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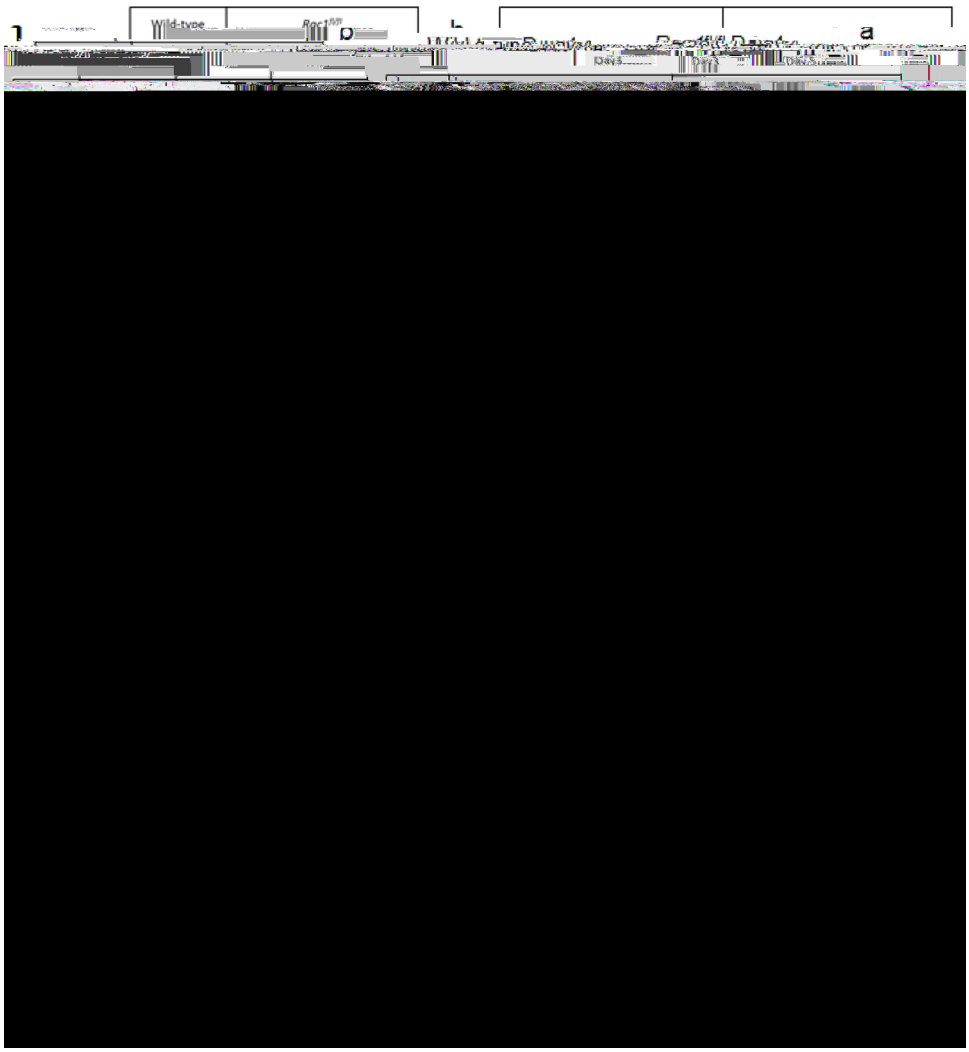


Fig. 1 Lo of Rac1 pe b ill homeo a i . a Images showing H&E, BrdU incorporation and Cleaved caspase-3 IHC in -,/P.2 (wild-type), -,/P.2, 1fl/fl (, 1fl/fl) mice day 3 post induction and -,/P.T2, 1fl/fl (, 1fl/fl) mice 3 and 5 days post induction. Red arrow indicates disintegrating villus. Scale bar represents 100 μm in each case (See amplified images in Supplementary Fig. 1d f). **b** Scanning EM on -,/P.2 (Wild-type) or -,/P.2, 1fl/fl (, 1fl/fl) intestines 4 days post induction. Red arrows indicate rounded, blebbing cells. Scale bar represents 100 μm in the upper panels and 50 μm in the lower panels. **c** -,/P.2 driving expression of

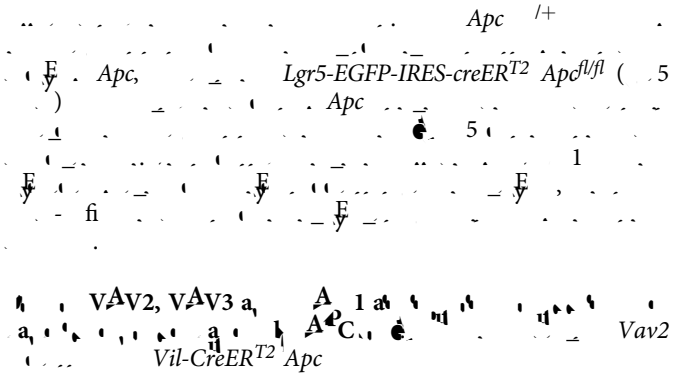
Re l and di c ion

AC1 a

Rac1 “ fi F14. F 1 fi 1 1 , Vil-CreER^{T2} Rac1$^{fl/fl}$ 2 2 F Rac1 42,43. 5 F ( ), F , F (. 1_), (. 1_ . 1_ , F . 1 , E . 1 _ F (. 1_ F . 1 ,). E F 1 _ F) _ F Vil-CreER^{T2} Rac1$^{fl/fl}$ 42,43 fl (. 1). 1 fi F Rac1 Vil-CreER^{T2} , Rac1 4 _ 5 (fi). , Rac1

Rac1 *Vil-CreER*^{T2} 2

Fig. 2 VAV3 and TIAM1 are upregulated following APC loss. a Heatmap derived from RNA-seq analysis comparing whole tissue from wild-type (*Villin1-Cre*^{ERT2}) and APC intestines (*Villin1-Cre*^{ERT2} *Apc*$^{fl/fl}$). $n = 3$ biologically independent animals for both APC and WT intestinal tissue. Log_2



(. 4). E - *Vil-CreER^{T2} Apc$^{fl/fl}$* _ *Vil-CreER^{T2} Apc$^{fl/fl}$ Vav2$^{-/-}$ Vav3$^{-/-}$ Tiam1$^{-/-}$* (2 3), F _ 2, 3 _ 1 F - _ (F . 4). E fi F . fi F F F E F E fi F _ fi _ (_ F) _ F 1 fi F _ (. 3 _ 4 ,). E fi (2 3) _ _ *Lgr5*, *Olfm4* _ F _ (. 4 _ - F . 7). F E , (2 3), F - 1 E

Fig. 4 Lo of ree GEF i able o ppre he lo of *Apc* pheno pe. a RNAscope staining for 2 in intestine from T2 fl/

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Vav3$^{-/-}$ *Tiam1$^{-/-}$*
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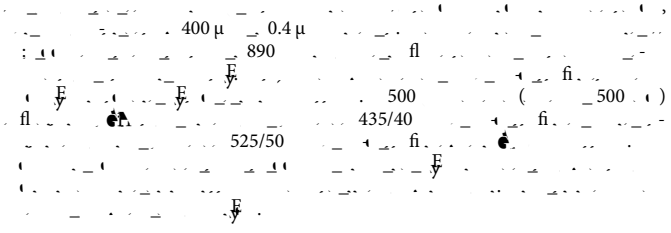
Vil-Cre^{ERT2} *Apc$^{fl/fl}$* *Kras$^{G12D/+}$* (. 6).
, 6

E- _ _ (24E10, 1:200; _ _ _ _#3195)[69], 9 (1:500; -
; _# 5535), β- _ (1:50; ; _#610154)[70], 44 (1:100;
; _# 550538)[71], (1:100; _ 6463);[13] 2 (1:200;



FLIM-FRET. *Vil-CreER* ^{2} *Apc*$^{fl/fl}$ *Vil-CreER*^{T2} *Apc*$^{fl/fl}$ *Vav2*$^{-/-}$ *Vav3*$^{-/-}$ *Tiam1*$^{-/-}$

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