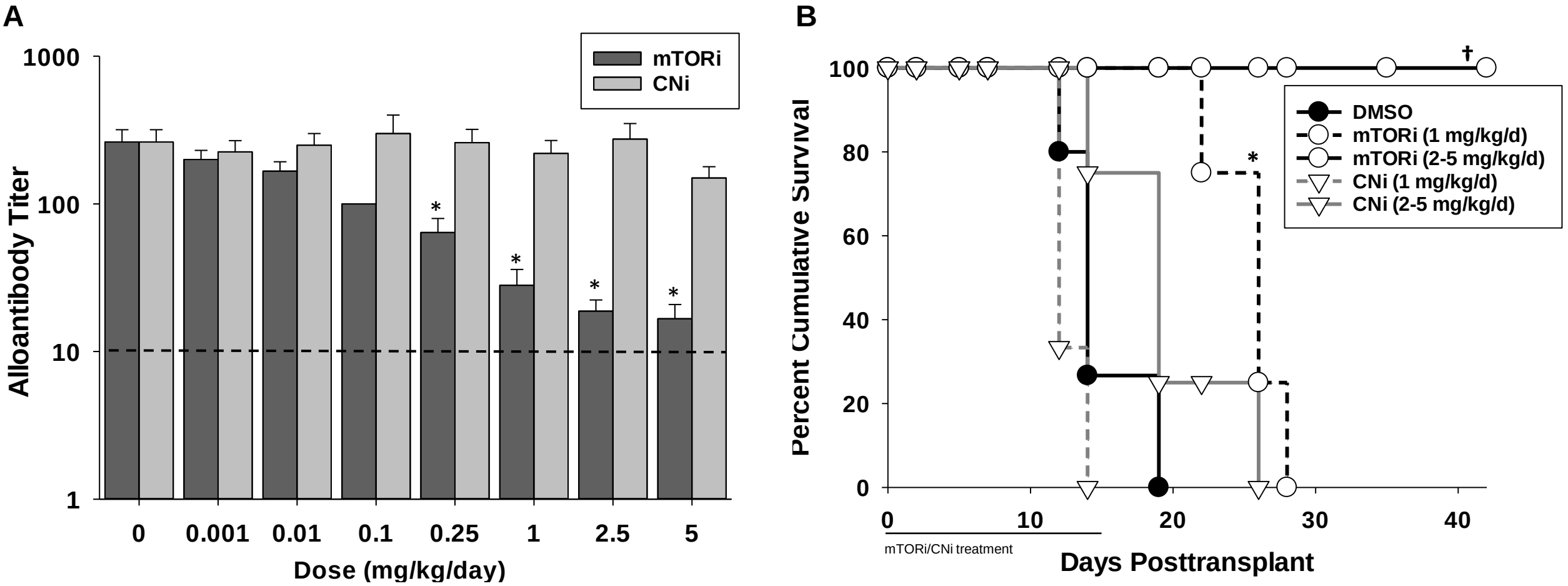
Supplemental Figure 1



Supplemental Figure 1: Dose response of mTORi or CNi on alloantibody production and allograft survival. A) To examine the effect of mTORi or CNi in high alloantibody producing transplant recipients, C57BL/6 (H-2^b, wild-type; WT) mice were transplanted with allogeneic FVB/N (H-2^q) hepatocytes and CD8-depleted (days -2, -1). On days 0-14 posttransplant cohorts of recipients were treated with 1-5 mg/kg/d mTORi or CNi or a 5% DMSO-vehicle control. **A)** Alloantibody was quantified by titering recipient serum on day 14 posttransplant. Treatment of recipients with as low a dose of mTORi as 0.25 mg/kg/d resulted in significantly reduced alloantibody (titer=64±16, n=5, $p<0.001$ for all comparisons as signified by "*") compared to control recipients (titer=263±55, n=4). Additionally the dose of mTORi inversely correlated with alloantibody level (alloantibody titer for 1.0 mg/kg/d=28±8, n=4; 2.5 mg/kg/d=19±4, n=4; 5.0 mg/kg/d=17±4, n=3, $p<0.001$ for all). CNi treatment did not inhibit alloantibody production even at the highest dose tested (5 mg/kg/d=150±29, n=4). Data was combined from duplicate experiments. **B)** To examine the effect of mTORi or CNi on allograft survival, CD8-depleted C57BL/6 recipients were treated on days 0 through 14 with 1-5 mg/kg/d mTORi or CNi or a 5% DMSO-vehicle control. Treatment with mTORi at 2-5 mg/kg/d significantly delayed graft rejection (MST >42 days, n=3) compared with CNi-treated groups (1 mg/kg/d: MST=12 days, n=6 and 2-5 mg/kg/d: MST=18 days, n=4) and DMSO treated controls (MST=14 days, n=15). $p<0.04$ for 2-5 mg/kg/day mTORi-treated versus all CNi and DMSO treated groups as signified by "†". mTORi at 1 mg/kg/d also significantly delayed graft rejection (MST=25 days, n=8) compared to DMSO and CNi at 1 mg/kg/d ($p<0.04$ for both comparisons, as signified by "*") but not when compared to the CNi 2-5 mg/kg/d group (p=ns). Treatment with CNi at the highest doses (2-5 mg/kg/d) did not delay rejection (MST=18 days, n=4) compared with DMSO treated controls (p=ns).