Supplementary Figure Legends

Supplementary Figure 1. WT (CD45.2+) mice were injected with OT-1 cells (CD45.1+). After 24h animals were injected with PBD (Uninfected) or with $2x10^5$ PFU mCMV-N4 (Infected). After 7 days, splenocytes were analyzed by flow cytometry. Shown is a typical gating strategy. Right-most plots show K^bm57^+ cells amongst $CD8^+$ recipient cells in uninfected mice (top), in OT-1 donor cells after infection (middle) and recipient $CD8^+$ T cells after infection (bottom).

Supplementary Figure 2. (a) WT mice were fed with a NCD or HFD for 12 weeks. Next, animals received 10^4 OT-1 cells ($CD45.1^+$) and were infected with LCMV-N4. After 5 days, viral titers were determined in liver. (b) Female WT ($CD45.2^+$) mice were fed with a NCD or HFD for 12 weeks. Next, animals received 10^4 OT-1 cells ($CD45.1^+$) and were infected with mCMV-N4. After 42 days, mice were re-infected with LCMV-N4. After 7 days, cytokine production after in vivo restimulation with PMA/Ionomycin was determined in splenic donor cells. (c) WT mice were fed with a NCD or HFD for 12 weeks. Next, animals were inoculated with 10^5 B16-N4 cells. After 14 days, metastases were quantified in the lungs. (a) Kruskal-Wallis test or Student`s t-test (b,c) was used to analyze differences between groups. Shown are means ± s.e.m of one experiment. * P<0.05, ** P<0.01, *** P<0.001.

Supplementary Figure 3. Purified WT ($CD45.1/2^+$) and IR^{CKO} ($CD45.1^+$) OT-1 cells were mixed in a 1:1 ratio, CFSE labeled and activated in vitro with ovalbumin (N4) peptide and anti-CD28 for 30h, followed by 5 days of IL-15 stimulation to induce memory differentiation. Cells were cultured in medium containing very low (1 mM), low (2.5 mM) or physiological (5 mM) concentrations of glucose and in the presence or absence of 1 U/ml fast-acting insulin. After 6 days (a) cell surface marker expression, (b) proliferation, (c) cytokine production after 4h N4-peptide restimulation was determined. (d) Ratio between WT and IR^{CKO} cells over time. Student`s t-test was used to determine statistical differences between groups. Shown is one of two experiments (n=3-5). Shown are means ± s.e.m. * P<0.05, ** P<0.01, *** P<0.001.

Supplementary Figure 4; Hyperglycemia impairs cytokine production by memory CD8 T cells. (a) Purified OT-1 cells were CFSE labeled and activated in vitro with ovalbumin (N4) peptide and anti-CD28 for 30h, followed by 5 days of culture in the presence of only IL-15 to induce memory differentiation. After 6 days, cells were analyzed by flow cytometry. Shown is proliferation segregated based on cell cycle. (b-e) WT ($CD45.2^+$) mice were made hyperglycemic through injection of a mixture of streptozotocin and alloxan (STZ/ALX). Mice were transferred with 10^4 OT-1 cells ($CD45.1^+$) and after one day infected with mCMV-N4. After 45 days, animals were re-infected with LCMV-N4. (a) fasting plasma levels. (b) blood glucose levels on day 14 after infection. (c-e) Donor cells in the blood were analyzed by flow cytometry on days (c) seven and (d) 37 days after primary infection or (e) seven days after re-infection. Shown is one of two experiments (n=4-5). Shown is one of two experiments (n=3-5). Shown are means ± s.e.m. ** P<0.01.