Figure S1. Peripheral Blood IFN-γ^+CD8^+ T cells Predominantly Express a Terminally Differentiated Effector Phenotype. Peripheral blood lymphocytes from kidney transplant recipients were analyzed using flow cytometry to determine the composition of naïve (CD62L^−CD45RO^−), central memory (T_{CM}; CD62L^+CD45RO^+), or terminally differentiated effector CD8^+ T cells (T_{EFF}; CD62L^−CD45RO^+). Cells were initially gated on lymphocytes and CD8^+ T cells. A) Representative data (DSA-negative recipient, 3 months posttransplant) shows that circulating CD8^+ T cells consist of 61% naïve CD8^+ T cells, 12% central memory CD8^+ T cells, 3% effector memory CD8^+ T cells, and 21% terminally differentiated effector cells. B) When CD8^+ T cells are further gated on IFN-γ^+ cells, IFN-γ^+CD8^+ T cells predominantly express a terminally differentiated effector phenotype (CD62L^CD45RO^−). Terminally differentiated effector IFN-γ^+CD8^+ T cells (CD62L^−CD45RO^−; red histogram) also express CD44 when compared to naïve cells (orange histogram) and CD44 FMO control (blue histogram). Expression of CD45RO^+CD8^+ T cells, CD62L^−CD44, and IFN-γ are shown in comparison to fluorescence minus one (FMO) controls for CD45RO, CD62L, CD44, and IFN-γ. Flow antibodies included anti-CD62L (clone DREG-56) and anti-CD45RO (clone UCHL1, both from BD).
Figure S2. Capture Rate for Peripheral Blood Samples to Assess Quantity of IFN-γ+CD8+ T cells and CXCR5+IFN-γ+CD8+ T cells in Primary Kidney Transplant Recipients Over the First Year Posttransplant. Peripheral blood sample collection was targeted for 6 time-points (pretransplant as well as follow-up visits at 1, 3, 6, 9, and 12 months posttransplant) from 95 consenting kidney transplant recipients (570 potential samples). A) Samples to analyze peripheral IFN-γ+CD8+ T cells were collected with overall 71% (402/570 samples) capture rate of targeted samples including 100% pretransplant, 72% 1 month, 73% 3 month, 57% 6 month, 54% 9 month, and 68% 12 month samples. Sample capture rates were similar for DSA-negative (70%) and DSA-positive (72%) recipients over the 1-year follow up (p=0.44). B) The peripheral blood sample collection for analysis of CXCR5+IFN-γ+CD8+ T cells was initiated later in the study and included 56% (320/570) capture rate of the targeted study samples including 72% pretransplant, 52% 1 month, 58% 3 month, 40% 6 month, 52% 9 month, 65% 12 month samples. Sample capture rates were similar for DSA-negative (57%) and DSA-positive (52%) recipients over the 1-year follow up (p=0.26).
Initial DSA was detected, on average, 6.0±3.7 months posttransplant in 23 of the 95 recipients (24.2%). Of the 23 DSA-positive recipients, recipients developed specificity to HLA I (7 recipients), HLA II (10 recipients), or to both HLA I and HLA II (6 recipients). HLA antigen specificity is listed for all recipients in each group.

**Figure S3. HLA Class I and HLA Class II Specificity of all DSA at the Time of Initial Detection.**
Figure S4. CD4⁺ T cells, CD8⁺ T cells, and White Blood cells in Peripheral Blood of DSA-positive and DSA-negative Kidney Transplant Recipients Over the First Year Posttransplant. Peripheral blood from DSA-positive (n=23) and DSA-negative recipients (n=72) was analyzed for quantity of total CD4⁺ T cells and CD8⁺ T cells and white blood cell count (WBC) (pretransplant and 1, 3, 6, 9, and 12 months posttransplant). A) Total peripheral CD4⁺ T cells and B) Total peripheral CD8⁺ T cells by flow cytometric analysis in DSA-positive and DSA negative recipients were similar (p=0.27 and p=0.86, respectively). C) WBC counts were slightly higher in DSA-positive recipients (p=0.03) but were in the normal range (4-10 x 10³) over the first year posttransplant. Graphed data represents geometric mean ± standard error.
Figure S5. Quantity of IL-17+CD4+ T cells, FoxP3+IL-10+CD4+ T cells, and IL-10+CD4+ T cells in DSA-positive and DSA-negative recipients Over the First Year Posttransplant. Peripheral blood from DSA-positive recipients (n=23) and DSA-negative recipients (n=72) was analyzed using flow cytometry to determine the quantity of IL-17+CD4+ T cells, FoxP3+IL-10+CD4+ T cells, and IL-10+CD4+ T cells. A-C) The quantities of IL-17+CD4+ T cells, FoxP3+IL-10+CD4+ T cells, and IL-10+CD4+ T cells were not significantly different between DSA-positive and DSA-negative recipients over the first year posttransplant (p=0.47, p=0.83, and p=0.94, respectively). Graphed data represents geometric mean ± standard error. D) Flow plots for IL-17, FoxP3, and IL-10 expression on CD4+ T cells are shown from representative DSA-negative and DSA-positive recipients (3 months posttransplant). Cells were gated on lymphocytes and CD4+ T cells. Flow antibodies included anti-IL-17 (clone N49-653), anti-FoxP3 (clone 259D/C7), and anti-IL-10 (clone JES3-9D7, all from BD).
Following kidney transplantation, recipients were maintained on an immunosuppressive regimen consisting of a combination of calcineurin inhibition (CNI, with Neoral) and mTOR inhibition (mTORi, with Rapamune or Zortress). Immunosuppression CNI 2 hour peak (C2) and mTORi trough levels were analyzed in 95 recipients at 1, 3, 6, 9, and 12 months posttransplant. A) DSA-negative (n=72) and DSA-positive recipients (n=23) had similar CNI C2 hour levels over the first year posttransplant (p=0.68). B) DSA-positive and DSA-negative recipients had similar mTORi trough levels over the first year posttransplant (p=0.69). Graphed data represents geometric mean ± standard error.
Figure S7. Cumulative Bacterial and Viral infections in 95 First-time Kidney Transplant Recipients Over the First Year Posttransplant. Following kidney transplantation (n=95), 43 recipients (45.3%) developed a bacterial (25 recipients) and/or viral (22 recipients) infection over the first year posttransplant. Most recipients with infection only developed 1 bacterial infection (17/25) and/or 1 viral infection (21/22) during the study period. Six recipients developed multiple bacterial infections, 4 recipients developed bacterial and viral infections (2 of whom also had multiple bacterial infections), and 1 recipient developed multiple viral infections. The majority of bacterial infections occurred in the first 4 months posttransplant (32 of 42 total infections; 8 patients with multiple bacterial infections). Viral infections (23 total) were less common than bacterial infections and their occurrence was more evenly distributed over the 1 year follow-up (1 recipient with 2 viral infections).