Store at -20°C

#44689

Human T Cell Co-inhibitory and Co-stimulatory Receptor IHC Antibody Sampler Kit

Cell Signaling TECHNOLOGY®

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For Research Use Only. Not For Use In Diagnostic Procedures.

Products Included	Product #	Quantity	Isotype/Source
PD-1 (D4W2J) XP® Rabbit mAb	86163	20 µl	Rabbit IgG
TIM-3 (D5D5R™) XP® Rabbit mAb	45208	20 µl	Rabbit IgG
LAG3 (D2G40™) XP® Rabbit mAb	15372	20 µl	Rabbit IgG
VISTA (D1L2G™) XP® Rabbit mAb	64953	20 µl	Rabbit IgG
B7-H3 (D9M2L) XP® Rabbit mAb	14058	20 µl	Rabbit IgG
4-1BB/CD137/TNFRSF9 (D2Z4Y) Rabbit mAb	34594	20 µl	Rabbit IgG
OX40 (E9U7O) XP® Rabbit mAb	61637	20 µl	Rabbit IgG
GITR (D9I9D) Rabbit mAb (IHC Preferred)	68014	20 µl	Rabbit IgG
CD40 Ligand (D5J9Y) Rabbit mAb	15094	20 µl	Rabbit IgG

See www.cellsignal.com for individual component applications, species cross-reactivity, dilutions, and additional application protocols.

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 antibody.*

Background References:

(1) Schildberg, F.A. et al. (2016) *Immunity* 44, 955-72.
(2) Anderson, A.C. et al. (2016) *Immunity* 44, 989-1004.
(3) Callahan, M.K. et al. (2016) *Immunity* 44, 1069-78.
(4) Ward-Kavanagh, L.K. et al. (2016) *Immunity* 44, 1005-19.
(5) Ara, A. et al. (2018) *Immunotargets Ther* 7, 55-61.
(6) Knee, D.A. et al. (2016) *Eur J Cancer* 67, 1-10.
(7) Chester, C. et al. (2018) *Blood* 131, 49-57.

Description: The Human T Cell Co-inhibitory and Co-stimulatory Receptor IHC Antibody Sampler Kit provides an economical means of detecting expression of receptors that modulate T cell activity in formalin-fixed, paraffin-embedded tissue samples.

Background: PD-1 (PDCD1, CD279), TIM-3 (HAVCR2), LAG3 (CD223), VISTA (PD-H1), and B7-H3 (CD276) 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. In addition to activated T cells, PD-1 is expressed by activated B-cells and monocytes. 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. Although primarily expressed by myeloid cells, VISTA is also expressed by CD4+, CD8+, and Treg cells. Research examining the biological function of B7-H3 suggested that B7-H3 can be both a positive and negative regulator of T cell response. B7-H3 is expressed by antigen presenting cells, activated T cells, and a few normal tissues, including placenta and prostate. Expression of B7-H3 is seen in several cancer types, including prostate, breast, colon, lung, and gastric cancers, and in endothelial cells from tumor associated vasculature. Therapeutic blockade of these immune checkpoint receptors is a promising strategy for neoplastic intervention by enabling anti-tumor immune responses (1-3).

4-1BB (TNFRSF9, CD137), GITR (TNFRSF18), OX40 (TNFRSF4, CD134), and CD40 ligand (CD40L, CD154, TRAP, gp39) are immune cell co-stimulatory receptors that promote effector T cell survival and activation, and enable optimal immune responses to pathogens. 4-1BB is expressed in activated CD4+ and CD8+ T cells, natural killer cells and dendritic cells. GITR is expressed constitutively at high levels on Tregs, at low levels on naive and memory T cells, and is induced upon T cell activation. Studies show GITR can also be induced on NK cells, macrophages, and DCs. GITR ligation has been shown to induce CD8+ T cell activation, cytoxicity, and memory T cell survival, and conversely inhibit Treg suppressive function while promoting effector T cell resistance to Treg suppression. OX40 is primarily expressed on activated CD4+ and CD8+ T cells, while CD40L is primarily expressed on the surface of T cells, but has also been reported in blood platelets, mast cells, basophils, NK cells, and B cells. Research studies show that agonists of these co-stimulatory receptors augment anti-tumor immunity in several cancer types. Due to the combined effects on both Treg suppression and effector cell activation, GITR represents a unique opportunity for immunotherapeutic intervention in cancer. These pathways are an important area of interest in the study of cancer, vascular diseases, and inflammatory disorders (4-7).

Specificity/Sensitivity: Each antibody included in the Human T Cell Co-inhibitory and Co-stimulatory Receptor IHC Antibody Sampler Kit recognizes endogenous levels of its target protein. CD40 Ligand (D5J9Y) Rabbit mAb recognizes endogenous levels of total membrane bound and soluble CD40 ligand protein.

Source/Purification: Monoclonal antibodies are produced by immunizing animals with a synthetic peptide corresponding to residues surrounding Ala274 of human PD-1 protein, Gln264 of human OX40 protein, Val142 of human GITR protein, Ala94 of human B7-H3 protein, or near the carboxy terminus of human VISTA protein. Monoclonal antibodies are produced by immunizing animals with a recombinant protein specific to the extracellular domain of human TIM-3 protein, human 4-1BB/CD137/TNFRSF9 protein, human CD40 ligand protein, or the amino terminus of human LAG3 protein.

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Applications: **W**—Western **IP**—Immunoprecipitation **IHC**—Immunohistochemistry **ChIP**—Chromatin Immunoprecipitation **IF**—Immunofluorescence **F**—Flow cytometry **E-P**—ELISA-Peptide **Species Cross-Reactivity:** **H**—human **M**—mouse **R**—rat **Hm**—hamster **Mk**—monkey **Mi**—mink **C**—chicken **Dm**—D. melanogaster **X**—Xenopus **Z**—zebrafish **B**—bovine **Dg**—dog **Pg**—pig **Sc**—S. cerevisiae **Ce**—C. elegans **Hr**—Horse **All**—all species expected Species enclosed in parentheses are predicted to react based on 100% homology.