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THSTI decoding the T-cell arsenal

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New Delhi, March 31: When CD4+ and CD8+ cells differentiate in response to a foreign pathogen, an array of complex molecular pathways is initiated. It is not a conclusion drawn from a single research. Instead, 25-30 years of ground-breaking research has provided novel insights into the working of T cells. Moreover, as technology advances, human comprehension increases, emerging research continues to knock down the secrets of T cell differentiation. A compilation of such inquisitive and noteworthy research papers forwarding understanding of T cell differentiation and function in tissue inflammation was published recently in Research Topics. Focusing mainly on prospects in anti-cancerous and autoimmune functions, the expanded subset of Th cells from Th1 and Th2 to Th17, Th9, Tfh, Tregs, and Th22 cells are studied. The differentiation of such T cells in carving a niche in the inflamed tissues of autoimmune disorders depends on several factors.

These include the strength of antigen-antibody interaction, the milieu of cytokines, degree of co-stimulation, expression of transcription factors, and interaction with histone modifiers. An essential part of the T cell response is their correct characterization and editing during thymic selection. However, the same receptors can be expressed by different and distinct T helper subsets, ultimately secreting typical cytokine. These can also be regulated by the same transcription factor, thereby urging the cautious use of markers for identifying T helper cells. It also relents the need to explore the physiological relevance of marker expression in these cells. The participation of different subsets has been indicated in the pathophysiology of inflammatory disorders. Besides the importance of marker expression, the role of metabolic properties, and checkpoints in determining the behaviour of CD4+ T cells also remains crucial.

For example, lipid metabolites act as a regulator of immune responses, while altered steroid pathways affect inflammation. Additionally, other metabolites such as NAD, ATP, Nitric Oxide remain crucial in T cell differentiation regulated through various metabolic checkpoints. The metabolic checkpoints are, in turn, regulated by mTOR and AMPK sensors by attenuating glycolysis and decreasing fatty acid metabolism, respectively. The AMPK

pathway can even impart an analgesic effect on inflammatory pain. Further, the AMP to ATP ratio influence the mTOR and AMPK function. Even the levels of amino acids Trp and Arg effect activation and function of effector T cells. Several different metabolic checkpoints can be thus targeted in various inflammatory diseases such as Type II diabetes, Chronic Obstructive Pulmonary Disease (COPD), ulcerative colitis, rheumatoid arthritis, and Crohn's disease. Thus, insights into the intricate network of transcription factors, metabolic checkpoints, and regulators can pave the way for improved understanding of the immunologic of diseases and their treatment.

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