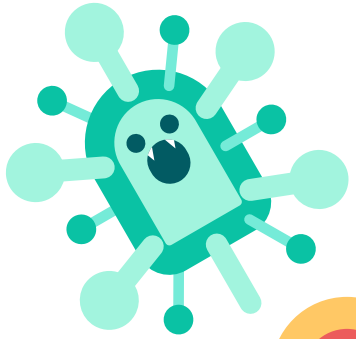
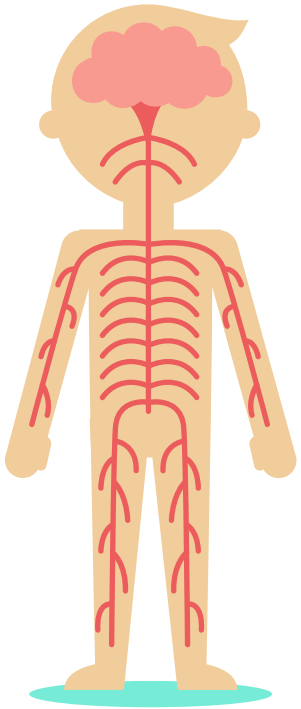
Diagnosis of an Immunodeficiency



Bianca Minter, Virginia Tam,
Victoria Walden

OUR PATIENT: JOHNNY



At 1

Recurring sinus infections (ethmoid sinuses), β- hemolytic streptococci

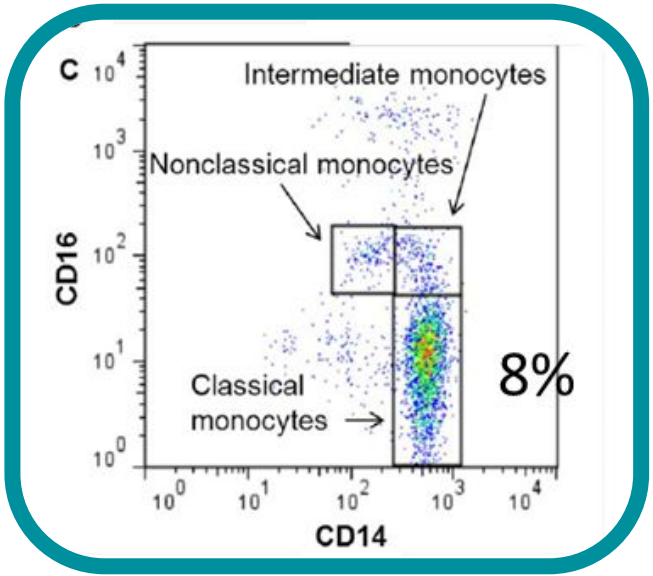
At 3

Pneumonia from *Pneumocystis jirovecii*

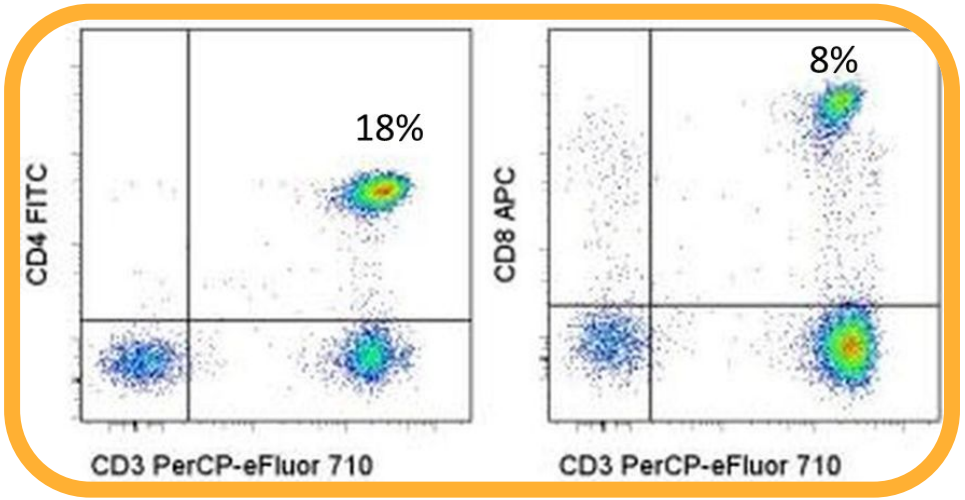
Family

No family history of immune disorders

Flow Cytometry

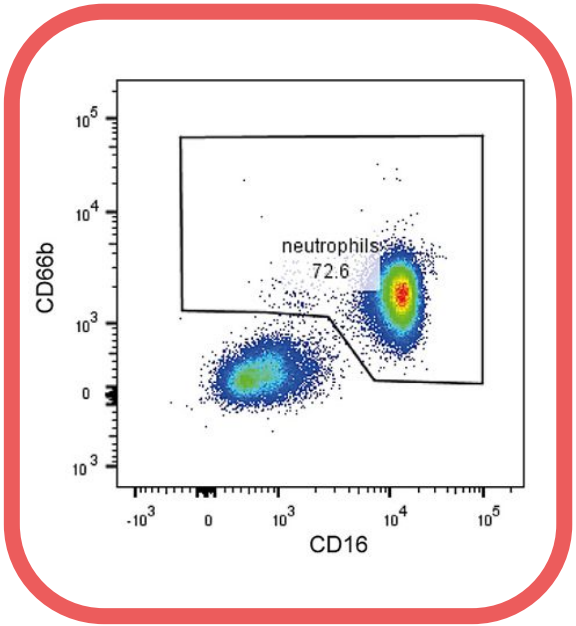


Normal % Monocytes: 2-8%

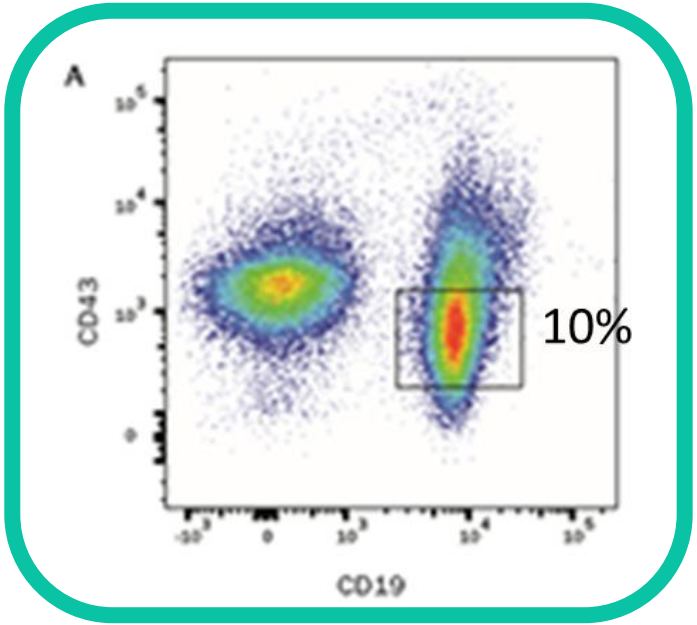


Normal % CD4 T cells:
10-20%
Normal % CD8 T cells:
3-10%

Flow Cytometry



Normal % Neutrophils: 40%-65%



Normal % B cells: 3-10%

Enzyme-Linked Immunosorbent Assay (ELISA)

IgM

Normal serum antibody levels (mg/dl): 75-150

IgA

Normal serum antibody levels (mg/dl): 150-225

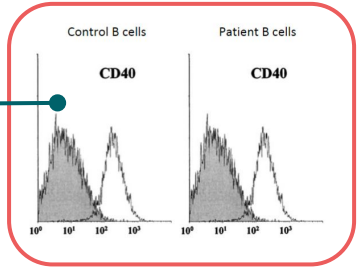
IgG

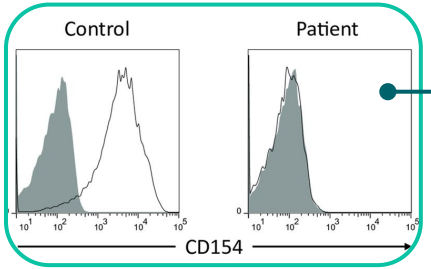
Normal serum antibody levels (mg/dl): 600-1500

More Flow Cytometry (And Western Blot Analysis)

B cells

Has CD40 on B cells



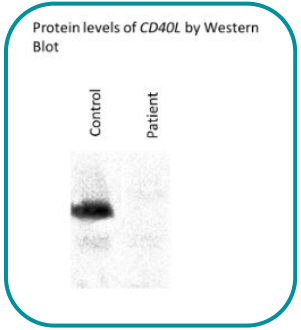


T cells

Has no CD40 ligand on CD3+ T cells

CD40L

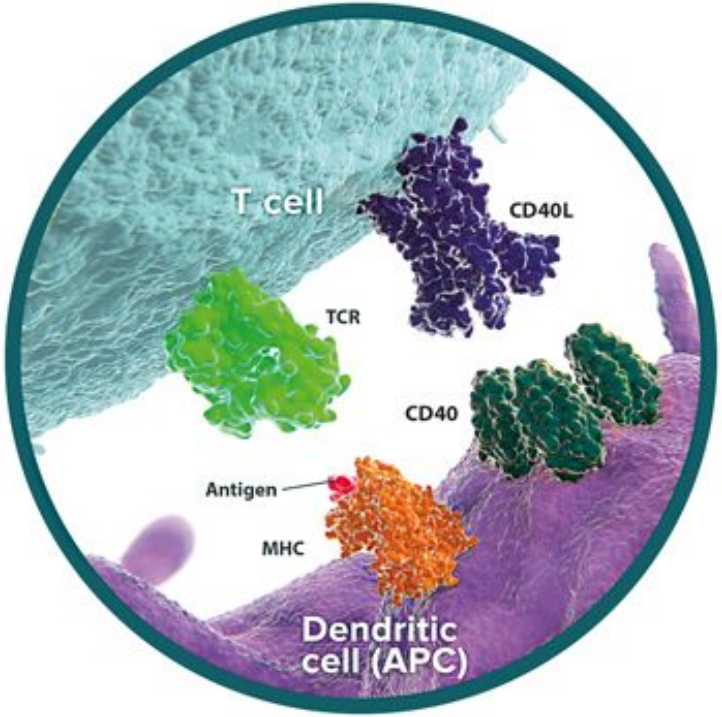
Confirmed absence of CD40L with western blot analysis



Activation of B Cells

CD40

- CD40 is a protein that binds to CD40L
- It is located on B cells



CD40L

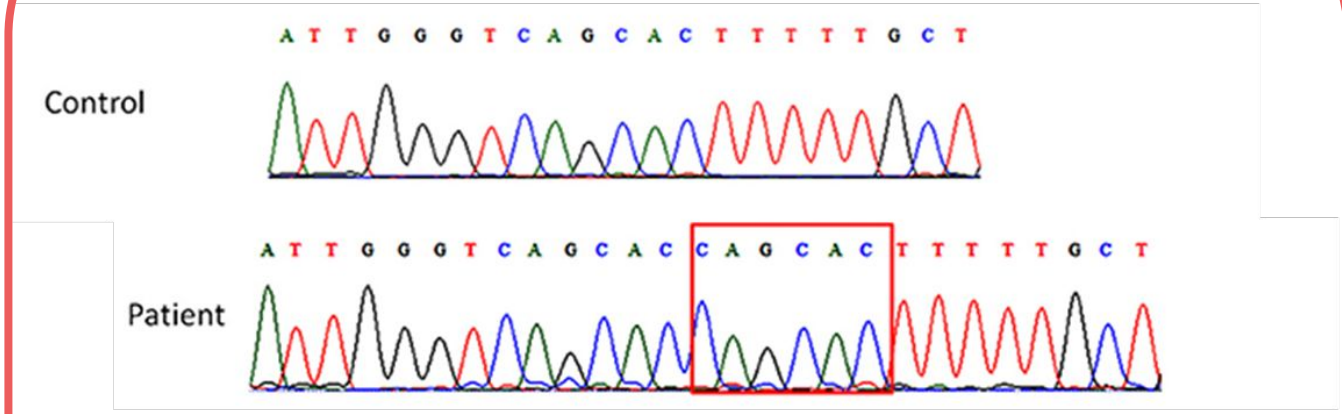
- CD40L is also called CD154
- It is located on CD3+ T cells and binds to CD40

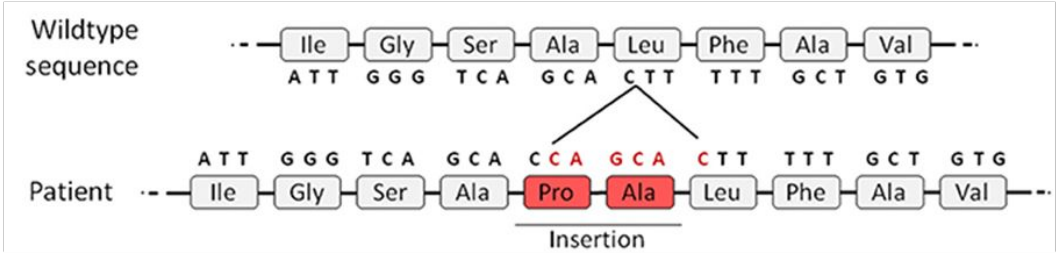
CD40\CD154 interactions

- CD40/CD40L interaction helps activate B cells and B Cell differentiation and producing immunoglobulins

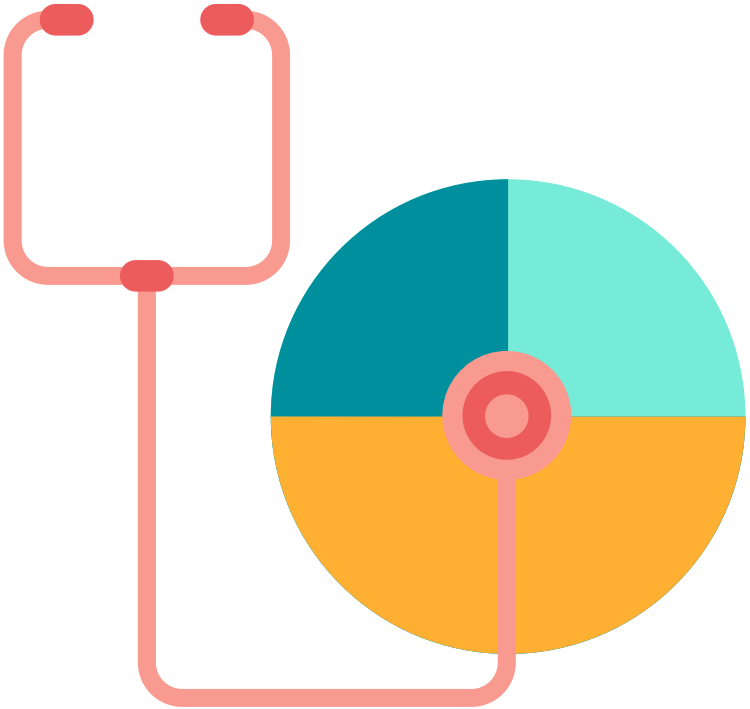
DNA Mutation Analysis

DNA Sequence Analysis of *Tnfsf5*/ *CD40L* gene





Diagnosis of Immunodeficiency



Immunoglobulin

Low levels of IgG and IgA

1

CD40L

Complete absence of CD40 ligand

2

Mutation

Mutation in TNFSF5/CD40L gene

3

What is X-linked Hyper IgM (Type 1)?

≥Normal IgM

Levels of IgM are elevated in sera.

Decreased IGs

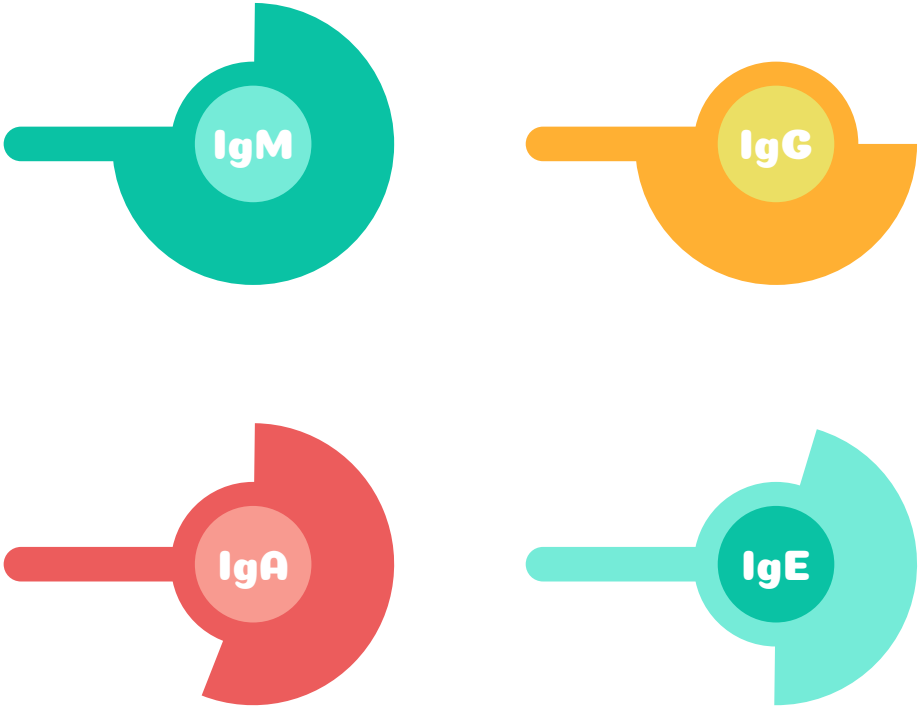
IgG, IgA, and IgE show unusually low concentrations.

Infections

Recurrent opportunistic bacterial and fungal infections

Disruption

B-cell activation is interrupted by absence of CD40L



CD40 Ligation Pathway Breakdown

Typical

CD40L function

CD40L enables T-cell activation of Ig differentiation.

HIGM1

CD40L function

Without CD40L, class switch does not occur.

HIGM1

Detection

Without differentiation, only IgM will be produced.

IgM

Overproduction

The result of this is elevated IgM levels.

Prevalence and Demographics of XHIGM1

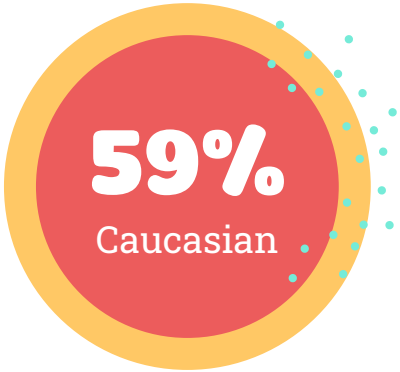
Statistics

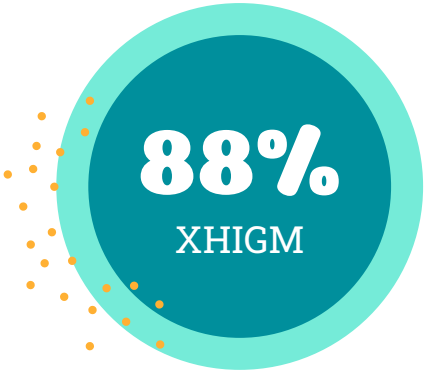
2 for 1,000,000 infant boys

All forms of HIGM are rare.

Ethnic Demographics

The next highest prevalence is African American at 10%, and APIA at 7%.





Other Diseases

XHIGM makes up 88% of HIGM conditions. 43% of patients had HIGM family history.

Most Common Treatments

Allogeneic Hematopoietic Stem Cell Transplant	Immunoglobulin Replacement Therapy

Summary

Tests Ran

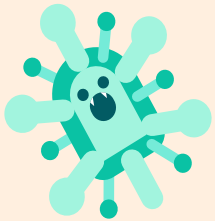
- Flow Cytometry
  - Tests to see white blood counts are normal
- ELISA
  - See if antibody levels are normal
- Another Flow Cytometry
  - Look at CD40 and CD40L on T cells
- Western Blot
  - Determine if the patient has CD40L proteins
- DNA Mutation Analysis
  - Look at where the DNA mutation is

Diagnosis

- X Linked Hyper IgM Syndrome Type 1
  - T cells and B cells cannot communicate with each other

Treatments

- Immunoglobulin Replacement Therapy
- Bone marrow transplant



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