Novel Single-Agent Immunotherapies

840 A THERAPEUTIC HUMANIZED ANTI-CARCINOMA MONOCLONAL ANTIBODY (MAB) CAN ALSO IDENTIFY IMMUNOSUPPRESSIVE REGULATORY T (TREGS) CELLS AND DOWN REGULATE TREG-MEDIATED IMMUNOSUPPRESSION

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Background NEO-201 is an IgG1 mAb reactive against many different human carcinomas expressing the NEO-201 antigen, but not against most normal epithelial tissues. NEO-201 can mediate antitumor activity against tumor cells through multiple mechanisms such as antibody-dependent cellular cytotoxicity (ADCC), complement dependent cytotoxicity (CDC), and blockade of the CEACAM5/CEACAM1 immune checkpoint inhibitory pathway. In addition to solid tumors, the NEO-201 target has also been found on human hematopoietic cells. Flow cytometry analysis has demonstrated that 98.9% of CD15+ granulocytes and about 4.6% of CD4+ T cells were positive for NEO-201 staining. No binding was observed with NEO-201 with respect to B cells, NK cells, monocytes, or CD8+ T cells and a majority of CD4+ T cells. This study was designed to characterize the subset of NEO-201+ binding CD4+ T cells and to evaluate the reactivity of NEO-201 to this subset of hematopoietic cells.

Methods Phenotypic analysis of PBMCs from healthy donors and cancer patients were performed by flow cytometry. Reagents used for flow cytometry were antibodies against human CD4, CD127, CD25, CD15s, FOXP3, CD39, CD73 and anti-NEO-201 mAb. Functional assays were performed using a flow cytometry based on CDC assay. Treg cells, isolated from 3 healthy donors using the EasySep™ Human CD4+CD127lowCD25+ Regulatory T (Treg) Cell Isolation Kit were used as target cells.

Results Flow cytometry analysis revealed that NEO-201+CD4+ T cells were also CD25+/CD127-/FOXP3+/CD15s+ in human PBMCs from both healthy donors and cancer patients. NEO-201 also binds to CD4+/CD25+/CD127-/Foxp3+/CD15s+ cells in Treg cells isolated from human PBMCs using a commercial isolation kit. NEO-201+CD4+ T cells were also CD25+/CD127-/FOXP3+/CD39+. In addition, NEO-201 mAb can kill these isolated Treg cells through CDC.

Conclusions This study demonstrated that the small subset of NEO-201+CD4+ T cell in human PBMCs are highly suppressive Treg cells and NEO-201 can be used as a novel marker to identify functionally suppressive Treg cells, Furthermore, NEO-201 can kill Treg cells through CDC, presenting an opportunity for therapeutic intervention to increase anti-tumor immunity.

Ethics Approval The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Institutional Review Board of National Institutes of Health (NIH). All subjects gave their informed consent for inclusion before they participated in the study.PBMCs from healthy volunteer donors were utilized under the appropriate Institutional Review Board approval (protocol code NCT00001846, first approved Nov 4, 1999; latest update 11/10/2020).PBMCs from cancer patients were utilized under the appropriate Institutional Review Board approval (protocol code NCT03476681, first approved 03/26/2018; latest update 01/08/2020).

Consent Informed consent was obtained from all subjects involved in the study.

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