Supplementary Fig. 1 CD56<sup>dim</sup> to CD56<sup>bright</sup> NK cell phenotypical change in response to OBZ and in patients receiving RTX infusion. 

- **a, b** PBMC were cocultured with Raji cells and OBZ or TRA for 7 days. OBZ induces enhanced expression of CD56 on NK cells. n=6.

- **c** Patients were treated by weekly single agent RTX infusion. CD19<sup>+</sup> target cells were eliminated 1 week after RTX treatment, but re-emerged on week 3 in the patient with circulating tumors.
Supplementary Fig. 2 RTX fails to induce CD56<sup>dim</sup> to CD56<sup>bright</sup> transition and proliferation of isolated NK cells. Isolated NK cells or unfractionated PBMCs were cocultured with Raji cells and RTX or TRA for up to 7 days. 

- **a, b** RTX has no impact on CD56 expression by isolated NK cells. n=4.
- **c** RTX fails to induce CFSE dilution by isolated NK cells at 7 days. n=5.
- **d** CD16 re-expression is seen with unfractionated PBMCs, but not with isolated PBMCs, after culture for 7 days with RTX.
- **e** The number of NK cells remaining after 7-day culture with RTX is greater with unfractionated PBMCs compared to isolated NK cells. n=5-8. Cell counts in the TRA group were used to normalize cell numbers.
Supplementary Fig. 3 T cell depletion doesn’t impact RTX-mediated NK cell activation. Unfractionated PBMC or PBMC depleted of CD3⁺ cells were cocultured with Raji or autologous B cells and RTX or TRA for 7 days. Depletion of T cells does not alter RTX-activated NK expression of CD25 (a, c) or CD69 (b, d). n=4-6
Supplementary Fig. 4 The depletion of CD14+ monocytes or CD19+ B cells does not suppress RTX-mediated NK cell responses. Unfractionated PBMC or PBMC depleted of CD14+ monocytes or CD19+ normal B cells were cocultured with Raji cells and RTX or TRA for 7 days and elimination of CD19+ target cells determined by flow cytometry. a, b The depletion of monocytes or B cells does not impact RTX-mediated NK elimination of CD19+ cells. c The depletion of monocytes or B cells does not impact on RTX-mediated NK cell viability. d, e The depletion of monocytes or B cells does not impact on RTX-mediated CD56dim to CD56bright NK cell transition. f, g The depletion of monocytes or B cells does not suppress RTX-mediated recovery of CD16. n=3 Cell counts in the TRA group were used to normalize cell numbers.
Supplementary Fig. 5 T cells, mainly CD4+ cells, are essential for RTX-mediated NK cell responses. Isolated NK cells were cocultured with Raji cells and RTX or TRA. T cell subsets were added to the culture based on their physiological proportion in the peripheral blood: 0.6 million CD3+, 0.4 million CD4+, or 0.2 million CD8+ T cells. a, b The elimination of CD19+ target cells is significantly enhanced with the presence of CD3+, CD4+ or CD8+ T cells at day 7. CD3+ and CD4+ T cells improve elimination of CD19+ target cells to a greater degree than CD8+ T cells. c The number of NK cells remaining in the culture after 7 days is increased by the addition of CD3+ or CD4+ T cells but not by CD8+ T cells. d, e CD56dim to CD56bright NK transition is only seen when T cells were present. CD3+ and CD4+ induce greater CD56dim to CD56bright NK transition than CD8+ T cells. f, g CD16 re-expression at 7 days is only seen when CD3+ or CD4+ T cells are present. n=6-8. Cell counts in the TRA group were used to normalize cell numbers.
Supplementary Fig. 6 T cells maintain CTX-mediated NK cell responses via IL2. Unfractionated PBMCs or PBMCs depleted of CD3+ T cells were cocultured with SQ20B cells and CTX or TRA. a-e On day 7, CTX induces CD56dim to CD56bright NK cell transition, maintains NK cell viability, and CD16 re-expression by NK cells after the initial downregulation at 20 hours in unfractionated PBMCs but not in T cell-depleted PBMCs. n=4. Unfractionated PBMCs or PBMCs depleted of CD3+ T cells were cocultured with SQ20B cells and CTX or IgG1 control. α-IL2 blocking mAb (10ug/ml) or recombinant IL2 (20ng/ml) was added to the coculture for 7 days. f-h On day 7, CTX-mediated NK cell viability, CD56dim to CD56bright NK transition, and CD16 re-expression on NK cells in unfractionated PBMCs were suppressed by α-IL2, and was maintained by recombinant IL2 supplementation on NK cells in T cell-depleted PBMCs. Cell counts in the TRA+PBMC group are used to normalize cell numbers. n=6.
Supplementary Fig. 7 T cell activation by α-CD3/28 beads enhances RTX-mediated NK cell responses. PBMC depleted of CD3+ T cells were cocultured with Raji cells and RTX or TRA for 7 days. Serial dilutions of either autologous resting or α-CD3/28-activated T cells were added to the coculture. RTX-mediated NK cell elimination of target cells (a), viability (b), CD56dim to CD56bright transition (c) and CD16 re-expression (d) is T cell dose dependent and further enhanced by T cell activation. n=7. Cell counts in the TRA group at 0% T cell dose were used to normalize cell numbers.