Neoantigen-specific antibodies for chemically directed immune targeting of KRAS tumors

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INVENTION NOVELTY

UCSF scientists have discovered novel antibodies that can specifically and selectively recognize tumor-derived neoantigens. The antibodies can be used for IgG, BiTE or CAR-T-based targeted immunotherapy and small molecule-based directed immune targeting via combination therapy. This dual therapeutic approach has the potential to specifically recognize and treat KRAS (G12C) cancer cell populations with high specificity, significantly improve cancer treatment outcomes, and overcome risk of treatment resistance in patients.

VALUE PROPOSITION

In the invention described here, researchers utilized a human naïve phage-displayed Fab library to identify and characterize novel antibodies that can recognize small molecule-bound neoantigens presented following KRAS tumor treatment with KRAS inhibitor ARS1620, a precursor of three clinical KRAS (G12C) inhibitors undergoing Phase I clinical trials (AMG510, MRTX849, JNJ-74699157. It was demonstrated that these antibodies can bind the neoantigen-small molecule complex with high specificity and affinity.

The antibodies identified have the following unique properties:

(i) High affinity to ARS1620/KRAS specific neoantigens on cancer cell surface,

(ii) No observable/quantifiable binding to healthy cell surface antigens,

(iii) Easy antibody format conversion for multiple combination immunotherapies.

TECHNOLOGY DESCRIPTION

UCSF researchers have used the Craik lab's biological panning platform with a human naïve phage-displayed Fab library to identify antibodies that specifically and selectively recognize KRas G12C+ tumor-derived neoantigens presented on tumor cells following treatment with ARS-1620 inhibitor molecules. The library has identified five unique Fabs that can recognize ARS-1620-labeled KRas G12C derived peptides with high specificity and affinity in cancer cells. Healthy cells do not display the small molecule bound neoantigens, therefore, this combination antibody and small molecule-based treatment allows specific recognition and targeting of the KRAS cancer cell population. The approach has shown efficacy to reduce proliferation in cancer cell line models. Additionally, antibodies in BiTE format have resulted in significant T-cell activation and mediated cytotoxic T-cell responses in cancer cells *ex vivo*. The

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OTHER INFORMATION

KEYWORDS

Oncogene derived neoantigens, cancer-targeting, combination therapy, antibody-mediated specific targeting

CATEGORIZED AS

- **Biotechnology**
  - Health
- **Medical**
  - Disease: Cancer
  - Therapeutics

RELATED CASES

2019-215-0

researchers are currently testing the efficacy of antibodies in preclinical animal models of KRas (G12C) cancer and also engineering the antibody to bind to related inhibitors.

APPLICATION

The invention will facilitate the development of the highly specific novel antibodies which have the following potential applications:

(i) Antibody-based therapeutics such as monoclonal antibody, biTE (bispecific T-cell engagers), and CAR-T for specific recognition of neoantigens on cancer cell populations,

(ii) Research-based applications in western blots, immunoprecipitation, ELISA, flow cytometry for recognition and quantification of neoantigens and peptides on cancer cell surface,

(iii) Antibody and small molecule combination therapies targeting tumor-specific intracellular oncoproteins and subsequent small molecule bound neoantigens.

LOOKING FOR PARTNERS

To develop and commercialize antibodies for developing novel combination therapeutics for cancer treatment.

STAGE OF DEVELOPMENT

Preclinical

RELATED MATERIALS

DATA AVAILABILITY

Under CDA/NDA

PATENT STATUS

Country	Type	Number	Dated	Case
Hong Kong	Published Application	40075694A.	01/27/2023	2019-215
European Patent Office	Published Application	3997131	05/28/2022	2019-215

Additional Patent Pending

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