CD47

CD47 also known as integrin associated protein is a transmembrane protein that in humans is encoded by the CD47 gene. CD47 belongs to the immunoglobulin superfamily and partners with membrane integrins and also binds the ligands thrombospondin-1 and signal-regulatory protein alpha.

CD47-SIRPα interaction refers to the binding of the protein CD47 on the surface of a cell to the receptor protein SIRPα on the surface of another cell. This interaction is a critical “don't eat me” signal that allows healthy cells to evade phagocytosis (engulfment) by the immune system. CD47 is expressed on a variety of cells, including red blood cells, platelets, and cancer cells, while SIRPα is primarily expressed on macrophages and dendritic cells, which are immune cells that engulf and eliminate foreign or damaged cells.

The interaction between CD47 and SIRPα triggers a signaling cascade that inhibits phagocytosis. Specifically, the binding of CD47 to SIRPα results in the activation of a tyrosine phosphatase called SHP-1, which then inhibits downstream signaling pathways that would otherwise lead to phagocytosis. This allows healthy cells to avoid being mistakenly targeted and eliminated by the immune system.

However, this interaction can also be exploited by cancer cells, which often overexpress CD47 to evade detection and elimination by the immune system. Researchers are currently exploring therapeutic strategies that target the CD47-SIRPα interaction to enhance the immune system's ability to recognize and eliminate cancer cells.

Results show that blocking CD47-SIRPα in a PV mouse model due to either anti-CD47 treatment or loss of the inhibitory SIRPα-signal corrects the polycythemia phenotype. Anti-CD47 treatment marginally impacted PV RBC production while not influencing erythroid maturation. However, upon anti-CD47 treatment, high-parametric single-cell cytometry identified an increase of MerTK+ splenic monocyte-derived effector cells, which differentiate from Ly6Chi monocytes during inflammatory conditions, acquire an inflammatory phagocytic state. Furthermore, in vitro, functional assays showed that splenic JAK2 mutant macrophages were more “pro-phagocytic,” suggesting that PV RBCs exploit the CD47-SIRPα interaction to escape innate immune attacks by clonal JAK2 mutant macrophages [1)].

CD47 is overexpressed in multiple tumours and plays an important role in immune escape and other biological processes of tumours. However, its role in adamantinomatous craniopharyngioma (ACP) remains unclear. Therefore, Zhang et al. from the Department of Neurosurgery, Nanfang Hospital, Southern Medical University, Guangzhou, China explored the functions of CD47 in ACP.

In this study, the expression of CD47 and the infiltration of immune cells in ACP was determined by immunohistochemistry (IHC) or immunofluorescence. Microglia-mediated phagocytosis was analysed using an in vitro phagocytosis assay. Using lentivirus transfection, CD47 was either silenced or overexpressed in primary ACP cells and the biological effects of CD47 on these cells were evaluated in vitro using cell viability, flow cytometry, wound healing, Transwell migration, and 3D hydrogel assays. The protein expression levels were analysed by western blotting.

Finger-like protrusions, which may be the key factor in the recurrence of ACP, were primarily found in the region of hypothalamic involvement. The expression of CD47 was higher in palisading epithelium compared to stellate reticulum and epithelial whorls. An in vitro phagocytosis assay showed that CD47 blockade could promote microglia-mediated phagocytosis. Functional assays revealed that CD47 promoted the growth, migration and invasion of ACP cells in vitro. Our mechanistic investigations showed that CD47 activated the MAPK/ERK pathway, thereby facilitating the biological behaviour of ACP cells.

Zhang et al. demonstrated that CD47 plays an important role in adamantinomatous craniopharyngioma cells, suggesting that CD47 could be a new potential therapeutic target for adamantinomatous craniopharyngioma treatment, and adding to the body of literature a role for the inhibition of MAPK/ERK in ACP [2)]

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