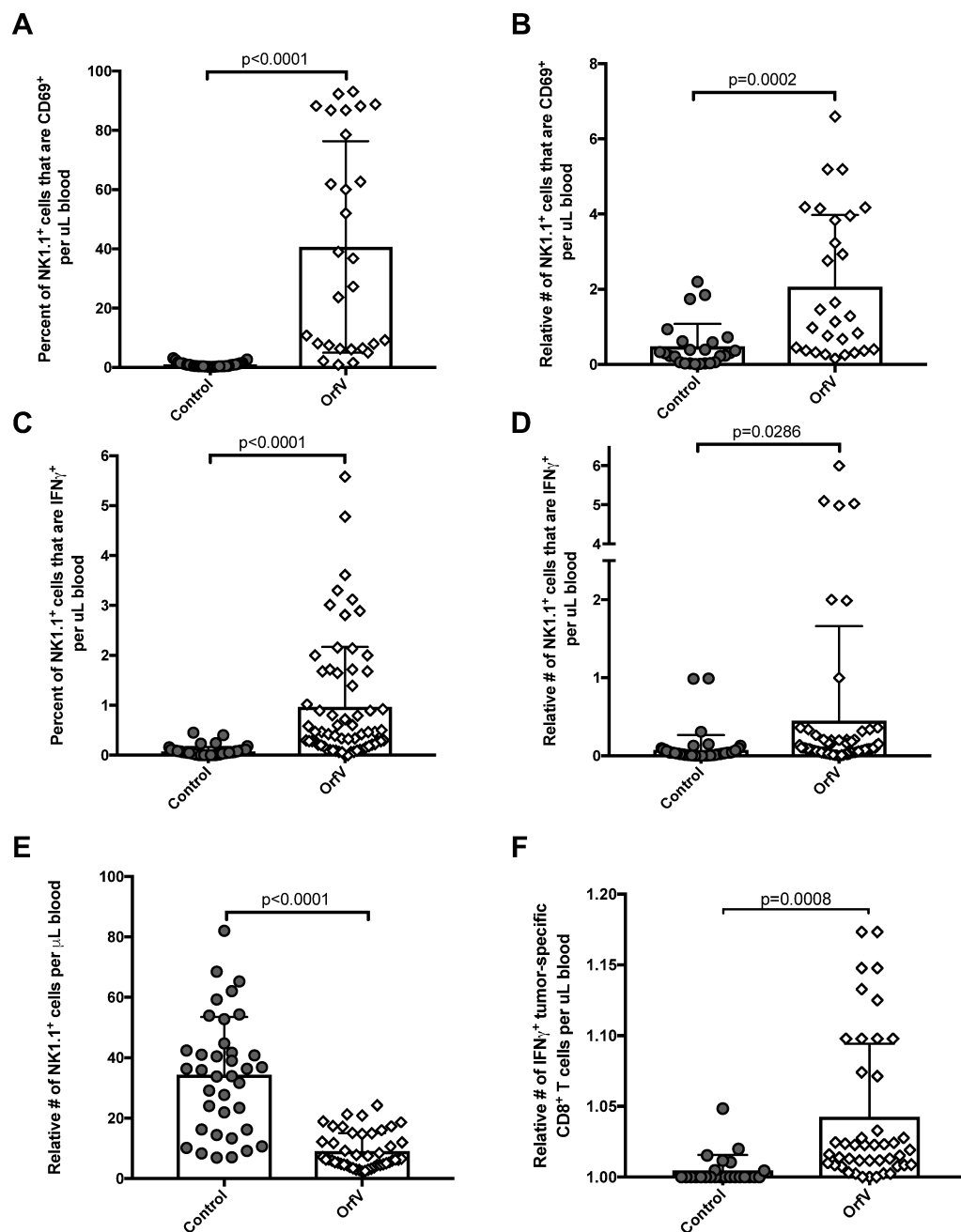


**Supplemental Figure 1: OrfV stimulates IL-12 production from BMDCs.** (A) Percent BMDCs expressing IL-12 following stimulation with LPS, OrfV or OrfV-infected ID8 cell supernatant as determined by flow cytometry. (B) Mean fluorescent intensity of IL-12 expressed by BMDCs following stimulation with LPS, OrfV or OrfV-infected ID8 cell supernatant as determined by flow cytometry.

Sample ID	Reads generated	Concordant alignment rates
OrfV_1	22991740	18311012 (79.64%)
OrfV_2	24023527	19012920 (79.14%)
OrfV_3	19829428	16171790 (81.55%)
Control_1	20484350	16319925 (79.67%)
Control_2	20909311	16494902 (78.89%)
Control_3	22690509	18393959 (81.06%)

**Supplementary Table 1.** Enriched NK RNA Seq Alignment Rates



**Supplementary Figure 2.** OrfV induces NK and T cell responses in peripheral blood. (A, B) ID8 tumor-bearing mice were treated with OrfV and peripheral blood was collected 36 hours later. The percent and number of NK cells expressing CD69 were quantified by flow cytometry. (C, D) The percent and number of NK cells in the peripheral blood expressing IFN $\gamma$  were quantified in ID8 tumor-bearing 36 hours following OrfV treatment. (E) The relative number of peripheral NK cells quantified in ID8 tumor-bearing animals 36 hours after OrfV therapy. (F) The relative number of peripheral CD8<sup>+</sup> T cells expressing IFN $\gamma$  in response to co-culture with autologous tumor cells were quantified in ID8 tumor-bearing mice ten days after OrfV treatment.