CANCER IN THE AGE OF BIOTECHNOLOGY

Dr. Carl June, a brief primer on immunotherapy and his research:

Before we can begin to understand some of the basics of the concept of immunotherapy, here is a quick review of some introductory human anatomy and physiology.

The circulatory system is a composed of several essential organs and tissues but for our purposes we will concentrate on the components of the blood. The three primary components of the blood include the red blood cells (erythrocytes), white blood cells (leukocytes) and platelets.

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While the erythrocytes are responsible for carrying the gasses of oxygen and carbon dioxide to and away from tissues and cells, it is the leukocytes that are required to fight off disease, infection and rid the body of foreign invaders. It is these cells that Dr. June works with during the development of immunotherapy technologies.

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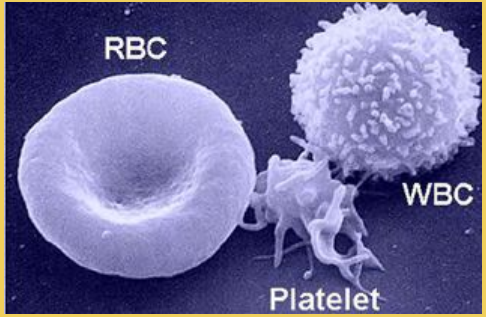
Leukocytes compose less than 1% of the total volume of cells within whole blood. That equates to 1 or 2 leukocytes for every 1000 erythrocytes. Leukocytes are larger than erythrocytes and when stained, have noticeable nuclei. Leukocytes come in several varieties each with a specific role to play in the defense of the body and the invasion of foreign substances.



Scanning electron micrograph of a white blood cells (WBC), a platelet and a red blood cell (RBC) (adapted from NCI-Frederick, 2005).

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The Leukocytes are divided into 5 varieties here from the most common to the least:

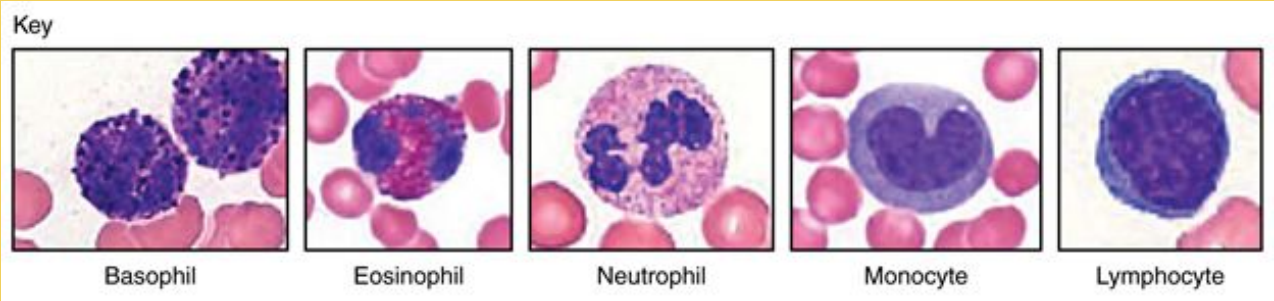
Neutrophils @ 60 – 70%

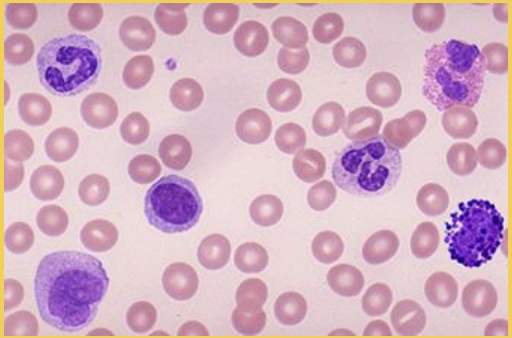
Lymphocytes @ 20 – 25%

Monocytes @ 3 – 8%

Eosinophils @ 2 – 4%

Basophils @ 0.5 – 1%





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Lymphocytes are further divided into B and T lymphocytes and they are the cells of the greatest interest in immunotherapy technologies. The T cells can be genetically modified to target specific cancer proteins.

The T cells operate by using receptors on their outer surface to identify and recognize a foreign invader. This system is extremely efficient for an outside foreign invader such as a virus or bacteria. Those cells have signature antigens (a type of protein) on their surfaces that allow the T cells to recognize them, seek them out and physically destroy them.

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However, in the case of a cancer cell, those cells are generally not recognized by the T cells because they are the normal cells of our bodies growing out of control in the form of a tumor. The T cells are not inclined to attack those cells because the T cells do not have a receptor on their surface to attack our cells, cancerous or not. Consequently, the T cells need to be genetically modified to identify the cancerous cells in order to destroy them.

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As researchers have learned, cancer cells within the human body have antigens on their surface, which T cells can be programmed to recognize. To accomplish this feat, the researchers identify the genetic sequence of the cancerous cell surface antigen. Once the surface antigen genetic signature is identified, a gene can be manufactured to have the T cell build the appropriate cancer receptor on the surface of the T cell. Recall that under normal conditions, the T cells would not have this receptor naturally because the infected cells are human in nature and not a foreign invader. But now, through genetic modifications, the T cells can build the appropriate receptor to recognize the cancerous cells and destroy them.

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During this process, T cells are removed from the patient's blood sample. The T cells are isolated and then reprogrammed by giving them the gene that builds the appropriate receptor, specific to the cancer antigen on the surface of their human cells. This new receptor is called a chimeric antigen receptor, CAR for short. The new T cells are called CAR-T cells and are now ready to recognize and attack the cancerous cells within the patient's body. The CAR-T cells are grown in the laboratory and eventually given to the patient by a blood infusion.

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Dr. June's research lab has developed a CAR-T technology to be used on acute lymphoblastic and chronic lymphocytic leukemia in young adults. In 2017, the FDA gave Dr. June permission to use his new CAR-T technology when all other common forms of cancer therapy have failed for the patient. Additionally, the patient needed to show a relapse in the amount of cancer within their bodies, and the CAR-T treatment would then be considered a last ditch effort to cure the patient and extend their lifespan.

So far, the results have been positive, so much so that new CAR-T cells are being developed for other forms of cancer as well. Those include blood, pancreatic and certain brain cancers.