Interferon Gamma Receptor 1 Deficiency presenting with *Mycobacterium avium intracellulare* (MAC) infection
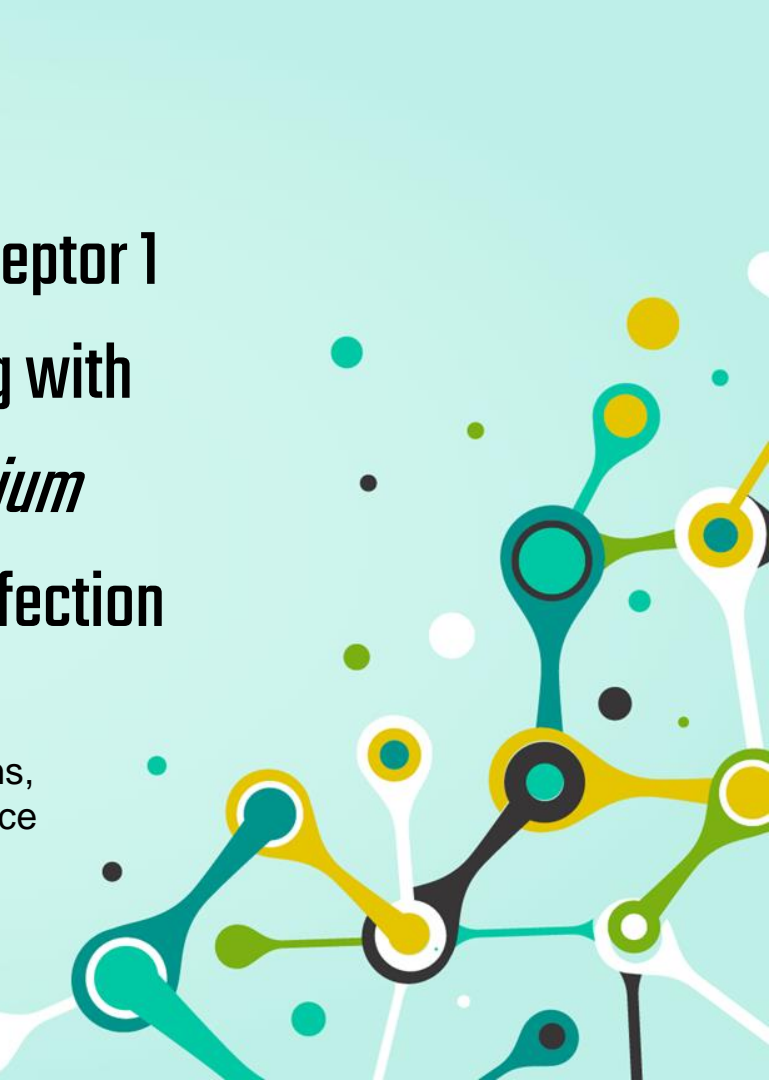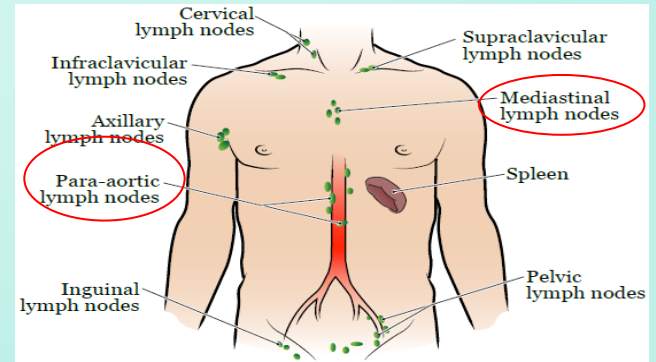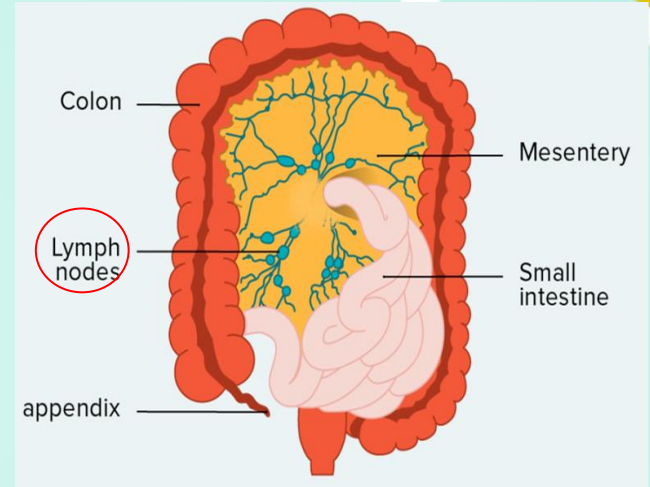
BIOL 404: Immunology
Presented by: Amy Helms, Tristana Foster, and Davice Jones

Summary of the Symptoms

- Female child
- 2 ½ years old
- Poor appetite
- Diarrhea
- Significant Weight Loss
- Enlarged Lymph Nodes in the mesentery and para-aortic region
- Repeated mycobacterial infections

Flow Cytometry Analysis

We wanted to run a Flow Cytometry to get a baseline understanding of the immune cells present in the patients system.

Flow cytometry is a common technology that uses lasers to produce **light signals** that are detected and converted into **electronic signals** which are analyzed by a computer.
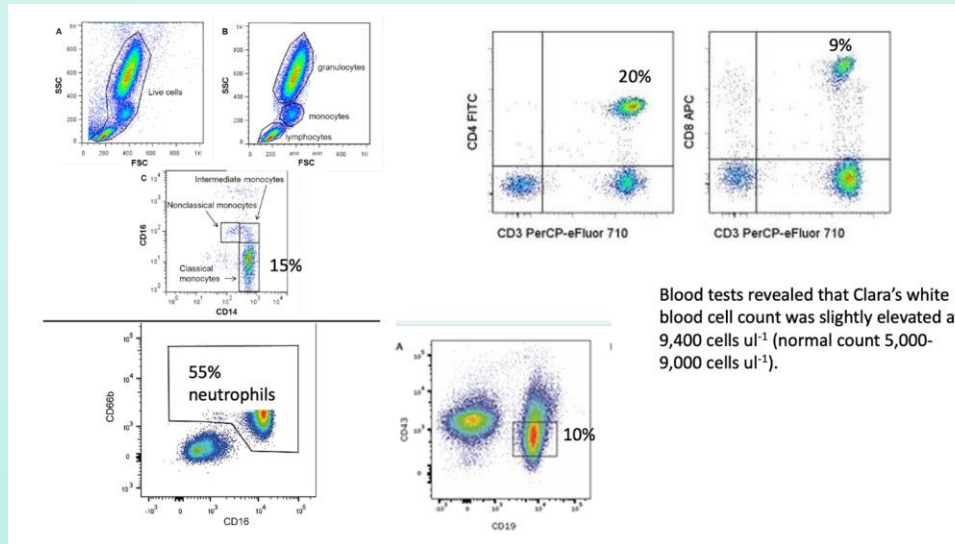
Flow Cytometry Results

These analyzed results for the patient showed cell populations of:

- White blood cell count= **9,400** (**Slightly abnormal:** average range is 5,000- 9,000)
- Neutrophils=**55%** (Normal: average range: 50-65%)
- Monocytes= **15%** (**Abnormal**: with a average range of 2-9%)
- CD4 T cells= **20%** (Normal: with an average of 20%)
- CD8 T cells= **9%** (**Top end of the range**: with an average 10%)
- B cells= **10%** (**Top end of the range**: with an average range of 10-15%)

The immune system was **not** functioning properly.

ELISA and Lymph node biopsy analysis

We wanted to run an ELISA (Enzyme-Linked Immunosorbent Assay) to measure **antibodies** in the patients blood.

We also conducted a lymph node biopsy to look at the **phagocytes** and **specific bacteria** because the patient had recurrent bacterial infections**.**

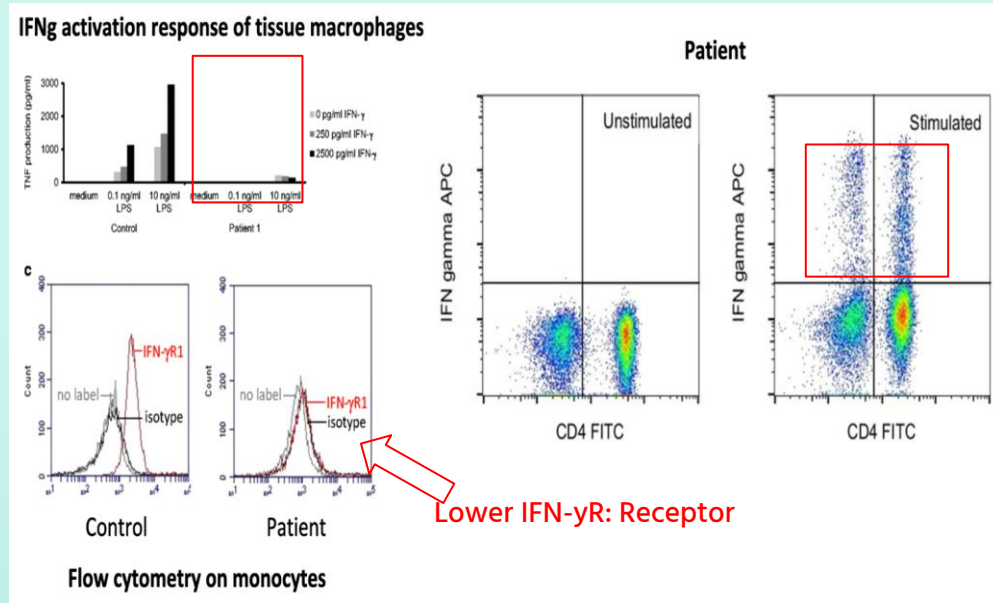| Antibody	Patient Serum antibody levels (mg/dl)	Range for Normal Serum Antibodies
IgM	175	75-150
IgA	450	150-225
IgG	1750	600-1500

Flow Cytometry

We wanted to measure if a Th1 response was present. The flow cytometry showed **normal** levels of CD40 and CD40L.
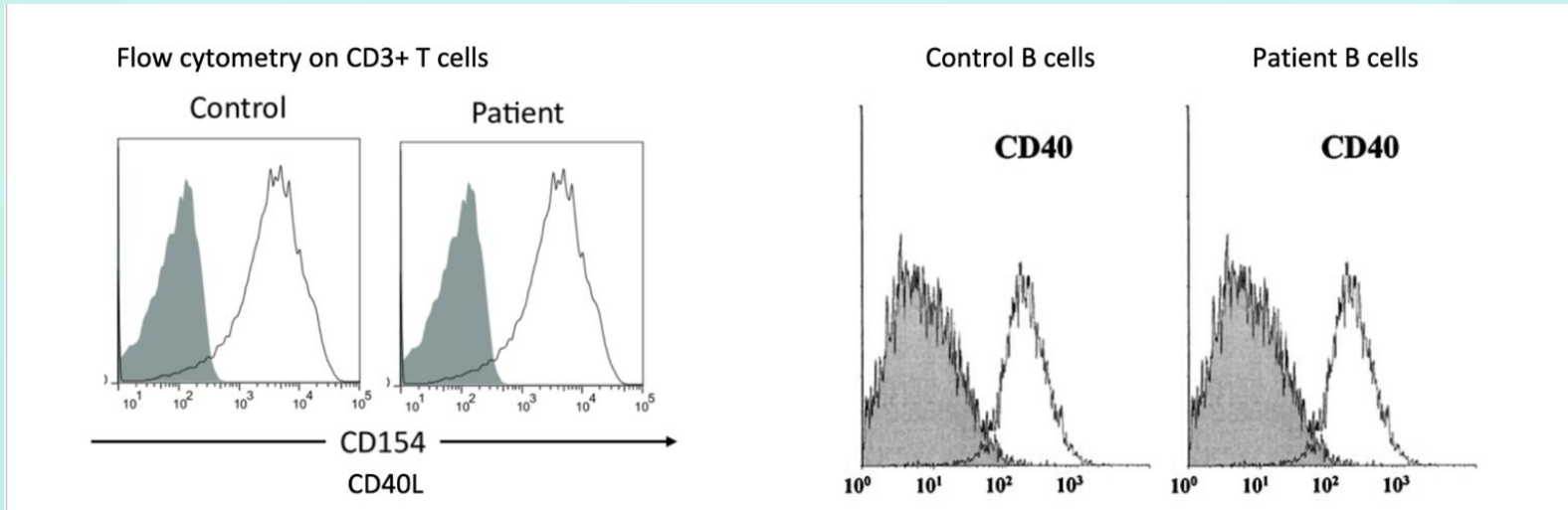
ELISA for IFNgR PBMCs and IFNg response

We then ran another Flow Cytometry and a **ELISA** to determine if the Interfering gamma (**IFNg**) and Interfering gamma receptor (**IFNgR**) was deficient.

TH1 activates macrophages

Intracellular Bacteria

- Macrophages present antigen to **re-stimulate activated CD4 T cells**
- **Th1 cells** produce **IFNγ** + express high levels of **CD40L**
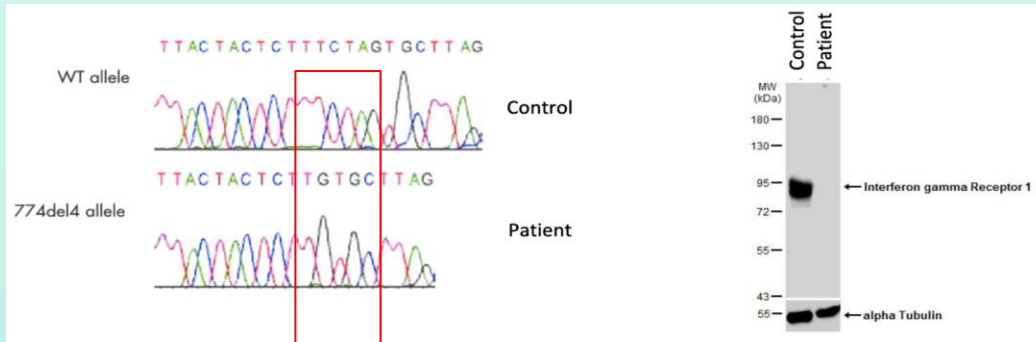- These **activate macrophages** to kill intracellular pathogens
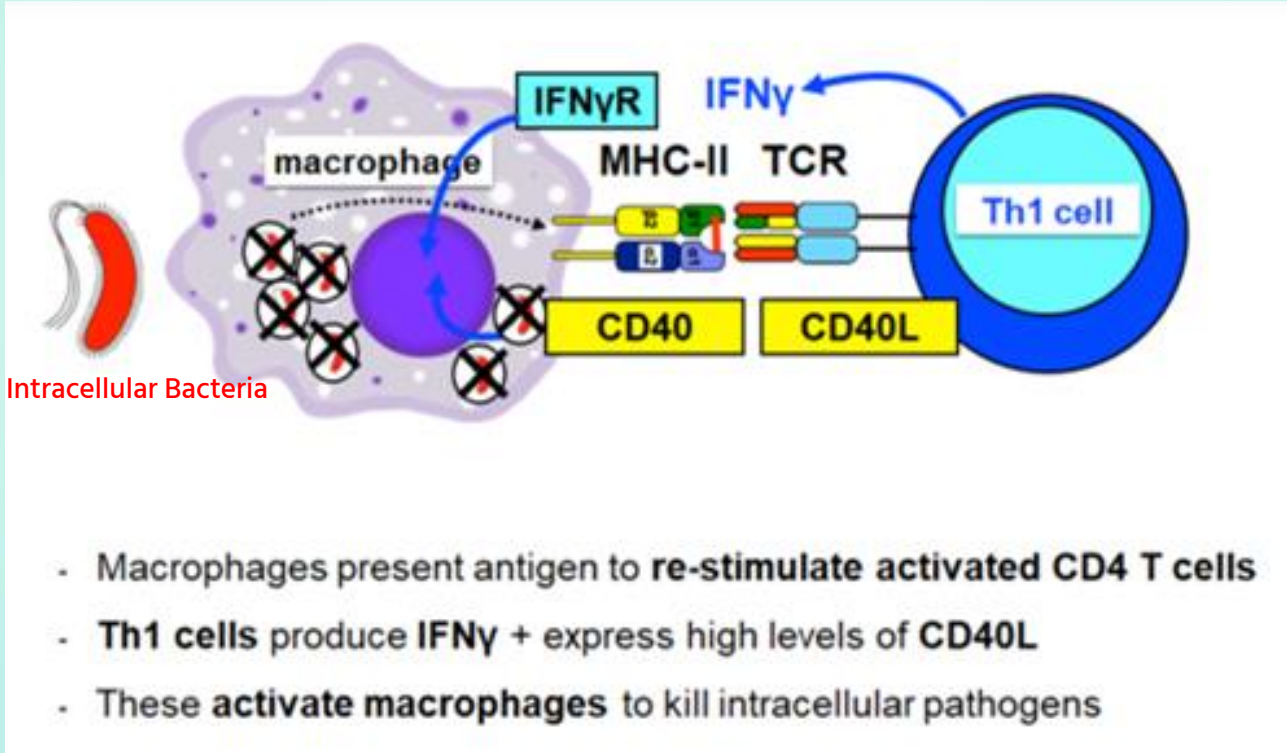
DNA Sequencing and Western Blot

DNA sequencing: is used to show changes in patients DNA.
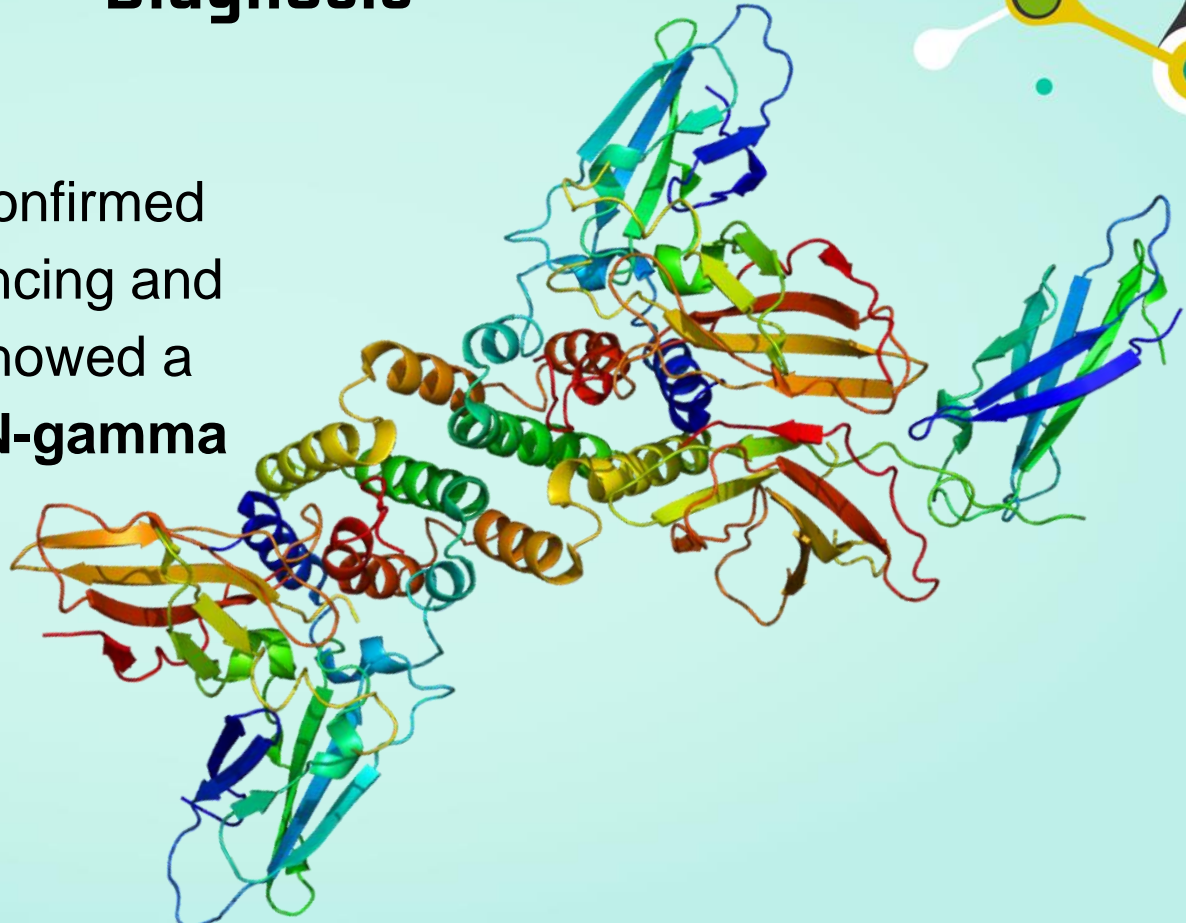- **Frameshift Deletion in DNA (TCTAGT) causing a nucleotide shift.**

Western Blot: is used to show proteins present in mixtures extracted from cells.
- **No protein levels of IFN-R1**

Diagnosis

- The diagnosis was confirmed through DNA Sequencing and Western Blots that showed a **deficiency** in the **IFN-gamma receptor 1**.

Background Information

- **Prevalence:** IFN-g receptor 1 deficiency is considered a **rare** disease. Approximately 1 to 8,000 people in the world and 1 to 300 people in USA.

- **Symptoms:** Symptoms appear in **newborns** to **infants**. Symptoms might included abnormal bronchitis physiology, anemia, anorexia, **diarrhea**, and **enlarged lymph nodes**.

- **Description:** IFN-g receptor 1 is not present within the patient. Without IFN-g receptor 1 the cytokines **cannot** bind and **activate** immune cells.

- **Similar Immunodeficiencies** based on similar gene descriptors**.**

    - Immunodeficiency 27a: 32.4% in common.

    - Osteomyelitis: 30.1% in common.

    - Mycobacterium Tuberculosis 1 (TB): 29.5% in common.

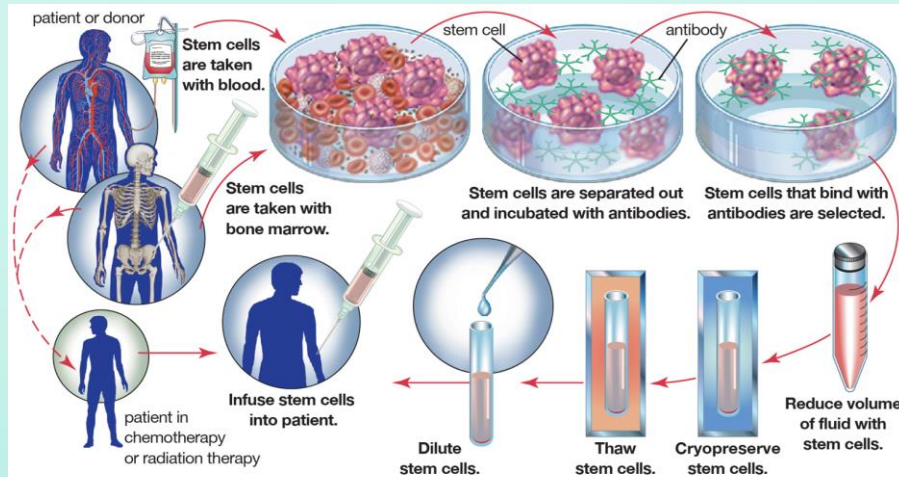10 11 12 13 14
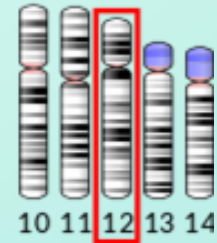
Therapy Options

Bone Marrow Transplant

- Where bone marrow is taken from a healthy individual and give it to the patient.

VS

Homologous Stem Cell Transplantation

- Bone marrow from the patient is removed and is genetically modified and then is given back to the patient.

patient or donor

Stem cells are taken with blood.

stem cell

antibody

Stem cells are taken with bone marrow.

Stem cells are separated out and incubated with antibodies.

Stem cells that bind with antibodies are selected.

Infuse stem cells into patient.

patient in chemotherapy or radiation therapy

Dilute stem cells.

Thaw stem cells.

Cryopreserve stem cells.

Reduce volume of fluid with stem cells.

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Preferred Therapy for Patient

Homologous Stem Cell Transplantation

- Reasons Why:

  - Chance of rejection with traditional bone marrow transplant.

  - The ability of generate of their own IFN-g receptors with Homologous Stem Cell Transplant.
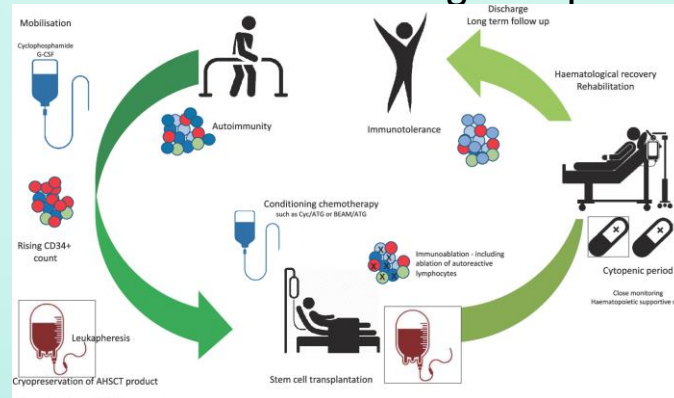
Questions?

RESOURCES

- Gutierrez, M. J., Kalra, N., Horwitz, A., & Nino, G. (2016). Novel Mutation of Interferon-γ Receptor 1 Gene Presenting as Early Life Mycobacterial Bronchial Disease. *Journal of investigative medicine high impact case reports*, *4*(4), 2324709616675463. https://doi.org/10.1177/2324709616675463
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- U.S. Department of Health and Human Services. (2021, November 8). *Interferon gamma, receptor 1, deficiency - about the disease*. Genetic and Rare Diseases Information Center. Retrieved March 20, 2022, from https://beta.rarediseases.info.nih.gov/diseases/3011/interferon-gamma-receptor-1-deficiency
- *Interferon Gamma, Receptor 1, Deficiency*. Malacards.org. (n.d.). Retrieved March 27, 2022, from https://www.malacards.org/card/interferon_gamma_receptor_1_deficiency?search=Interferon+Gamma%2C+Receptor+1%2C+Deficiency