T-cell activation: Mechanisms, pathways, and immune response.

Chongbo Shang*

Department of Neurology, Fudan University, China

Introduction

T-cells are a crucial component of the adaptive immune system, playing a central role in recognizing and eliminating pathogens. Understanding the mechanisms and pathways of T-cell activation is essential for advancing immunotherapy, vaccine development, and the treatment of autoimmune diseases [1].

T-cell activation is initiated when a naïve T-cell encounters an antigen-presenting cell (APC) that presents a specific antigen via the major histocompatibility complex (MHC). This process requires three key signals. The T-cell receptor (TCR) binds to the peptide-MHC complex on the APC. CD4+ T-cells recognize antigens presented by MHC class II, while CD8+ T-cells recognize antigens associated with MHC class I [2].

Cytokines secreted by APCs and surrounding immune cells determine the differentiation and function of T-cells. Key cytokines include interleukin-2 (IL-2), interferon-gamma (IFN-γ), and transforming growth factor-beta (TGF-β) [3].

Once the TCR engages with the antigen-MHC complex, several intracellular signaling cascades are activated: Lck kinase phosphorylates the immunoreceptor tyrosine-based activation motifs (ITAMs) in the CD3 complex. ZAP-70 (zeta-chain-associated protein kinase 70) is recruited and activated, initiating downstream signaling. Activation of the Ras/MAPK pathway leads to gene transcription for T-cell proliferation and differentiation [4].

TCR stimulation induces calcium influx, activating calcineurin. Calcineurin dephosphorylates nuclear factor of activated T-cells (NFAT), leading to IL-2 gene expression. Phosphoinositide 3-kinase (PI3K) activation leads to Akt phosphorylation, promoting cell survival and metabolism [4].

The mechanistic target of rapamycin (mTOR) controls T-cell proliferation and differentiation. The recruitment of protein kinase C (PKC-θ) activates IκB kinase (IKK), leading to NF-κB nuclear translocation [5].

NF-κB regulates genes associated with T-cell survival and immune response. Following activation, T-cells differentiate into various subsets based on cytokine signals: Differentiate into Th1, Th2, Th17, or Treg cells, each with distinct cytokine profiles and immune functions. Kill infected or malignant cells by releasing perforin and granzymes [6].

Provide long-term immunity by quickly responding to previously encountered antigens. Understanding T-cell activation has significant implications in medicine [7].

Checkpoint inhibitors, such as PD-1 and CTLA-4 blockers, enhance T-cell activation against cancer. Dysregulated T-cell activation contributes to diseases like rheumatoid arthritis and multiple sclerosis [8].

The binding of costimulatory molecules, such as CD28 on T-cells with B7-1 (CD80) or B7-2 (CD86) on APCs, enhances activation and prevents anergy. Effective vaccines rely on robust T-cell responses to generate lasting immunity [9].

T-cell activation is a complex process that involves antigen recognition, costimulatory signaling, and intracellular signaling cascades leading to immune responses [10].

Conclusion

T-cell activation is a highly regulated process that determines immune responses against pathogens and tumors. The intricate signaling pathways and differentiation mechanisms involved provide valuable insights into developing targeted therapies for cancer, autoimmune disorders, and infectious diseases.

References

1. Kazemi T, Younesi V, Jadidi-Niaragh F, et al., Immunotherapeutic approaches for cancer therapy: an updated review. Artif Cells Nanomed Biotechnol. 2016;44(3):769-79.
2. Mellman I, Coukos G, Dranoff G. Cancer immunotherapy comes of age. Nat. 2011;480(7378):480-9.
3. Farkona S, Diamandis EP, Blasutig IM. Cancer immunotherapy: the beginning of the end of cancer?. BMC Med. 2016;14(1):1-8.
4. Riley RS, June CH, Langer R, et al., Delivery technologies for cancer immunotherapy. Nat Rev Drug Discov. 2019;18(3):175-96.
5. Lesterhuis WJ, Haanen JB, Punt CJ. Cancer immunotherapy–revisited. Nat Rev Drug Discov. 2011;10(8):591-600.
6. Fukumura D, Kloepper J, Amoozgar Z, et al., Enhancing cancer immunotherapy using antiangiogenics: opportunities and challenges. Nat Rev Clin Oncol. 2018;15(5):325-40.
7. Martin JD, Cabral H, Stylianopoulos T, et al., Improving cancer immunotherapy using nanomedicines: progress, opportunities and challenges. Nat Rev Clin Oncol.2020;17(4):251-66.
8. Parish CR. Cancer immunotherapy: the past, the present and the future. Immunol Cell Biol 2003;81(2):106-13.

***Correspondence to:** Chongbo Shang, Department of Neurology, Fudan University, China. E-mail: c.shan@fudan.edu.cn

***Received:** 03-Feb-2025, Manuscript No. AAJCIT-25-161373; **Editor assigned:** 04-Feb-2025, Pre QC No. AAJCIT-25-161373(PQ); **Reviewed:** 17-Feb-2025, QC No AAJCIT-25-161373; **Revised:** 21-Feb-2025, Manuscript No. AAJCIT-25-161373(R); **Published:** 28-Feb-2025, DOI:10.35841/aajcit-8.1.247*

***Citation:** Shang C. T-cell activation: Mechanisms, pathways, and immune response. J Cancer Immunol Ther. 2025;8(1):247*

9. Baxevanis CN, Perez SA, Papamichail M. Cancer immunotherapy. Crit Rev Clin Lab Sci. 2009;46(4):167-89.
10. Huang X, Pan J, Xu F, et al.,. Bacteria-based cancer immunotherapy. Adv Sci. 2021;8(7):2003572.

Citation: *Shang C. T-cell activation: Mechanisms, pathways, and immune response. J Cancer Immunol Ther. 2025;8(1):247*