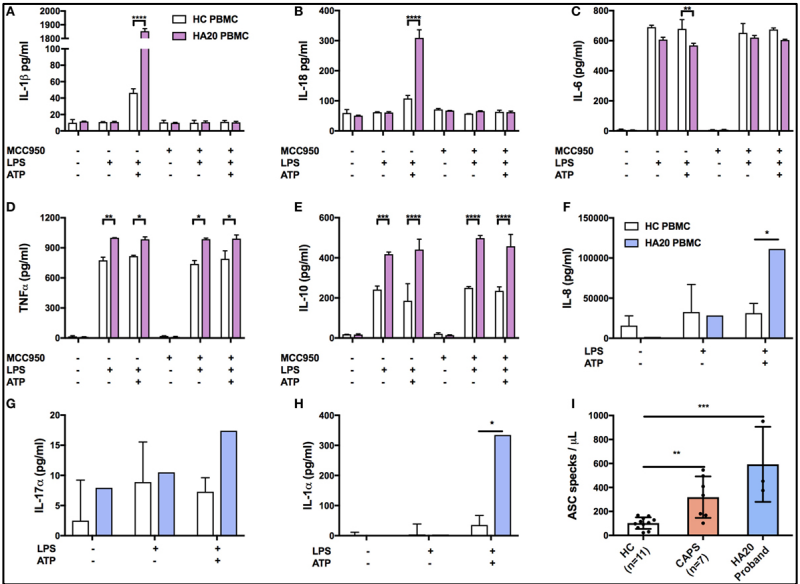


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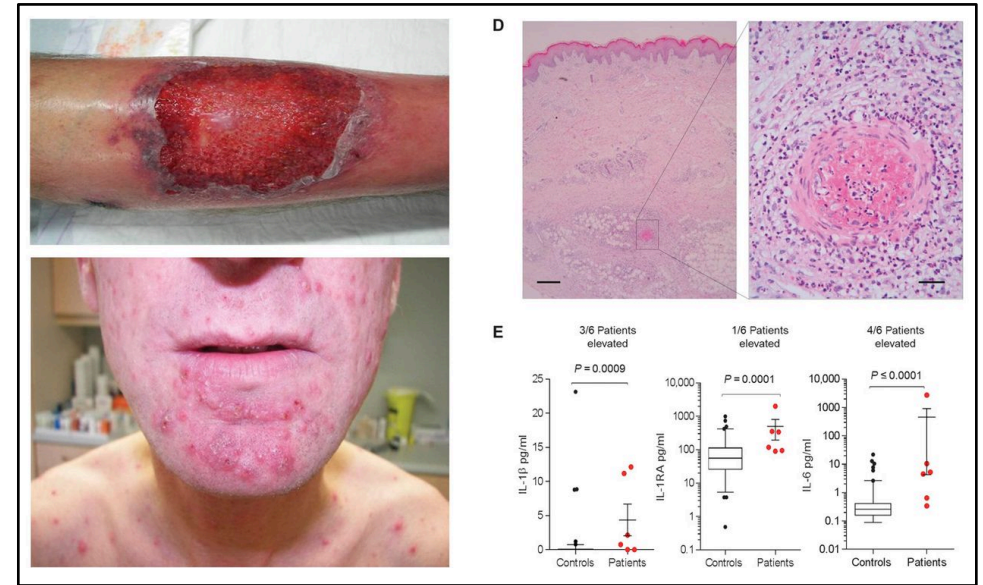


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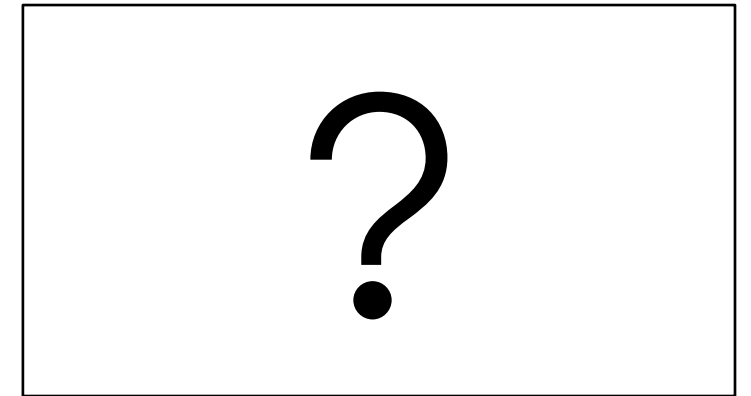


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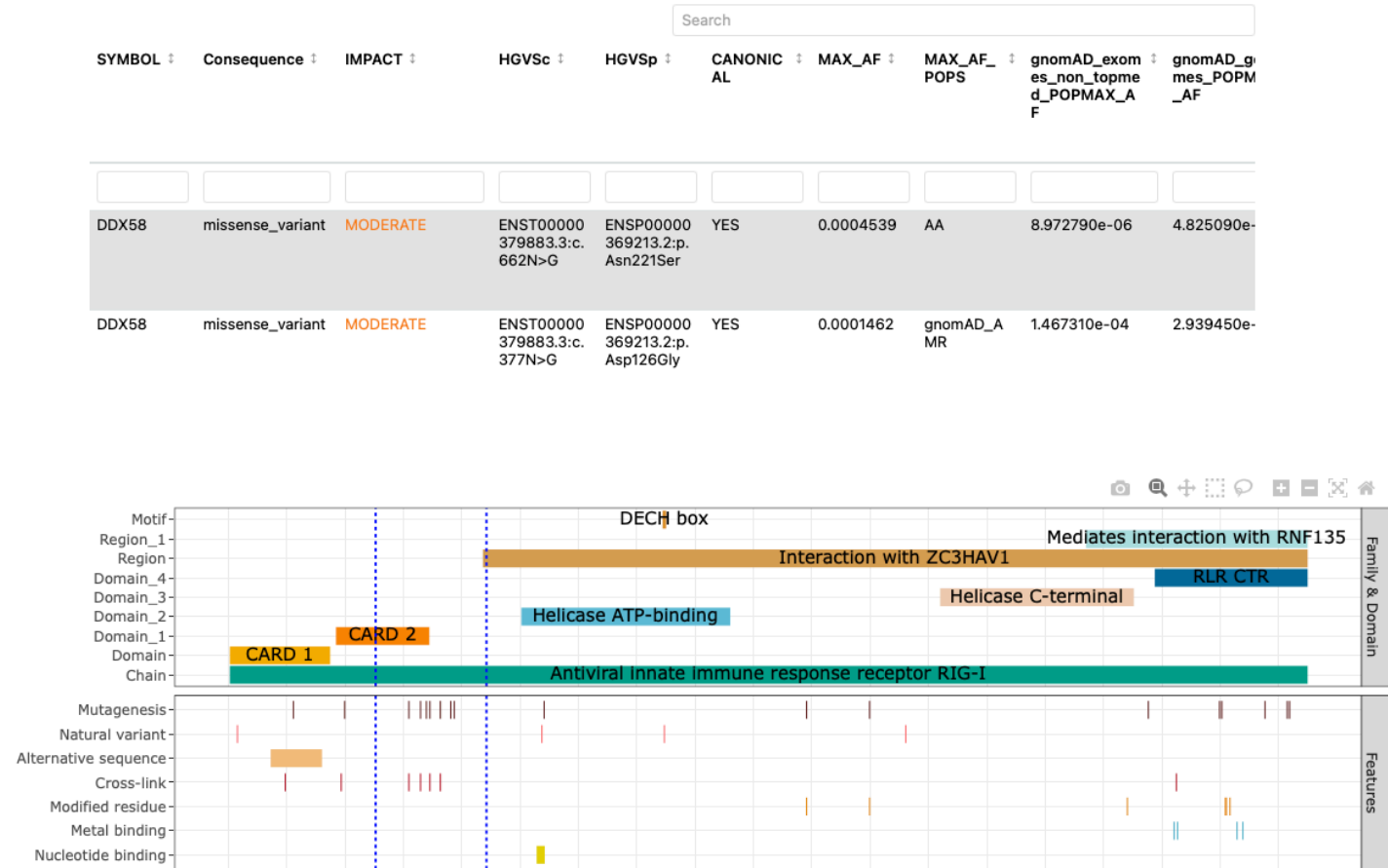
## Evidence builder

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

Protocol

Evidence source

Simple report

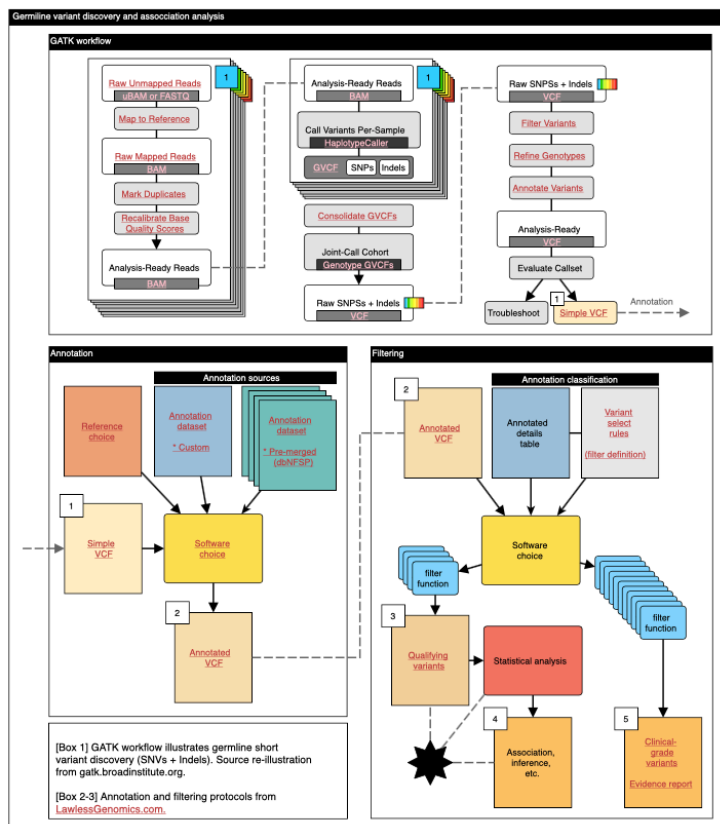


# Protocol

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.

**Accurately report your finding**

- ACMG standards and guidelines: for the interpretation of variants.
- Use accurate HGVS variant nomenclature: for precise clinical genetics.
- Use accurate HGNC gene names: for precise clinical genetics.
- Find other genes: outside of IUIS IEI genes.
- Coming soon: summarise all diagnostic evidence sources.

**IUIS IEI table**

Disease	Gene symbol	Inheritance	Inheritance detail	T cell count	B cell count	Immunoglobulin levels
CD3d deficiency	CD3D	AR		Very low	Normal	Low
CD3e deficiency	CD3E	AR		Very low	Normal	Low
CD3z deficiency	CD3Z	AR		Very low	Normal	Low
Coronin-1A deficiency	CORO1A	AR		Very low	Normal	Low
gc deficiency (common gamma chain SCID, CD132 deficiency)	IL2RG	XL		Very low	Normal to high	Low
IL7Ra deficiency	IL7R	AR		Very low	Normal to high	Low

# PharmVar

Allele	Protein	Archival changes (2010)	Transcript	Effect	Enzyme activity	Reference
CYP2A6*1	CYP2A6	None	Normal	Normal	Normal	Shimada et al., 2010
CYP2A6*2	CYP2A6	Y100H	Normal	Normal	Normal	Shimada et al., 2010
CYP2A6*3	CYP2A6	Y100H	Normal	Normal	Normal	Shimada et al., 2010
CYP2A6*4	CYP2A6	Y100H	Normal	Normal	Normal	Shimada et al., 2010
CYP2A6*5	CYP2A6	Y100H	Normal	Normal	Normal	Shimada et al., 2010
CYP2A6*6	CYP2A6	Y100H	Normal	Normal	Normal	Shimada et al., 2010
CYP2A6*7	CYP2A6	Y100H	Normal	Normal	Normal	Shimada et al., 2010
CYP2A6*8	CYP2A6	Y100H	Normal	Normal	Normal	Shimada et al., 2010
CYP2A6*9	CYP2A6	Y100H	Normal	Normal	Normal	Shimada et al., 2010
CYP2A6*10	CYP2A6	Y100H	Normal	Normal	Normal	Shimada et al., 2010

[Link: example evidence page](#)

# HGNC

Symbol report for IL7R

IL7R (Interleukin 7 receptor) is a protein-coding gene located on chromosome 2 (2p11.2). It is a member of the IL7R family and is involved in the regulation of T cell development and function.

Gene structure: 11 exons, 10 introns.

Protein structure: 317 amino acids, 3 domains (IL7R-α, IL7R-β, IL7R-γ).

Gene expression: Expressed in T cells, B cells, and other immune cells.

Gene function: Involved in the regulation of T cell development and function.

# OMIM

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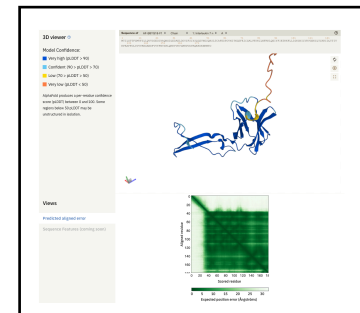
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# Alpha fold



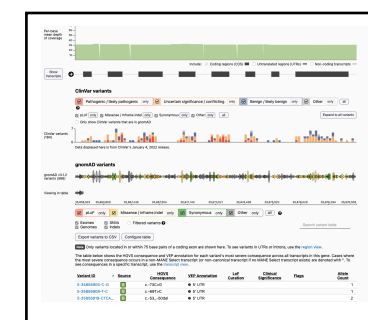
many more

# UniProt

UniProt is a comprehensive resource for protein sequence and functional information. It provides a central repository for protein sequences, structures, and functional data from a wide range of organisms.

The UniProt entry for IL7R provides detailed information about the protein, including its sequence, structure, and function.

# GnomAD



# ClinGen

ClinGen is a clinical genetics resource that provides information on the clinical significance of genetic variants. It includes data on the frequency of variants in different populations and tissues, as well as information on the clinical significance of specific variants.

The ClinGen entry for IL7R provides a clinical significance assessment for the protein, including information on the frequency of variants in different populations and tissues, as well as information on the clinical significance of specific variants.

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](https://doi.org/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](https://doi.org/10.3389/fimmu.2018.01527) D. Lawless, *et al.*

Blood. Germline TET2 Loss-Of-Function Causes Childhood Immunodeficiency and Lymphoma. [10.1182/blood.2020005844](https://doi.org/10.1182/blood.2020005844) J. Spegarova, and D. Lawless, *et al.*

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](https://doi.org/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.

