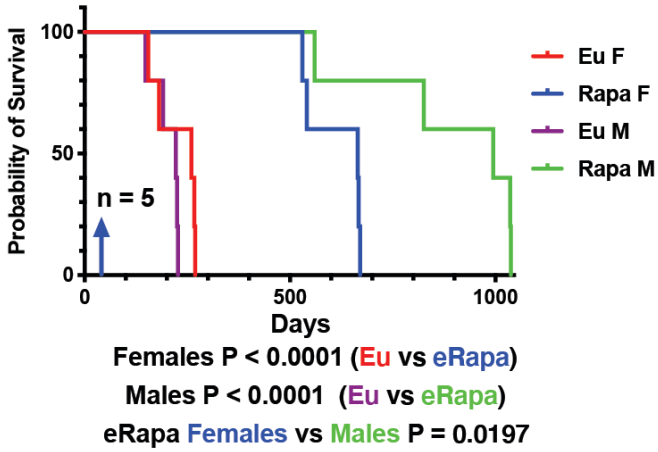

Figure 1. *Chronic rapamycin extends longevity of male Apc$^{Min/+}$ mice greater than females.* Blue arrow indicates the start of eRapa 42 ppm and control (Eudragit) diets at 4 weeks of age. Life span statistics for the groups was the Log-rank (Mantel-Cox) test. P values are below the graph.

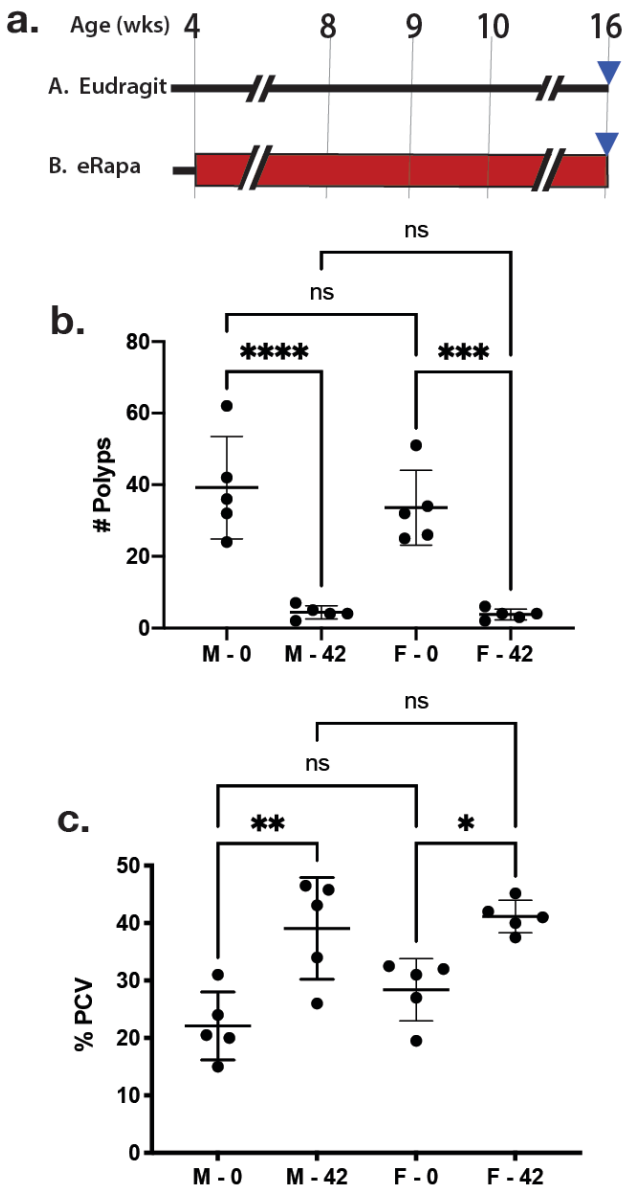

Figure 2. *Rapamycin reduces small intestine polyposis in female and male Apc$^{Min/+}$ mice.* **a)** Experimental design for cross-section experiments. Red rectangle indicates rapamycin treatment period. Blue triangles indicate the age at which we collected tissues. **b)** Graphs of the number of polyps for females (F) and males (M) on the indicated diets (0 or 42 ppm eRapa). **c)** Rapamycin prevents anemia in *female and male Apc$^{Min/+}$ mice. PCV = packed cell volume*. Graphs showing packed cell volume (PCV) percentages for females and males on the indicated diets. * P≤0.05, ** P≤0.01, *** P≤0.001, **** P≤0.0001

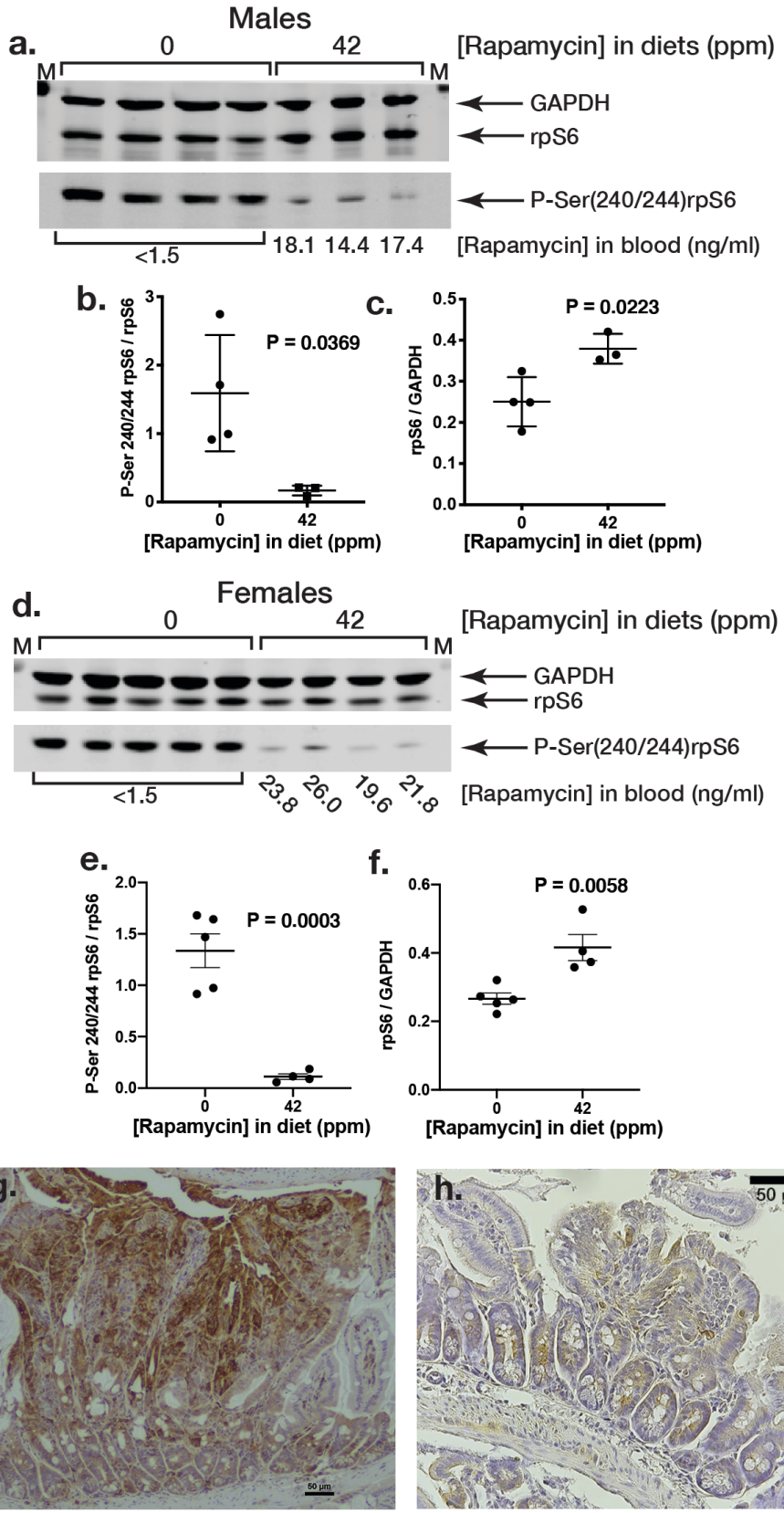
Males
a.
0
42
[Rapamycin] in diets (ppm)
M
M
GAPDH
rpS6
P-Ser(240/244)rpS6
<1.5
18.1 14.4 17.4
[Rapamycin] in blood (ng/ml)
b.
P-Ser 240/244 rpS6 / rpS6
P = 0.0369
[Rapamycin] in diet (ppm)
c.
rpS6 / GAPDH
P = 0.0223
[Rapamycin] in diet (ppm)
Females
d.
0
42
[Rapamycin] in diets (ppm)
M
M
GAPDH
rpS6
P-Ser(240/244)rpS6
<1.5
23.8
26.0
19.6
21.8
[Rapamycin] in blood (ng/ml)
e.
P-Ser 240/244 rpS6 / rpS6
P = 0.0003
[Rapamycin] in diet (ppm)
f.
rpS6 / GAPDH
P = 0.0058
[Rapamycin] in diet (ppm)
g.
h.
50 µm

Figure 3. *eRapa effects on mTORC1.* Representative immunoblot assay of small intestine lysates prepared from *Apc*$^{Min/+}$ male **(a)** and female **(d)** mice respectively. Diets indicated above the blots, antibodies to the left of each lane, and rapamycin concentrations in blood below. Graphs show the quantification of the immunoblot data as measured by the ratio of the intensity values for phosphorylation state-dependent signal (P(240/244)rpS6) to phosphorylation state–independent (rpS6) signal (**b** and **e**) and rpS6 intensity values relative to GAPDH (**c** and **f**). Phosphorylated rpS6 expression in small intestine of control (**g**) and eRapa treated (**h**) mice, bars represent 50μm.

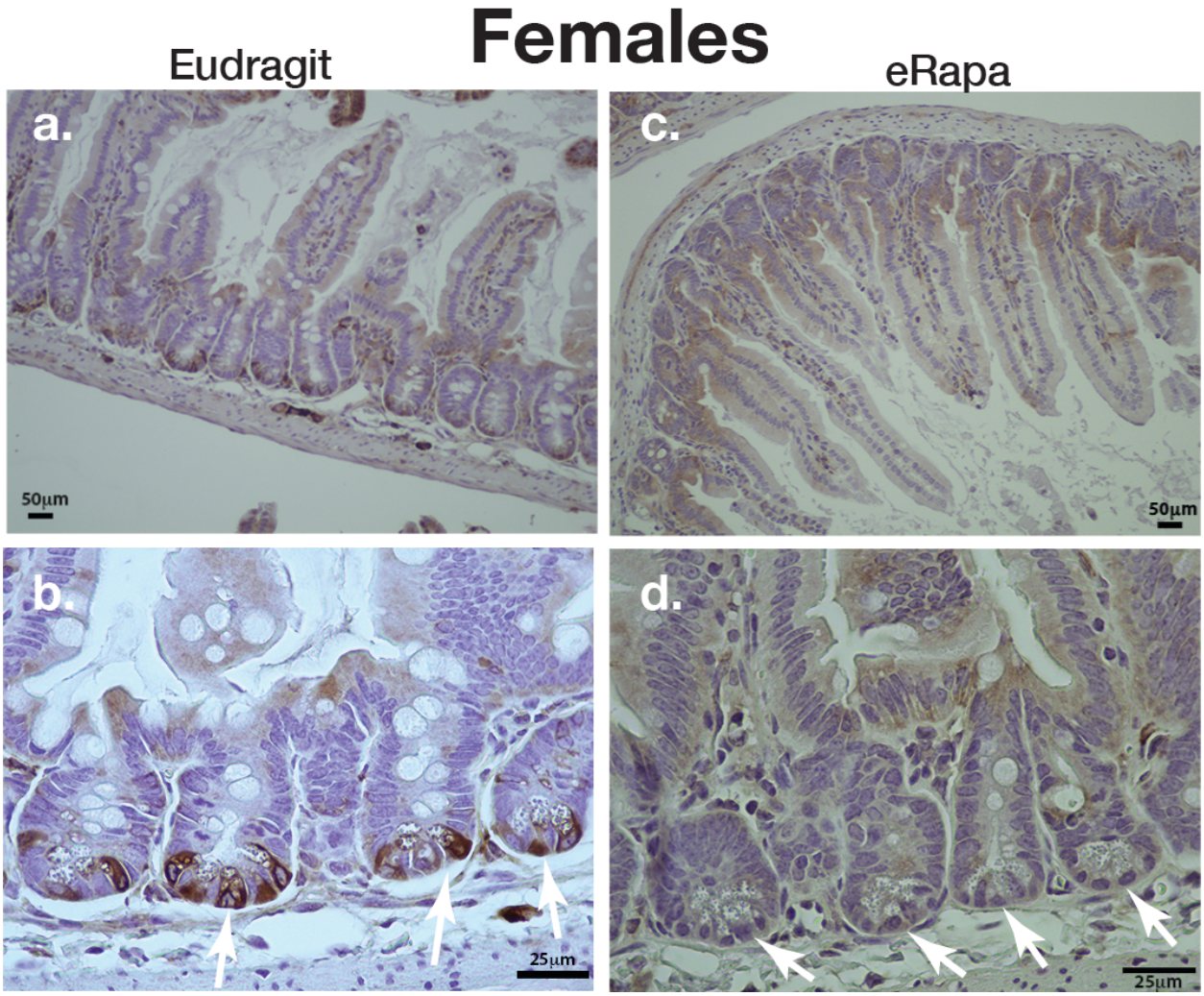

Figure 4. *Chronic eRapa represses mTORC1 activity in female intestinal crypt niche primarily in Paneth cells*. **a and b**. Intestinal preparations from Eudragit fed females. Arrows in panel b point to prominent staining of crypt cells with an antibody specific for P-Ser(240/244)-rpS6. In eRapa fed specimens (**c and d**.), no signal is detected in the crypt niches (arrows in panel d). Panels a and c show lower magnification of villi and crypts in mice fed Eudragit and eRapa diets respectively.

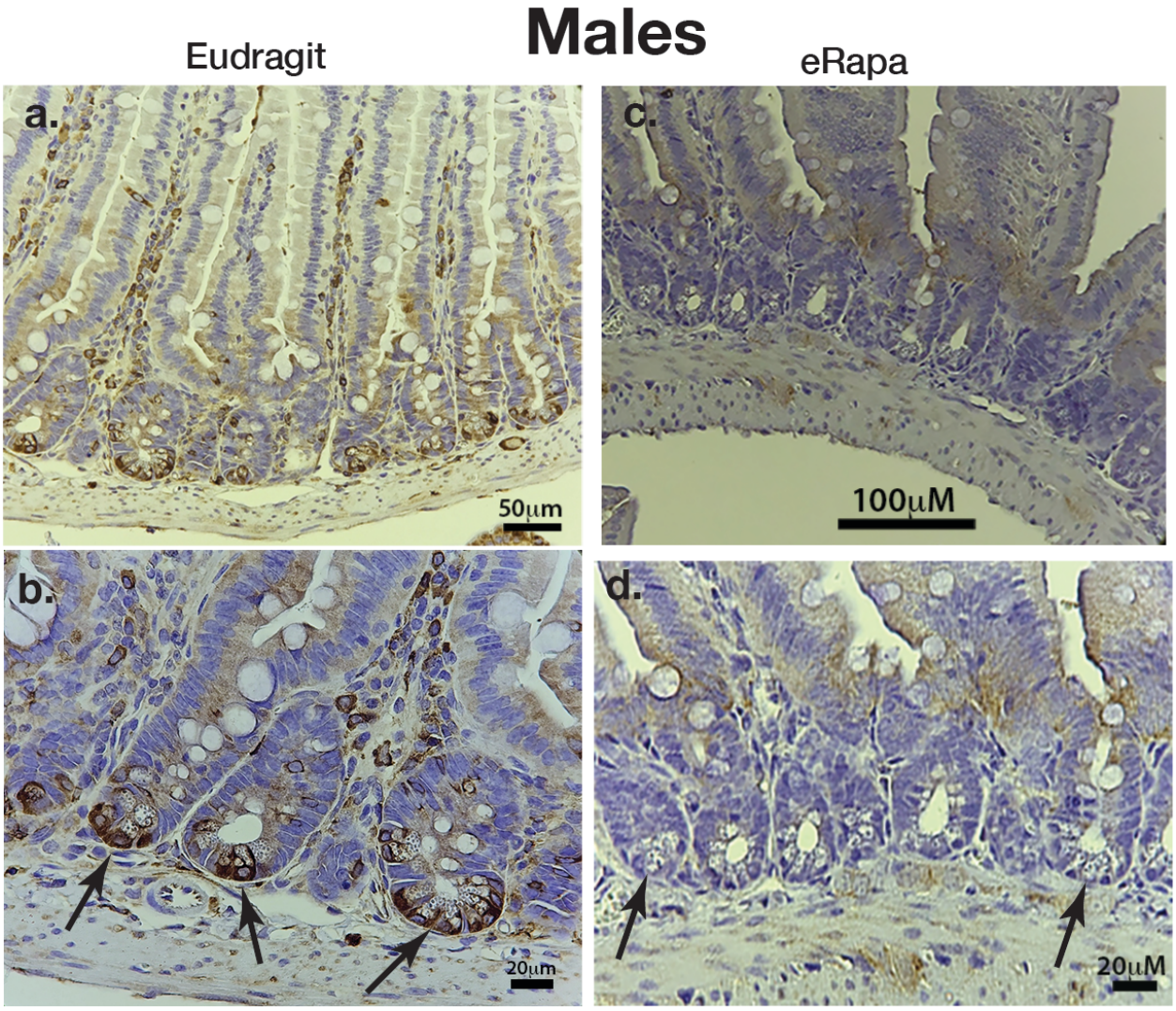

Figure 5. *Chronic eRapa represses mTORC1 activity in male intestinal crypt niche primarily in Paneth cells*. **a and b**. Intestinal preparations from Eudragit fed females. Arrows in panel b point to prominent staining of crypt cells with an antibody specific for P-Ser(240/244)-rpS6. In eRapa fed specimens (**c and d**.), no signal is detected in the crypt niches (arrows in panel d). Panels a and c show lower magnification of villi and crypts in mice fed Eudragit and eRapa diets respectively.

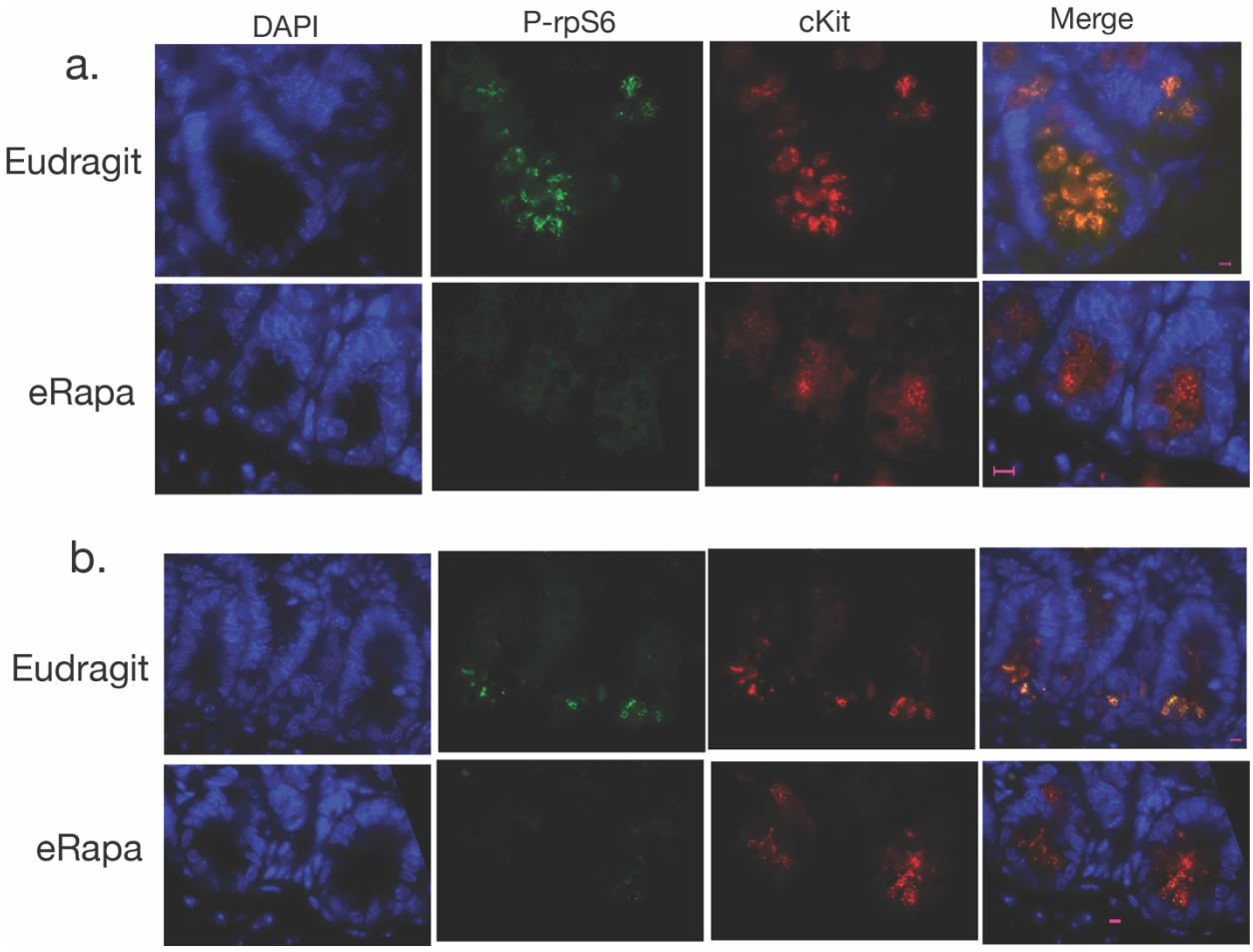

Figure 6. *Co-localization of cKit and reduced phosphorylated rpS6 by chronic rapamycin in intestinal crypts.* Panels a and b show results using tissue sections from females and males respectively, which were prepared from mice fed eRapa diets (42 ppm rapamycin) or Eudragit controls. DAPI identifies nuclei (blue). Antibodies specific for P-Ser(240/244)rpS6 are green and those specific for cKit are red. Magnification bars are 5 μM.

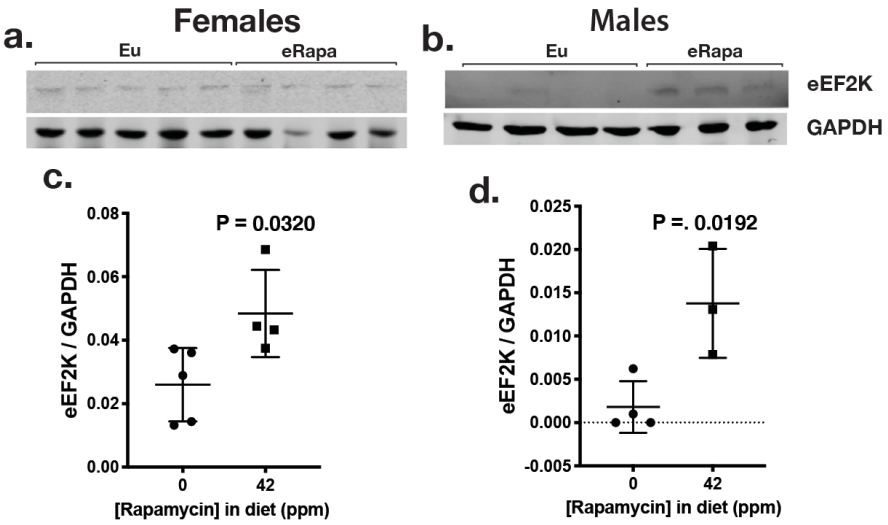

Figure 7. *eRapa effects on eukaryotic elongation factor 2 kinase (eEF2K).* Representative immunoblot assay of small intestine lysates prepared from *Apc*$^{Min/+}$ female **(a)** and mal **(b)** mice respectively. Diets indicated above the blots, antibodies to the right the lanes. Graphs showing the quantification of the immunoblot data as measured by the ratio of the intensity values for eEF2K signal relative to GAPDH signal (**c** and **d**).

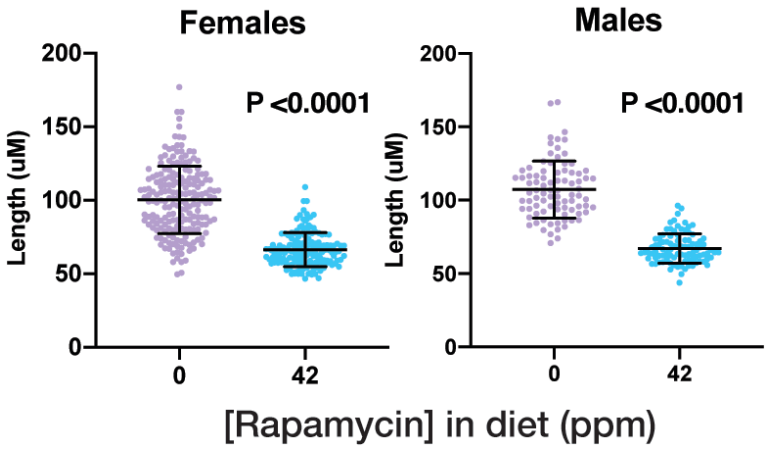

Figure 8. Rapamycin reduced crypt depths in female and male intestinal crypt measurements.