TACONIC
Models For **Life.**

NOG-EXL Application Note

Head-to-head comparison of humanized NOG-EXL and NSG-SGM3 demonstrates NOG-EXL mice best mimic human immune cell composition and have improved survival.

Based on: Maser I-P, Hoves S, Bayer C, Heidkamp G, Nimmerjahn F, Eckmann J, and Ries CH (2020) The Tumor Milieu Promotes Functional Human Tumor-Resident Plasmacytoid Dendritic Cells in Humanized Mouse Models. *Front. Immunol.* 11:2082. https://doi.org/10.3389/fimmu.2020.02082

Maser et al. generated humanized immune system mice via busulfan preconditioning and engraftment of cord blood-derived hematopoietic stem cells in young adult female mice. The same protocol and donors were used across three mouse strains: NOG, NOG-EXL, and NSG-SGM3.

KEY TAKEAWAYS

- Humanized NSG-SGM3 mice have decreased survival compared to humanized NOG-EXL or humanized NOG mice.
- Humanized NOG-EXL mice develop a reconstituted human immune system which more closely resembles the human immune cell composition compared to humanized NSG-SGM3 or NOG mice.
- Humanized NOG-EXL mice develop all three major types of human dendritic cells, including classical CD1c$^+$ DCs (cDC2), cross-presenting CD141$^+$ DCs (cDC1), and plasmacytoid CD303$^+$ DCs (pDC).
- The human pDC cells in humanized NOG-EXL mice are present in large quantities and are functional, as shown by successful stimulation with TLR7/8 or TLR9 agonists. Thus this model may be suitable for study of immuno-oncology approaches directed at activation of pDCs without resorting to techniques such as *ex vivo* expansion.
- The composition of tumor-infiltrating immune cells is influenced more by the tumor than by choice of humanized model.

Figure 1: All strains were humanized via the same protocol and with the same HSC donors.

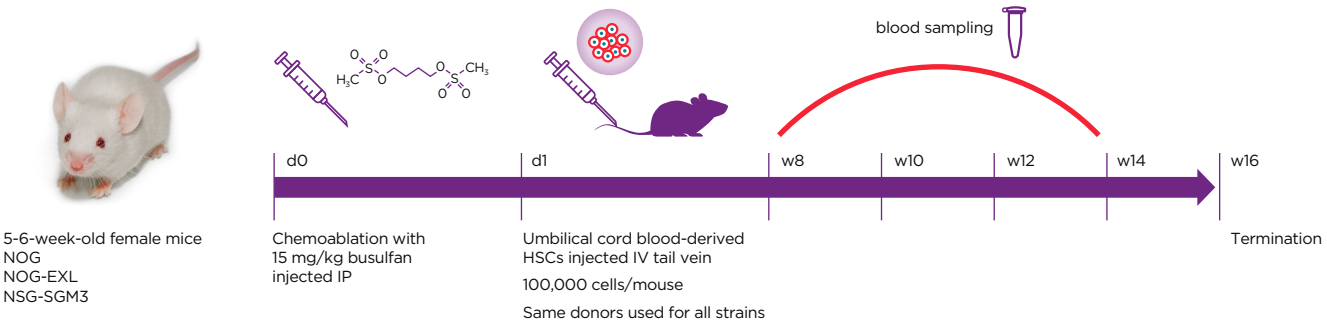
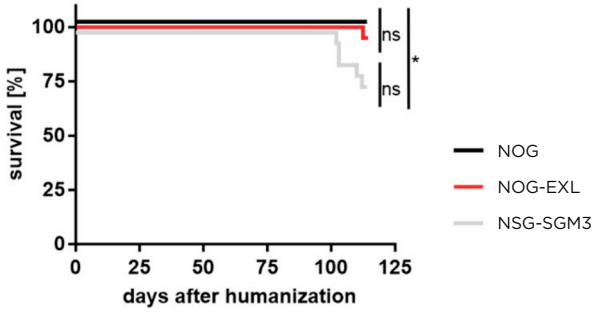


Figure 2: Humanized NOG-EXL mice exhibit improved overall survival compared to humanized NSG-SGM3 mice.



*p<0.05.

Figure 3: Following humanization, both NOG-EXL and NSG-SGM3 demonstrate significantly increased human cytokine profiles compared to NOG mice. Humanized NOG-EXL mice have a more physiological, low-inflammatory cytokine profile compared to a pro-inflammatory profile in humanized NSG-SGM3. Human cytokines and chemokines analysis by Bio-Plex in sera of humanized mice.

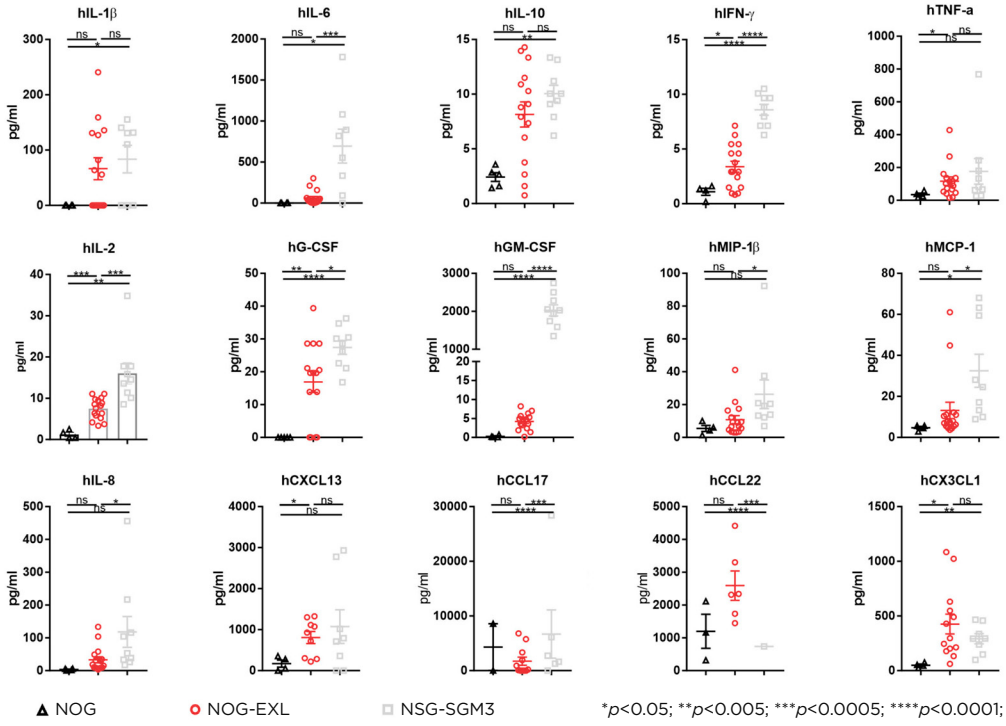
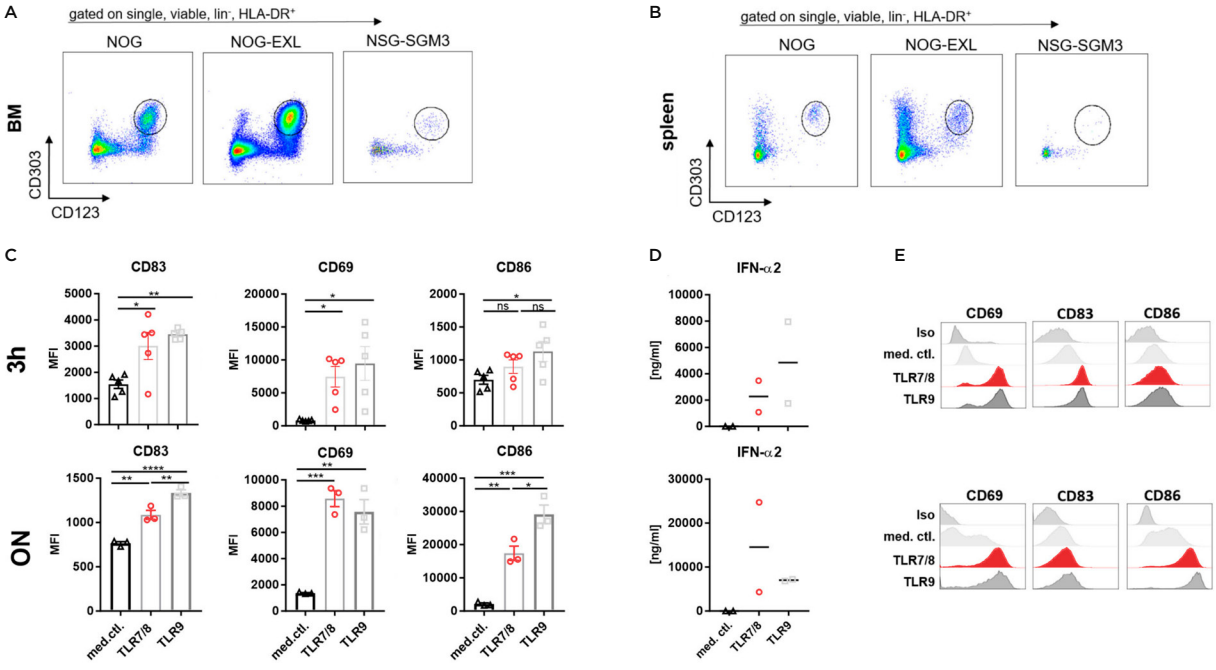


Figure 4: Humanized NOG-EXL mice develop human pDCs and these cells are functional. (A) Representative FACS plots of human pDCs (CD303⁺/CD123⁺) in bone marrow and (B) spleen. (C) Activation marker MFIs (CD83, CD69, CD86), gated on pDCs (CD123⁺/CD303⁺) enriched from pooled humanized NOG-EXL bone marrow with TLR7/8 or TLR9. (D) IFN-α2 levels in supernatant of TLR-agonist treated or non-treated pDCs enriched from pooled bone marrow from humanized NOG-EXL mice measured after 3 h or overnight (ON) stimulation. (E) Representative activation marker histograms with (TLR7/8 or TLR9) or without stimulation (media control = med. ctl.) ON.



*p<0.05; **p<0.001; ***p<0.0005; ****p<0.0001, n=3/condition.

IF YOU HAVE STRUGGLED WITH

- Finding a humanized model to study human myeloid cells with
- Understanding whether your cell type of interest is present and functional in a humanized model
- Mortality in humanized mouse studies

Request a scientific consultation to discuss selection of the most appropriate humanized model for your research.
We can help you plan your study and maximize success working with these technically complex but valuable models.