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Biomedical Engineering +
Leonard Gelfand Center

League of Immuno-Legends

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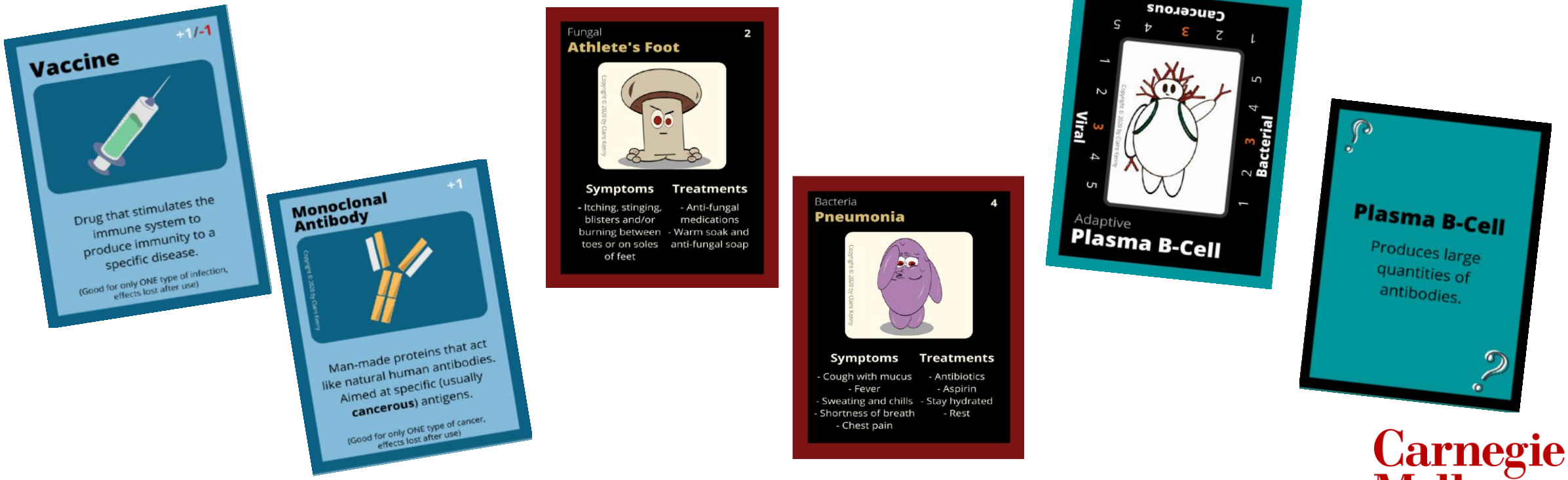
This educational resource for high school audiences was developed as a project by Carnegie Mellon student, Claire Kenny, for the course *Experiential Learning through Projects*, Section O, taught by Dr. Conrad Zapanta and Dr. Judith Hallinen during the summer of 2020.



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Outline

What is the immune system?

- What are the main components of the immune system?
- How does the immune system combat different attacks?
- What happens when the immune system fails?

How can biomedical engineering address problems that arise?

- Immunoengineering
- Applications
  - *Antibiotics*
  - *Vaccines*
  - *Cancer Therapy*

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Vocabulary

Antibody: (also known as immunoglobulins) Y-shaped proteins that can recognize and bind to antigens, further signaling to others involved in the immune system responses

Antigen: Molecules capable of stimulating an immune response, could be proteins on the surfaces of bacteria, fungi and viruses

Cytokine: Protein involved in cell signaling, especially between immune cells

Cytotoxic: Substance or process that results in cell damage or cell death

Heparin: Anticoagulant that inhibits blood clotting and promotes the movement of white blood cells in an area

Histamine: Chemical that widens blood vessels and increases the flow of blood to injured tissue

Pathogen: Organisms or infectious agents that invade the body and can cause health issues

What is the Immune System?

The role of the immune system — a collection of structures and processes within the body — is to protect against disease or other potentially damaging foreign bodies.

4 main functions to accomplish this:

- Immune Recognition
- Immune Effector Functions
- Immune Regulation
- Immune Memory

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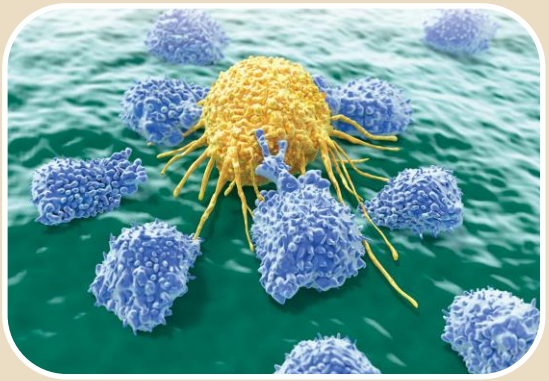
Two Main Categories

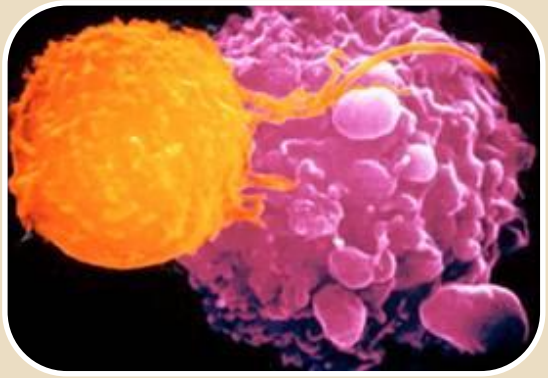
	Innate Immunity	Adaptive Immunity
Specificity	• Non-specific • No memory	• Antigen specific • Has memory
Duration	• Initiates in minutes to hours • Lasts days to weeks	• Initiates in days to weeks • Lasts months to years
Components	• The skin & all mucous membranes • Different defensive white blood cells • Various substances in blood and body fluids	• T and B cells • Antibodies • Cytokines

Meet the players:



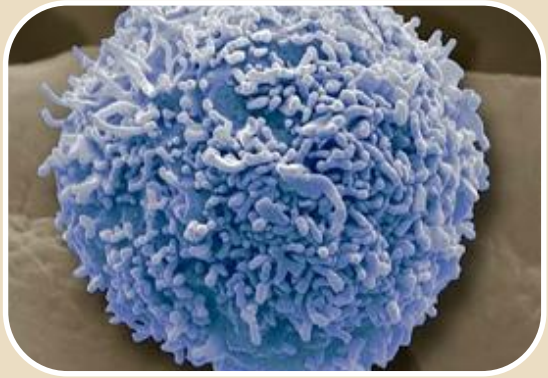
Natural Killer Cells

- **Innate**
- Defend the host from tumors and virally infected cells
- Do not require prior activation
- Release cytotoxic granules that destroy altered cells



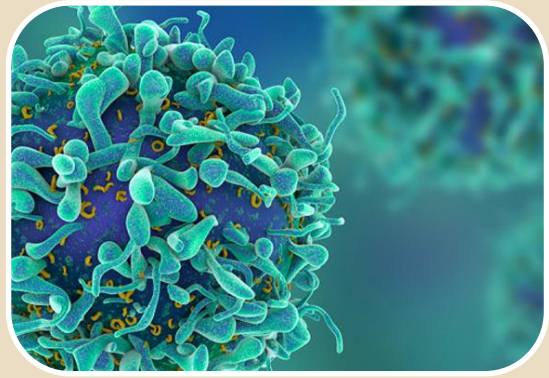
Cytotoxic T-Cells

- **Adaptive**
- Also known as: Killer T-Cells or CD8+
- Produce toxic granules containing enzymes that induce the death of pathogen-infected cells



Helper T-Cells

- **Adaptive**
- Also known as: CD4+
- Produce cytokines to direct an immune response against a pathogen
- Necessary to activate B-cells and Cytotoxic T-Cells



Regulatory T-Cells

- **Adaptive**
- Act to suppress immune response
- Help maintain homeostasis and self-tolerance
- Able to inhibit T-cell proliferation, cytokine production and autoimmunity

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Note: See speaker notes for full image citations

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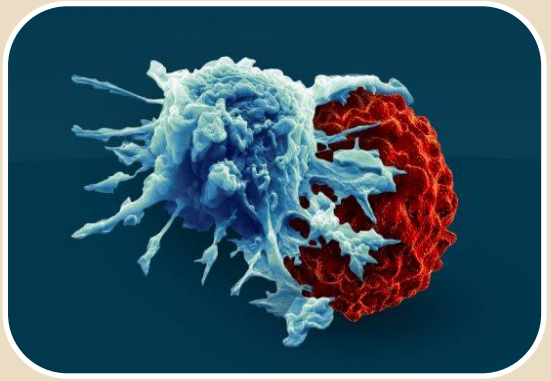
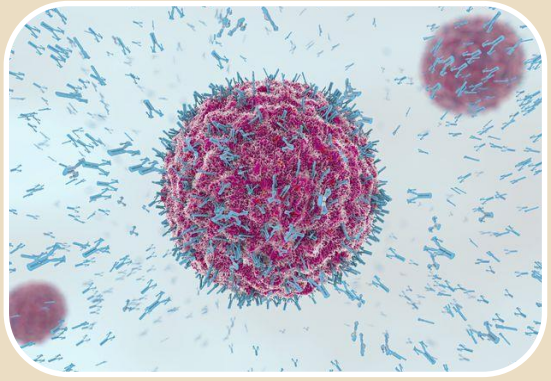


Macrophages

- **Innate**
- Detect, consume by phagocytosis and destroy bacteria and other harmful organisms
- Can present antigens to T-Cells
- Can release cytokines to initiate an inflammation response

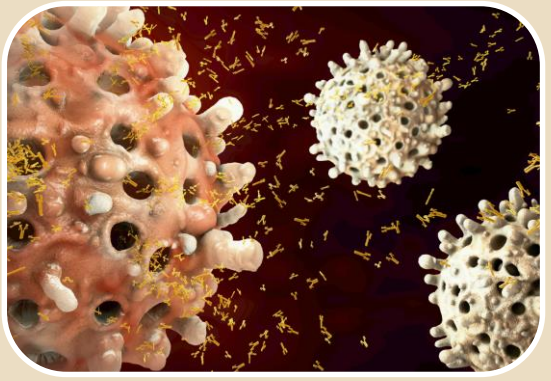
Dendritic Cells

- **Innate**
- Bind and retain antigens to be presented to T-Cells
- Induce the differentiation of germinal B-cells into memory B-cells



Plasma B-Cells

- **Adaptive**
- Activated B-cells that produce antibodies specialized for one pathogen
- Can release several thousands of antibodies in response to an antigen



Memory-B Cells

- **Adaptive**
- Important for maintaining immunity
- Makes any secondary exposures to an antigen quicker (and possibly stronger), sometimes before you even feel sick again

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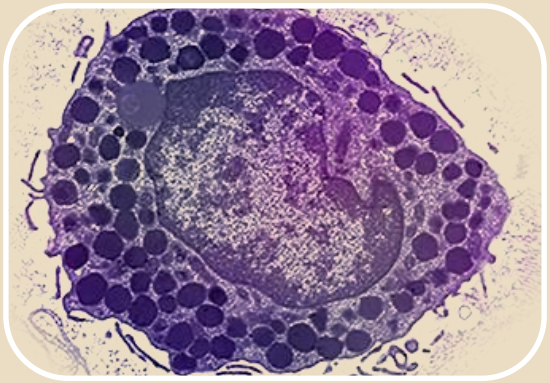
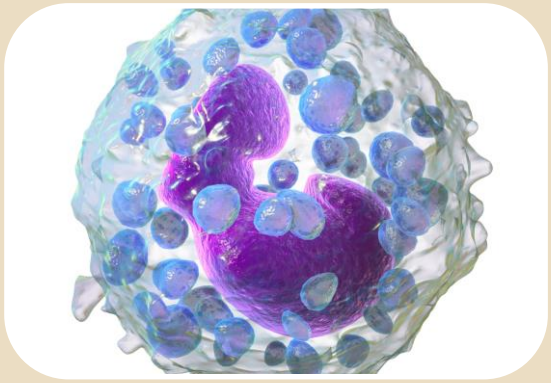


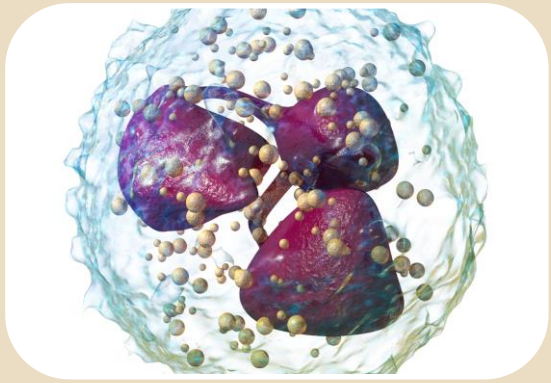
Mast Cells

- **Innate**
- Carry granules containing histamine and heparin
- Play a role in the inflammatory process



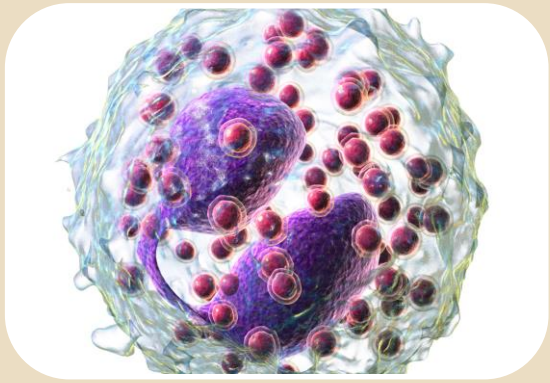
Basophils

- **Innate**
- Important for allergic and antigen response
- Excrete histamine and heparin
- Can also release chemical signals to attract eosinophils and neutrophils to an infection site
- *Lifetime*: Hours to days



Neutrophils

- **Innate**
- Usually first responder to a microbial infection
- Active in the phagocytosis of bacteria and can be found in pus
- Effective against bacterial or fungal infections
- *Lifetime*: Hours to days



Eosinophils

- **Innate**
- Responds to allergies, parasitic infections, collagen diseases, and diseases of the spleen and central nervous system.
- Secretes chemicals to destroy large parasites
- *Lifetime*: 8-12 days

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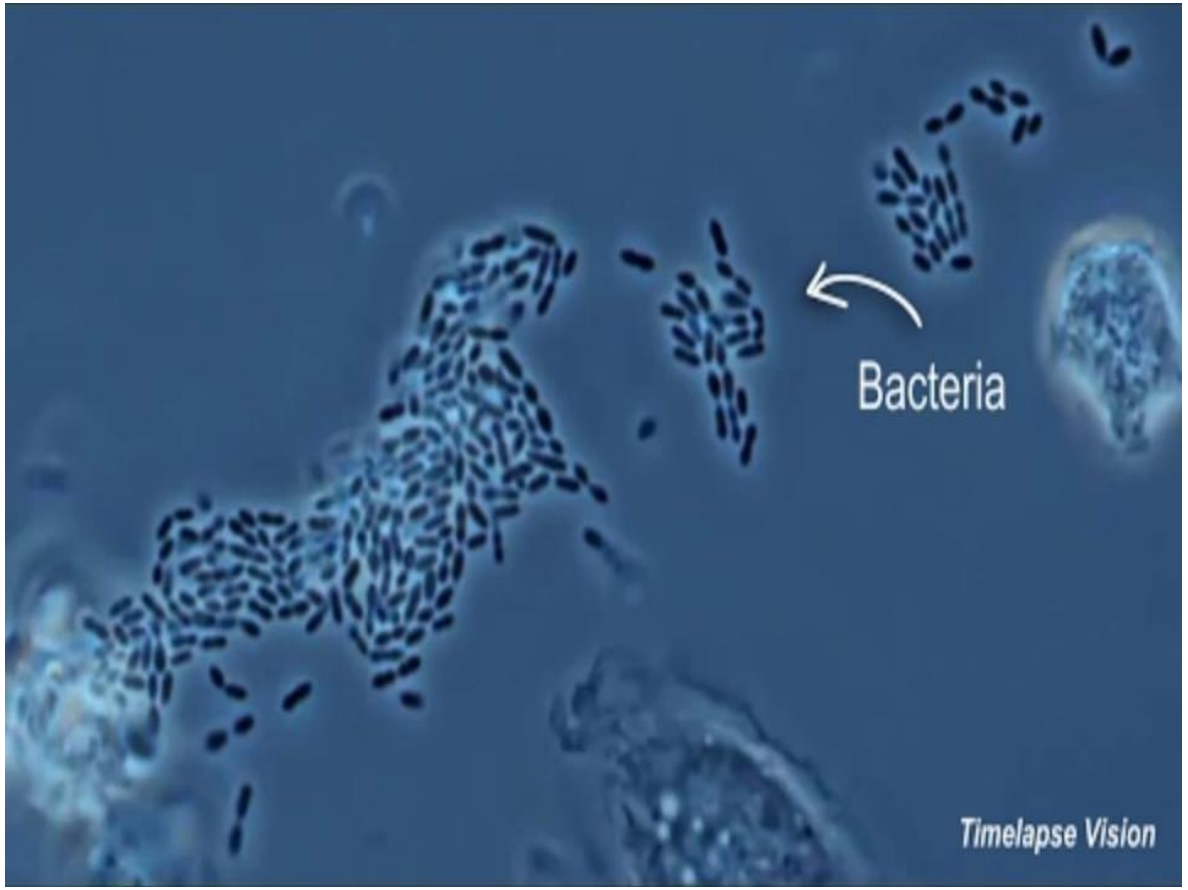
Macrophages at work!



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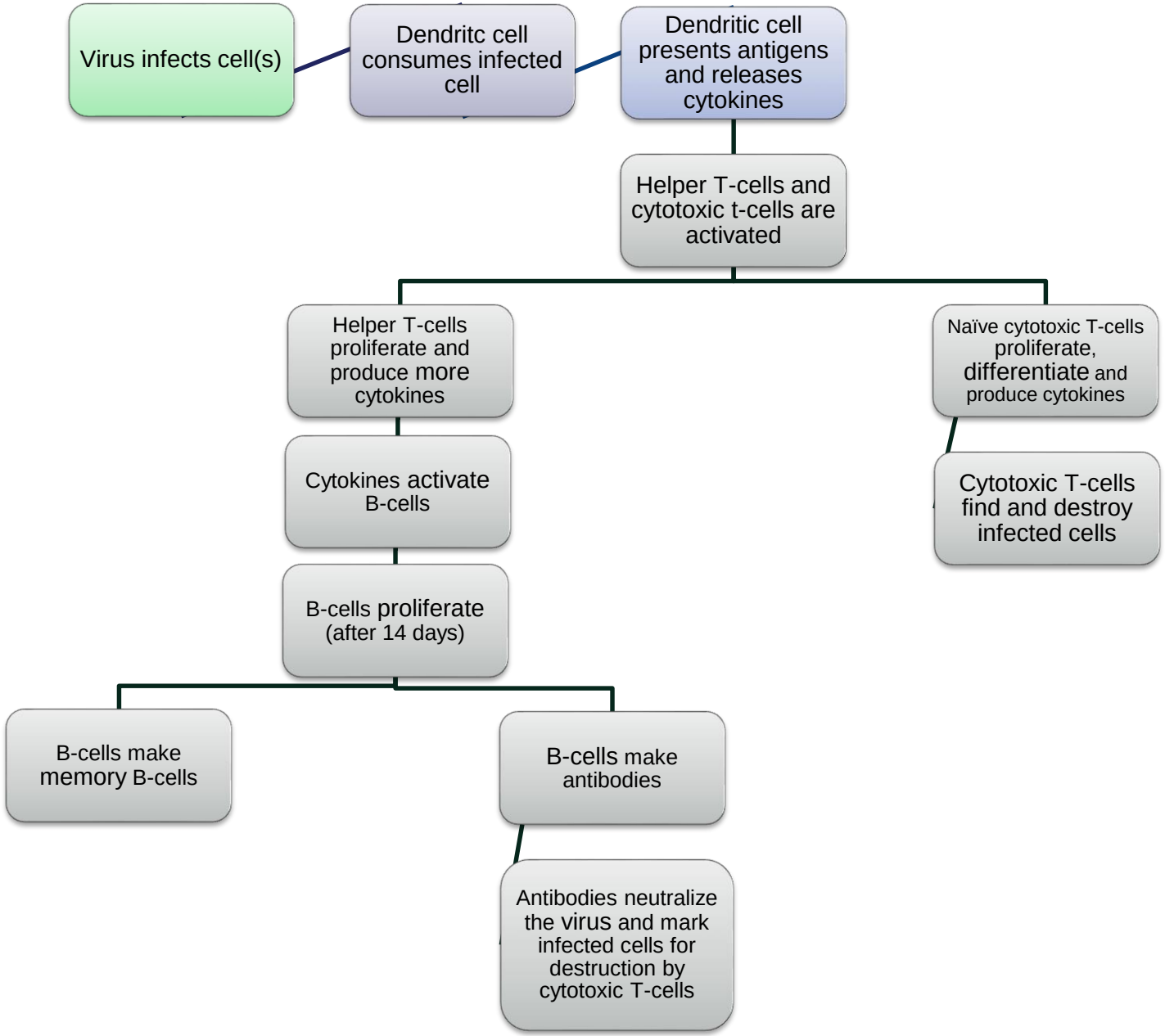
This is a simplified version of the body's immune response to

Viral Infections



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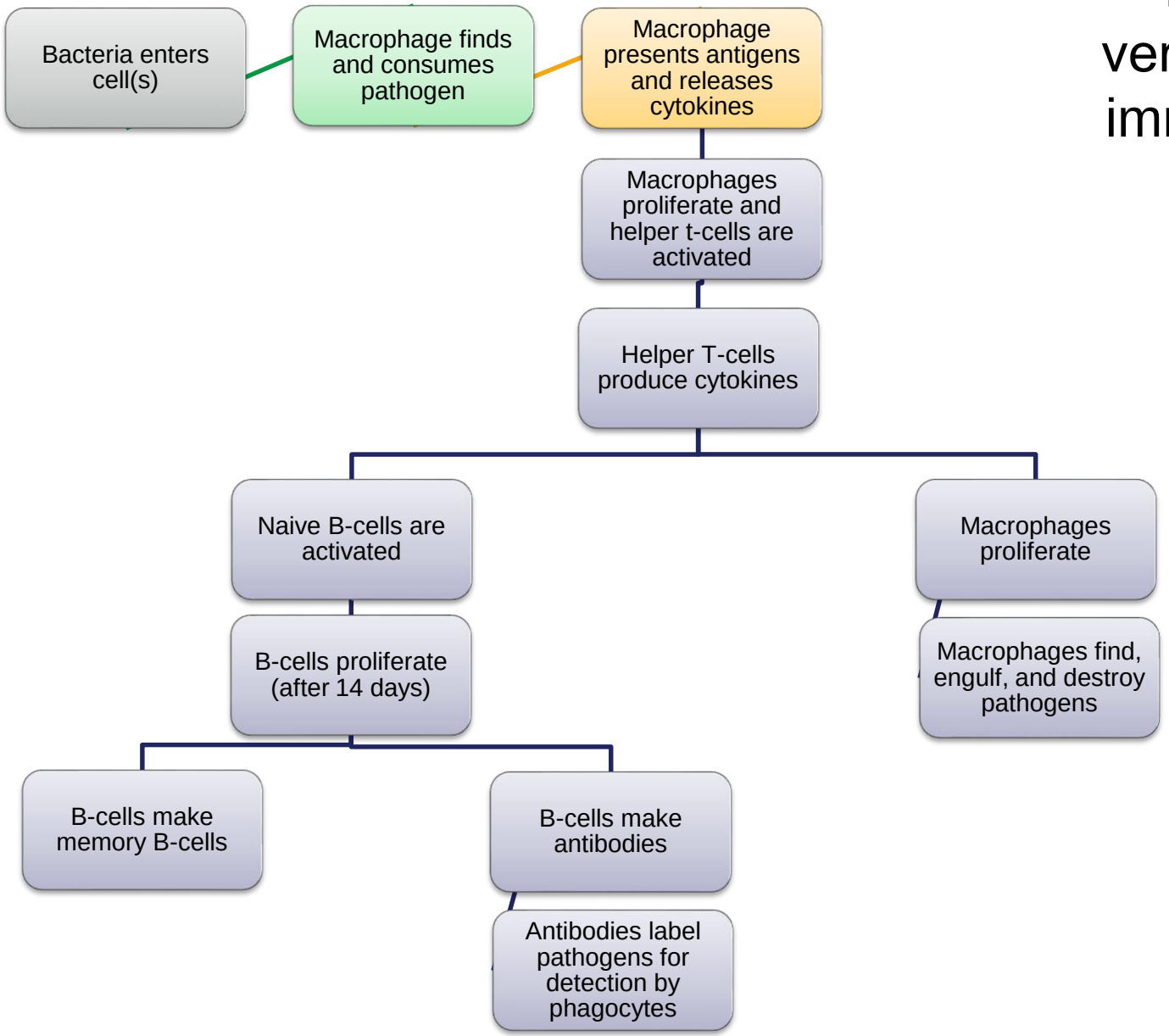
This is a simplified version of the body's immune response to

Bacterial Infections



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Other Infections

Fungal Infections

There are many fungi in the world but only some can cause an infection

Infectious fungi are **opportunistic pathogens,** meaning they wait for optimal conditions, such as when the immune system is weakened

Recognized by innate immune system (dendritic cells and macrophages)

Parasitic Infections

Many of these infections occur in developing parts of the world

Established when the innate immune system fails to eliminate the parasite

The adaptive immune system will, in turn, begin a cascade of events to make antibodies against the parasite

Macrophages, mast cells, basophils, neutrophils, eosinophils and NK cells will then bind to and eliminate the antibody coated parasite

Note: See speaker notes for full image citations

Immune System Failures - Allergies

Allergies are one of the *unwanted* reactions of the immune system.

- Caused by an **overreaction** to different substances or allergens
- The body produces antibodies that "attack" the allergen
- Symptoms can include:
  - Wheezing
  - Itching, runny nose
  - Watery or itchy eyes
  - And more
- **Anaphylactic shock** is a life-threatening reaction to an allergen, can cause trouble breathing, shock, vomiting, and more

Note: See speaker notes for full image citations

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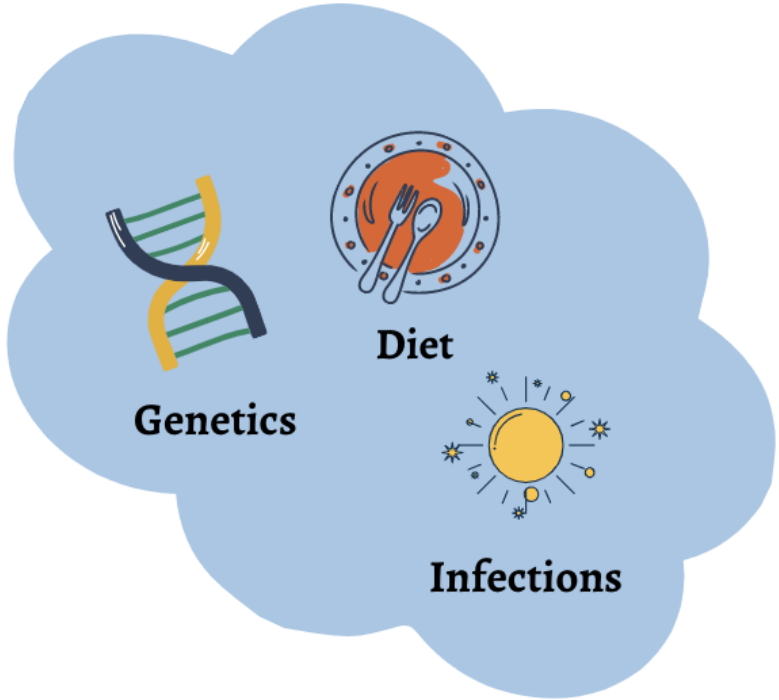
Immune System Failures - Autoimmune Diseases

- Conditions where the immune system mistakenly attacks the body.
- The immune system mistakes the body as foreign, and releases proteins, known as autoantibodies, to attack healthy cells.
- Common autoimmune diseases include:
  - Type 1 Diabetes
  - Rheumatoid Arthritis
  - Psoriasis
  - Celiac Disease
  - HIV/AIDS



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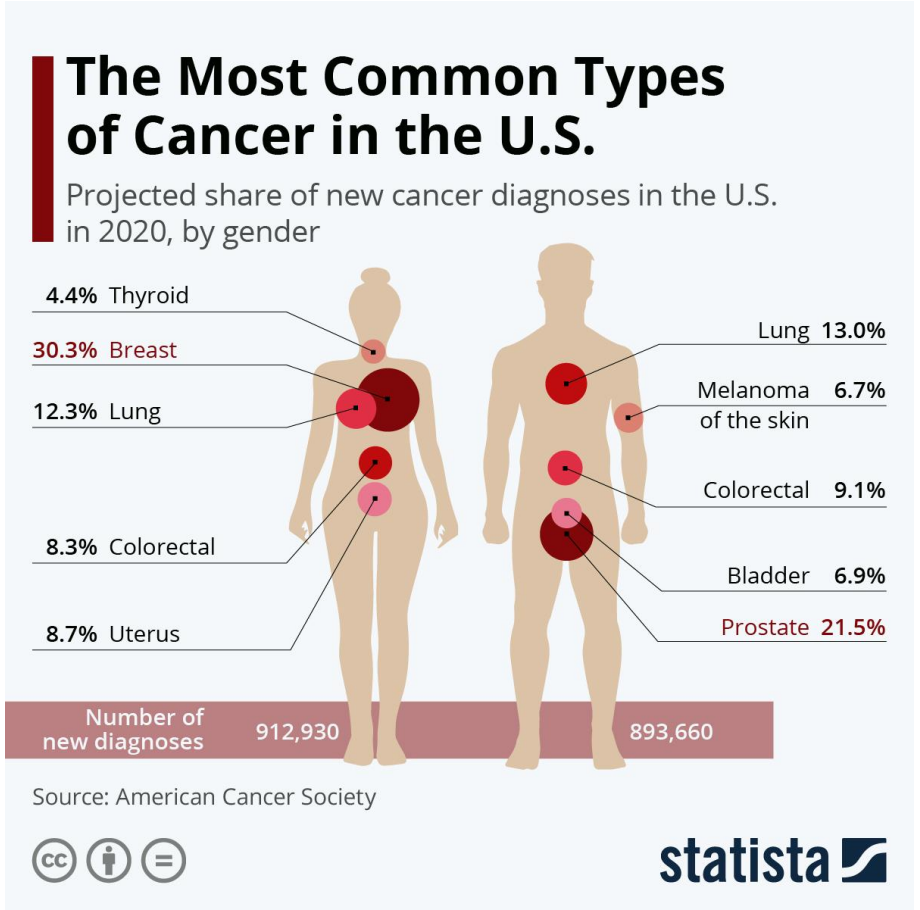
Immune System Failures - Cancer

Cancer is a very large and broad term that can be summed up as a disease where the *"body's cells begin to divide without stopping and spread into surrounding tissues."*

Usually, the immune system can regulate cell survival and production. However, cancer sees old or damaged cells surviving, and new cells forming when they are not needed.

The greatest challenge with cancer is the immune systems inability to recognize cancer, as the cancerous cells "hide".



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Georgia Tech Defines Immunoengineering as …

> “An emerging area that involves the application of engineering tools and principles to quantitatively study the immune system in health and diseases and to develop therapeutic interventions for precisely controlling and modulating a patient’s immune response.”

Immunoengineering applications - Vaccines, antibiotics, and antivirals

Vaccines

- A small amount of a specially treated antigen or pathogen often injected
- Goal is that the individual does not get sick but will still produce antibodies
- Prepares the immune system and leads to a more rapid response in the future
- Heavily reduces possibility of individual getting sick

Antibiotics

- Helps fight bacterial infections
- Can kill or inhibit the growth of bacteria
- Attacks cell wall coating the bacteria, interferes with or blocks production of a molecule that the cell needs to live in a body
- **Antibiotic resistance** occurs when bacteria adapt and become accustomed to an antibiotic, making the antibiotic ineffective

Antivirals

- Less common as most viral infections can be taken care of by the immune system
- Work by inhibiting replication of virus
- Limited number of diseases treatable by antivirals
- Most antivirals work on specific infections, meaning one does not solve all

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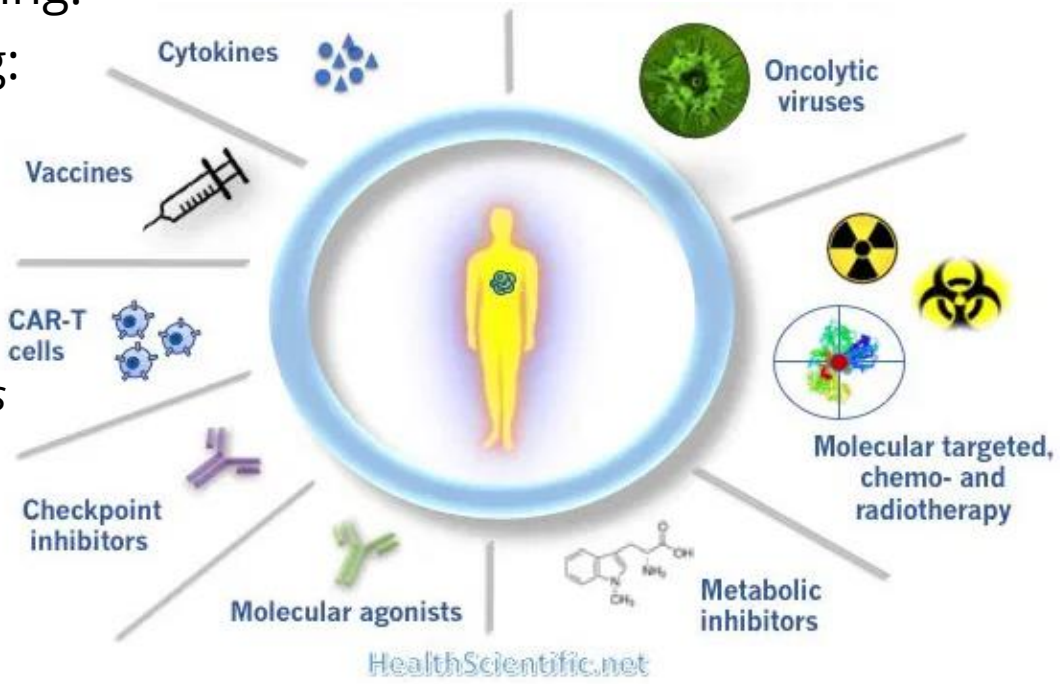
Immunoengineering applications - Cancer Therapy

There are numerous cancer therapies out, or in-the-making.

The newer approaches commonly used are the following:

1. Adoptive Cell Therapy:
   - *Expanding immune cell numbers or genetically modifying*
2. Cancer Vaccines:
   - *Educate the immune system about what cancer cells "look like"*
   - *Mainly for prevention*
3. Immunomodulators:
   - *Modulates "brakes and gas pedals" of the immune system*
4. Targeted Antibodies:
   - *Creating and customizing antibodies against specific cancer targets*



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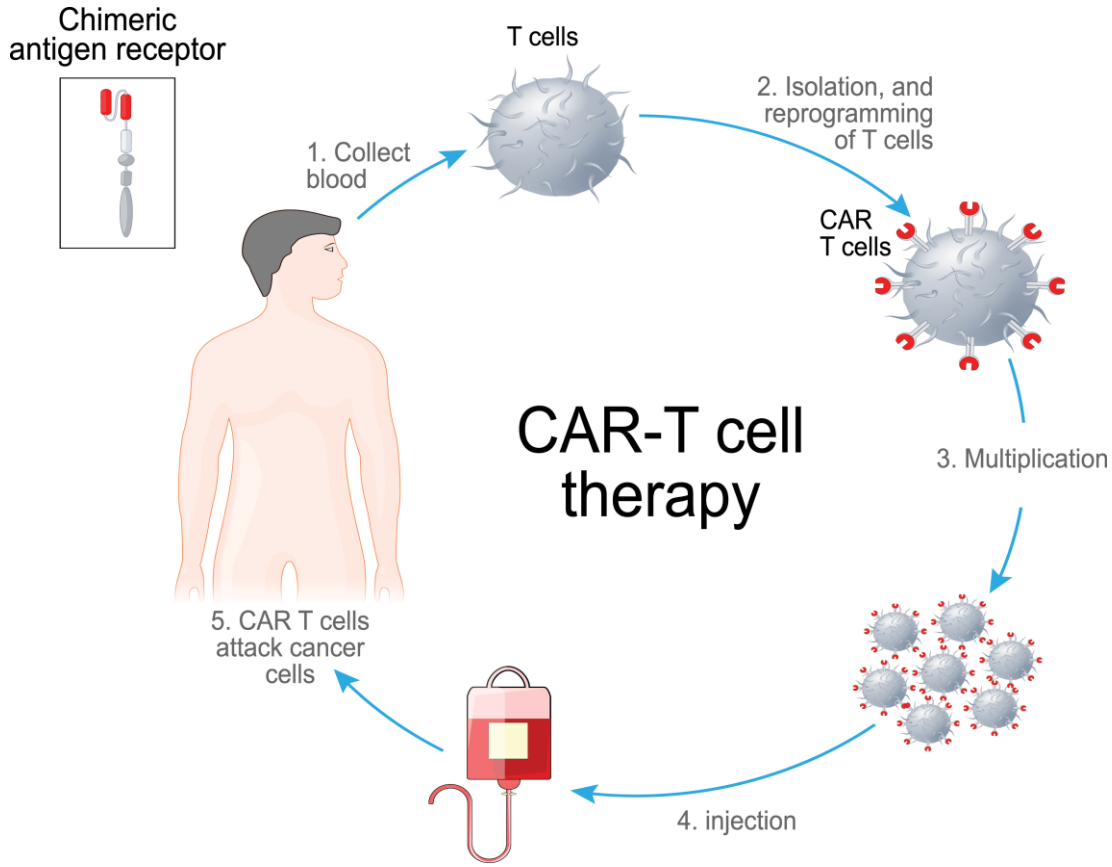
Cancer therapies: CAR-t Cell Therapy

Is an adoptive cell therapy that stands for: **Chimeric Antigen Receptor-T cell therapy**

The process includes:

1. Extracting T-cells from the patient's body
2. Genetically modifying the T-cells to develop additional characteristics to recognize cancer cells
3. Growing those cells in large numbers
4. Placing the cells back into the body



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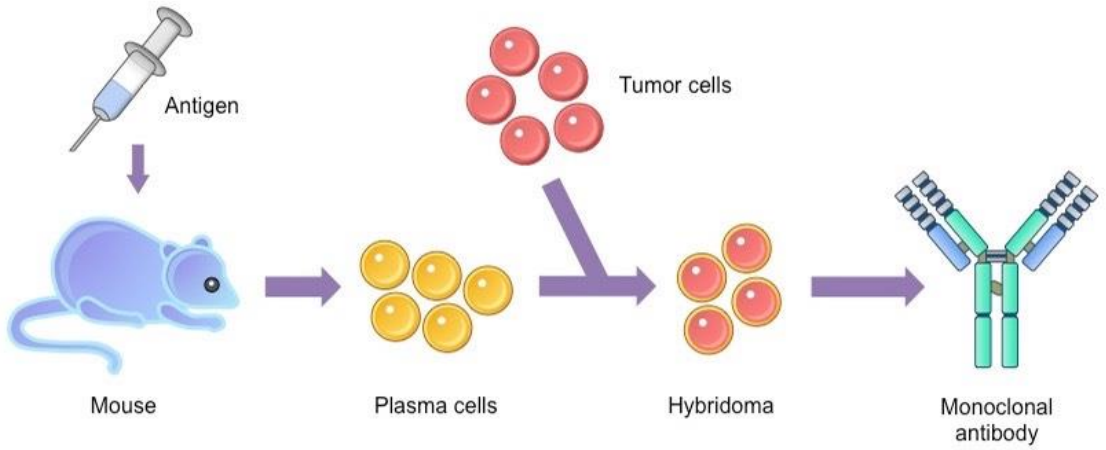
Cancer therapies : Monoclonal Antibodies [mAb]



Can be identified as any therapy ending – mAb

Could be Murine: (mouse), Chimeric (part mouse, part human), Humanized (small parts mouse attached to human proteins) or Human

The process includes:

1. Injecting an antigen and extracting the resulting B-cells
2. Fusing the B-cells with tumor cells to make hybridoma cells
3. Culturing the newly made cells and and purifying the resulting antibodies

Note: See speaker notes for full image citations

References

1. G. (n.d.). Immunoengineering. Retrieved June 26, 2020, from https://bme.gatech.edu/bme/areas/immunoengineering
2. Zimmermann, K. (2018, October 17). Immune System: Diseases, Disorders & Function. Retrieved June 26, 2020, from https://www.livescience.com/26579-immune-system.html
3. InformedHealth.org [Internet]. Cologne, Germany: Institute for Quality and Efficiency in Health Care (IQWiG); 2006-. The innate and adaptive immune systems. 2010 Dec 7 [Updated 2016 Aug 4]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK279396/
4. Allergies and the Immune System. (n.d.). Retrieved July 26, 2020, from https://www.hopkinsmedicine.org/health/conditions-and-diseases/allergies-and-the-immune-system
5. Watson, S. (2002, May 15). Autoimmune Diseases: Types, Symptoms, Causes, Diagnosis & More. Retrieved July 26, 2020, from https://www.healthline.com/health/autoimmune-disorders
6. Department of Health & Human Services. (2014, March 30). Immune system. Retrieved July 27, 2020, from https://www.betterhealth.vic.gov.au/health/conditionsandtreatments/immune-system
7. Immune Deficiency Foundation. (2013). Retrieved July 27, 2020, from https://primaryimmune.org/immune-system-and-primary-immunodeficiency
8. The immune system: Cells, tissues, function, and disease. (2018, July 11). Retrieved July 27, 2020, from https://www.medicalnewstoday.com/articles/320101
9. Network, H. (2003, October 16). How Do Antibiotics Work? How Long They Take to Work and More. Retrieved July 27, 2020, from https://www.healthline.com/health/how-do-antibiotics-work
10. Iallonardo, M. (2020, May 18). Antivirals work in a couple of ways that can prevent the virus from spreading once inside you or by preventing infection from ever taking hold. Retrieved July 28, 2020, from https://www.insider.com/how-antivirals-work
11. Types of cancer immunotherapy. (2019, October 07). Retrieved July 28, 2020, from https://healthscientific.net/types-of-cancer-immunotherapy/
12. What Is Cancer? (n.d.). Retrieved July 28, 2020, from https://www.cancer.gov/about-cancer/understanding/what-is-cancer
13. Drummond, R. (n.d.). Immune responses to fungal pathogens. Retrieved July 28, 2020, from https://www.immunology.org/public-information/bitesized-immunology/pathogens-and-disease/immune-responses-fungal-pathogens
14. Stewart, J. (2012, May 24). Parasitic infections: Pathogenesis and immunity. Retrieved July 28, 2020, from https://www.sciencedirect.com/science/article/pii/B9780702040894000263

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