Osmosis Magazine

Volume 2019
Issue 2 *Osmosis Magazine - Fall 2019*

Article 3

2019

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George Qiao
University of Richmond, claprade@richmond.edu

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By George Qiao

Diabetes, the seventh leading cause of death in the United States, is caused by excessive blood glucose.1 Type 1 diabetes is a variation of the disease characterized by a deficiency in insulin, a hormone produced in the pancreas that allows cells to take up glucose from the blood and receive energy. Lack of insulin results in accumulation of sugar in the bloodstream, and subsequently dehydration, excessive urination, and tissue damage.2 The need to prevent the disease is urgent, as over a million children or young adults in the world have type 1 diabetes, and over 100,000 cases of type 1 diabetes are diagnosed every year.3 Type 1 diabetes is known as an autoimmune disease because the immune system destroys insulin-producing beta cells in the pancreas.2 What is not certain is the mechanism by which this occurs. However, recent research has linked the disease to a newly found cell called the X lymphocyte.4

We are familiar with the B and T lymphocytes, which are involved in the acquired immune response in our bodies for fighting against extracellular pathogens. B cells function to secrete antibodies that recognize antigens and are involved in humoral immunity. During maturation in the bone marrow, B cells that react with self-antigens are negatively selected; that is, they undergo apoptosis or receptor modification so that they are not a threat to the body. The surviving B cells then travel to the spleen to complete maturation and become naive B cells, which are mature cells that are not yet activated.5 T cells arrive in different classes and fight against intracellular pathogens through cell-mediated immunity. During maturation in the thymus, , T cells also undergo negative selection, and once matured, are known as naive T cells.6

Antigen-presenting cells (APCs) recognize protein antigens and display them to T cells. A B cell can act as an APC and recognize protein antigens using its B-cell receptor (BCR) to internalize the antigen and process and display the antigen on an MHC II molecule. A helper T cell can recognize the presented antigen through its T-cell receptor (TCR), and the interaction between the MHC II on the B cell and CD4 molecule on the T cell results in T cell activation. The T cell secretes cytokines that activate the B cell, which differentiates into plasma cells that secrete antibodies and memory cells that remain for future invaders.5 Cytotoxic T cells, unlike helper T cells, directly target pathogen-infected cells and destroy the cells along with the pathogen inside.6

Normally, the only two types of lymphocytes that the body produces are B and T lymphocytes. What is previously known regarding the mechanism of insulin destruction is that insulin can bind to a molecule on APCs known as HLA-DQ8. However, the binding is not strong enough to trigger a reaction that leads to type 1 diabetes. Researchers at Johns Hopkins Medicine recently utilized computer simulations that revealed dual-expressor (DE) cells which express both the BCR and TCR. A protein coded by the BCR of DE cells, named the x-Id peptide, can bind to HLA-DQ8 very tightly compared to insulin, and the binding is strong enough to bring out a T cell response that can result in type 1 diabetes.4

To test the strength of the T cell response by DE cells, the researchers produced a genetically-

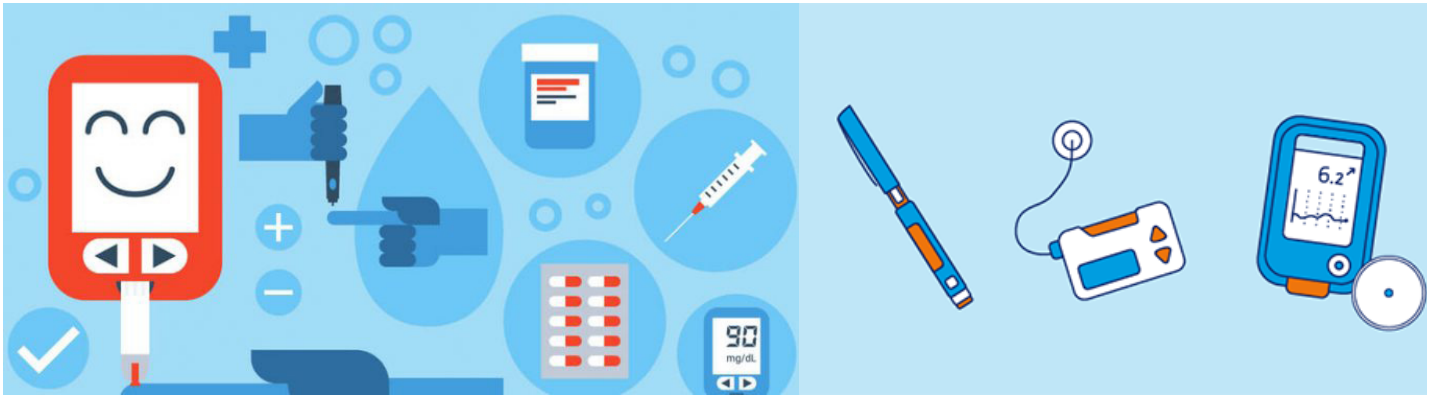
engineered insulin mimic called the "superagonist," which has a higher affinity for HLA-DQ8 than normal insulin and is 1,000 times more immune-stimulating. The team ran computer simulations which illustrated that the x-Id protein resulted in a T cell response with tenfold increased strength over that of the superagonist; hence, the x-Id protein displayed a trigger in T cell activity that is 10,000 times stronger than that produced by normal insulin. These results suggest that the x-Id protein found in DE cells can elicit strong T cell responses that can then attack insulin-producing cells.4, 7

To confirm the existence of the DE cell, which can be referred to as the "X" lymphocyte, the researchers used a virus to produce genetically-identical duplicates of the cell, and found that the clone cells all expressed both BCRs and TCRs, illustrating that the cell is a hybrid of the B cell and the T cell. Furthermore, the researchers obtained blood samples from donors with type 1 diabetes and healthy donors and found that the DE lymphocytes appeared more frequently in patients with type 1 diabetes than nondiabetic subjects.4, 7

The discovery of the X lymphocyte helps deepen our understanding of type 1 diabetes and can be insightful for those searching for a cure for the condition. While the results of the X lymphocyte study at Johns Hopkins yields valuable information, more studies should be done to further confirm and analyze the new type of cell. In the future, more information regarding the X lymphocyte and its behavior can bring us closer to finding a cure for type 1 diabetes.

References

1. Nichols, H. (2019, July 4). The top 10 leading causes of death in the United States. Retrieved from https://www.medicalnewstoday.com/articles/282929.php.
2. Type 1 Diabetes Mellitus. (2018, December). Retrieved from https://www.health.harvard.edu/a_to_z/type-1-diabetes-mellitus-a-to-z.
3. International Diabetes Federation. (2017). Idf Diabetes Atlas (8th ed.).
4. Newly Discovered Immune Cell Linked to Type 1 Diabetes. (2019, May 30). Retrieved from https://www.hopkinsmedicine.org/news/newsroom/news-releases/newly-discovered-immune-cell-linked-to-type-1-diabetes.
5. Microbiology. (n.d.). Retrieved from https://courses.lumenlearning.com/microbiology/chapter/b-lymphocytes-and-humoral-immunity/.
6. Microbiology. (n.d.). Retrieved from https://courses.lumenlearning.com/microbiology/chapter/t-lymphocytes-and-cellular-immunity/.
7. Ahmed, R., Omidian, Z., Giwa, A., Cornwell, B., Majety, N., Bell, D. R., … Hamad, A. R. A. (2019). A Public BCR Present in a Unique Dual-Receptor-Expressing Lymphocyte from Type 1 Diabetes Patients Encodes a Potent T Cell Autoantigen. Cell, 177(6).



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