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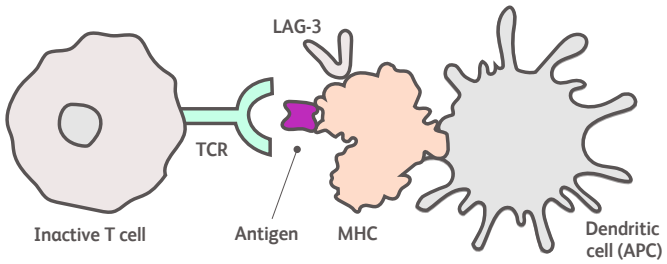
Lymphocyte-Activation Gene 3 (LAG-3)

About LAG-3

Lymphocyte-activation gene 3 (LAG-3) is an immune checkpoint receptor protein found on the cell surface of effector T cells and regulatory T cells (Tregs) and functions to control T cell response, activation and growth.[1]

T cells are a type of white blood cell that are part of the immune system. Activation of cytotoxic T cells by antigens enables them to kill unhealthy or foreign cells.[1]



LAG-3 and Immune Function

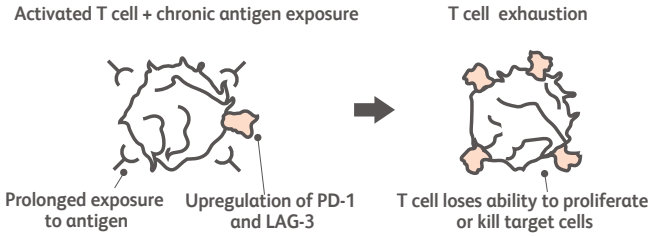
- After a T cell is activated to kill its target cell, LAG-3 expression is increased to turn off the immune response, so that the T cell does not go on to attack healthy cells.2
- Inhibition of the immune response is accomplished through activation of the LAG-3 pathway, which can occur via binding of LAG-3 to a type of antigen-presenting complex called MHC II.

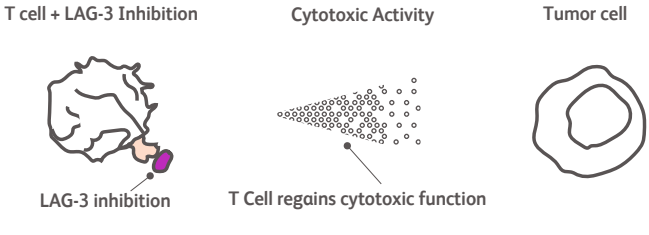
LAG-3 and T Cell Exhaustion

- However, in certain situations where T cells experience prolonged exposure to an antigen, such as cancer or chronic infection, the T cells become desensitized and lose their ability to activate and multiply in the presence of the antigen.[4]
- The desensitized T cell will also progressively fail to produce cytokines (proteins that assist in the immune response) and kill the target cells.[4]
- This process is called T cell exhaustion and is associated with an increased expression of inhibitory receptors such as LAG-3.[4]

LAG-3 and Cancer

- Because of its critical role in regulating exhaustion of cytotoxic T cells and Treg function, LAG-3 has become a target of study in the cancer field.
- In cancer, LAG-3 expressing exhausted cytotoxic T cells and Tregs expressing LAG-3 gather at tumor sites.[5,6]
- Preclinical studies suggest that inhibiting LAG-3 allows T cells to regain their cytotoxic function and potentially inhibit tumor growth.[7]





Interactions with Other Checkpoints

Preclinical studies suggest that targeting LAG-3 in combination with other potentially complementary immune checkpoints may be a key strategy to more effectively activate the antitumor immune response.

Learn more about our research and development efforts by visiting:
www.bms.com/media/media-library/scientific-media-resources.html

[1] Nicholas Durham, Charles G. Drake et al. Lymphocyte Activation Gene 3 (LAG-3) modulates the Ability of CD4 T- cells to Be Suppressed in Vivo. PLoS ONE. November 2014. DOI: 10.1371/journal.pone.0109080.
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[3] Maçon-Lemaître L, Triebel F. The negative regulatory function of the lymphocyte-activation gene-3 co-receptor (CD223) on human T cells. Immunology 2005; 115:170–8.
[4] Wherry, E. J. T cell exhaustion. Nature Immunol. 12, 492–499 (2011).
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[6] Camisaschi C, Casati C, Rini F, et al. LAG-3 Expression Defines a Subset of CD4+ CD25high Foxp3+ Regulatory T Cells That Are Expanded at Tumor Sites. J Immunol. 2010; 184(11):6545-6551.
[7] Grosso JF., Kelleher CC, Harris TJ, et al. LAG-3 regulates CDS+ T cell accumulation and effector function in murine self and tumor-tolerance systems. J Clin Invest. 2007;117(11):3383-3392.
[8] Seng-Ryong Woo, Dario A.A. Vignali, et al. Immune inhibitory molecules LAG-3 and PD-1 synergistically regulate T cell function to promote tumoral immune escape. Cancer Res. 2012 Feb 15; 72(4): 917–927