Metabolic regulation in innate immunity

Abstract

The metabolic parameter dependent on the central nervous system (CNS) can regulate the storage and release of energy. Macrophages are the main effector cells that represent the innate immune system and have multiple roles, such as phagocytosis, secretion of cytokines, and antigen presentation. These responses are intervened by the generation of reactive oxygen/reactive nitrogen species (ROS/RNS), such as superoxide. In macrophages, G6PD (glucose 6-phosphate dehydrogenase) stimulates the expression of ROS- and RNS-producing genes. The immune response function requires rapid and extensive cell growth, proliferation, and production of effector cytokines. The metabolic and biosynthetic demand of lymphocytes increases after activation in relation to glucose metabolism via increasing glucose transporter 1. During the immune system response to pathogens, a special group of cytokines (chemokines) signals immune cells such as T-cells and macrophages to travel to the site of infection. These cytokines activate their cells to stimulate production of more cytokines. Many metabolic processes react directly or indirectly to proinflammatory cytokines to ensure a steady supply of nutrients for proliferation of phagocytes. This review has focused on energy metabolism regulation with neuroimmunity dependent cells.

Keywords: glucose, Immune system, toll like receptor

Abbreviations: CNS, central nervous system; G6P, glucose 6-phosphate; GluT, glucose transferase; ATP, Adenosine three phosphate; NADPH, nicotinamide adenine dinucleotide phosphate; MAPKs, mitogen activated protein kinases; ROS/RNS, reactive oxygen/reactive nitrogen species; G6PD, glucose-6-phosphate dehydrogenase; NF-κB, nuclear factor-κB nox: NADPH Oxidase 2; MIF, migration inhibitory factor; PKC, protein kinase C; TLR, toll-like receptors; PRRS, pattern recognition receptor; Myd88, myeloid differentiation primary response gene 88; TIR, toll/Interleukin-1 receptor; IRAK4, IL-1 receptor-associated kinase 4; TRAF6, TNF receptor associated factor; AP-1, activator protein 1 IKK: IκB kinase; JNK, c-Jun N-terminal kinases; TCR, T-cell receptor; TNF-α, tumor necrosis factor-α; IL-6, Interleukin-6; LIF, leukemia inhibitory factor; IL-18, Interleukin-18 IL-1; Acp, The IL-1 accessory protein; Gp130, Glycoprotein 130; JAK, Janus kinase; STAT, signal transducer and activator of transcription; CRP, C-reactive protein.

Introduction

Metabolism is the chemical reaction that converts food into energy in the body. According to the first law of thermodynamics, energy cannot be created or destroyed; it has to be used or stored within biological systems. The metabolic processes in biological systems do not happen at random, but are tightly regulated to enable the most efficient use of the energy in ingested food. The metabolic parameter depends on the central nervous system (CNS), which can regulate the storage and release of energy. Metabolic regulation is modulated with enzyme activity. Glucose, one of the most important factors in metabolism, regulates the energy metabolism. Glucose 6-phosphate (G6P) is one of the glucose derivatives which is phosphorylated on carbon 6 and has two major metabolic pathways, glycolysis and pentose phosphate. Glucose 6-phosphate can also be converted to glycogen. This reaction is mediated through the enzymatic activity of hexokinase through the action of one molecule adenosine three phosphates (ATP). Glycogen can undergo a glycol genolysis reaction and form glucose-1-phosphate. Excessive production of Nicotinamide Adenine Dinucleotide Phosphate (NADPH) may lead to formation of G6P by glucose 6-phosphate dehydrogenase(G6PD), which is the first step of the pentose phosphate pathway. In addition, if the body needs nucleotide precursors of DNA for growth and synthesis, G6P will also be dehydrogenated and enter the pentose phosphate pathway. The production of NADPH by G6PD is an essential enzyme in red blood cells, which carry oxygen from the lungs to tissues throughout the body. This enzyme helps protect red blood cells from damage and premature destruction. Many scientists have demonstrated the relationship between glucose and immune receptors and responses. Consider et al. verified the relationship between high glucose inhibitions which can induce an inflammatory response. Also it has been confirmed that the macrophage infiltration depends on glucose levels in the body; they also demonstrated that some effectors could inhibit the glucose levels or G6PD genes and contribute to inflammatory diseases.

Metabolic regulation of cytokines

The human immune system is energy intense and protection of immune functions has been thought to account for as much as 25% of the daily energy expenditure in healthy persons. During the process of the immune system fighting pathogens, a special group of cytokines (chemokines) signals immune cells, such as T-cells and macrophages, to migrate to the site of infection. These cytokines can activate their cells and stimulate production of more cytokines. Many metabolic processes react directly or indirectly to proinflammatory cytokines to ensure a steady supply of nutrients for proliferation of phagocytes and antibody production. The current hypothesis is that during an immune response, cytokines direct nutrients away from tissue growth. Therefore infection causes major modification in human metabolism. During sickness energy is reduced, fatty acid oxidation is increased to provide energy, and protein degradation is enhanced to supply amino acids for production of acute phase proteins. Some studies explained that the immune cells use glucose as their main fuel and also express the insulin receptor and respond to insulin. In addition, glutamine is essential for immune cell function and is highly used both as a primary fuel and as a carbon and nitrogen donor for nucleotide
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Integrated Metabolic Regulation

Stress and infections may cause high circulating levels in the body. Increasing polymorphism in IL-6 and IL-1 variations are associated with the risk of various diseases, including metabolic disorders. C-reactive protein is an important predictor and strong risk factor for atherosclerosis and cardiovascular diseases. TNF can be fueled with more glucose by inhibiting the uptake of glucose into the muscle and adipose cells governed by insulin sensitivity. Glucose transfer into immune cells is mediated through GluT1 activity. However, cytokines play an important role in metabolic regulation. Proinflammatory cytokines such as IL-6, IL-1, and TNF-α can act through a heterodimer consisting of the IL-1RI and the IL-1 accessory protein (IL-1AcP). Binding of agonists induces the recruitment of MyD88 and initiates the activation of IRAK/TRAF pathway, leading to NF-kB activation. The IL-6 cytokine family, including IL-6, IL-1, and LIF, shares the gp130 signal transducer and signal through gp130 and a ligand specific receptor. Although the gp130 expresses across all cell types, it cannot transduce signals without the ligand specific receptor. The IL-6 cytokine family shares the gp130 signal transducer and signal through gp130 and a ligand specific receptor. The IL-6/IL-6Ra fusion-protein Hyper-IL-6 can activate all cells with gp130 even in the absence of the ligand specific receptor. Binding of agonists induces phosphorylation of JAK and initiates the activation of JAK/STAT or JAK/MAPK pathway.

Conclusion

Metabolism is the chemical reaction that converts food to energy which can be regulated by the central nervous system. Brain function is linked to glucose infiltration and transportation of energy, which can be altered by cytokines and proinflammatory cytokines via the immune system. Glucose infiltration in the immune system can manage innate immunity by regulating the complement cascades and also by producing adaptive immunity components. Energy metabolism has a major role in homeostasis and occurrence of CNS immune diseases.

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Conflict of interest

Author declares there is no conflict of interest.

References


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