Influence of inflammation in the process of T lymphocyte differentiation: Proliferative, metabolic, and oxidative changes

Moro-García M.A.

Mayo J.C.

Sainz R.M.

Alonso-Arias R.

T lymphocytes, from their first encounter with their specific antigen as naïve cell until the last stages of their differentiation, in a replicative state of senescence, go through a series of phases. In several of these stages, T lymphocytes are subjected to exponential growth in successive encounters with the same antigen. This entire process occurs throughout the life of a human individual and, earlier, in patients with chronic infections/pathologies through inflammatory mediators, first acutely and later in a chronic form. This process plays a fundamental role in amplifying the activating signals on T lymphocytes and directing their clonal proliferation. The mechanisms that control cell growth are high levels of telomerase activity and maintenance of telomeric length that are far superior to other cell types, as well as metabolic adaptation and redox control. Large numbers of highly differentiated memory cells are accumulated in the immunological niches where they will contribute in a significant way to increase the levels of inflammatory mediators that will perpetuate the new state at the systemic level. These levels of inflammation greatly influence the process of T lymphocyte differentiation from naïve T lymphocyte, even before, until the arrival of exhaustion or cell death. The changes observed during lymphocyte differentiation are correlated with changes in cellular metabolism and these in turn are influenced by the inflammatory state of the environment where the cell is located. Reactive oxygen species (ROS) exert a dual action in the population of T lymphocytes. Exposure to high levels of ROS decreases the capacity of activation and T lymphocyte proliferation; however, intermediate levels of oxidation are necessary for the lymphocyte activation, differentiation, and effector functions. In conclusion, we can affirm that the inflammatory levels in the environment greatly influence the differentiation and activity of T lymphocyte populations. However,

little is known about the mechanisms involved in these processes. The elucidation of these mechanisms would be of great help in the advance of improvements in pathologies with a large inflammatory base such as rheumatoid arthritis, intestinal inflammatory diseases, several infectious diseases and even, cancerous processes.

Differentiation

Exhaustion

Inflammation

Metabolic reprogramming

Redox balance

T lymphocytes

adenosine triphosphate

catalase

CD27 antigen

CD28 antigen

gamma interferon

glucose transporter

granulocyte macrophage colony stimulating factor

interleukin 12

interleukin 15

interleukin 1beta

interleukin 2 receptor beta

interleukin 6

peroxidase

pyruvate dehydrogenase kinase

reactive oxygen metabolite

superoxide dismutase

telomerase

thioredoxin

transcription factor T bet

tumor necrosis factor

aerobic glycolysis

cell death

cell growth

cell proliferation

human

infection

inflammation

lymphocyte differentiation

memory cell

metabolism

mitophagy

oxidation

oxidative stress

pentose phosphate cycle

Review

T lymphocyte

tumor growth

tumor microenvironment