**The New Scientific Exploration of Synthetic Immunology**

**ABSTRACT**

“Synthetic Immunology: Hacking Immune Cells to Expand Their Therapeutic Capabilities” introduces, to the reader, the new scientific area of Synthetic Immunology. Synthetic Immunology seeks to aim to synthetically manipulate the cells of the immune system, to enhance their natural function as well as target specific diseases that the body normally is unable to control such as autoimmunity and cancer. What makes an immune cell a favorable target to manipulate is due to the fact that they can be easily extracted from serum and harvested as well as easily modified outside of the body and can also be easily imported back into the body. These synthetically modified immune cells are manipulated through the use of altered cell surface receptors to interact specifically for a distinct disease. The advantages of such manipulation includes a stronger more specified immune response to normally difficult to manage diseases. Synthetically manipulating immune cells to recognize and combat specific diseases can contribute to a new kind of therapeutic practice. Synthetic immunology can provide the means to fight and get rid of diseases that are detrimental and even fatal to the human body. The most recent synthetic immunology advancement has been the synthetic, ex vivo, modification of the T Cell to directly identify cancer cells and malignant tumors. This was done by altering the T Cell receptor of the T Cell through the addition of a synthetic extracellular recognition domain that recognizes tumor specific antigens. Many of these engineered T Cells with these modified T Cell Receptors have been shown to attack tumor cells that express certain intracellular antigens. Although, this article provided a numerous amount of examples on how synthetic immunology can be applied and how it can benefit the immune system against certain diseases, most of these examples only worked in theory and have not be scientifically tested.

**INTRODUCTION**

The immune system is a critical systematic element of our body. It is made up of essential components that aid in the recognition and destruction of various pathogenic diseases. The Immune System is comprised of innate immunity and adaptive immunity. The innate immune system, also known as the first line of defense, is comprised of various physical barriers and chemical components such as hair, skin, cilia, mucosal membranes and lysozyme the fluid-like secretion found in body secretions such tears and saliva. Macrophages and natural killer cells also play a role in destroying and phagocytizing pathogenic bacteria. The adaptive immune system has a major role in taking over after the innate immune system fails to contain a pathogen. The adaptive immune system is comprised of the major T Cells and B Cells. T Cells are made up of two main classes, Cytotoxic T Cells and T Helper cells. Cytotoxic T cells function to naturalize and destroy foreign pathogens and T Helper Cells work to activate other T Helper Cells and B Cells. B Cells are plasma cells that produce antibodies. Antibodies take the shape of a Y shaped fork with two heavy chains and two light chains. These chains are what defines what class an antibody resides in. Antibody’s also contain a variable region and a constant region. These regions are what recognize antigens. Antigens are pathogens which are recognized by antibodies. Antibodies coat pathogens which are then engulfed by phagocytizing cells through the process of opsonization. Other components and cells also come into play within the immune system such as cytokines, chemokines, attractants, and complement pathways. Cytokines are signaling molecules that regulate other cells of the immune system, control inflammation and hematopoiesis. Chemokines are a subclass of cytokines that act as signaling factors which causes immune cells to migrate to sites of infection to defend and fight off foreign invaders. There are three different pathways that make up the complement pathway. These pathways are each activated by different mechanisms and employ complement to induce opsonization by coating microbes, promoting inflammation, and breaking down other complement proteins.

Synthetic Immunology employs the manipulation of all of the components described above, by cell surface receptor modification, to specifically identify and attack diseases such as cancer and auto immunity. Current research, places emphasis on the T Cell. In order to successfully modify an immune cell, more specifically the T Cell, there is a series of steps and procedures that must by thoroughly carried out. T cells have been targeted for manipulation due to their cytotoxic activity, which makes them favorably for tumor cell destruction. In order to successfully program a T Cell to specifically detect and destroy tumor cells, the T cell must be capable of properly detecting tumor cells and differentiate them from normal cells, migrate to the target location of where the tumor cells reside, survive, expand and persistence in order to continue to attack such aggressive cells, overcome and undo the suppressiveness of an immunosuppressive environment that these tumor cells create. To program a T Cell the first step is to modify it’s cellular receptor to enable it to sense a diseased cell from a normal one. The most successful of these receptors is the Chimeric Antigen Receptor that contains a synthetic extracellular recognition domain that recognizes a tumor specific surface antigen. By altering the receptor on the T cell this will allow for an engineered attack by the T Cell on cells that express this specific intracellular antigen such as tumor cells. Another way that T Cells are engineered to attack cancer cells is through the modification Chemokine receptors. One factor that limits T cell attack on tumor cells is the lack of migration to the tumor cell environment. Modifying T Cells to have chemokine receptors can allow for the T Cell to better sense and migrate toward the tumor cell environment.

**Recent Progress**

Recent progress in the study of synthetic immunology involves using an engineered chemokine receptor CCR2b to migrate T Cells toward Xenograft Nueroblastoma and a mesothelioma model which each worked successfully (Raybal). Many tumor antigen specific T receptors have been recognized that respond well to the modified T Cells. Although theoretically the modified CAR T Cells work well there has been concerns about the persistence of the cells within the body, the variations in duration ranges from as little to thirsty days to up to four years depending on the type of Chimeric antigen receptor on the T Cell (Raybal).

**Discussion**

Theoretically, synthetic immunology would be promising and be an ideal therapeutic treatment. The idea of modifying the components in the immune system to better fight off and destroy infections and infectious diseases would provide for promising treatment with little to no detrimental effects. The research results presented in this article were deemed to produce successful results but the amount of research results shown were very minimal. The idea of synthetic immunology is seen to be still in the theoretical stage due to the small amount of data presented. The article gave a wide variety of examples detailing how modifying immune cells could work but these detailed examples were not backed by current research trials and results. In order for synthetic immunology to be a successful area of science there must be more extensive research and trials conducted. If the study of modified immunology comes to produce consistent and successful outcomes, then the using this as a form of therapeutic treatment could help the human body manage and suppress a various amount of disease and chronic illness.

**References**

Roybal, Kole T., and Wendell A. Lim. “Synthetic Immunology: Hacking Immune Cells to Expand Their Therapeutic Capabilities.” Annual Review of Immunology, vol. 35, no. 1, 2017, pp. 229-253., doi:10.1146/annurev-immunol-051116-052302.

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