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#43049**Human Exhausted CD8⁺ T Cell IHC
Antibody Sampler Kit****Orders:** 877-616-CELL (2355)
orders@cellsignal.com**Support:** 877-678-TECH (8324)**Web:** info@cellsignal.com
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3 Trask Lane | Danvers | Massachusetts | 01923 | USA

1 Kit (9 x 20 microliters)

For Research Use Only. Not for Use in Diagnostic Procedures.

| Product Includes | Product # | Quantity | Mol. Wt | Isotype/Source |
|--|-----------|----------|---------------|----------------|
| CD3ε (D7A6E™) XP® Rabbit mAb | 85061 | 20 µl | 23 kDa | Rabbit IgG |
| CD8α (D8A8Y) Rabbit mAb | 85336 | 20 µl | 29 kDa | Rabbit IgG |
| Tox/Tox2 (E613Q) Rabbit mAb | 73758 | 20 µl | 60-80 kDa | Rabbit IgG |
| TCF1/TCF7 (C63D9) Rabbit mAb | 2203 | 20 µl | 48, 50 kDa | Rabbit IgG |
| Granzyme B (D6E9W) Rabbit mAb | 46890 | 20 µl | 30 kDa | Rabbit IgG |
| PD-1 (Intracellular Domain) (D4W2J) XP® Rabbit mAb | 86163 | 20 µl | 52-65 kDa | Rabbit IgG |
| TIGIT (E5Y1W) XP® Rabbit mAb | 99567 | 20 µl | 18, 30-40 kDa | Rabbit IgG |
| TIM-3 (D5D5R™) XP® Rabbit mAb | 45208 | 20 µl | 45-70 kDa | Rabbit IgG |
| LAG3 (D2G4O) XP® Rabbit mAb | 15372 | 20 µl | 60-80 kDa | Rabbit IgG |
| Anti-rabbit IgG, HRP-linked Antibody | 7074 | 100 µl | | Goat |

Please visit cellsignal.com for individual component applications, species cross-reactivity, dilutions, protocols, and additional product information.**Description**

The Human Exhausted CD8⁺ T Cell IHC Antibody Sampler Kit provides an economical means of characterizing the extent of exhaustion in T cells in formalin-fixed, paraffin-embedded tissue samples.

Storage

Supplied in 10 mM sodium HEPES (pH 7.5), 150 mM NaCl, 100 µg/ml BSA, 50% glycerol and less than 0.02% sodium azide. Store at -20°C. *Do not aliquot the antibodies.*

Background

Cluster of Differentiation 3 (CD3) is a multiunit protein complex expressed on the surface of T cells that directly associates with the T cell receptor (TCR). CD3 is composed of four polypeptides: ζ, γ, ε, and δ. Engagement of the TCR complex with antigens presented in major histocompatibility complexes induces tyrosine phosphorylation in the immunoreceptor tyrosine-based activation motif (ITAM) of CD3 proteins. CD3 phosphorylation is required for downstream signaling through ZAP-70 and p85 subunit of PI-3 kinase, leading to T cell activation, proliferation, and effector functions (1). CD8 is a transmembrane glycoprotein expressed primarily on cytotoxic T cells, but has also been described on a subset of dendritic cells in mice (2,3). On T cells, CD8 is a co-receptor for the TCR, and these two distinct structures are required to recognize antigen bound to MHC Class I. CD8 ensures specificity of the TCR-antigen interaction, prolongs the contact between the T cell and the antigen presenting cell, and recruits the tyrosine kinase Lck, which is essential for T cell activation (2).

Tox, Tox2, and TCF1/TCF7 play key roles in T cell development. Tox is also induced by high antigen stimulation during chronic viral infection or cancer, regulating T cell persistence and exhaustion. TCF1/TCF7 preserves the effector function of exhausted T cells during viral infection or cancer. EOMES is a key transcription factor for memory T cells and for full effector differentiation of CD8⁺ T cells. The dynamic expression of these transcription factors help characterize the extent to which a T cell is exhausted and will respond to antigen stimulation (4-8). Granzyme B is a serine protease expressed by cytotoxic T lymphocytes and natural killer (NK) cells and is a key component of immune responses to pathogens and transformed cells (9).

PD-1 (PDCD1, CD279), TIGIT (VSIG9, VSTM3), TIM-3 (HAVCR2), and LAG3 (CD223) are immune cell co-inhibitory receptors (also known as immune checkpoints) that negatively regulate T cell function and dampen the immune response to pathogens and cancer (10-15). In addition to activated T cells, PD-1 is expressed by activated B cells and monocytes. Following interaction with its ligands, PD-L1 and PD-L2, PD-1 is phosphorylated at ITIM and ITSM motifs leading to recruitment of protein tyrosine phosphatases SHP-1 and SHP-2 and suppression of TCR signaling. TIGIT is expressed at low levels on subsets of T cells and NK cells, and is upregulated at the protein level following activation of these cells. TIGIT marks exhausted T cells in the tumor microenvironment and during human immunodeficiency virus (HIV) infection. TIM-3 is expressed by exhausted T cells in the settings of chronic infection and cancer. Tumor-infiltrating macrophages and dendritic cells also express TIM-3. LAG3 is primarily expressed by activated CD4⁺ T cells, CD8⁺ T cells, FoxP3⁺ T regulatory cells (Tregs), and natural killer (NK) cells. Co-expression of multiple immune checkpoints help characterize the extent to which a T cell is exhausted and will respond to antigen stimulation. Therapeutic blockade of several of these immune

checkpoint receptors is a promising strategy for neoplastic intervention by enabling anti-tumor immune responses (10-15).

Background References

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