Indoleamine 2,3-dioxygenase (IDO) is an intracellular enzyme that initiates the breakdown of tryptophan in the tumor microenvironment. Tryptophan is an essential amino acid obtained from the diet that is a fuel required by the body to build proteins needed for cellular growth as well as immune function.

**IDO and Immune Function**
- IDO regulates immune function through control of tryptophan levels.
- In a healthy person, IDO ensures the immune system does not over-respond to threats.
- By reducing the level of tryptophan, IDO removes the fuel needed for immune activity and acts to suppress the immune system through two mechanisms:
  - Suppression of effector T cell activity which signals to stop the immune response
  - Promotion of T regulatory cell (Treg) activity which acts to actively suppress the immune response

**IDO and Cancer**
- Tumor cells hijack this immunosuppressive process by upregulating IDO activity and depleting tryptophan in the tumor microenvironment.
- Without tryptophan to fuel the immune cells, cytotoxic T cells starve and immunosuppressive Tregs are upregulated leading to a failure of the immune system to respond appropriately to the cancer.
- IDO expression is upregulated in several types of cancer.

**Clinical Implications and Interactions**
- Preclinical studies suggest that targeting the IDO pathway in combination with other potentially complementary immune pathways may be a key strategy to more effectively activate the antitumor immune response.

The IDO pathway is just one of many immune pathways under investigation at Bristol-Myers Squibb. Learn more about our work in Immuno-Oncology by visiting: https://iopathway.web.bms.com