

***Supplemental Figure 1) T cell depletion in AJ mice.*** No difference in tumor number, size or incidence was evident between AJ mice depleted of T lymphocytes with anti CD4 and CD8 antibodies (500 µg of GK1.5 and YTS169.4 i.p. followed by 250µg of each weekly for 4 months after urethane treatment) vs. isotype control-treated mice.

***Supplemental Figure 2) Cytotoxicity of neutrophils and monocytes/macrophages.*** Only minimal cytotoxicity was evident by neutrophils (isolated using the “no touch” technique of biotinylated antibodies followed by magnetic cell depletion) or monocytes and macrophages (isolated by CD115<sup>+</sup> selection from the bone marrow) with no differences between AJ, 129SvEv or B6 mice.

***Supplemental Figure 3) Strain-specific differences in Yac-1 cytotoxicity.*** Unlike the case for lung cancer cell lines, 129/SvEv NK cells are able to lyse YAC-1 cells at similar levels to those isolated from B6 mice while AJ NK cells demonstrate a virtual absence of YAC-1 cytotoxicity. Data demonstrates 100:1 effector:target ratio and is representative of two separate experiments.

***Supplemental Figure 4) Cytotoxicity of NK cells from C57BL/10 and Balb/c mice.*** C57BL/10 mice, which share the NKC with the B6 strain, are able to lyse LLC cells more efficiently than NK cells from Balb/c mice, which have a NKC locus similar to 129 and AJ strains.

***Supplemental Figure 5) Microsatellite mapping of the 129/SvEv.B6-NKC Rag<sup>2-/-</sup> mouse.*** The 129/SvEv.B6-NKC Rag<sup>2-/-</sup> mouse contains B6 alleles only in chromosome 6 in the NKC region (detailed in Figure 4). The indicated mice were genotyped for 138 microsatellites, as indicated.

***Supplemental Figure 6) SNP rs13459098 in the Pas-1 locus is of 129 origin in 129/SvEv.B6-NKC Rag<sup>2-/-</sup> mice.*** SNP rs13459098, located at 145123190 bp, was analyzed and was determined to be of the 129 strain (identical results obtained using 129SvEv and 129 Ola mice).