WHITEPAPER

Meet the Marker: OX40

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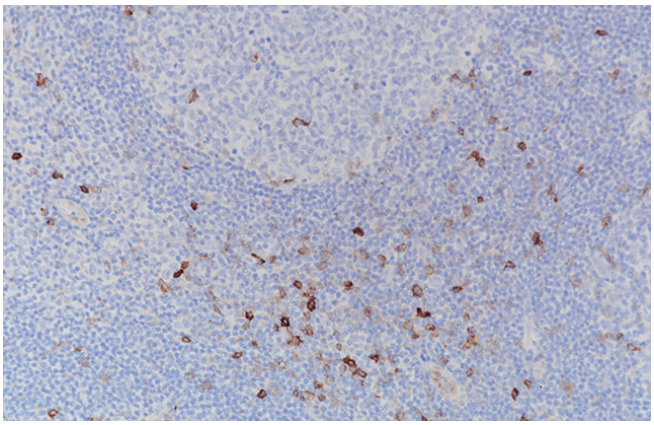
OX40, also known as CD134, is a well-known T-cell activation marker and is a member of the tumor necrosis factor (TNF) superfamily of proteins. [1,2] OX40 is a costimulatory receptor that binds to OX40L (CD252), its only known ligand, and initiates cellular signaling events required for full activation of T cells following their recognition of a foreign antigen.[2] Binding of OX40 and OX40L plays roles in T-cell survival, maintenance of memory CD8 T cells, differentiation of CD4 T cells, and Treg inhibition.[1] OX40 and its ligand also regulate cytokine production from T cells, antigen-presenting cells, NK cells and NKT cells, and modulate cytokine receptor signaling.

As a co-stimulatory receptor, OX40 can enhance T-cell receptor signaling on the surface of T lymphocytes, steering their activation by a specifically recognized antigen. For instance, OX40 antibody engagement by ligands on dendritic cells dramatically increases the proliferation, effector function, and survival of T cells.[3] Preclinical studies demonstrated OX40 agonists increase anti-tumor immunity and improve tumor-free survival by increasing T and B cell responses to reporter antigen immunizations, leading to preferential up-regulation of OX40 on CD4(+) FoxP3(+) regulatory T cells in tumor-infiltrating lymphocytes, and increased the anti-tumor reactivity of T and B cells in patients with melanoma.[3] Findings such as this render OX40 as a promising therapeutic target, as this protein can favorably influence the antitumor properties of circulating T cells, B cells, and intratumoral regulatory T cells.[3]

With the success of anti-CTLA-4 and anti-PD-1 therapeutics in cancer immunotherapy, TNF members have been recognized as ideal targets to provide co-stimulatory signals in combination with immune checkpoint blocking antibodies.[4] To maximize therapeutic benefit, researchers are evaluating a triple combination of OX40 with PD-1 and CTLA-4. This “triple threat” immunotherapy approach is an intriguing combination, as OX40 stimulation may help augment the efficacy of dual PD-1/CTLA-4 blockade by enhancing the expansion, survival, and cytolytic activity of tumor-reactive effector T cells.[5] Another combination researched was a CTLA-4 inhibitor, a 4-1BB agonist, and an OX40 agonist. When this cocktail was administered via an intratumoral injection into a mouse lymphoma and colon cancer model, significant antitumor effects were demonstrated, as tumors were cleared in between 70% and 100% of mice and survival was significantly extended.[2] Additionally, combination of anti-OX40 monoclonal antibody treatment plus the HER2 cancer vaccine promoted anti-tumor functions of CD8 T cells and led to tumor regression.[1]



Tonsil stained with OX40/CD134 antibody

Looking to Add OX40 to Your Antibody Menu?

Biocare Medical’s rabbit monoclonal OX40 demonstrates robust specificity and sensitivity and is available in concentrated and prediluted formats. For additional information, please visit our website https://biocare.net/product/ox40-cd134/ or call 800-799-9499.

1. Jeong S, Park SH. Co-Stimulatory Receptors in Cancers and Their Implications for Cancer Immunotherapy. Immune Netw. 2020 Feb; 20(1):e3

2. De Lartigue, H. OX40 Agonists Forge a Path in Combination Immunotherapy. OncologyLive, Vol. 18/No. 05, Volume 18, Issue 5

3. Curti, Brendan D *et al.* “OX40 is a potent immune-stimulating target in late-stage cancer patients.” Cancer research vol. 73,24 (2013): 7189-7198. doi:10.1158/0008-5472.CAN-12-4174

4.Kuang Z, Jing H, Wu Z, Wang J, Li Y, Ni H, Zhang P, Wu W, Wu M, Zhou S, Qiu X, Wu D, Prinz B, Baruah H, Chen B, Yu M, Liu J. Development and characterization of a novel anti-OX40 antibody for potent immune activation. Cancer Immunol Immunother. 2020 Jun;69(6):939-950. doi: 10.1007/s00262-020-02501-2. Epub 2020 Feb 20. PMID: 32078015.

5. Linch SN, *et al.* OX40 Agonists and Combination Immunotherapy: Putting the Pedal to the Metal. Front Oncol. 2015; 5:34.