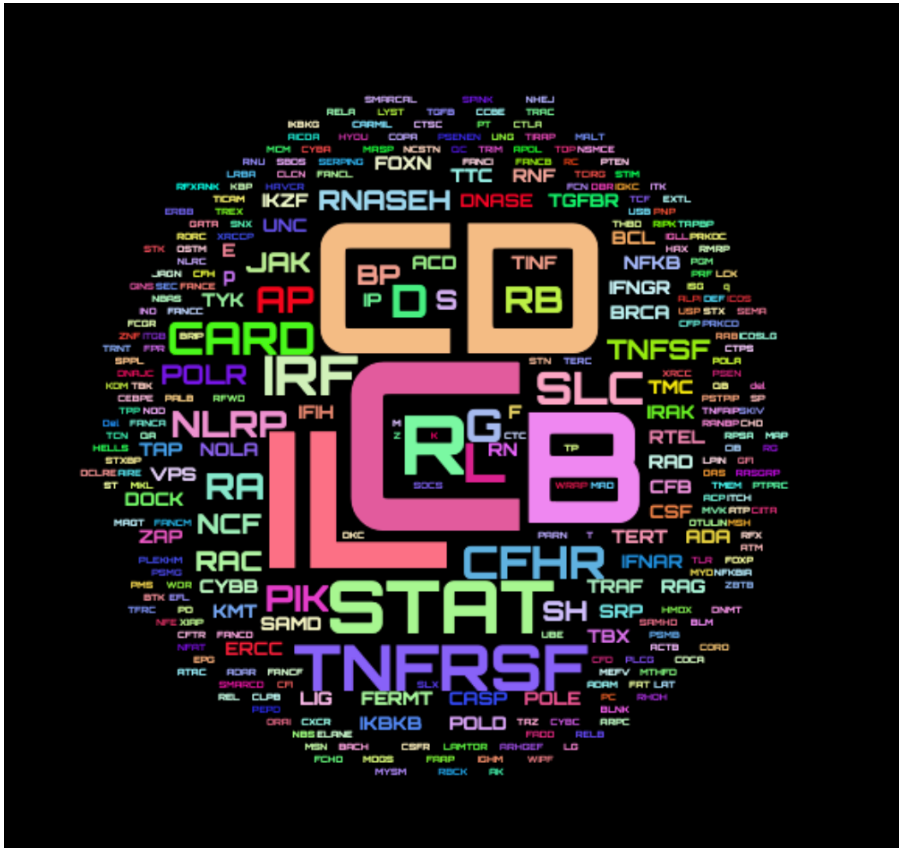
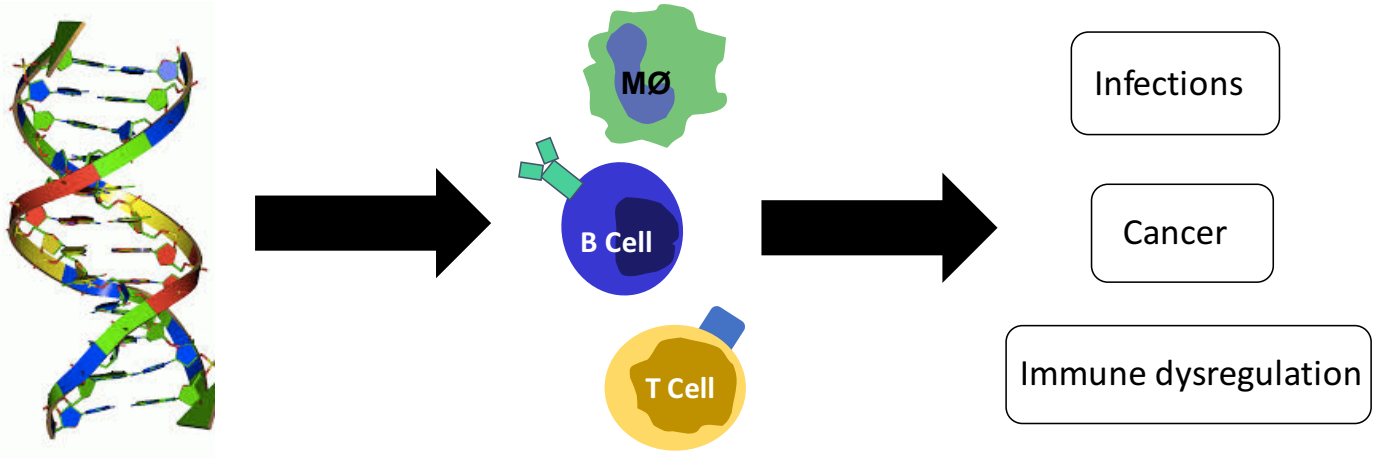
The immune system is made up of several hundred components, each encoded by their own gene



Created using ABCYa.com

Clinical immunologists treat inborn errors of immunity (IEIs)

- Group of genetic conditions affecting immune system development, function or both



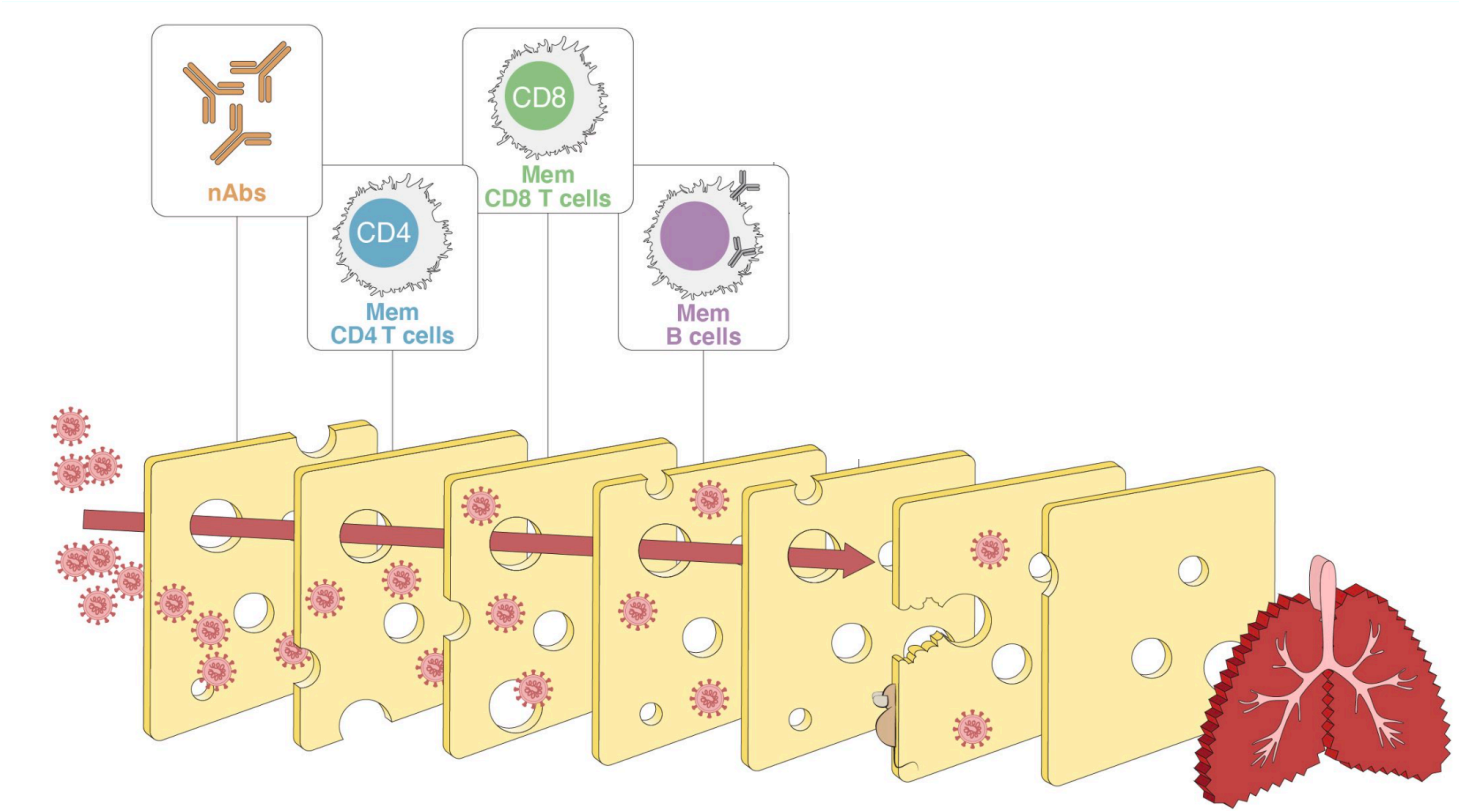
- More than 500 unique IEIs described

Clinical immunologists treat inborn errors of immunity (IEIs)

Individually rare

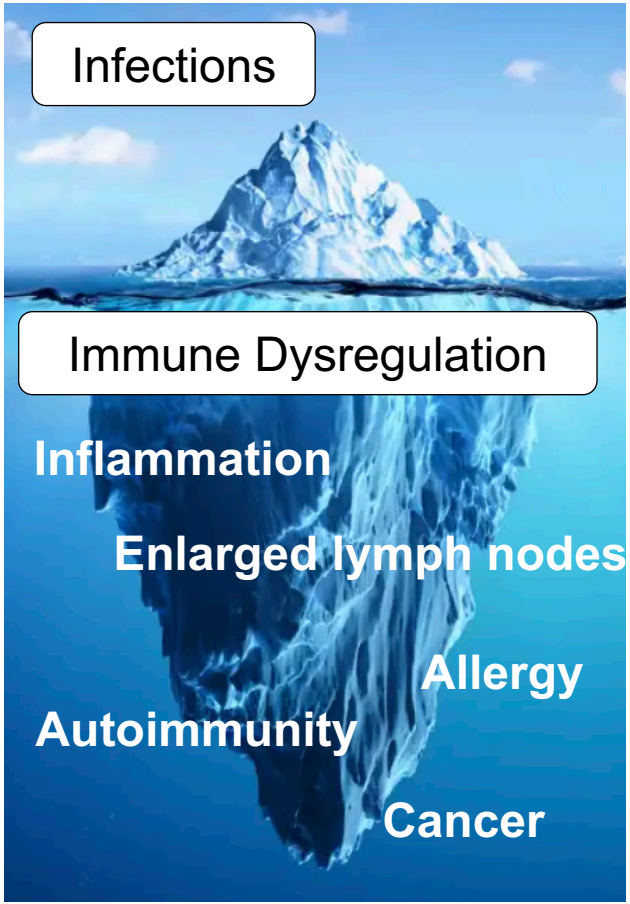
Collectively common

Inborn errors of immunity: when one piece of the immune system is missing



Adapted from Prof. Shane Crotty (@profshanecrotty)

IEIs have broad clinical features



Inborn errors of immunity don't just predispose to infections

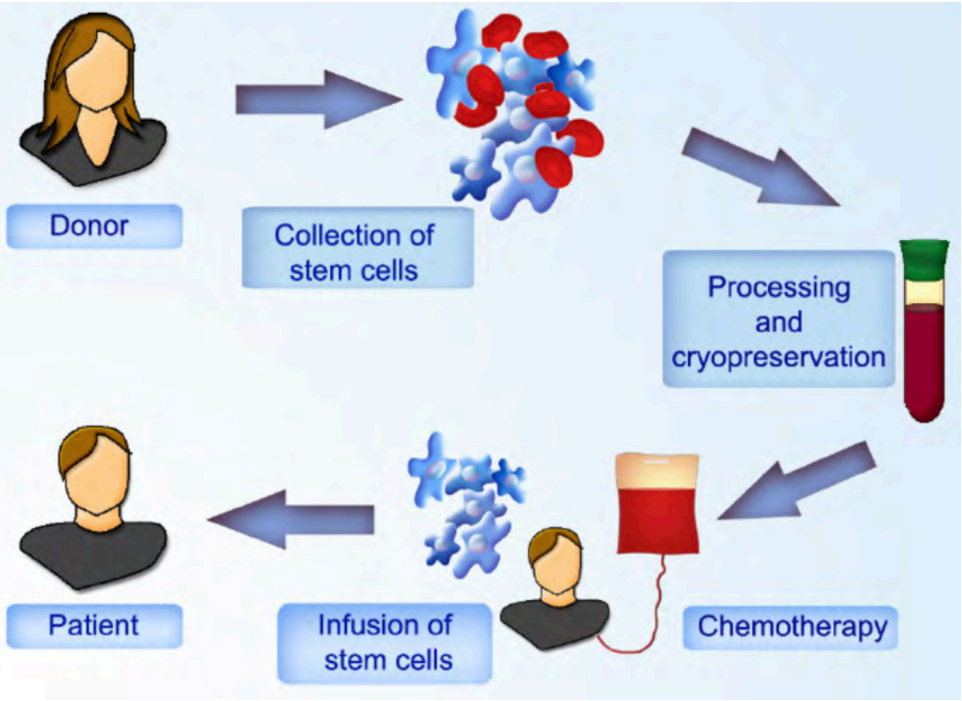
- Also predispose to 'immune dysregulation'
- → when the immune system has a hard time controlling itself

Cortesi M et al. Front Immunol. 2024 Dec 19;15:1497921.
Fischer A et al. J Allergy Clin Immunol. 2017.

How do we treat inborn errors of immunity?

- Depends on the particular type of IEI a person has
- May include measures to:
- Protect against infection
- Provide medicine to calm over-active immune responses
- Targeted therapies
- Replace immune system with a healthy donor’s

Allogeneic hematopoietic stem cell transplantation



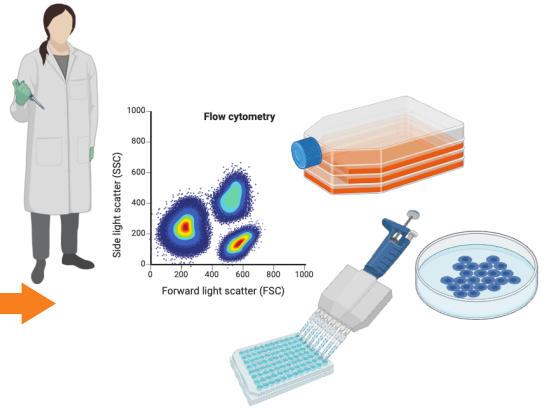
- Patient with SCID receives stem cells from a healthy donor
- These stem cells travel to the patient's bone marrow, where they will repopulate and replace the patient's immune system with a healthy immune system

L Huergo-Zapico *et al*. INTECH Open Access Publisher 2012

Pipeline for discovering rare genetic immune diseases

Person with severe, unusual infection or inflammation (suspected IEI)

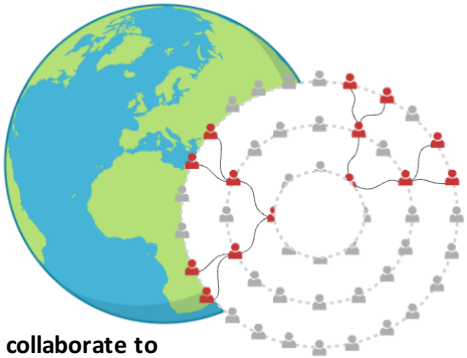
Genomic sequencing and identification of candidate variants



Functional validation to establish genotype-phenotype relationship

In vitro treatment testing

Communicate results with care team and patient + family



Share findings and collaborate to identify similarly affected individuals

Slide adapted from Maryam Vaseghi-Shanjani

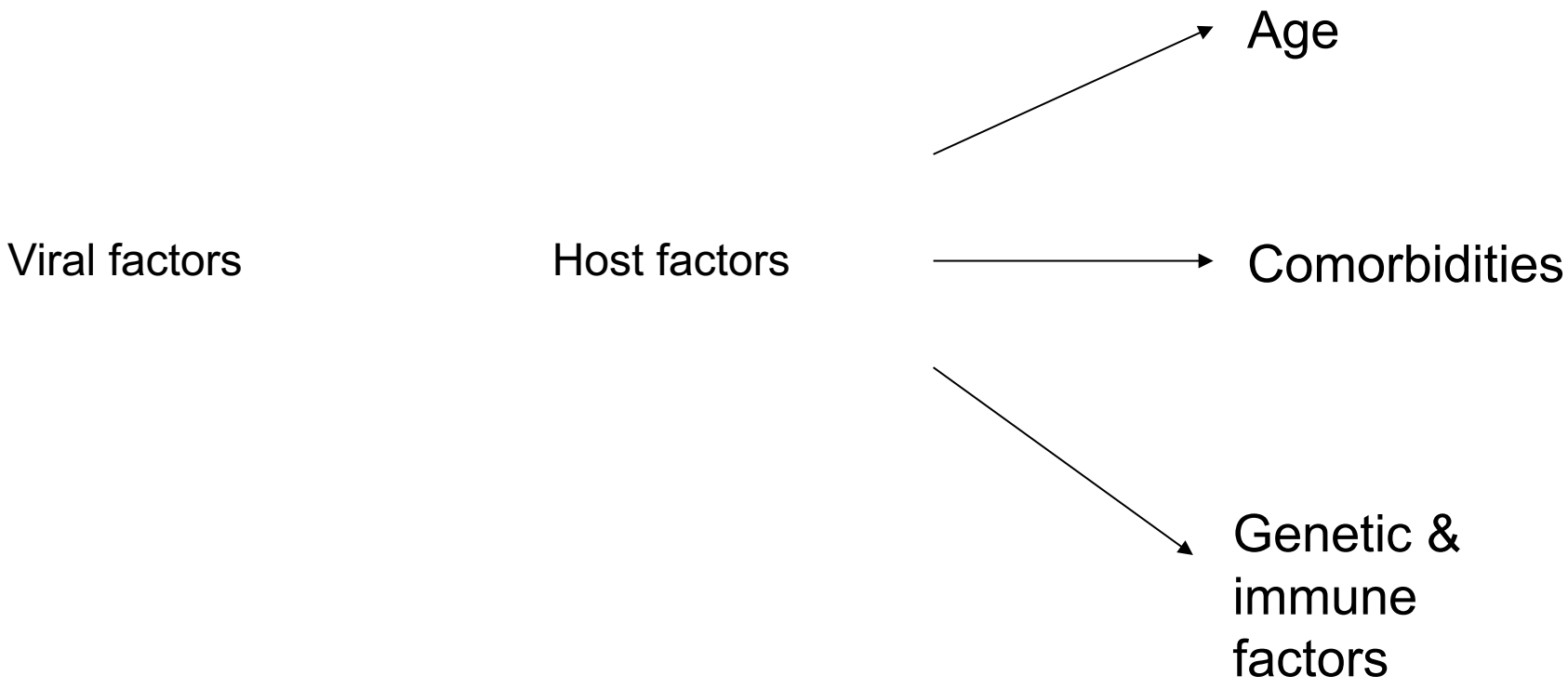
Severe acute respiratory syndrome coronavirus 2 (SARS-CoV2)

- Virus underlying coronavirus disease 2019 (COVID-19)
- Wide spectrum of disease severity

Asymptomatic

Severe

What accounts for spectrum of COVID-19 severity?

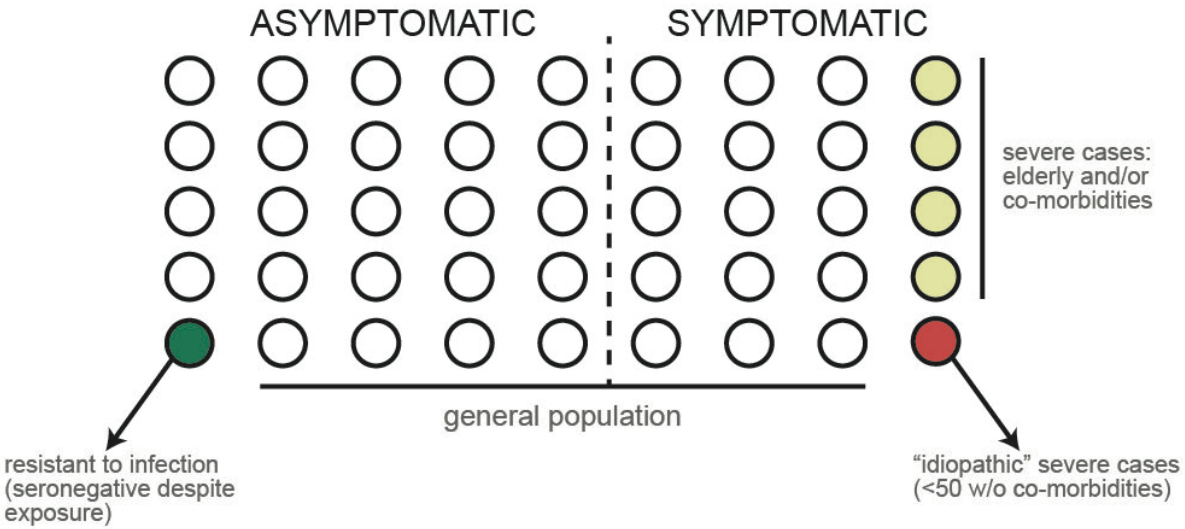


Lancet 2020; 395:1054-62.

COVID Human Genetic Effort: learning from outliers

Hypothesis:

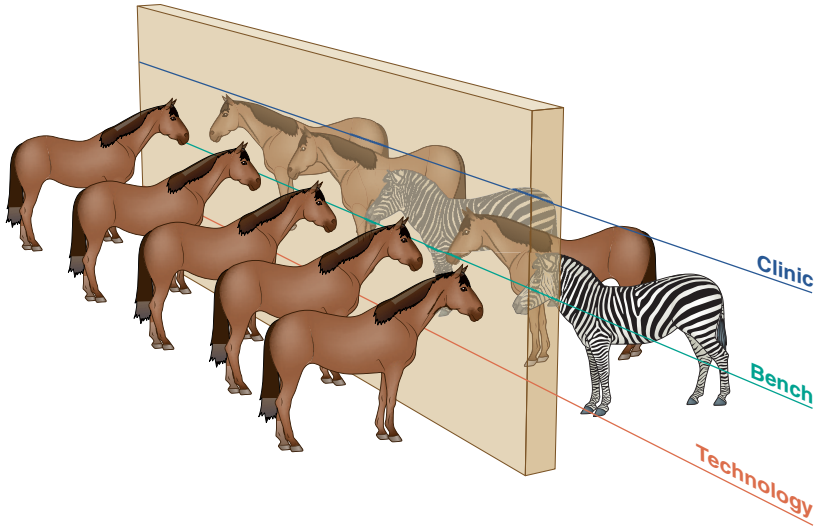
monogenic causes of susceptibility
and resistance to SARS-CoV-2 infection



https://www.covidhge.com/

Summary

- Identifying rare diseases is crucial so that affected individuals can receive access to appropriate care
- Clinician-scientist is a rewarding career path to consider!



Biggs CM, Lu HY, Turvey SE. Nat Genet. 2017 Jul 27;49(8):1162-1163.

Acknowledgement

Thank you for your time!

Thank you to patients and families

Figures created using BioRender

Canadian Allergy, Asthma and Immunology Foundation

CIHR IRSC
Canadian Institutes of Health Research
Instituts de recherche en santé du Canada

Primary Immune Deficiency Treatment Consortium

PROVIDENCE HEALTH CARE
Research Institute
Pursuing **real life** health solutions.

AllerGen
Allergy, Genes and Environment Network

Michael Smith Health Research BC

BC Children's Hospital
Research Institute