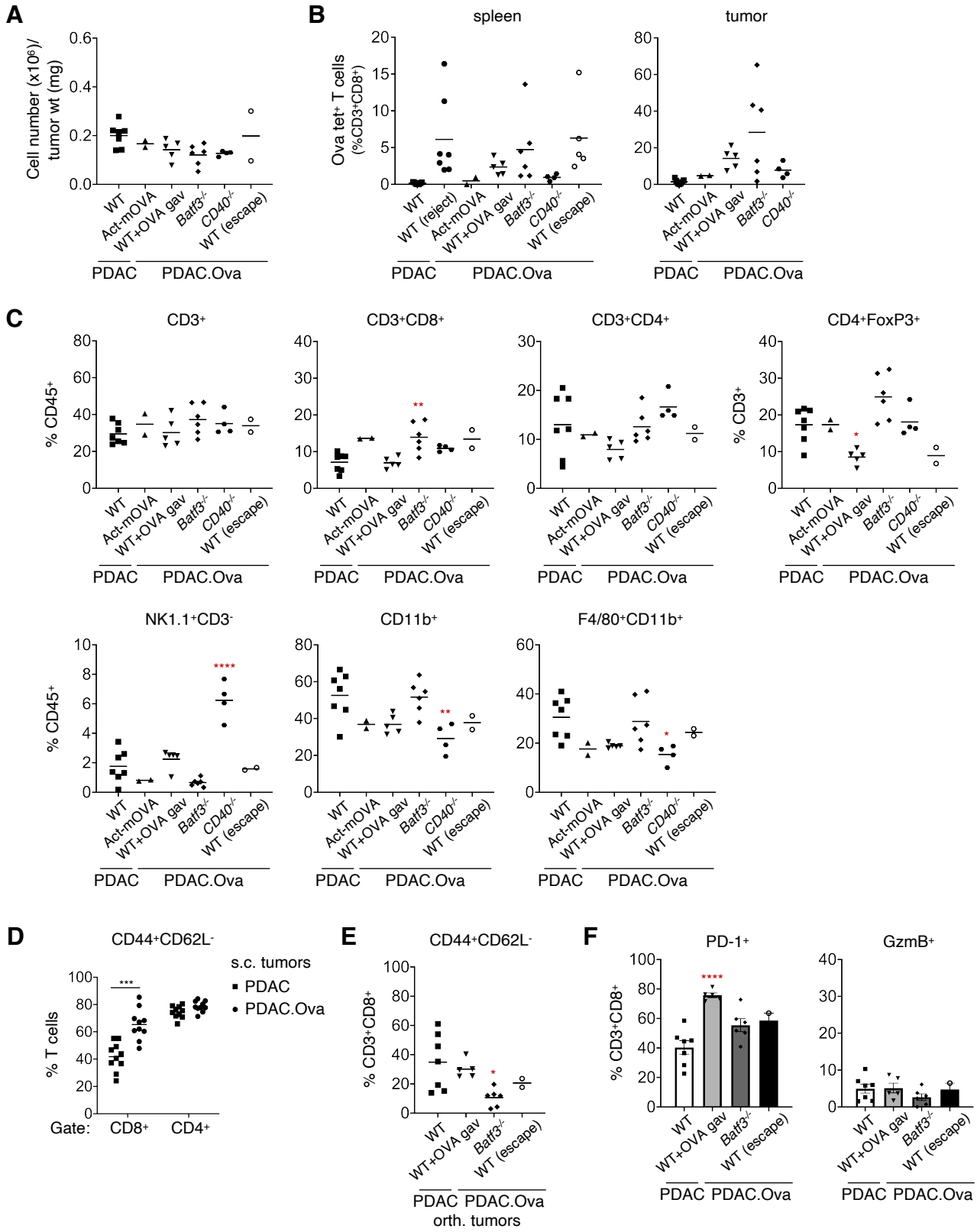Supplementary Fig. S4