

Optogenetic Fc Receptor for Precise Control Over Macrophage Anti-Cancer Response

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BACKGROUND

Macrophages are critical components of immune responses that eliminate bacteria and other harmful cells in human tissue, including cancer cells. An appropriately activated macrophage can initiate phagocytosis of cancer cells and kill cytotoxic tumors. Macrophage-based cancer therapies are a promising treatment for killing solid tumors, but they are still limited by needing to know tumor-specific antigens, ligand binding requirements, a low number of cancer cells killed per macrophage, and poor control over macrophage activation. The field requires a more controlled technique of activating macrophages to promote increased phagocytosis of cancer cells.

DESCRIPTION

Researchers at the University of California, Santa Barbara have leveraged optogenetics to activate highly phagocytic macrophages without requiring a native ligand to activate the signaling pathway. Due to its reversibility, this technique allows for precise temporal control over activation and deactivation. The key feature of this invention is the Optogenetic Fc Receptor (optoFcR) which consists of a plasma membrane localization sequence followed by the functional domain of the Fc receptor (Internal Tyrosine Activating Motif or ITAM), a fluorescent marker, and the plant protein cryptochrome 2 (cry2). Upon blue light stimulation, cry2 undergoes a conformational change and in turn activates the native signaling pathway. This activation is reversible with removal of the blue light stimulus. Activating optoFcR with blue light makes macrophages more sensitive to future stimuli and can be used to increase macrophages' appetite for antibody opsonized cancer cells. The optogenic properties of this molecule could be used to specifically activate macrophages in a cancer site with no effect on the rest of the body, creating a highly effective and highly controlled treatment opportunity.

ADVANTAGES

- ▶ Activates highly phagocytic macrophages for combination with monoclonal antibody therapies
- ▶ Tunable activation for increased cancer cell killing with minimal toxicity
- ▶ Long-term sensitization of CAR macrophages for increased phagocytic and inflammatory ability
- ▶ Achieves activation without known antigen
- ▶ Reversible process provides precise control over activation and deactivation
- ▶ Targets specific cancer sites without affecting the rest of the body

APPLICATIONS

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OTHER INFORMATION

KEYWORDS

optogenetics, cancer,
macrophage, phagocytic,
phagocytosis, solid tumor,
activation, CAR, inflammatory,
antigen, monoclonal

CATEGORIZED AS

- ▶ **Medical**
 - ▶ [Disease: Cancer](#)
 - ▶ [Therapeutics](#)

RELATED CASES

2023-849-0

► Cancer therapies

PATENT STATUS

Patent Pending

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

► [Methods of Treating Lymphoma with a Phagocyte Having a Chimeric Antigen Receptor](#)

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