

Figure S1. Macrophage depletion in NOD/SCID mice receiving intravenous injection of clodronate-liposomes. NOD/SCID mice were treated with clodronate-liposomes or PBS-liposomes (controls) at days 0 (100 μ l) and 2 (50 μ l); spleens were harvested 7 days later, fixed in 10% buffered formalin and embedded in paraffin. Immunohistochemistry was performed on spleen sections with primary antibody rat anti-mouse F4/80 (BM8) and secondary biotinylated goat anti-rat IgG (F4/80) or with secondary antibody alone (CTRL), and F4/80⁺ cells (brown color) were visualized by the avidin-biotin peroxidase complex (ABC) technique. Section was counterstained with Hematoxylin. Compared to PBS-liposome treated mice, mice treated with clodronate-liposomes showed severe splenic atrophy (A), which was associated with a paucity of hematoxylin positive nuclear cells and the lack of F4/80⁺ cells (B; x400). Shown are representative samples from clodronate-liposome-treated mice.



Figure S2. Flow cytometric analysis of human CD235a⁺ **cells in tissues from humanized mice.** Shown are CD235a staining of single cell suspensions of liver, spleen, kidney, and lung from a representative humanized mouse.



Figure S3. Presence of human CD235a⁺CD45⁻ nucleated erythroid cells in bone marrow of humanized mice. Bone marrow cells were harvested from humanized NSG mice 20 weeks after transplantation with human fetal thymus and CD34⁺ FLCs, and stained with anti-human CD45, CD235a and propidium iodide (PI). Shown are representative flow cytometric profiles.



Figure S4. Human RBCs remained undetectable in blood from humanized mice after sublethal irradiation. Shown are representative flow cytometric profiles from a representative humanized mouse before (A) and after (B) irradiation (2.5 Gy).