

Magnone M, Nencioni A, Bruzzone S. NAD⁺ Levels Control T Cell Calcium Signaling and Activation (2015). *Messenger* 4, 1-6.

NAD⁺ plays a central role in key cellular functions, being a co-enzyme in redox reactions or representing a substrate for NAD⁺-utilizing enzymes, which drive several cellular processes. Here we will focus on the crucial role of NAD⁺ in regulating human T lymphocyte survival, cytokine secretion, and response to mitogens. More specifically, we will discuss the NAD⁺-dependent control of intracellular Ca²⁺ homeostasis, in terms of Ca²⁺ increase in response to mitogen stimulation and in terms of NAD⁺-mediated Ca²⁺ content in ER stores, in conditions of different levels of intracellular NAD⁺ in T cells. Modulation of intracellular NAD⁺ levels is obtained either by inhibiting NAMPT, a key enzyme in NAD⁺ biosynthesis, or, alternatively, by supplementing cells with NAD⁺ precursors, up-regulating intracellular NAD⁺ production. The NAD⁺-dependent molecular mechanisms discussed support the rationale for the use of NAMPT inhibitors in immunosuppressive/anti-inflammatory therapies, or the use of vitamin B3, precursors of NAD⁺, for the boosting of immune response.