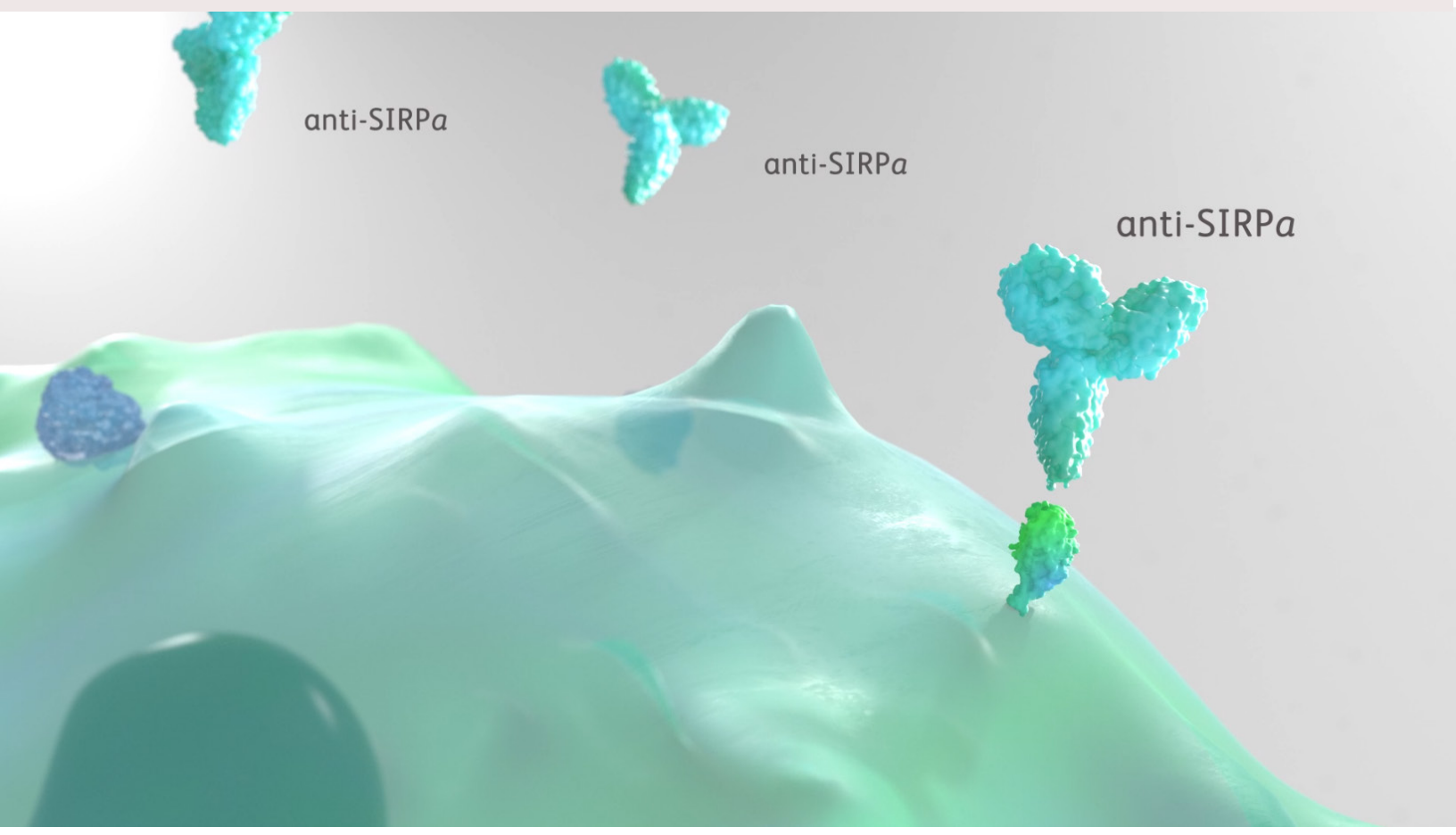
Bristol Myers Squibb™

Signal regulatory protein α (SIRPα)

SIRPα and its Role in the Immune Response



Signal regulatory protein α, or SIRPα, is a **receptor selectively expressed on macrophages**.[1]

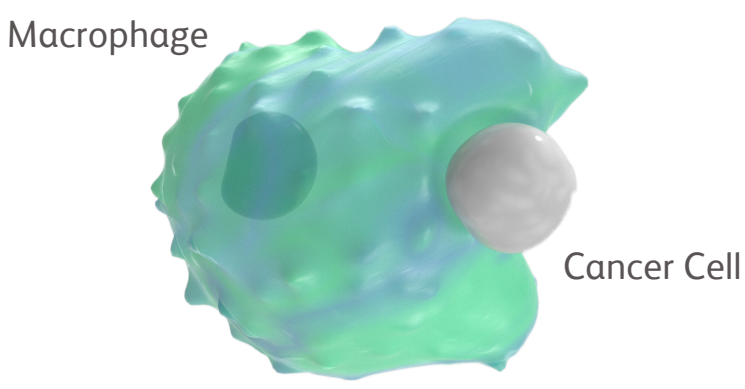
Macrophages are effector cells of the innate immune system that play an important role in cancer immunosurveillance. Macrophages can recognize, engulf and degrade cancer cells through a process called phagocytosis.

CD47, a protein found on the surface of most normal cells, binds SIRPα. This binding initiates an inhibitory signaling pathway that tells macrophages not to attack these cells, also referred to as a "don't eat me" signal.[1]

The CD47/SIRPα Axis and Cancer

Cancer cells can **overexpress CD47** on their surfaces, allowing the cancer cells to escape detection by the immune system and limiting the body's anticancer immune response.[2]

One key way a macrophage recognizes a cancer cell is through the presence of an "eat me" signal on the cancer cell. This signal is separate from the CD47/SIRPα axis and is important because it helps macrophages distinguish which cells to destroy.[2,3]



Blocking SIRPα

The CD47/ SIRPα axis is a promising new target for cancer immunotherapy and researchers are exploring strategies to disrupt it.

- The effect of disrupting the CD47/SIRPα axis in cancer has been clinically validated with an anti-CD47 monoclonal antibody **in combination with an "eat me" signal partner**.[4]

Another approach is to block the SIRPα receptor on macrophages using a monoclonal antibody so that SIRPα cannot bind to CD47.

Blocking SIRPα to inhibit the CD47/SIRPα axis may offer a promising approach for drug development due to how and on which cells SIRPα is expressed versus CD47.

- CD47 is expressed on all cells and upregulated on cancer cells
- SIRPα, however, is mainly restricted to myeloid cells, such as macrophages

By blocking cancer cell-expressed CD47 from binding to SIRPα on the surface of macrophages, researchers aim to **improve and enhance macrophage recognition and phagocytosis of cancer cells** triggered by opsonic therapeutic antibodies (antibodies marking the cell for destruction) and other "eat me" signals.

Bristol Myers Squibb aims to design novel therapeutics by identifying new ways to disrupt immune suppression and promote cancer cell death.

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2. Zhang W, Huang Q, Xiao W, et al. Advances in Anti-Tumor Treatments Targeting the CD47/SIRPα Axis. *Front Immunol.* 2020;11. doi:10.3389/fimmu.2020.00018
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4. Sallman D. The First-in-Class Anti-CD47 Antibody Magrolimab Combined with Azacitidine Is Well-Tolerated and Effective in AML Patients: Phase 1b Results. In: ASH; 2020. Accessed March 30, 2021. https://ash.confex.com/ash/2020/webprogram/Paper134728.html