Supplementary figure 1: IEC-subset specific gene expression in the ileal and colonic epithelium.



Supplementary figure 2: Intestinal crypt density and goblet cell numbers are DDX5-independent.





Supplementary figure 3: Tuft cell gating strategy.

Α.





Supplementary figure 4. DDX5 dependency of IEC subset defining genes in the small intestinal ISC and secretory lineage progenitors.



Lgr5^{hi}

Supplementary figure 5. DDX5 is not involved in intestinal organoid survival and growth.



Supplementary figure 6. Similar type 2 cytokines and trichomonas levels in WT^{IEC} and DDX5^{ΔIEC} mice.



Supplementary figure 7. IL-13 driven tuft cell hyperplasia is DDX5-independent.



Supplementary figure 8: Restoring CDC42 protein levels in DDX5^{ΔIEC} small intestinal organoids.



Β.



Supplementary figure 9: Transient inhibition of CDC42 activity did not alter wildtype intestinal organoid viability, growth, or response to IL-13 stimulation.



Supplementary figure 10: DDX5 promotes both type 1 and type 2 tuft cell programs in the small intestine.



Α.

Q2 0.65

Q3 28.7

Q2 0.042 Q2 0.77

03 28.5 2021 03 20.9





2369 CD45m CD45mid 1.79 31.0 CD45-50.0 CD45mid 1.23 C



Small Intestine_5656_KO_002.tcs Q2: CD24+, Siglec-F+ 168 Small Intestine_5656_KO_001.tcs Q2: CD24+, Siglec-F+ 162





Small Intestine_5656_KO_002.fcs Q2: CD24+ , Siglec-F+ 168



Β.



Supplementary figure 11: DDX5-dependent and -independent genes among small intestinal IEC lineages.



Supplementary figure 12: **DDX5-dependent viral and bacterial populations in the murine intestine.**



Supplementary figure 13: DDX5-dependent programs in colonic tumors.



-1.50

Column mean normalized expression

DDX5^{△IEC} Pair 1 DDX5^{△IEC} Pair 2