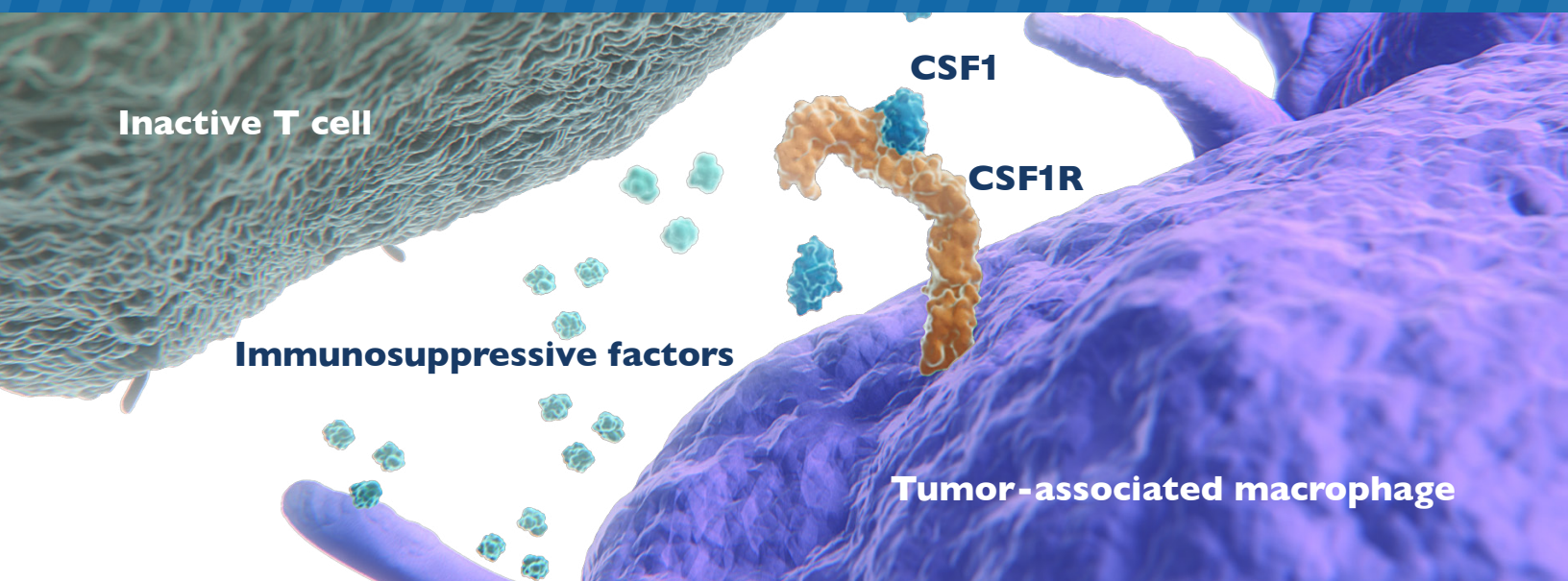


Colony-stimulating Factor 1 Receptor (CSF1R) Immune Pathway



About CSF1R

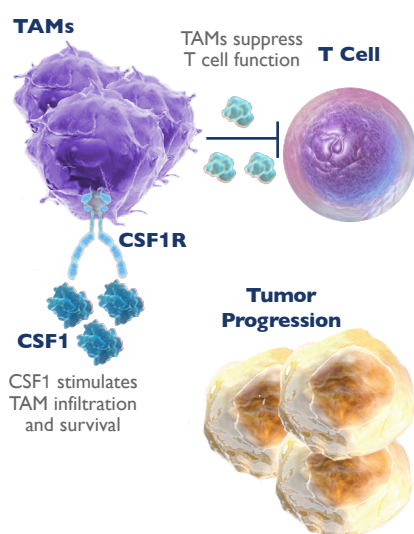
Colony-stimulating factor 1 receptor (CSF1R) is a cell-surface tyrosine kinase receptor expressed by macrophages and other cells of the myeloid lineage.¹ The CSF1R tyrosine kinase is activated when bound by its ligands, CSF1 and IL-34.²

Cancer and Macrophages

CSF1 in the tumor microenvironment promotes the infiltration and survival of immunosuppressive tumor associated macrophages (TAMs).

High levels of TAMs in tumors are associated with poor prognostic outcomes.

High levels of CSF1 in tumors stimulate more M2-like macrophages, which further support tumor progression through suppressing effector T cell functions.

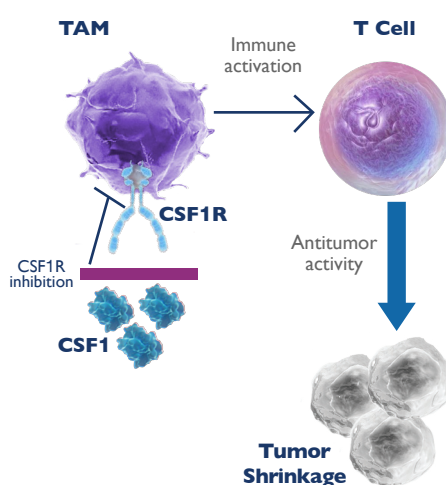


Effects of CSF1R Blockade

Preclinical research suggests that a blockade of CSF1R or inhibition of its kinase activity may reduce the tumor burden by:

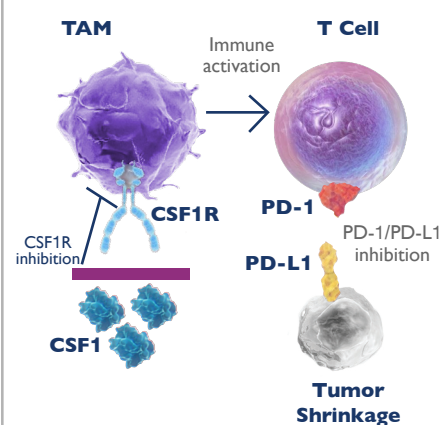
- Decreasing the number of immunosuppressive M2-like TAMs. Targeting M2-like TAMs could improve antitumor response across multiple tumor types.
- Promoting immune-stimulatory cytokines, such as IFN γ , which enhance T cell responses.

The net effect is promotion of antitumor immunologic effects.



Clinical Implications and Interactions

As a consequence of the decrease in the immunosuppressive signals mediated by M2 TAMs, some cancer cells may upregulate PD-L1. Preclinical studies suggest that targeting the CSF1R pathway in combination with other potentially complementary immune pathways may be a key strategy to more effectively activate the antitumor immune response.^{3,4}



The CSF1R 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 Stanley ER, Chitu V. CSF-1 receptor signaling in myeloid cells. Cold Spring Harb Perspect Biol. 2014;6:a021857. ² Hume, D.A., & MacDonald, K. P. (2012). Therapeutic applications of macrophage colony-stimulating factor-1 (CSF-1) and antagonists of CSF-1 receptor (CSF-1R) signaling. Blood, 119(8), 1810-1820. Accessed September 27, 2017 ³ Ries CH, Cannarile MA, Hoves S, et al. Targeting tumor-associated macrophages with anti-CSF-1R antibody reveals a strategy for cancer therapy. Cancer Cell. 2014;25:846-859. ⁴ Mitchem JB, Brennan DJ, Knolhoff BL, et al. Targeting tumor-infiltrating macrophages decreases tumor-initiating cells, relieves immunosuppression, and improves chemotherapeutic responses. Cancer Res. 2013;73:1128-1141.