

TARGET FOR ANTI-TUMOR IMMUNE RESPONSES

REFERENCE NUMBER

E-070-2010

PRODUCT TYPE

- Research Materials

KEYWORDS

- Cancer
- cell line
- melanoma
- 888-mel

COLLABORATION OPPORTUNITY

This invention is available for licensing.

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DESCRIPTION OF TECHNOLOGY

The Surgery Branch of the National Cancer Institute is seeking statements of capability or interest from parties interested in collaborative research to carry out genotypic as well as phenotypic analysis of the 888 mel cell line in order to better understand the nature of tumor cells that respond to therapy. In addition, this cell line can be used as a target of humoral or cell mediated immune responses as a part of studies characterizing the nature of immune responses directed against tumor cells.

A human melanoma cell line designated 888-mel has been developed from the resected tumor of a 26-year old Caucasian female (patient 888) diagnosed with metastatic melanoma, a frequently terminal cancer. The 888-mel cell line was derived from three separate subcutaneous melanoma lesions on the patient and possesses many characteristics representative of melanoma cell lines developed by these researchers. Most prominently, the 888-mel cell line was used to develop a tumor infiltrating lymphocyte (TIL) culture with high affinity for the tumor cells of patient 888. When the TIL 888 culture was provided as an autologous adoptive immunotherapy treatment to patient 888 in combination with interleukin-2 (IL-2), a complete remission of subcutaneous, lung, and mucosal metastases was observed in the patient for over three years.

Since this medical breakthrough, the 888-mel cell line has been well characterized through various laboratory procedures and data involving this cell line has been published as part of numerous articles. Studies have shown that the cell line expresses a variety of tumor associated antigens (TAAs), including tyrosinase, TRP1, TRP2, gp100, MART-1, p15, gp75, mutated beta-catenin, and p53. However, 888-mel does not normally express the MAGE 1, 2, or 3 TAAs. Many melanoma cell lines are HLA-A2 restricted, but the 888-mel cell line is HLA-A2 negative. The HLA class I typing for this cell line is as follows: HLA-A0101, A2402, B55, B62, Cw5201, Cw55, DRb1*1502, DRb1*1610, DQb1*0601, DRb5*0102, DRb50*203. 888-mel is a validated source of HLA class I peptides utilized in screens that test the reactivity of TIL cultures that are candidates for adoptive immunotherapy trials. 888-mel is also a standard cell line for studying immune responses in cancer, particularly T cell responses. Other experiments show that roscovitine, a cyclin-dependent kinase inhibitor, can induce apoptosis in the 888-mel cell line, so these cells may be useful in various cell death studies.

POTENTIAL COMMERCIAL APPLICATIONS

- Research tool for investigating the key immune responses required to mediate the remission of metastatic melanoma in order to identify the immune cell types necessary to produce an effective immunotherapy
- Research tool for investigating the tumor associated antigens that contribute to the dampening of the immune response in many melanoma tumors so that researchers can better understand how to boost immunogenicity against these antigens
- Source material for tumor associated peptides that could serve as melanoma vaccine candidates or utilized to determine the reactivity of tumor infiltrating lymphocyte (TIL) cultures being considered for clinical trials
- Source material for the development of TIL cultures for use in adoptive immunotherapy protocols to treat melanoma patients

COMPETITIVE ADVANTAGES

- Cell line is derived from a melanoma patient that underwent complete tumor remission: Immune cell cultures capable of treating melanoma patients in adoptive immunotherapy protocols could be derived from the tumor associated antigen epitopes found on the 888-mel cell line. This cell line may be a source of novel antigenic peptides capable of triggering immune responses in melanoma patients that lead to tumor regression or stabilization. 888-mel cells have been shown to retain many features of primary melanoma samples, including the expression of common tumor associated antigens.
- 888-mel is an HLA-A2 negative cell line: A majority of the cancer vaccines and immunotherapies developed to date have focused on utilizing HLA-A2 restricted tumor epitopes since this HLA allele is largely expressed in the human population. However, therapies restricted to HLA-A2 recognition will not be successful in melanoma patients that do not express this allele. For these patients, additional therapies are needed that are directed against melanoma tumor epitopes presented by different HLA alleles.

- The 888-mel cell line has been well characterized through multiple years of study and is a fundamental cell line for melanoma studies: The collection of tumor associated antigens expressed by this cell line have been determined through multiple studies, many of which were performed by researchers in the inventors's laboratory. A significant amount of data has also been compiled detailing the immune responses triggered by 888-mel cells.

PUBLICATIONS

1. J Weber et al. Expression of the MAGE-1 tumor antigen is up-regulated by the demethylating agent 5-aza-2''-deoxycytidine. *Cancer Res.* 1994 Apr 1;54(7):1766-1771. [PubMed: 7511051]
2. PF Robbins et al. Recognition of tyrosinase by tumor-infiltrating lymphocytes from a patient responding to immunotherapy. *Cancer Res.* 1994 Jun 15;54(12):3124-3126. Erratum in: *Cancer Res.* 1994 Jul 15;54(14):3952. [PubMed: 8205528]
3. PF Robbins et al. Multiple HLA class II-restricted melanocyte differentiation antigens are recognized by tumor-infiltrating lymphocytes from a patient with melanoma. *J Immunol.* 2002 Nov 15;169(10):6036-6047. [PubMed: 12421991]

PATENT STATUS

- **Not Patented:** Research Tool. Patent protection is not being pursued for this technology.