




COMPARISON OF CYTOKINE TRANSGENICS FOR IMPROVED MYELOID LINEAGE RECONSTITUTION

Several super immunodeficient models expressing cytokines designed to drive myeloid cell lineage commitment have been generated. Explore the features of each model in the comparison table below.



| MODEL |  huNOG-EXL |  Humanized NSG-SGM3 (or hu-CD34-SGM3) |  Humanized MISTRG |
|---|--|--|--|
| STRAIN | hGM-CSF/hIL3-NOG | NSG™-SGM3 | MISTRG |
| ALSO KNOWN AS | IL3/GM-Tg | NSGS | - |
| NOMENCLATURE | NOD.Cg- <i>Prkdc</i> ^{scid} <i>Il2rg</i> ^{tm1Sug} Tg(SV40/HTLV-IL3,CSF2)10-7Jic/JicTac | NOD.Cg- <i>Prkdc</i> ^{scid} <i>Il2rg</i> ^{tm1Wjl} Tg(CMV-IL3,CSF2,KITLG)1Eav/MloySzJ | C;129S4- <i>Rag2</i> ^{tm1Flv} <i>Csf1</i> ^{tm1(CSF1)Flv} <i>Csf2</i> / <i>Il3</i> ^{tm1.1(CSF2,IL3)Flv} <i>Thpo</i> ^{tm1.1(TPO)Flv} <i>Il2rg</i> ^{tm1.1Flv} Tg(SIRPA)1Flv/J |
| BACKGROUND | NOG (NOD strain background) | NSG™ (NOD strain background) | Mixed BALB/c x 129S4 |
| CYTOKINES EXPRESSED (other modifications) | Human GM-CSF (CSF2) Human IL-3 | Human GM-CSF (CSF2) Human IL-3 Human KITLG (SF) | Human GM-CSF (CSF2) Human IL-3 Human M-CSF (CSF1) Human TPO <i>Human SIRPα</i> |
| CYTOKINE LEVELS | hGM-CSF ~35 pg/ml hIL-3 ~80 pg/ml ¹ | hGM-CSF, hIL-3 and hKITLG ~2000-4000 pg/ml ⁷ | Not reported |
| PROMOTER | SV40 | CMV | All under endogenous mouse promoters except GM-CSF under human promoter. |
| INCREASE IN MYELOID CELLS OVER BASE MODEL | ~3 fold relative to NOG ¹ | ~1.5 to 5 fold relative to NSG ³⁻⁴ | ~9 fold compared to Rag2/ <i>Il2rg</i> null and ~6 fold compared to NSG ⁶ |
| LIFESPAN UNENGRAFTED | Expected normal lifespan. | Expected normal lifespan. | Not reported. |
| LIFESPAN AFTER CD34+ HSC ENGRAFTMENT | Up to 7 months reported. High chimeric ratio mice develop anemia after engraftment. ² | Up to 4 months reported. Mice develop anemia after engraftment. ⁵ | 3 weeks after engraftment reaches 10-20% chimerism in peripheral blood if pre-conditioned with irradiation (~10-12 weeks post-engraftment); lifespan may be prolonged by using less potent stem cells, lower cell numbers or avoiding pre-conditioning. ⁶ |
| OTHER COMMENTS | Stable engraftment through lifespan of mouse. | Loss of human graft after 3-4 months ⁵ . | Not available to companies or for commercial use. ⁸ |
| TERMS OF USE | Label license – no signatures or license fees required. May be used for contract or sponsored studies when purchased under for-profit terms and price. | Research institutions require an MTA, companies require a license prior to shipping. ⁷ | |
| AVAILABLE FROM | Taconic Biosciences taconic.com/hunog-exl Naive: taconic.com/13395 | The Jackson Laboratory | The Jackson Laboratory (Not available as of Mar 2016) ⁸ |

1. Ito R, Takahashi T, Katano I, Kawai K, Kamisako T, Ogura T, Ida-Tanaka M, Suemizu H, Nunomura S, Ra C, Mori A, Aiso S, Ito M. (2013) Establishment of a human allergy model using human IL-3/GM-CSF-transgenic NOG mice. *J Immuno*. 191(6):2890-9:2890-9.

2. Personal communication, Takeshi Takahashi, CIEA, and results of studies at Taconic.

3. Miller PH, Cheung AM, Beer PA, Knapp DJ, Dhillon K, Rabu G, Rostamirad S, Humphries RK, Eaves CJ. (2013) Enhanced normal short-term human myelopoiesis in mice engineered to express human-specific myeloid growth factors. *Blood*. 121(5):e1-4.

4. Billerbeck E, Barry WT, Mu K, Dorner M, Rice CM, Ploss A. (2011) Development of human CD4+FoxP3+ regulatory T cells in human stem cell factor-, granulocyte-macrophage

colony-stimulating factor-, and interleukin-3-expressing NOD-SCID IL2Rγ(null) humanized mice. *Blood*. 117(11):3076-86.

5. 5th International Workshop on Humanized Mice, workshop discussion.

6. Rongvaux A, Willinger T, Martinek J, Strowig T, Gearty SV, Teichmann LL, Saito Y, Marches F, Halene S, Palucka AK, Manz MG, Flavell RA. (2014) Development and function of human innate immune cells in a humanized mouse model. *Nat Biotechnol*. 32(4):364-72.

7. The Jackson Laboratory website: www.jax.org/strain/013062

8. The Jackson Laboratory website: www.jax.org/strain/017712