CC Chemokine Receptor 8 (CCR8) Immune Pathway

**CCR8 and Its Role in Immune Response**

CC chemokine receptor 8 (CCR8) is a protein found mainly on the surface of a highly immunosuppressive subset of regulatory T cells (Tregs) within tumors. It is a regulator of immune response.1,2

As a chemokine receptor, CCR8 serves as a mediator of activity in concert with its chemokine CC chemokine ligand 1 (CCL1).3 Chemokines are signaling molecules that direct the immune response through chemotaxis, attracting and binding to their receptors and facilitating cell movement.4

Receptors like CCR8 and their chemokines play an important role in the immune system's response to cancer.

Chemokine and chemokine receptor expression influence the recruitment of immune cells to the tumor microenvironment (TME) where tumors use those cells and mechanisms to evade or suppress the natural anti-cancer immune response, allowing cancer to grow.1

CCR8 expression is upregulated on a highly immunosuppressive subset of Tregs in multiple cancer types.4

- CCR8 is found to be particularly upregulated on Tregs in the TME, with lower levels of CCR8+ Tregs found in the blood and normal tissues.4,5
- Tregs act via many mechanisms within the TME, including suppression of antigen-presenting cell (APC) function, consumption of interleukin 2 (IL-2) and production of immunosuppressive cytokines and metabolites.2,6
- High Treg infiltration in the TME is correlated with poor prognosis in multiple cancer types.1,2,4

**CC8R and Its Role in Cancer**


Preclinical data suggested that CCR8 antibody–mediated Treg depletion drove a proinflammatory response, which resulted in inhibition of tumor growth.4

- Researchers are using non-fucosylated anti-CCR8 antibodies that have increased antibody-dependent cellular cytotoxicity (ADCC) activity and are therefore good depleters of CCR8-expressing Tregs.
- This approach is being explored as a monotherapy as well as in combination with immune checkpoint blockade.

Bristol Myers Squibb has launched a first-in-human study of this approach, investigating antibody-mediated Treg depletion targeting CCR8 as an immunotherapeutic mechanism.

Targeting CCR8 has the potential to be more specific in anti-tumor activity than other current approaches to Treg depletion.1,3

- Other Treg target molecules are also found on Tregs peripherally (in the blood), in normal tissue and on effector T cells.
- As such, a highly selective target is needed that allows for the specific depletion of tumor-infiltrating Tregs without affecting Tregs in the blood and normal tissues or destroying effector T cells.

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Bristol Myers Squibb is dedicated to the continued pursuit of innovation in cancer therapy as an integral part of our vision of transforming patients’ lives through science.