CD33 MONOCYTES AS A BIOMARKER

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority under 35 U.S.C. § 119(e) to U.S. Provisional Application No. 62/681,560, filed Jun. 6, 2018, the content of which is hereby incorporated by reference in its entirety.

[0002] This invention was made with support under grants R01 CA202987, P01 HL136275, and U01 CA224766 awarded by the National Institutes of Health. The government has certain rights in this invention.

BACKGROUND

[0003] Lung cancer is the most common and deadly cancer type worldwide, accounting for nearly 1.8 million deaths in 2018[1]. Immune checkpoint blockade (ICB), including anti-PD-1 monoclonal antibodies (aPD-1), produces positive clinical responses in approximately 30% of advanced non-small cell lung cancer (NSCLC) patients receiving aPD-1 monotherapy[2]. Although aPD-1's primary mechanism of action is believed to be through reinvigoration of intratumoral antigen-experienced T cells[3], monocytes and their macrophage/dendritic cell (DC) progeny are key regulators of the tumor immune microenvironment (TIME)[4] and are reshaped by ICB[5,6].

[0004] Immunotherapies that broadly target monocytes/macrophages have displayed minimal success in early clinical trials, which may be due to the significant heterogeneity observed in these cell types and their ability to adopt both pro- and anti-tumor functions.

[0005] Thus, a need exists in the art to identify the cancers most suitably treated by these powerful new therapies. This disclosure satisfies this need and provides related advantages as well.

SUMMARY OF THE DISCLOSURE

[0006] This summary is provided to introduce a selection of concepts in a simplified form that are further described below in the Detailed Description. This Summary is not intended to identify key aspects or essential aspects of the claimed subject matter.

[0007] The present disclosure aims to at least identify, characterize and/or isolate a population of cells that act as a biomarker for response to immunotherapy. Via the examination of the myeloid compartment in human cancer patients, the applicants have found that CD33 can be used as a predictive biomarker of patient response to immunotherapy.

[0008] The present disclosure relates broadly to a method of determining whether a subject will respond to a treatment for a neoplasia, neoplastic disorder, tumor, cancer or malignancy, the method comprising detecting the amount of CD33 in a biological sample from the subject, comparing the measured amount to a reference amount, wherein an increased measured amount compared to the reference amount is indicative that the subject will respond to the treatment for a neoplasia, neoplastic disorder, tumor, cancer or malignancy.

[0009] In certain aspects of the present disclosure, a method for determining whether a subject will respond to a treatment for a neoplasia, neoplastic disorder, tumor, cancer or malignancy is provided, the method comprising detecting the amount of CD33 in a biological sample from the subject, comparing the measured amount to a reference amount, wherein a decrease in the measured amount compared to the reference amount is indicative that the subject will not respond to the treatment for a neoplasia, neoplastic disorder, tumor, cancer or malignancy

[0010] In certain alternative aspects of the present disclosure, a method for determining whether a subject will respond to a treatment for a neoplasia, neoplastic disorder, tumor, cancer or malignancy is provided, the method comprising measuring the amount of CD33 in a biological sample from the subject, wherein a high amount of CD33 indicates that the subject will respond to a treatment for a neoplasia, neoplastic disorder, tumor, cancer or malignancy and a low amount of CD33 indicates that the subject will not respond to the treatment for a neoplasia, neoplastic disorder, tumor, cancer or malignancy.

[0011] In certain aspects of the present disclosure, a method for determining whether a subject will respond to a treatment for a neoplasia, neoplastic disorder, tumor, cancer or malignancy is provided, the method comprising detecting the amount of cells with high expression of CD33 in a biological sample from the subject, comparing the measured amount to a reference amount, wherein an increased measured amount compared to the reference amount is indicative that the subject will respond to the treatment for a neoplasia, neoplastic disorder, tumor, cancer or malignancy.

[0012] In other aspects of the present disclosure, a method for determining whether a subject will respond to a treatment for a neoplasia, neoplastic disorder, tumor, cancer or malignancy is provided, the method comprising measuring the presence or amount of cells with high expression of CD33 in a biological sample from the subject, wherein the presence or a high amount of cells with high expression of CD33 indicates that the subject will respond to the treatment for a neoplasia, neoplastic disorder, tumor, cancer or malignancy.

[0013] In alternative aspects of the present disclosure, a method of determining whether a subject will respond to a treatment for a neoplasia, neoplastic disorder, tumor, cancer or malignancy is provided, the method comprising detecting the amount of cells with low expression of CD33 in a biological sample from the subject, comparing the measured amount to a reference amount, wherein a decreased measured amount compared to the reference amount is indicative that the subject will not respond to the treatment for a neoplasia, neoplastic disorder, tumor, cancer or malignancy.

[0014] In certain aspects of the present disclosure, a method of determining whether a subject will respond to a treatment for a neoplasia, neoplastic disorder, tumor, cancer or malignancy is provided, the method comprising measuring the presence or amount of cells with low expression of CD33 in a biological sample from the subject, wherein the presence or a high amount of cells with low expression of CD33 indicates that the subject will not respond to the treatment for a neoplasia, neoplastic disorder, tumor, cancer or malignancy.

[0015] In certain other aspects of the present disclosure, the method comprises detecting or measuring the amount of $CD33^{hi}$ myeloid cells in the biological sample. In alternative aspects of the present disclosure, the method comprises detecting CD33 monocytes or $CD33^{hi}$ macrophages in the biological sample.