Creating an Immune System Forever

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ABSTRACT

People have been researching how to live longer in our world, as the only thing we cannot escape is death itself. They looked at animals and everything, but recent studies have shown that our immune system is the secret to living longer. By keeping our immune systems in top condition, we can maximize our time to live in this world. Firstly, adopting a healthy lifestyle can make our immune system far healthier. Doing exercise always enhances immunity by promoting circulation and reducing chronic inflammation. A diet of plenty of fruits, vegetables, grains, and proteins provides essential nutrients and antioxidants for immune cell function. Sufficient sleep allows for optimal immune system recovery and regulation. Vaccines stimulate the immune system to produce antibodies and memory cells, which provide protection against pathogens. Routine immunizations, such as influenza and pneumonia vaccines, are essential for older adults at higher risk of severe complications from these infections. Finally, not using drugs or Alcohol keeps our body in the best condition possible, allowing us to produce many immune cells and overall making our body more robust. In specific, Additionally, emerging fields like personalized medicine and immune rejuvenation therapies to individual immune profiles and rejuvenating immune function. In these aspects, this research paper will dive deep into why our immune system declines and how we can prevent that from happening by applying these methods. Methods such as these will be present throughout this research paper. This immune system research paper is attached below.

Introduction

In our world, most of us think about life and death. We all try our best to cheat death and get around it or delay it as long as possible. Most people look at cures or even put themselves in an AI, but this is all in vain. We can't get around death but can delay it by keeping our immune systems healthy. Our immune system is very complex, but two key players make up the majority of our immune system and do the most. The T cells are what we think about when we think of the immune system. Your white blood cells charge at a virus and try to kill it immediately. If we didn't have this, many simple weak viruses may be more potent and affect our bodies more if we didn't kill them early on. However, we have more specialized B cells for viruses that multiply or take over the body quickly. B cells are the cells that are known for producing antibodies to counter a specific virus. Unlike T cells, B cells take days to gather information about that virus to create antibodies to counter that particular virus. B and T cells are the polar opposite as one fights any virus at any time (T cells); however, B cells specialize in defeating one singular virus. Nevertheless, together, these two cells help our bodies defeat viruses but weaken over time.

We can do things to keep them as healthy as possible, allowing us to live longer. However, there are some things we can't overcome, as even though we do all these, death is inevitable and will happen to us no matter what we do. There has been lots of research done on this, such as eating healthier, getting more exercise, and not doing drugs or Alcohol. My research will go more into depth about this and see if these methods truly work or if they don't work. My research will also go into depth about these topics in the reduction of eating or what we can do as we age to keep our immune system healthy, as elders may not be able to do all the things they could do when they were younger. We can use all of these methods, along with medications or vitamins, to keep our immune system as healthy as possible

for the rest of our lives. B and T cells are just a tiny part of the immune system, but let us learn more about the other areas of the immune system.

Parts of the Immune System

There are hundreds of immune cells, most of which form in the bone marrow, similar to B and T cells. T cells, known as white blood cells, are just one of many types of white blood cells. Three other white blood cell types are Neutrophils, Lymphocytes, and Macrophages. Although when we think of white blood cells, we think of T cells as the most common, that place goes to neutrophils. Neutrophils are what we think of when we hear of white blood cells. They are the most common form of white blood cells, and they can fight away viruses by swallowing them whole and then degrading the bacteria inside of them. Lymphocytes are the overarching categories of what we know as B and T cells.
T cells kill viruses by attacking them early, while B cells take some time to make antibodies, finishing off more potent viruses. Macrophages are very similar to Neutrophils as they are the first two cells to show up at the scene. They first eat the virus whole, identical to Neutrophils, but then they use acids inside of them to kill the bacteria. They have a secondary function: to clean up the dead virus/bacteria after the white blood cells kill them. Macrophages and Neutrophils use the same method of using acids and enzymes to eradicate the virus, known as Phagocytosis (also commonly referred to as "cell eating").

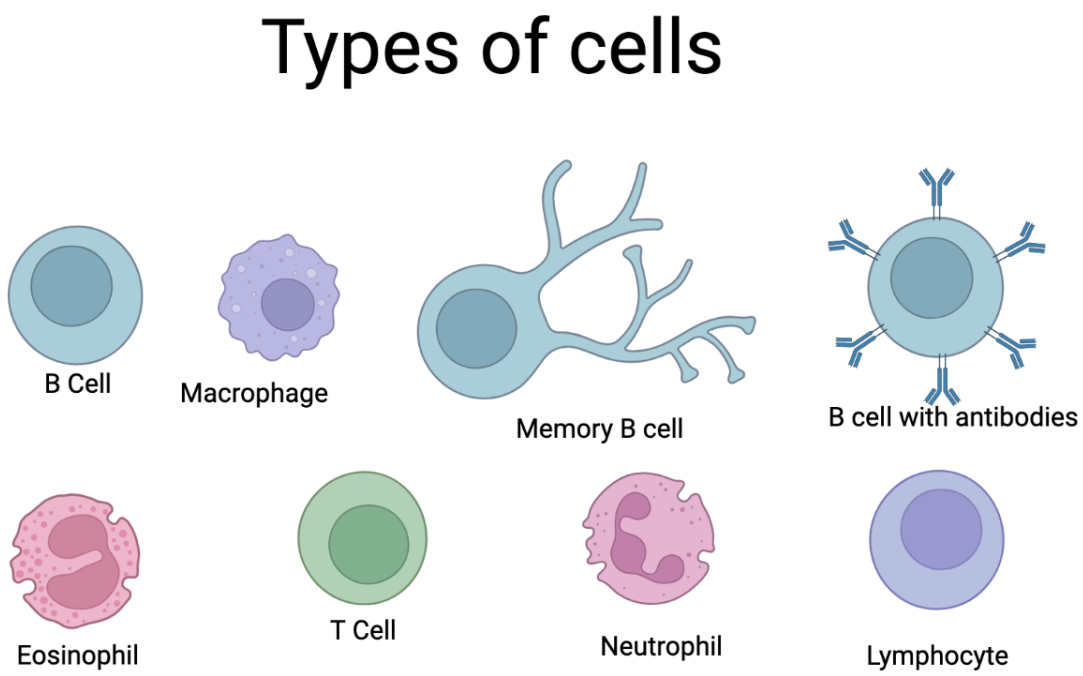

Fig 1 Caption: This table displays all the immune cells in one area. The chart includes T cells, B cells, Lymphocytes, Memory B cells, B cells with antibodies attached, Macrophages, Eosinophils, and Neutrophils. This chart gives readers an easy view of all the immune cells in one area. It also allows them to visualize what they will read more about in the rest of the paper. Made by Pranish Mandava.

Why does the Immune system Decline?

A study analyzing stem and progenitor cells found that aging affected all cells in your body. For example, alterations in the PI3K pathway are often side effects of aging cells. In a study done with mice to find out if the immune system ages, these observations were done by JCI. "Consistent with this observation, HSCs deplete due to the build-up of ROS in mice, a key downstream PI3K component, is deleted." (JCI). The article talks about how we can control the ROS levels in cells by using ATM kinase and age-related declines in the signs of ATM, and the results show an increase in ROS in cells. Increased expression of tumor suppressor proteins also occurs in aging cells from multiple tissues. There also is a mystery of why the quality of lymphoid progenitors gets worse as you age, and recent studies have shown that Arf expression increases in B cells from old mice and partially reverses the effects of aging. This mystery allows us to find a possible breakthrough in how we can keep our immune system young again to enable us to have an opportunity to live longer.

Other age-related problems can be tied to the hematopoietic system. For example, changed expression of various B lineage transcription factors has shown declines in B lymphopoiesis. Recently, researchers have explored BATF in the decrease of HSCs during aging. Researchers showed that BATF levels increased in HSCs due to DNA damage, causing change in HSCs at the expense of their self-renewal.

Although considerable focus has been on stem and progenitor cells, aging also affects gene expression patterns in mature B and T cells. New T cell signaling has also proven to correlate with aging, and the list of unregulated genes grows, as shown by several recent reports, two of which focused on altered expression of DUSPs. DUSPs turn off target kinases. They also turn off the MAPK pathway, whose activity is critical for T cell activation in areas such as bone marrow, the lymphatic system, or your blood. A study done by researchers in JCI reported, "Induction and sustained transcription of DUSP4 in activated CD4+ memory T cells from humans 65 and older, which correlated with their altered cytokine production and an impaired ability to help B cells." (JCI). Another report from the same laboratory elaborated on the increase of DUSP6 in naive CD4+ human T cells, activating a lower fraction of Th cells, particularly in response to low-affinity stimuli. As mentioned above, these abnormalities in HSCs, lymphoid progenitors, and B and T cells can occur partly due to age-related alterations in all immune cells' significant areas. For example, over time, exposure to an inflammatory area can induce epigenetic modifications that affect the genes required for growth, survival, or differentiation. Nevertheless, cell-autonomous events may be a significant cause of aging and the potential for us to solve aging as a whole.

B and T cell declination

As we know, when an illness strikes, the B and T cells are activated first. When these cells are activated, our body quickly uses our T cells to kill the outsiders, and then B cells take their time to produce antibodies, which destroy the virus. When a virus gets killed, the stronger the virus, the weaker your immune system is, as it has already spent most of its energy trying to kill the first virus. If a second powerful virus attacks simultaneously, this can lead to death, which is very unlikely. Usually, over time your immune system strengthens again and falls again repeatedly. After time takes its toll, both cells have reasons for declining over time. T cells deteriorate over time because they eventually die, and your body can't produce the same amount as it once could. Another reason for this is thymic involution.

The Thymus is a small lymphatic gland mainly used to train our T cells. As you age, the Thymus starts to shrink because of a process known as Immunosenescence. Immunosenescence means that your body gets weaker and less powerful as you age. This process makes the lymphatic system start to shrink because the lymphatic system has been attacked for many years now and is shrinking because of overuse. Since the Thymus is a part of the lymphatic system, it declines over time alongside the rest. Since the overall Thymus has shrunk, the T cell production is far lower, as a smaller thymus can't produce the same amount as an average or larger Thymus.

A weaker Thymus decreases T cell production as you age, which is a constantly declining factor and will only worsen as you age. B cells differ slightly from T cells because they produce far slower due to a different production site. Unlike T cells grown in the Thymus, B cells form in the bone marrow. Since as we get age, the cellularity of our bone marrow decreases significantly. This factor leads to a decrease in B cell production. Due to these reasons caused by Immunosenescence, B cell and T cell production heavily decline as we age. These are only two of their critical immune cells, but the rest of the white blood cells have their reason.

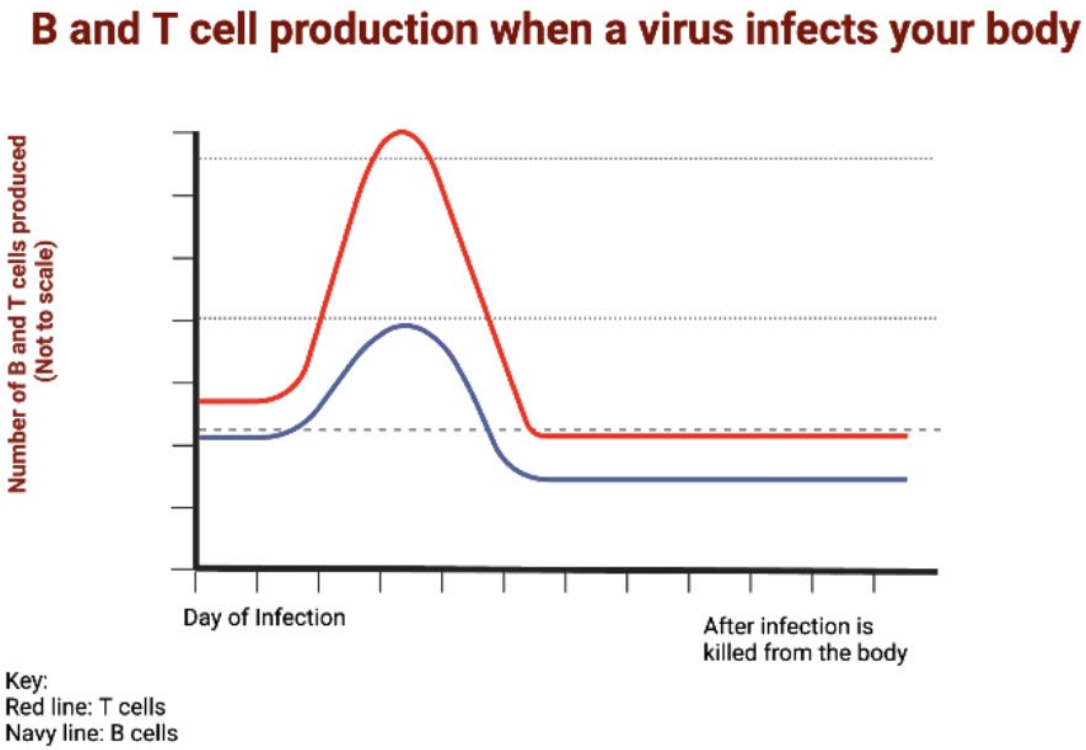

Fig 2 Caption: This graph illustrates how B and T cell production significantly spikes when infected with a disease/virus. This virus infection will lead to an immune response by rapidly producing these cells, as shown in the graph above. The disease is one of the reasons why we get severe side effects after we feel sick as our body raises our internal temperature to fight the virus. After this repeatedly happens, our immune system weakens as we cannot muster the same number of immune cells as we could at a younger age, leading to eventual death. Made by Pranish Mandava.

Other Immune cell declination

Neutrophils, similar to T cells, also correlate with their decrease in Immunosenescence. Many studies have shown a correlation between age and Neutrophil decline because they overuse their enzymes and acids to break down the virus inside them. Another reason why they decline is also similar to B cells. Most of our immune cells form in the bone marrow inside our bones. As we age, our body can't create the same amount of Neutrophils, which is why Neutropenia happens (a lack of Neutrophils in the blood flow). Macrophages are very similar to Neutrophils; as they age, they reduce their productivity. They cannot be as productive in Phagocytosis as by breaking down the cells.

Another problem is that as we age, bone marrow can't produce as many immune cells as it once could. This problem in the bone marrow heavily affects Macrophages more than any cell. After all, they are relatively big cells

because they have to contain a whole organism, unlike Neutrophils, which work together to consume an entire organism. The larger they get, the more energy is used and is harder to produce, which makes Macrophage production and usability go down. Since Macrophages are the frontline fighters alongside Neutrophils and B cells, many Macrophages die, and only a few form, leading to the overall decrease of Macrophages in our body. Due to these reasons, Macrophage and Neutrophil production in our body heavily decrease as we age due to Immunosenescence and so much more. Although we can't truly stop this, we can keep our immune system as robust as possible by doing these methods.

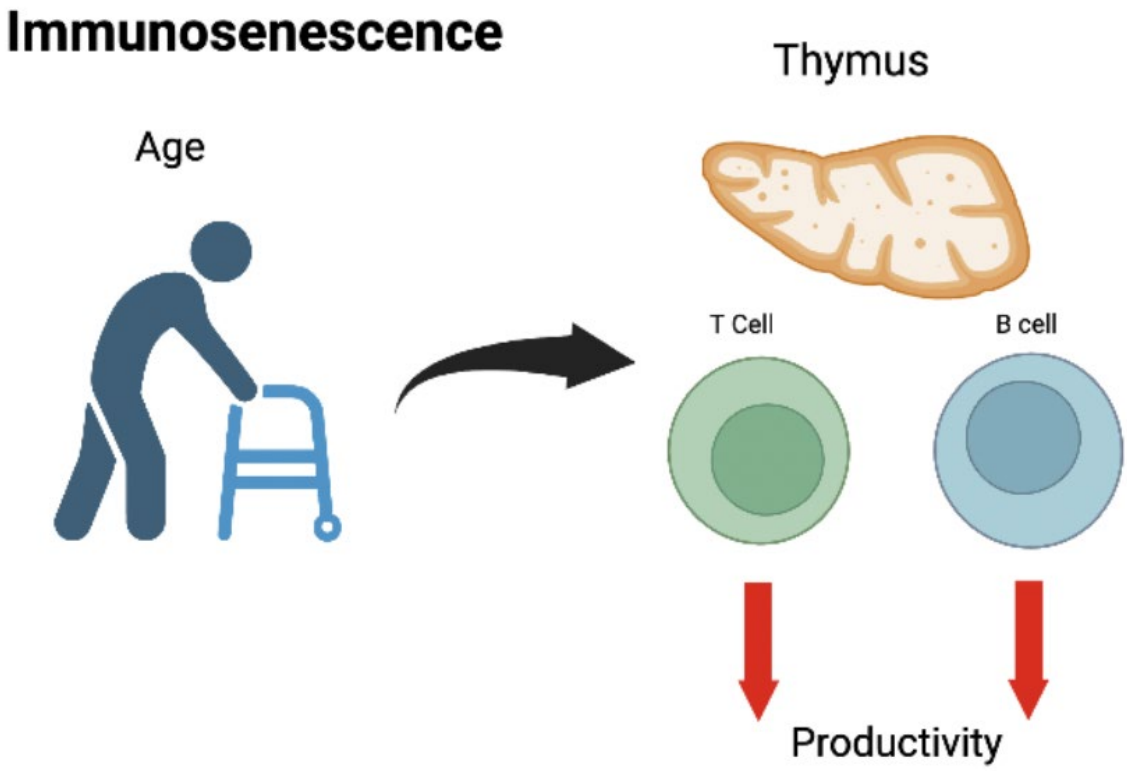

Fig 3 Caption: This image illustrates that Immunosenescence significantly impacts the Thymus (known for producing these immune cells). This graph reinforces that idea by showing it in a visual form. It shows how B and T cell production severely decreases as we age. Immunosenescence is the idea that as we age, our body gradually gets worse. This idea is applied in this image showing how our body (Thymus specifically) is affected by this process. Made by Pranish Mandava.

How can we prevent Immune System Declination?

Our immune system is one of the key reasons we live for so long, but as we age, it weakens. We can use many methods, such as having a healthy lifestyle, exercising, not doing drugs or Alcohol, not smoking, and having a healthy diet. A healthy lifestyle allows your immune system to be in the best shape possible. For example, doing Yoga or breathing practice your lungs and immune system, allowing your body to be overall more substantial in countering viruses. It will enable our immune system to be as strong as possible and give us the best chance to keep our body as strong as possible. Exercising (cardio) allows your heart to keep pumping blood (which contains your white blood cells) around the body, creating an easier way to access bacterial breakouts. Cardio enables the heart to quickly move around blood because the healthier the heart, the easier we can move blood; the more beneficial it is, the better. Not doing drugs and

Alcohol just keeps your body healthy, as doing these kills your body and weakens your immune system, allowing viruses a greater chance to take over your body. Drugs and Alcohol wholly ruin your body; when you overuse Alcohol, it can lead to liver cancer, and drugs can lead to mental addiction and financial ruin. Both of these together will ruin your life. Not smoking can keep your lungs healthy, which is essential for breathing. Breathing allows oxygen to enter the body more effectively, which is vital to survival, as oxygen is necessary for the body to stay. Finally, a healthy diet can keep your immune system healthy because certain fibers can keep your immune system healthy because they can break down fatty acid chains. In modern society, people don't care much about their diet as they eat fast food every day, which is very oily, or they eat chips, which are all unhealthy for you. We have to worry about our diet the most nowadays, but our bodies may need even more vitamins than usual if we are older. In addition to this, organic and nonorganic foods do affect our immune system. Organic food, also known as natural foods, are very powerful as they don't have any pesticides and such, allowing our bodies to stay healthy. In contrast, nonorganic foods are raised with pesticides, ruining the food by corrupting it with pesticides. Vitamin medication, especially vitamins A and D, may help us keep our immune system healthy when we cannot exercise as much or such.

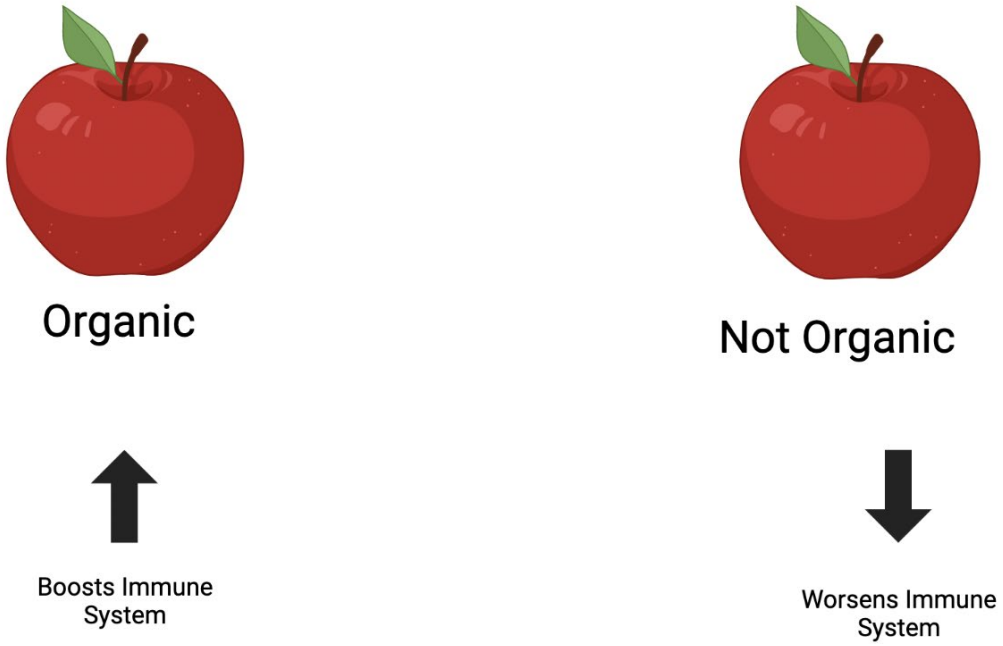

Fig 4 Caption: This image is used to demonstrate further how organic and nonorganic foods affect our immune system. Organic foods use far more natural and fewer pesticides, providing us with more and better nutrients. Nonorganic foods can be pesticide raised, making us sick at first and even affecting us long-term by affecting our organs and tissues by burning or even destroying them. Made by Pranish Mandava.

How can we prevent B and T cell declination?

Fixing age-related deficiencies in lymphocyte progenitors or mature T and B cells may significantly restore immune function in older people. However, these cells would be in an aged microenvironment that could eventually make them as aged cells once again. Researchers found that CD4+ T cells created from old HSCs were functional in younger people but not more seniors. This means that the aged thymic or peripheral microenvironments significantly impact

how the Immune system regenerates itself. From this perspective, interventions may need to lower the effects of aging on many cellular targets.

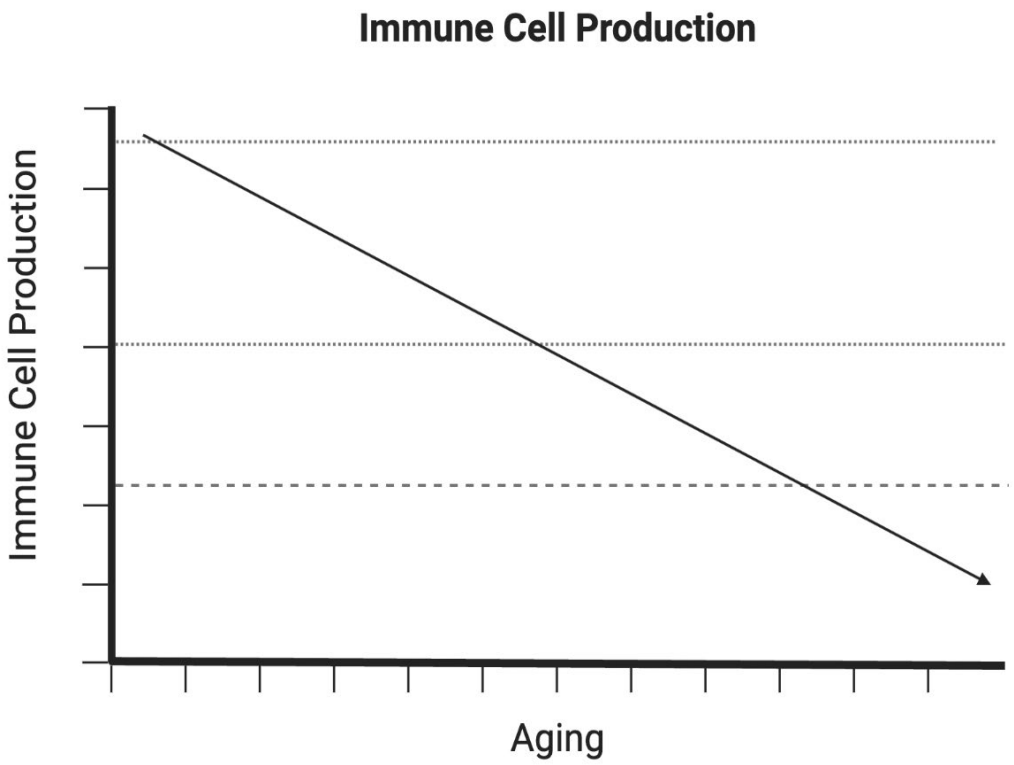

Fig 5 Caption: This image further demonstrates how aging leads to lower production of immune cells, reinforcing the idea that Immunosenescence heavily affects our body and immune system functions. This is the major area of focus in this research article as we are analyzing how we use our immune system and how we can prevent its decline. This graph provides a clear example by showing how aging leads to Immunosenescence and that eventually leads to a decline in our cell functions, creating a worse immune system and life. Made by Pranish Mandava.

The possibility of multiple hormones and growth factors to improve the harmed Thymus has been tested in numerous clinical trials. Many of these factors can be categorized in 3 ways. Those in the first, such as IL-7, connect with Thymus and bone marrow progenitors. There is little evidence that IL-7 has any effect on thymic cells. However, the benefit of IL-7 lies in its ability to stimulate peripheral T-cell survival/expansion. The second category includes hormones such as GH have been demonstrated in clinical trials to promote Thymic performance and size. Many GH effects are mediated through IGF-1. IGF-1 may bind to receptors in the thymic stroma. However, it is primarily mediated through effects on the former cells. Stromal cells–derived factors presumably act on thymocytes (curved arrow). A third category of factors, typified by FGF7, binds to stromal cells but not to thymocytes. Factors caused by stromal cells then act on thymocytes, and we have recently demonstrated the effects of Ink4a in ETPs.

Vitamins A and D are two of the most important ones we know. Vitamin D can be obtained through many means, such as vegetables and the sun. Vitamin A is primarily obtained through food. In Vitamin D, the significant type of Vitamin D is Vitamin D3 (VD3). VD3 is obtained through sunlight (ultraviolet rays) or Vitamin pills. Vitamin A is found in almost all foods, and it is beneficial for helping our organs by keeping them healthy. These 2 Vitamins, in specific, have been known for keeping our immune system healthy and allowing our body to be strong, but what do these two vitamins do to our immune system?

Effects of Vitamin D

For over two decades, it has been recognized that VD3 metabolites affect the immune system by significantly suppressing adaptive immune cells. T cells experience growth inhibition, reduced production of IL-2 and IFN mRNA and protein, and CD8 T-cell-mediated cytotoxicity when exposed to VD3. The VDR-RXR complex binds to VDRE in the promoters of genes producing IL-2 and IFN to reduce their production. The most noticeable inhibitory effects of VD3 occur in memory T-cells, which express higher levels of VDR than naive T-cells. VD3 also increases T-cell capacity to suppress primary mixed-lymphocyte reactions and cytotoxic T-cell responses. Overall, VD3 blocks the induction of TH1-cell cytokines, particularly IFNγ, while promoting TH2-cell responses by indirectly decreasing IFNγ production and directly enhancing IL-4 production. VD3 suppresses the synthesis of IL-12, a cytokine that supports TH1-cell responses in antigen-presenting DCs, further enhancing its effect on effector T-cell differentiation. Additionally, VD3 inhibits TH17-cell responses, partly by inhibiting IL-6 and IL-23 production, and induces the reciprocal differentiation of Treg cells. VD3 also decreases B-cell proliferation, plasma-cell differentiation, and IgG secretion, which might be indirectly mediated through its effect on B cells.

The role of VD3 in the immune system has yet to be fully understood due to conflicting reports on its direct effect on B cells. In patients with inactive SLE, VD3 inhibits mitogen-stimulated IgG production by B cells, but not in those with active SLE, suggesting memory B cells and ASCs may be refractory to VD3 inhibition. Low levels of VD3 in SLE patients during active disease may exacerbate humoral immunity. VD3 can inhibit the differentiation and maturation of DCs, decrease TH1-cell responses, and induce IL-10-producing TR1 cells. However, it can also stimulate human monocyte proliferation and increase the production of IL-1 and cathelicidin by monocytes and macrophages. VDR-deficient mice have an average immune-cell population and reject transplants at the same rate as wild-type mice. Animal models with VDR deficiency in T, B, and myeloid cells are needed to understand VD3's effects on the immune response.

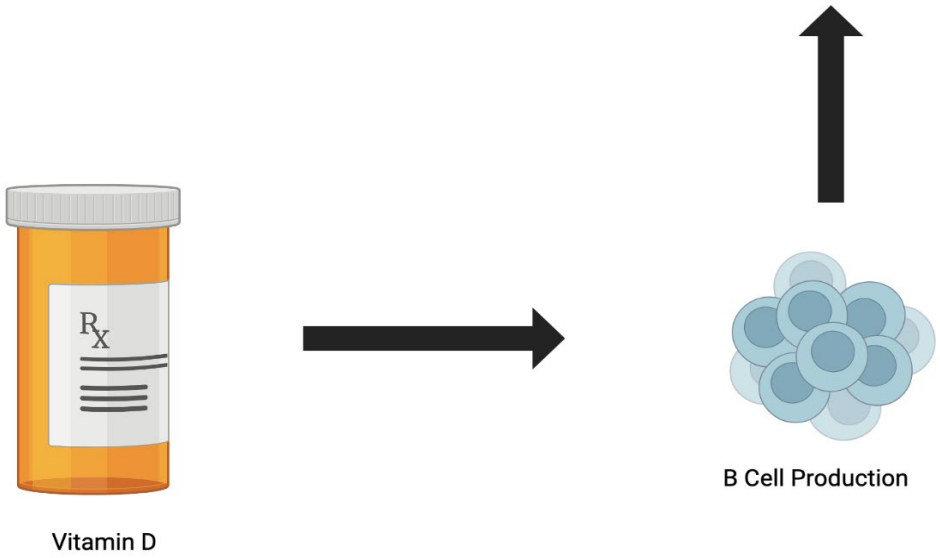

Fig 6 Caption: This image directly represents how the use of Vitamins such as Vitamin D can lead to B cell production. The use of VD3 in cells and our immune system leads to a significant immune response allowing our body to create more immune cells. The VD3 will focus near the Thymus, allowing more immune cells to form. This allows for a more robust immune system as we still produce more immune cells at a longer age, getting us even close to living for as long as we want. Made by Pranish Mandava.

Effects of Vitamin A

The adaptive immune response can also be affected by Vitamin A. Retinoic acid metabolites, for instance, can enhance T-cell proliferation and cytotoxicity, likely by increasing IL-2 secretion and signaling. Vitamin A-deficient mice exhibit impaired T-cell function, suggesting an in vivo role for Vitamin A in this regard. One possible explanation is that retinoic acid cannot compete with VD3 for their shared nuclear binding partner RXR in the absence of Vitamin A. Consequently, VD3's inhibitory effects on T-cell function, including TH-cell activity, are not counterbalanced by retinoic acid.

It's worth noting that certain types of vitamin A metabolites, known as retro-retinoids, can impact general lymphocyte functions, such as B-cell proliferation and T-cell activation and proliferation. While 14-hydroxy-retro retinol positively affects proliferation, anhydro retinol can block B-cell proliferation and induce apoptosis in T cells. Retro-retinoids don't signal through RAR or RXR receptors and may compete for a standard yet unknown receptor. Retinoic acid, on the other hand, can directly affect DC function and modulate antigen presentation. It can increase the expression of matrix metalloproteinases, which boosts tumor-specific T-cell responses by increasing the migration of tumor-infiltrating DCs to the draining lymph nodes. In the presence of inflammatory stimuli, retinoic acid enhances DC maturation and antigen-presenting capacity. However, retinoic acid can be stored by DCs and released to act directly on T cells or other cells and impact the final outcome of an immune response. Vitamin A metabolites also have specific effects on the immune response, such as modulating the TH1-TH2 cell balance and differentiating TReg and TH17 cells. Retinoic acid, in particular, promotes TH2-cell differentiation by inducing IL4 gene expression and blocking the manifestation of T-bet, the TH1-cell master regulator. Vitamin A supplementation was associated with an increase in disease severity in a mouse model of asthma. In contrast, vitamin A deficiency had the opposite effect, linked to decreased TH2-cell cytokines. Retinoic acid may promote TH2-cell differentiation indirectly through the modulation of APCs, but it can also act directly on T cells through RAR proteins.

Conclusion

In conclusion, we can do many things to improve our immune system. We can do this by having a healthy lifestyle, exercising, not doing drugs or Alcohol, not smoking, having a nutritious diet, and using vitamins. We can have a healthy lifestyle to keep our immune system and the body more robust, exercising to prevent our immune system from going into Immunosenescence and not doing drugs, Alcohol, or smoking to keep our immune system as strong as possible. We can have a healthy diet to keep our body strong and use vitamins, especially Vitamins A and D, to keep our immune systems healthy.

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