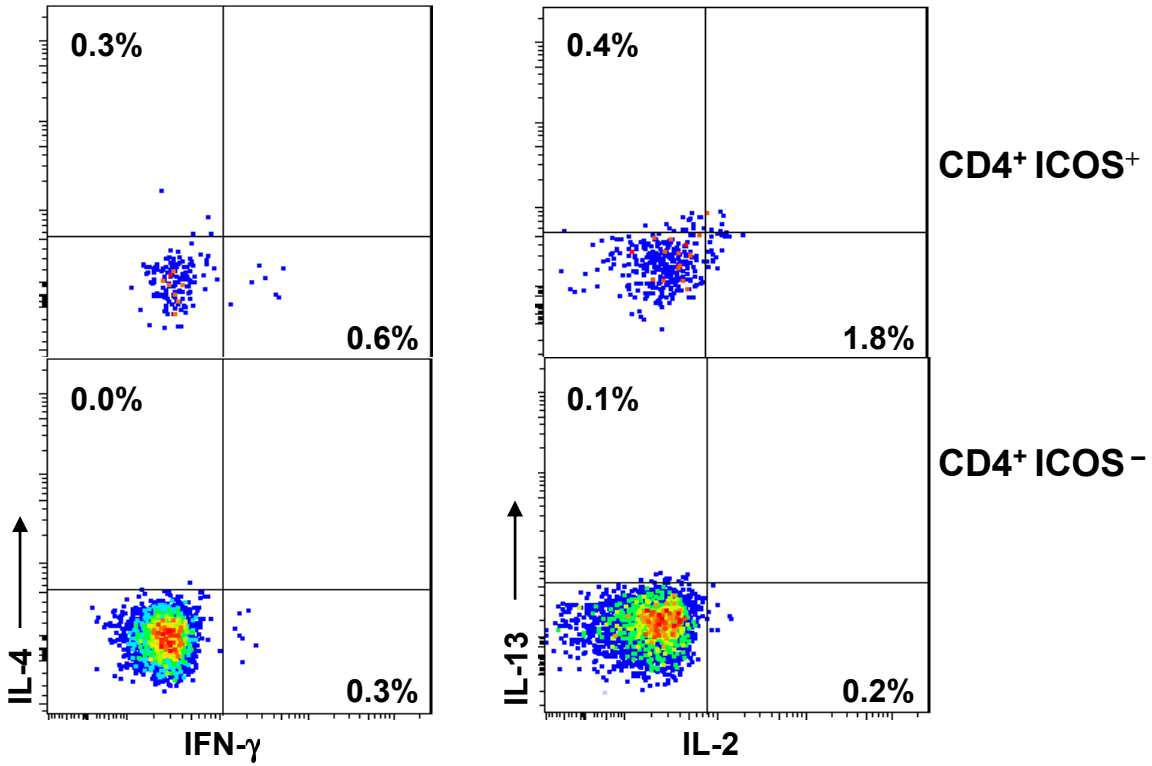Supplementary Fig. 3