Effects of Excess or Insufficient Energy on Immune System of Mice

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Abstract. Nowadays, people have found that excessive or too little energy intake has a great impact on the immune system. Excess energy may lead to weakened immunity, making obese patients more prone to chronic inflammation and tumors. However, the specific molecular mechanism of excess energy acting on the immune system is still not clear. There are also differences in the total impact of too little energy on the human immune system. Therefore, by summing up various opinions and drawing on the research results of a large number of papers, this paper systematically summarizes the impact of energy on the immune system in order to let others have a more comprehensive and profound understanding of the progress in related fields. Through the research, the paper finds that energy deficiency can affect the properties of immune organs and especially reduce the weight of the spleen. Obesity and splenomegaly are closely related and have a certain causal relationship. Obese patients can significantly reduce or keep the peripheral blood T cells unchanged, and their impact on immunity is controversial. Dieting has a positive effect on obese patients and a negative effect on normal people. On the one hand, obesity can promote the activation of macrophages and Th1 cells and strengthen the inflammatory response. On the other hand, adipose tissue itself can secrete cytokines such as leptin to cause chronic inflammation. Obesity can inhibit tumor immunity by affecting the tumor microenvironment, leading to tumor formation.

Keywords: diet restriction · obesity · excess energy · immunity

1 Introduction

With the gradual improvement of people's living standards, obesity has become a very serious social problem. Obese patients will have a series of diseases such as hypertension, hyperlipidemia, arteriosclerosis, and heart disease. In addition, obese patients are more likely to have diabetes, gout, and some tumor-related diseases.

Nowadays, people have found that excessive or too little energy intake has a great impact on the immune system. Excess energy may lead to weakened immunity, making obese patients more prone to chronic inflammation and tumors. The immune organs in different parts of people with low energy intake will also have positive or negative changes. However, the specific molecular mechanism of excess energy acting on the

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immune system is still not clear. There are also differences in the total impact of too little energy on the human immune system. Many people do not fully understand the impact of obesity or weight loss on the immune system. Therefore, by summing up various opinions and drawing on the research results of a large number of papers, this paper systematically summarizes the impact of energy on the immune system in order to let others have a more comprehensive and profound understanding of the progress in related fields.

2 Definitions

2.1 Obesity

Obesity is a common group of metabolic disorders. When the human body eats more calories than it consumes, the excess calories are stored in the body in the form of fat. When the amount exceeds the normal physiological needs and reaches a certain value, it will evolve into obesity. The weight of adipose tissue in normal male adults accounts for 15% ~ 18% of body weight, and that in female adults accounts for 20% ~ 25%. The proportion of body fat increased with age. The evaluation methods of obesity include anthropometry, dual energy X-ray absorptiometry, ultrasound, CT, infrared induction, etc. If there is no obvious cause, it is called simple obesity, and if there is a clear cause, it is called secondary obesity.

2.2 Immune System

The immune system has the functions of immune surveillance, defense, and regulation. This system consists of immune organs (bone marrow, spleen, lymph nodes, tonsils, small intestine lymph nodes, appendix, thymus, etc.), immune cells (lymphocytes, mononuclear phagocytes, neutrophils, basophils, eosinophils, mast cells, platelets (because there is IgG in platelets), etc.), and immune active substances (antibodies, lysozyme, complement, immunoglobulin, interferon, interleukin, tumor necrosis factor, and other cytokines). The immune system is divided into innate immunity (also known as non-specific immunity) and adaptive immunity (also known as specific immunity). Adaptive immunity is divided into humoral immunity and cellular immunity.

2.3 Inflammation

Inflammation is a term that refers to people's defensive responses to motivation, which manifests as edema, heat, pain, and immune system dysfunction.

Usually, inflammation is a favorable and spontaneous defense response of people. However, under some circumstances, inflammation is also negative, like impairing people's own cells, killing other people's transplanted tissue, and so on.

2.4 Tumor Immunity

Tumor immunity is to study the relationship between cancer antigen, the immune system and tumorigenesis, improvement or prognosis. Cancer forms by the malignant diffusion of normal cells in the body, which is characterized by constant increase and diversion in the body. Consequently, the striking feature of cancer in immunology is the production of some novel antigen markers that cannot appear in the same kinds of common cells. Cancer antigens are found continuously. On the other hand, some cancer Ag is specific to cancer cells; on the other hand, some associated Ag mostly refers to antigens in the infant, which are shared by embryonic tissue and tumor tissue.

3 Effects on Immune Organs

Immune organs include both central and peripheral immune organs. Central immune organs include bone marrow and the thymus, while peripheral immune organs include the spleen and lymph nodes. In the immune system, T cells and B cells are generated in the bone marrow at the same time, and then T cells transfer to the thymus to mature, while B cells remain in the bone marrow to mature.

Some people have conducted experiments to limit the energy intake of rats. They artificially gave rats 40% of the daily energy required by diet [1], and established a rat obesity model (DIO model) to study the effects of the two on the immune system. Researchers found that the weight and size of the spleen of rats with an artificially controlled diet will be smaller, and the spleen index will also be reduced [7].

At the same time, studies have shown that obesity is closely related to the incidence of breast cancer [8]. Some researchers have found that obese breast cancer patients have a higher probability of lymph node metastasis and lymph node resection than non obese breast cancer patients. Therefore, obesity may affect the immune function of lymph nodes.

At the same time, traditional Chinese medicine has a direct relationship between the spleen and obesity. The spleen is the main organ of water and grain transportation in the human body. When spleen deficiency occurs, the metabolism of water and grain will inevitably be abnormal. The moisture in the body will stop accumulating, and the excessive moisture in the human body will lead to obesity. In other words, traditional Chinese medicine believes that spleen deficiency is one of the direct causes of obesity.

4 Effect on Immune Cells

Immune cells include B lymphocytes, T lymphocytes, NK cells, antigen-presenting cells (dendritic cells and phagocytes) and stem cells. Lymphocytes can recognize antigens specifically or nonspecifically according to different classifications, and then produce different coping strategies. It plays an important role in innate immunity and adaptive immunity.

Some researchers have artificially restricted the diets of rats to study the effects of diet on the immune system. They found that the proportion of lymphocytes in the spleen of obese rats on a diet changed, and the content of cd8+ T cells in the spleen

and blood decreased significantly, resulting in an increase in the proportion of cd4+t cells/cd8+t cells in the spleen. The study speculated that diet might be conducive to enhancing the immunity of obese rats. At the same time, some researchers also observed the impact of energy intake restriction on normal rats, and finally, surprisingly, found that dieting would reduce the number of T cells and inhibit the immunity of normal rats [1]. Therefore, dieting has different effects on the immune systems of rats in different states, which should be classified and discussed [9].

As for the effect of excess energy on the immune system of mice, the researchers found that the contents of cd4+t and cd8+t cells in peripheral immune organs (spleen and lymph nodes) and peripheral blood of long-term obese rats decreased significantly, but the aggregation of cd4+t cells and cd8+t cells was also more obvious, and the content of T cells in adipose tissue of rats increased significantly. It seems that obesity has a negative effect on the immune systems of rats. However, the conclusions derived from rats' behavior may not be applicable to humans. Some scientists have compared the proportion of lymphocytes in the blood of obese and non-obese young people at the same age and found that there was no significant difference between them. However, other scientists found that the proportion of peripheral blood lymphocytes increased significantly in obese women. Different scientists have produced different experimental results here [2]. Therefore, the specific impact of obesity on human immune cells is still inconclusive and controversial.

5 Impact on Immune Molecules

5.1 Inflammatory Reaction

Adipose tissue is closely related to the systemic chronic inflammatory response, and its formation may have a variety of mechanisms.

One theory is that the accumulation of fat in abnormal organs can lead to the weakening of insulin action, resulting in insulin resistance [3], and then metabolic disorders. In the past, chronic inflammation could occur. At the same time, M1 macrophages and Th1 cells that produce inflammation can also secrete cytokines to cause insulin resistance [6]. Other studies have found that when obese patients consume a large amount of saturated fatty acids and cholesterol, they can activate the inflammatory receptor NLRP3 and then trigger a cascade reaction to produce inflammation; On the contrary, a certain amount of unsaturated fatty acids can inhibit the activation of this receptor and the production of chronic inflammation. Therefore, NLRP3 also plays an important role in the production of inflammation. It has also been found that adipose tissue can secrete a variety of adipokines, such as leptin. On the one hand, leptin can promote the survival and activation of innate immune cells (macrophages) and then release more inflammatory mediators to cause inflammation; on the other hand, it can also affect adaptive immunity by promoting the presentation of antigens by dendritic cells. At the same time, leptin also helps B cells release more cytokines to cause inflammation (Fig. 1) [11].

5.2 Tumor Immunity

The researchers found that in obese mice with excess energy, the tumor will use fatty acids as the main energy material to replace glucose. This leads to the reduction of free

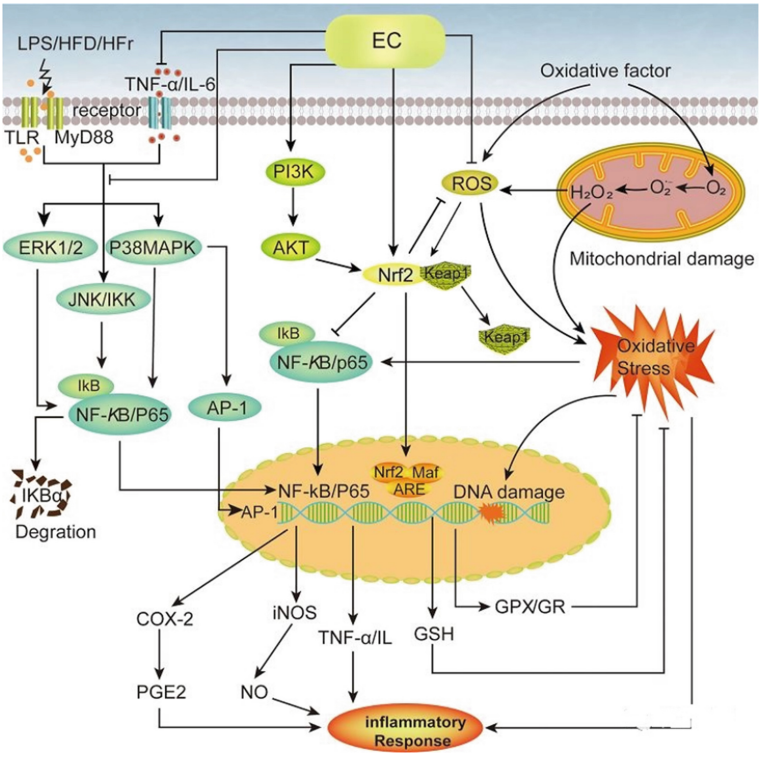

Fig. 1. Inflammation effect

fatty acids absorbed by cd8+ CTL cells in the tumor microenvironment [4], which in turn leads to the weakening of anti-tumor immunity [12] (Fig. 2). At the same time, some studies have found that obese mice with excess energy can up-regulate the expression of PD-L1, which is an immune checkpoint molecule [5], and its activation is conducive to the production of tumors. People speculate that fat cells secrete TNF-α and IL-6 to promote PD-L1 in tumor cells. At the same time, exosomes secreted by adipocytes up-regulate PD-L1 expression in tumor cells, which may also be involved [7].

At the same time, it has been found that obesity is closely related to the incidence rate of breast cancer. Researchers speculate that obesity may affect the incidence rate of breast cancer through insulin, inflammatory mediators, estrogen, and even leptin. The current view is that for premenopausal women, the degree of obesity is negatively correlated with the incidence rate of breast cancer; for postmenopausal women, the degree of obesity is positively correlated with the incidence rate of breast cancer [10].

6 Conclusion

In conclusion, through the research above, the paper finds that energy deficiency can affect the properties of immune organs, especially reducing the weight of the spleen. Obesity and splenomegaly are closely related and have a certain causal relationship.

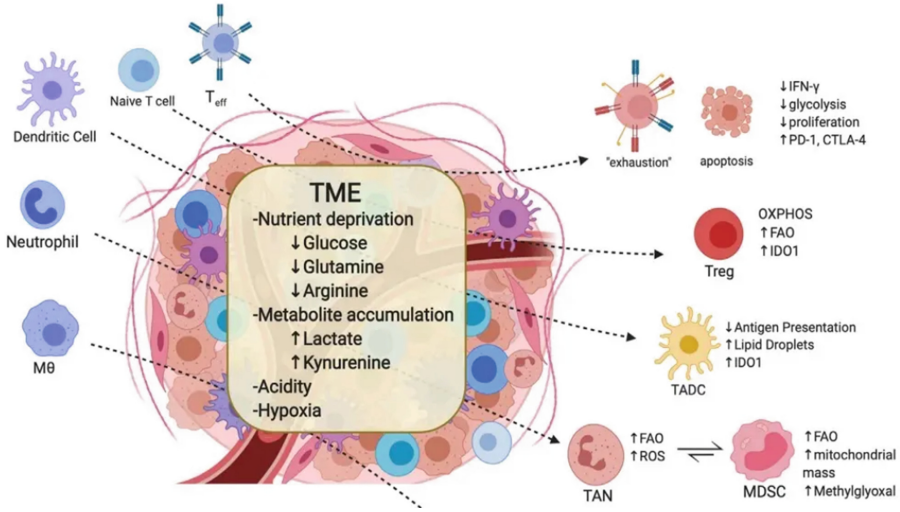

Fig. 2. Tumor microenvironment

Besides, obese patients can significantly reduce or keep peripheral blood T cells unchanged, and their impact on immunity is controversial. Dieting has a positive effect on obese patients and a negative effect on normal people.

On the one hand, obesity can promote the activation of macrophages and Th1 cells and strengthen the inflammatory response; on the other hand, adipose tissue itself can secrete cytokines such as leptin to cause chronic inflammation. In addition, obesity can inhibit tumor immunity by affecting the tumor microenvironment, leading to tumor formation.

The above is the main discussion about energy and immunity. However, there are still many deficiencies in this paper. For example, it has not conducted a detailed and rigorous investigation. The research is not comprehensive enough, and the number of references is not comprehensive enough. Further research in this area will be carried out in the future.

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