Therapeutics & Vaccines

COMPOSITIONS AND METHODS TO ENHANCE IMMUNE CHECKPOINT BLOCKADE THERAPY AGAINST HYPOXIC TUMORS

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The Invention

UW-Madison researchers have developed an improved delivery system that is able to penetrate the extracellular matrix (ECM) and shuttle surface-conjugated protein cages, composed of collagenases and anti-PD-L1 antibodies, to cancerous cells (e.g., pancreatic ductal adenocarcinoma (PDAC) tumor parenchyma). The delivery system is based on the probiotic E. coli strain Nissle 1917 (EcN), which has hypoxia tropism and excellent motility, and a protein cage comprised of linkers that degrade upon exposure to reactive oxygen species (ROS). As a result, when the EcN-protein cage enters the PDAC microenvironment, which has elevated levels of ROS, the cage degrades and releases collagenases and anti-PD-L1. These collagenases destroy oncogenic collagen and block the integrin α3β1-FAK signaling pathway, thereby overcoming immunosuppression and reducing the proliferation of tumor cells. Finally, the anti-PD-L1 antibodies are then able to activate infiltrating T cells for enhanced PDAC immunotherapy. While initial results have focused on PDAC, ongoing work has demonstrated utility against breast cancer, showing the potential for this novel platform.

Publications

- Read a news story about this technology.

Tech Fields

- Therapeutics & Vaccines : Oncology

For current licensing status, please contact Rafael Diaz at rdiaz@warf.org or 608-960-9847