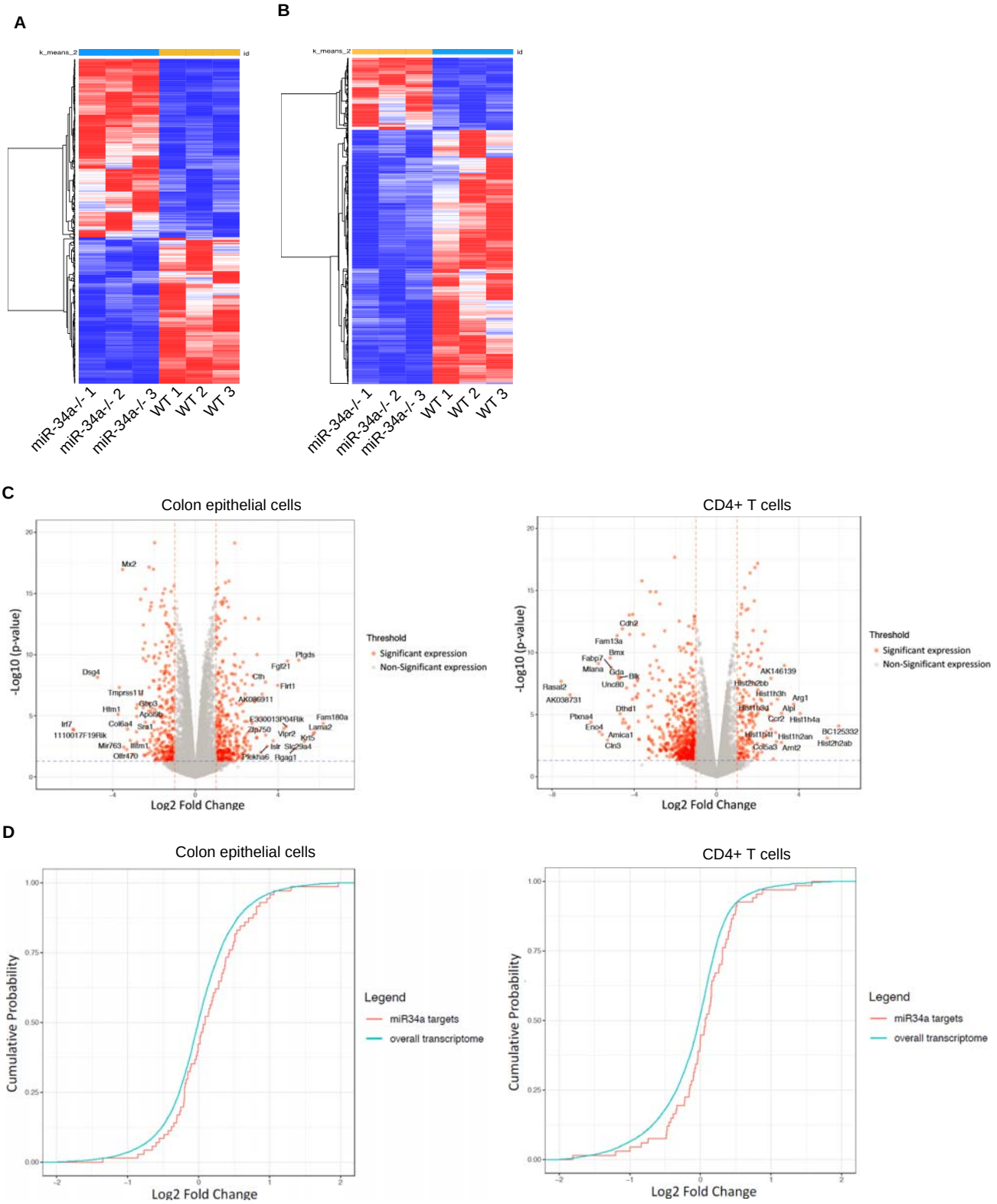Figure 3-figure supplement 4