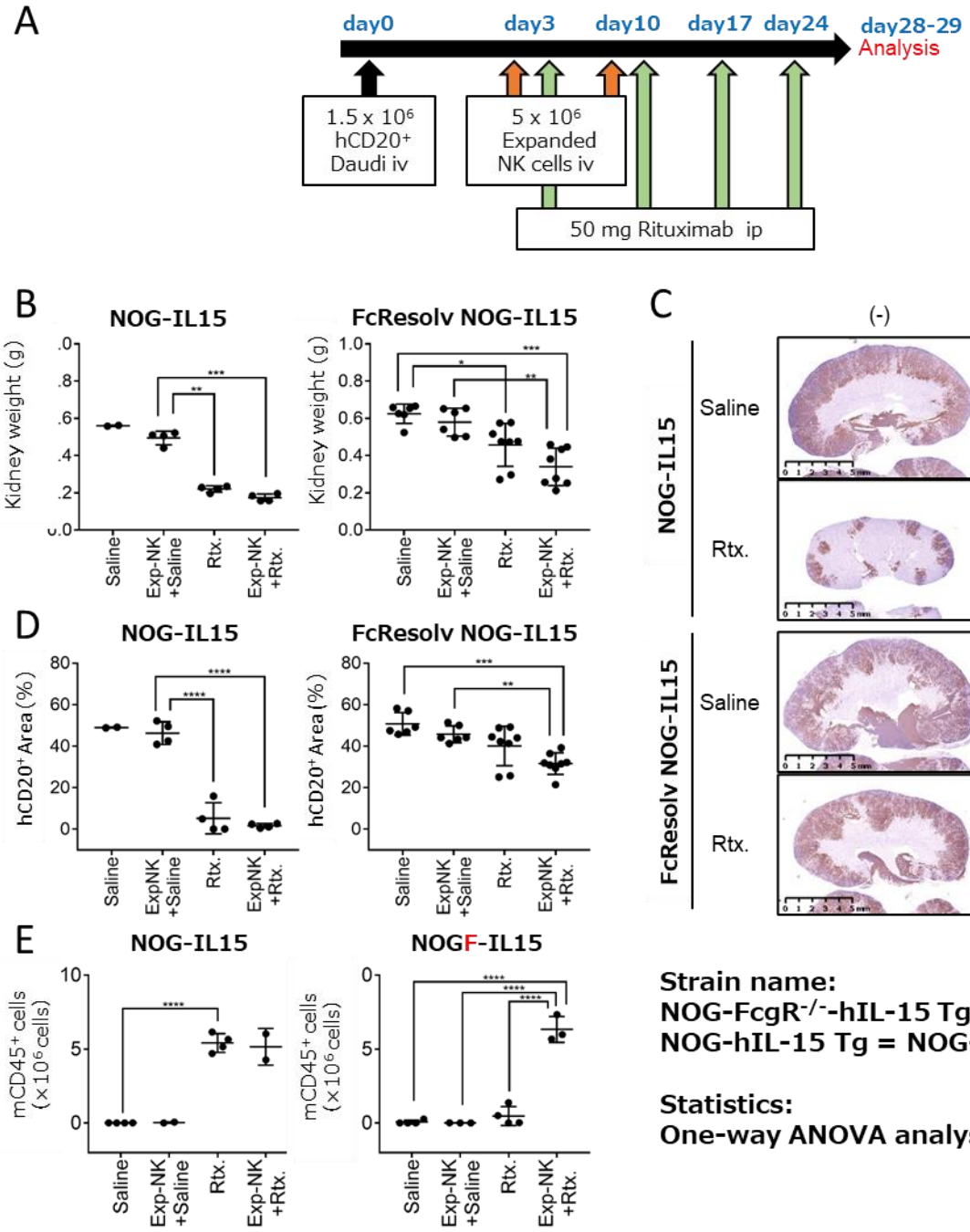
# FcResolv NOG-IL15 mouse : Validation of the *in vivo* ADCC model




**Strain name:**
**NOG-FcgR$^{-/-}$-hIL-15 Tg = FcResolv NOG-IL15**
**NOG-hIL-15 Tg = NOG-IL15**

**Statistics:**
**One-way ANOVA analysis, *p<0.05,**p<0.01**

# Validation of the *in vivo* ADCC model

- We investigated whether ADCC mediated by human NK cells was specifically detected in the new strain.
- Mice were inoculated with Daudi cells and then subjected to three different treatment protocols: human NK cells, rituximab, or a combination of the two (Fig A).
- Engrafted human NK cells were lost rapidly when using NOG or FcResolv NOG mouse, and no protective effect could be detected in any of the mouse (data not shown).
- Comparing NOG-IL15 and FcResolv NOG-IL15 mouse, engraftment of human NK cells alone did not induce tumor suppression in either strain, as indicated by increased kidney weight (Fig. B).
- As same as NOG mouse, rituximab treatment potently suppressed renal swelling in NOG-IL15 mouse, and this suppression was evident regardless of the presence of human NK cells (Fig. B, left).
- In contrast, in FcResolv NOG-IL15 mouse, combined therapy with human NK cells and rituximab induced a significant reduction in kidney weight compared with saline-treated or NK cell engrafted groups. Rituximab-treated mouse showed an intermediate reduction in kidney weight, with no statistical significance between this group and the combination therapy group (Fig. B, right). Consistent results were also obtained by immunohistochemical analysis (Fig. C, D).
- Interestingly, image analysis of multiple sections by immunohistochemistry showed that mouse receiving the combination therapy had enhanced suppression of Daudi when compared with the rituximab-treated group, and it was suggested that human NK cells killed Daudi cells via ADCC (Fig. C, D). Bone marrow (BM) analysis also demonstrated that the combination therapy was effective in preventing devastating BM destruction by Daudi cells.
- In NOG mouse, Daudi cells significantly deplete mouse CD45+ cells in the BM by an unknown mechanism (data was not shown).
- In NOG-IL15 mouse, rituximab treatment rescued murine CD45+ cells regardless of NK cell engraftment, whereas untreated mouse or mouse receiving only human NK cell engraftment had significantly reduced murine CD45+ cells ( Fig. 3E).
- On the other hand, in FcResolv NOG-IL15 mouse, only the group receiving the combination therapy avoided BM disruption (Fig. 3E).
- These results suggest that this new mouse strain enables specific detection of ADCC via human NK cells.

*Katano et. al.,* Frontiers in Immunology, Oct. 2020., the content has been revised and posted separately.