**Supplementary Figure 1 Intravenously administered mRNA-LNPs target the liver.** Representative IVIS image (24 hours post-injection) of BALB/c mice injected with 5 µg LNP-complexed firefly luciferase-encoding mRNA by the intravenous route.
Supplementary Figure 2 Repeated delivery of nucleoside-modified mRNA into immunocompetent mice. BALB/c mice were intraperitoneally injected weekly for 5 weeks with 0.1 μg of murine erythropoietin (muEPO) encoding nucleoside-modified mRNA. (a) Animals were bled 1 week after each injection and antibody responses to muEPO protein were measured in the plasma by ELISA. (b) To measure the sensitivity of the ELISA, recombinant anti-muEPO antibodies (10, 1 and 0.1 ng) were spiked into mouse plasma and analyzed. Group size is 5 animals.
Supplementary Figure 3 Characterization of BLT humanized mice. BLT humanized mice were engrafted with 100,000 CD34+ human hematopoietic stem cells. (a) Chimerism was measured in peripheral blood 16 weeks later by enumerating human CD45+ cells in blood. (b) Percent of T cells (CD3+) and B cells (CD19+) of CD45+ cells in BLT mice. (c) Percent of CD4+ and CD8+ T cells of total CD3+ T cells in BLT mice. Group size is 28 animals.
Supplementary Figure 4 Characterization of humanized CD34-NSG mice.

NSG humanized mice were engrafted with 100,000 CD34+ human hematopoietic stem cells. Chimerism was measured in peripheral blood 12 weeks later by enumerating human CD45+ cells in blood. Group size is 8 animals.