1449 NCG-M IS A TRIPLE IMMUNODEFICIENT MOUSE WITH INCREASED RECONSTITUTION OF HUMAN MYELOID CELL POPULATIONS FOR USE IN IMMUNOTHERAPY PRECLINICAL RESEARCH

[1]Steven Bronson*, [2]Jenny Rowe, [3]Christoph Eberle, [3]Robert Mihalek, [3]Ann Fiore, [2]Stephen Festin. [1]*Charles River Laboratories, Inc., Manhattan, KS, USA*; [2]*Charles River Laboratories, Inc., Wilmington, MA, USA*; [3]*Charles River Laboratories, Inc., Worcester, MA, USA*

Background Immune humanized mice are immunodeficient mice that have been engrafted with human hematopoietic stem cells or peripheral blood mononuclear cells. These research models offer a unique tool that has been used extensively to study the effects of immunotherapies. One of the current limitations of this model occurs because of differences between human and mouse cytokines. These differences affect the development of human immune system including limiting the development of the myeloid cell populations. Myeloid cells including macrophages and dendritic cells are an essential component of the immune system and are involved in anti-tumor immunity which can impact how a therapeutic affects the growth of a tumor. Next generation models including the NCG-M are being developed to further enhance humanized mouse models and the development of the human immune system.

Methods NCG-M were genetically modified from the NCG mouse strain (NOD-*Prkdc*^{em26Cd52}*Il2rg*^{em26Cd22}/NjuCrl) to produce human granulocyte-macrophage colony stimulating factor (GM-CSF), interleukin 3 (IL-3) and stem cell factor (SCF). NCG-M mice were weighed across multiple weeks and peripheral blood was collected at multiple timepoints to examine the levels of mouse leukocytes and the expression of human factors. 5–7-week-old mice were irradiated with a sublethal dose of total body irradiation and engrafted with cord-blood derived human hematopoietic stem cells. Peripheral blood was collected from immune humanized mice to examine human cell populations.

Results NCG-M mice lacked T, B, and NK cells exhibited a similar level of immunodeficiency as the NCG mouse. These mice also had increased levels of human GM-CSF, IL-3 and SCF in the peripheral blood when compared to NCG. Humanized NCG-M had similar levels of mice had increased levels of $CD33^+$ myeloid cells compared to humanized NCG mice.

Conclusions The humanized NCG-M exhibits higher levels of myeloid lineage cells when compared to the humanized NCG. These cells are important to anti-tumor immunity making this immune humanized model ideal to assess cancer therapeutic including immunotherapies in a preclinical study.

Ethics Approval Animal procedures were reviewed and approved by CRL IACUC and performed in an AAALAC accredited facility.

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