SITC 2019 – Friday November 8, 2019

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Abstract: P771

An anti-carcinoma monoclonal antibody (mAb) NEO-201 can also target and eliminate human immunosuppressive regulatory T cells (Tregs)

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Journal for ImmunoTherapy of Cancer 2019, 7(Suppl 1):P771

Background

NEO-201 is an IgG1 mAb reactive against many different carcinomas, but not reactive against most normal tissues. Functional analysis revealed that NEO-201 is capable of engaging innate immune effector mechanism (ADCC, CDC and enhancing NK activity) to kill tumor cells. Previous studies showed that NEO-201 attenuates growth of human tumor xenografts in mice, and demonstrates safety/tolerability in non-human primates with a transient decrease in neutrophils being the only adverse effect observed. A clinical trial evaluating NEO-201 in adults with chemo–resistant solid tumors is ongoing at the NIH Clinical Center. Preclinical evaluation showed that NEO-201 reacts against human regulatory T cells (Tregs) and here we further investigated the phenotypic and functional effects of NEO-201 on human Tregs in vitro.

Methods

PBMCs were collected from 5 normal donors and used for phenotypic and functional analysis. EasySep StemCell Treg isolation kits anti-biotin kits (biotin-labeled NEO-201 mAb) were used to isolate Tregs from PBMCs. Phenotypic analysis was conducted by flow cytometry for markers: CD4, CD25, CD127, FoxP3, CD15s, CD45RA, CCR4, NEO-201 antigen, CEACAM5 and CEACAM6. The ability of NEO-201-isolated Tregs to suppress autologous CD4+ T responder cell proliferation was assessed using a co-culture suppression assay and the ability of NEO-201 to mediate killing of opsonized Tregs was evaluated using a CDC assay.

Results

The % of NEO-201+ cells in the population of CD4+CD25highCD127-negFoxP3+CD15s+CCR4+Tregs ranged from 60%-80%. NEO-201+Tregs were CD45RA negative. Isolated CD4+NEO-201+ Tregs were capable of suppressing CD4+ T responder cell proliferation, and NEO-201 mAb mediated CDC activity against Tregs.

Conclusions

NEO-201 reacts against human Tregs and can be used as a novel marker to identify and to purify Tregs. Tregs isolated using NEO-201 mAb were functionally suppressive and could be eliminated by CDC. This study demonstrates for the first time that this tumor-targeting mAb may also mediate through a novel mechanism down regulating Treg-mediated immunosuppression of anticancer immunity.