The LAG-3 pathway is just one of many immune pathways under investigation at Bristol-Myers Squibb. Learn more about our work in Immuno-Oncology by visiting: www.immunooncology.bmsinformation.com

**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. 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.

**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.
- Inhibition of the immune response is accomplished through the binding of LAG-3 to an antigen-presenting complex called MHC II, which together signal the T cell to stop activation and multiplication.

**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.
- The desensitized T cell will also progressively fail to produce cytokines (proteins that assist in the immune response) and kill the target cells.
- This process is called T cell exhaustion and is associated with an increased expression of inhibitory receptors such as LAG-3.

**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.
- Preclinical studies suggest that inhibiting LAG-3 allows T cells to regain their cytotoxic function and potentially affect tumor growth.

**Interactions with Other Pathways**

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