



**Supplementary Figure S2.** Experimental schema to study the HLH phenotype after LV vector gene transfer. Prf1<sup>-/-</sup> bone marrow lineage<sup>-</sup>Sca<sup>+</sup>Kit<sup>+</sup> (LSK) hematopoietic stem and progenitor cells were transduced with MND4T, PGK4T, and PRF0T vectors and transplanted into myeloablated Prf1<sup>-/-</sup> mice. Wild-type (WT) or Prf1<sup>-/-</sup> LSK cells were also similarly transplanted into Prf1<sup>-/-</sup> mice as positive and negative controls. Mice were monitored for 12 weeks after hematopoietic stem cell transplantation (HCT) when they were assessed for NK cell tNGFR chimerism in peripheral blood. At 16 weeks, the mice were challenged with LCMV: 8 days after LCMV, small subsets were sacrificed for cytotoxicity assays. The rest were bled at 2 weeks for assessment of gene-modified cell chimerism, IFN- $\gamma$  levels, and cytopenias. These mice were also assessed two or three times per week for clinical assessment of the HLH phenotype and survival studies. In addition, at the time of LCMV infection at 16 weeks, a group of WT and Prf1<sup>-/-</sup> mice (untransplanted mice) were concurrently infected with LCMV as the historical HLH controls.