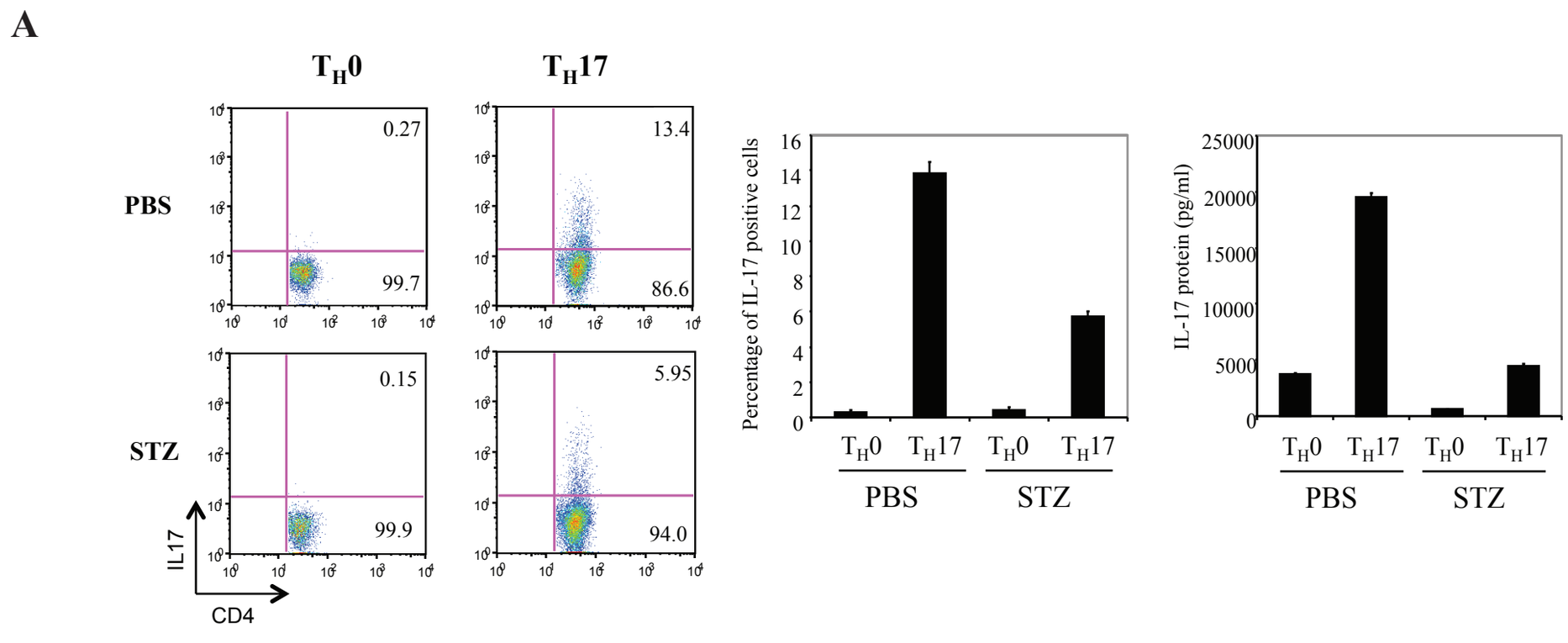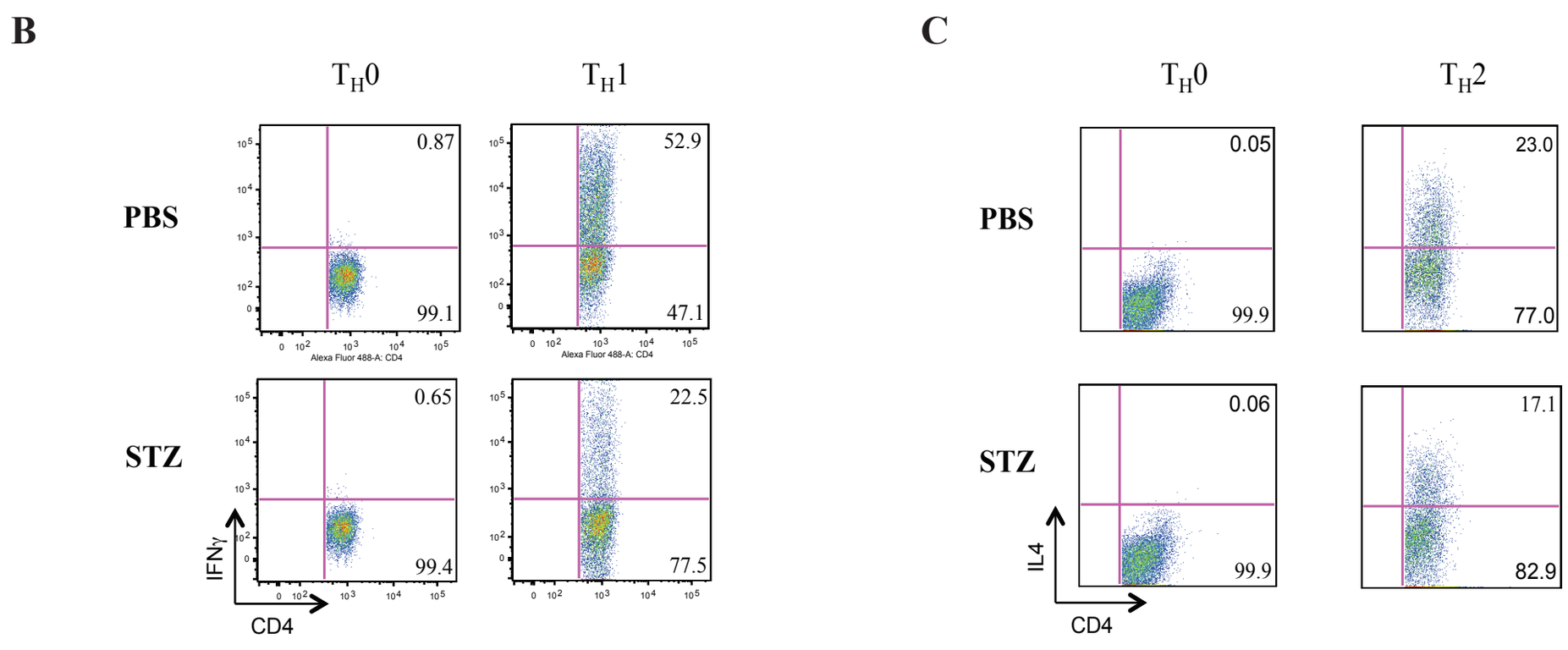Supplymentary Figure 3