



**Supplementary information Fig. S6 Hyper-organoids contained functional Lgr5<sup>+</sup> regenerative stem cells**

**a**, Representative images and relative organoid-forming efficiency of single Lgr5<sup>+</sup> cells from ENR and Hyper organoids.

**b**, FACS analysis of tdTomato<sup>+</sup> cells in different organoids shown in Fig. 2f.

**c**, Immunofluorescence staining of regenerative and differentiated intestinal marker genes expressed in Hyper-organoids using the lineage tracing system. Scale bars, 10  $\mu$ m.

**d**. Quantification of the proportion of cells expressing tdTomato and differentiated intestinal marker gene. *P* values were determined using one-way ANOVA.

e. qPCR analysis of differentiated intestinal gene expression in ENR and Hyper-organoids treated with differentiation medium for 3d or untreated.

\*\*\* $P < 0.001$ ; \*\* $P < 0.01$ ; \* $P < 0.05$ ; ns, not significant ( $P > 0.05$ ). All experiments were independently replicated at least twice with similar results.