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DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government Owned Invention Available for License: MC38 B2m KO Cell Line

AGENCY: National Institutes of Health, HHS.

ACTION: Notice.

SUMMARY: The National Cancer Institute (NCI) seeks licensees for a CRISPR/Cas9-engineered MC38 B2m knockout murine colon cancer cell line that models tumor resistance to PD-1/PD-L1 checkpoint blockade caused by loss of MHC-I antigen presentation. This research tool provides an opportunity to study checkpoint-refractory tumors and evaluate alternative or combination immunotherapy strategies for cancers that evade conventional T-cell–mediated recognition.

FOR FURTHER INFORMATION CONTACT: Inquiries related to this license opportunity should be directed to: Michael Pollack, Ph.D., Unit Supervisor, NCI, Technology Transfer Center, Email: *PollackM@mail.nih.gov* or Phone: 240-276-5519.

SUPPLEMENTARY INFORMATION: Immune checkpoint blockade (ICB) is a type of cancer immunotherapy targeting proteins such as programmed cell death protein 1 (PD-1) and programmed death-ligand 1 (PD-L1), which tumors use to reduce T-cell immune activity. These therapies can be effective in some patients. However, ICB targeting PD-1/PD-L1 fails to provide clinical benefit for most cancer patients due to primary resistance. In such cases, tumors either do not respond from the outset or acquire resistance after initially responding. One important cause of resistance is defective antigen presentation, the process by which tumor cells display internal protein fragments on their surface using major histocompatibility complex class I (MHC-I) molecules for cancer-killing T cell recognition. Researchers at the NCI have developed and validated an MC38 B2m knockout murine colon cancer cell line designed to reproduce a clinically relevant form of immunotherapy resistance. Using CRISPR/Cas9, NCI researchers eliminated B2m, a gene required for tumor cells to display MHC-I antigen-presenting molecules to cancer-killing T cells. The resulting MC38 B2m KO cell line produces tumors that lack this key immune-recognition signal and are resistant to anti-PD-1 and anti-PD-L1 therapy in syngeneic mouse

models. This gives researchers a defined, practical preclinical model to: (1) study tumor immune escape and (2) evaluate new immunotherapy strategies in a checkpoint-resistant setting. This is a superior approach versus models only in tumors that remain responsive to checkpoint blockade. This model uses a clinically relevant checkpoint-resistance mechanism by deleting B2m, which causes loss of MHC-I antigen presentation and prevents conventional CD8+ T-cell recognition. It is based upon the MC38 colon cancer model, which has significant response to PD-1/PD-L1 immune checkpoint blockade before B2m knockout. MC38 B2m KO tumors show abrogated response to anti-PD-1 and anti-PD-L1 treatment *in vivo*, while wild-type MC38 tumors showed significant tumor growth reduction under the same treatment framework.

The Center for Immuno-Oncology seeks licensees interested in using this cell line as a research tool for immuno-oncology studies. This model may be useful for evaluating alternative or combination immunotherapy strategies for checkpoint-refractory tumors, including cancers that evade conventional T-cell-mediated recognition due to defective antigen presentation. It facilitates mechanistic studies of tumor immune escape, CD8+ T-cell recognition, and tumor microenvironment remodeling.

"This Notice is in accordance with 37 C.F.R. § 404.4 Authority to grant licenses."

NIH Reference Number: E-123-2026-0.

Related Technologies: N/A.

Product Type: Research Tool.

Therapeutic Area(s): Oncology.

Development Stage: N/A.

Publications:

- Chariou, PL, et al. Generation of murine tumor models refractory to αPD-1/-L1 therapies due to defects in antigen processing/presentation or IFNγ signaling using CRISPR/Cas9 (PMID: 38427670)

Patens: N/A.

Potential Commercial Applications:

- Development of cancer therapeutics overcoming of PD-1/PD-L1 checkpoint blockade resistance.
- Development of alternative or combination immunotherapies for checkpoint-refractory tumors.

- Pre-clinical screening of alternative or combination immunotherapies for checkpoint-refractory tumors.
- Evaluation of cancer therapeutic strategies for cancers with defective antigen processing/presentation or loss of MHC-I expression.
- Companion model for comparing checkpoint-resistant MC38 B2m KO tumors against checkpoint-responsive wild-type MC38 tumors.

Competitive Advantages:

- Uniquely models a clinically relevant checkpoint-resistance mechanism.
- Uses the MC38 colon cancer model, which is well-established and regulatorily de-risked.
- Unique model permitting the interrogation of abrogated response to anti-PD-1 and anti-PD-1 treatment.

Collaboration Opportunity: Licensing.

Dated: August 7, 2026.

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