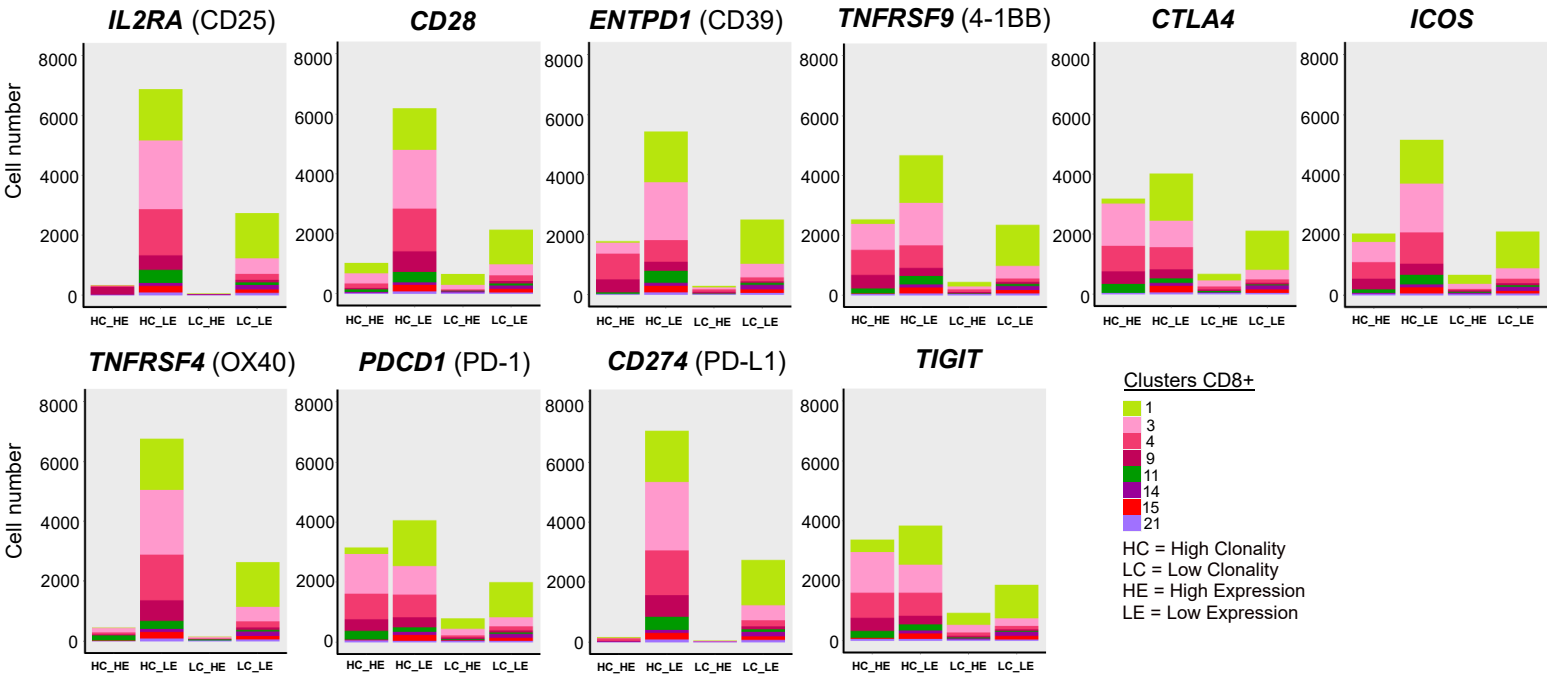Supplementary Data 12