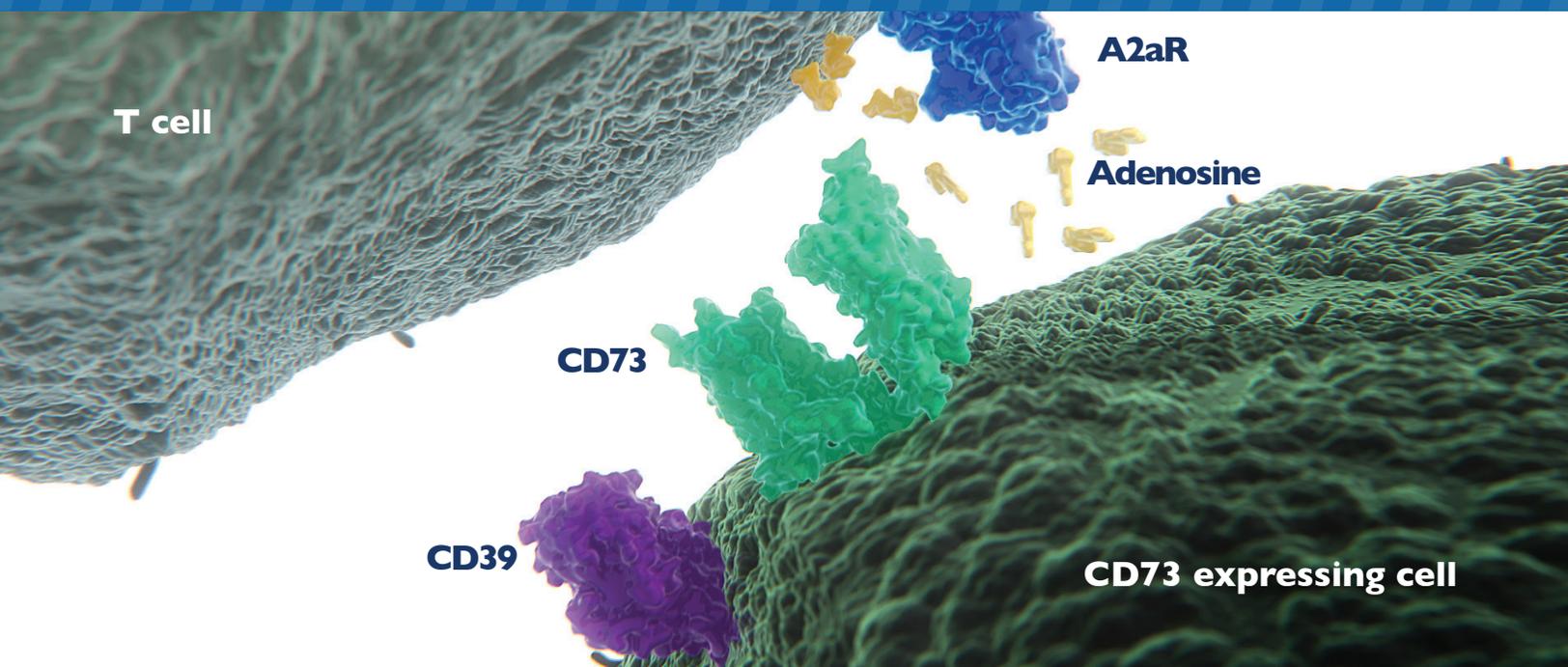


CD73 Immune Pathway



About CD73

CD73 is a cell surface enzyme which is overexpressed in the tumor microenvironment and promotes tumor growth by limiting anti-tumor immunity via the adenosine receptor pathway.^{1,2}



CD73 and Immune Function

- CD73 converts extracellular adenosine monophosphate (AMP) into immunosuppressive adenosine, which shuts down anti-tumor immune surveillance at the level of T and natural killer (NK) cells, dendritic cells (DCs), myeloid-derived suppressor cells (MDSCs) and tumor associated macrophages (TAMs).^{2,3}



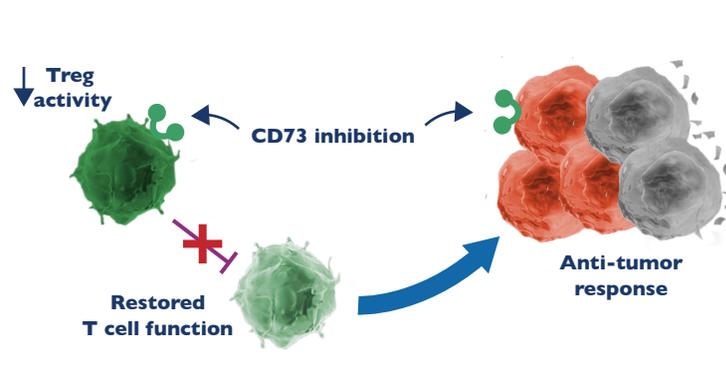
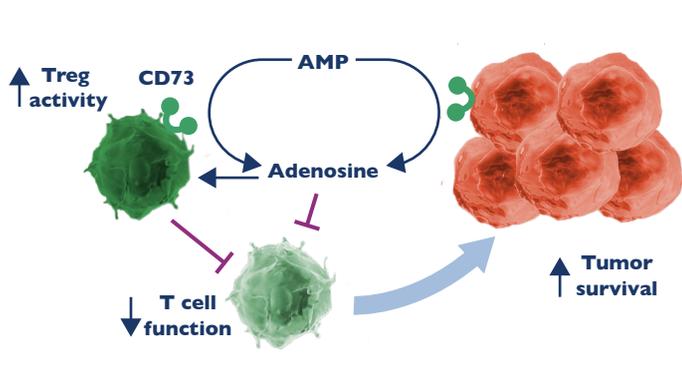
CD73 and Cancer

- In cancer, upregulation of CD73 expression in tumor cells and cells in the tumor stroma results in an increase in adenosine production,^{2,3} which:
 - Inhibits T cell and NK cell cytotoxicity, cytokine production and proliferation as well as suppression of antigen-presenting cells (APCs).
 - Promotes regulatory T cell (Treg) proliferation and suppressive activity.
 - Stimulates MDSCs and macrophage M2 polarization.
- These changes enable tumor growth and disease progression.



Research Implications and Interactions

- Preclinical research has identified CD73 as a contributor to immune escape in cancer, therefore, inhibition of CD73 activity may enhance anti-tumor immune surveillance at the level of T cells and other immune cells regulated by adenosine.⁴
- Targeting the CD73 pathway, in combination with other potentially complementary immune pathways, may be a key strategy to help activate an anti-tumor immune response.



The CD73 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://www.bms.com/life-and-science/science/immuno-oncology-pathway.html>

¹ Kobie JJ, Shah PR, Yang L, Rebhahn JA, Fowell DJ, Mosmann TR. T regulatory and primed uncommitted CD4⁺ T cells express CD73, which suppresses effector CD4⁺ T cells by converting 5'-adenosine monophosphate to adenosine. *J Immunol.* 2006;177(10):6780-6786. ² Antonioli L, Yegutkin GG, Pacher P, Blandizzi C, Hasko G. Anti-CD73 in cancer immunotherapy: awakening new opportunities. *Trends Cancer.* 2016;2(2):95-109. ³ Whiteside TL. Targeting adenosine in cancer immunotherapy: a review of recent progress. *Expert Rev Anticancer Ther.* 2017;17(6):527-535. ⁴ Stagg J, Divisekera U, McLaughlin N, et al. Anti-CD73 antibody therapy inhibits breast tumor growth and metastasis. *Proc Natl Acad Sci U S A.* 2010;107(4):1547-1552