

[Open Peer Review on Qeios](#)

Anti-SIRPa Monoclonal Antibody CC-95251

National Cancer Institute

Source

National Cancer Institute. *Anti-SIRPa Monoclonal Antibody CC-95251*. NCI Thesaurus. Code C157501.

A monoclonal antibody targeting signal-regulatory protein alpha (SIRPa; CD172a) with potential immunostimulating and antineoplastic activities. Upon intravenous administration, anti-SIRPa monoclonal antibody CC-95251 targets and binds to SIRPa, a cell surface protein expressed on macrophages, thereby blocking the interaction between SIRPa and cluster of differentiation 47 (CD47) expressed on tumor cells. This prevents CD47/SIRPa-mediated signaling and abrogates the CD47/SIRPa-mediated inhibition of phagocytosis. This induces pro-phagocytic signaling mediated by the binding of calreticulin (CRT), which is specifically expressed on the surface of tumor cells, to low-density lipoprotein (LDL) receptor-related protein (LRP), expressed on macrophages. This results in macrophage activation and the specific phagocytosis of tumor cells. In addition, blocking CD47/SIRPa-mediated signaling activates both an anti-tumor T-lymphocyte immune response and T cell-mediated killing of CD47-expressing tumor cells. SIRPa, also known as tyrosine-protein phosphatase non-receptor type substrate 1, mediates negative regulation of phagocytosis, mast cell activation and dendritic cell activation. CD47, also called integrin-associated protein (IAP), is a tumor-associated antigen (TAA) expressed on normal, healthy hematopoietic stem cells (HSCs) and overexpressed on the surface of a variety of cancer cells. Expression of CD47, and its interaction with SIRPa, leads to the inhibition of macrophage activation and protects cancer cells from phagocytosis, which allows cancer cells to proliferate.