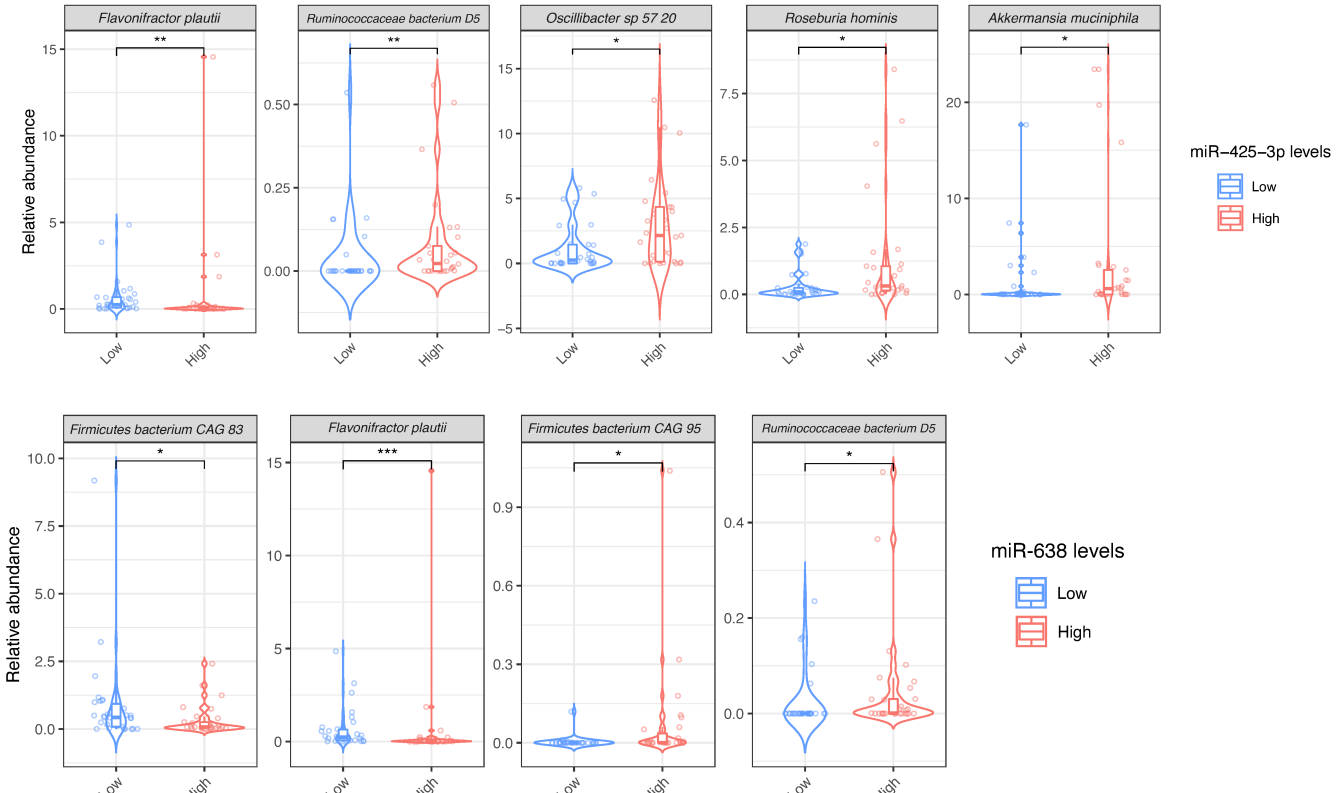Supplementary Figure 4