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ADENOSINE IN THE ROLE OF IMMUNOMODULATOR

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Adenosine is a purine nucleoside composed of adenine and ribose which acts as a neuromodulator as well as an immunomodulator, regulating the balance of energy in the body as well as immune responses through signaling of cellular stress in energy depletion. Broken down from ATP, it acts throughout all systems of the body providing inhibitory effects towards overreactive cells. It is a key regulator in balancing the immune system responsible for signaling stress in the body, as well as responding with receptor mediated processes which work to suppress inflammation and maintain basic homeostasis throughout the cells.

This research reviewed the mechanisms of adenosine function as well as the importance for proper function for the immune system cells. In research of the individuality of adenosine function specifically as an immunomodulator, the molecular mechanisms and clinical relevance of the effect of adenosine regulation function of immune cells, an extensive analysis of existing research was conducted. Using databases such as Google Scholar, PubMed and publications from John Hopkins University were used. Terms searched included «adenosine as an immunomodulator», «mechanisms of adenosine» and «clinical implications of adenosine immunomodulation dysfunction». Studies published from 1993 to 2023 were included, with a particular focus on observation studies in tested subjects and subject reviews of the importance of proper immune cell response to inflammation.

Typically, when cells become stressed in the form of inflammation, hypoxia or generally exhausted through physical exertion, ATP is released into the extracellular space. Effectors, primarily CD39 and CD73 break down the ATP into adenosine, shifting it from a pro-inflammatory signal to an anti-inflammatory signal. Adenosine then binds to immune cell receptors, activates intracellular signaling by increasing cAMP where it suppresses the inflammatory pathways, with immune cells ultimately becoming less active (Chenglai et al., 2023). With adenosine initiating the immunosuppressive signaling, it forms the responses on a tissue-level. Evidence indicates that after its bonding with receptors (primarily A2A or A2B) the T cells suppress excessive inflammation, notably proliferation and cytokine production. This process is vital for preventing any future autoimmune diseases. Macrophages, which are key regulators of the immune system, contain sensors for inflammation. Adenosine primarily acts on the M2 phenotype due to its anti-inflammatory and tissue repairing properties. It is at this point that macrophages along with dendritic cells alert killer T cells, reducing cytotoxicity and any further damage to tissues. Adenosine plays a role as an important endogenous regulator for homeostasis. It resolves inflammation, protecting any tissue damage from overactive immune responses, signaling a protective response to any acute or large scale tissue or cell stress and in case of its dysfunction or impairment, overactivation of T cells and macrophages may result in serious conditions such as lupus, multiple sclerosis or tissue necrosis. (Giulia et al., 2020)

Functionally a neuromodulator as well as an immunomodulator, adenosine acts a beacon for signaling cellular stress and damage or ineffective homeostasis. It moderates activity of macrophages, T cells and dendritic cells working closely together to stop tissue damage and rather promote tissue repairment.