co-floxing the mTORC1 essential component Raptor. Translational status was assessed by sucrose gradient ultracentrifugation of intestinal epithelial extract from these mice and 35S methionine incorporation and harringtonine chase assays on organoid cultures. The role of downstream mTORC1 effectors was established by assessing the intestinal regeneration following IR irradiation of 4EBP1/2DKO, S6K1/2DKO, rpS6mut and eEF2k−/− mice. Survival studies for Apcfl/fl mice treated with rapamycin were performed both prior to, and on development of, symptoms

Results mTORC1 activity is absolutely required for the proliferation of Apc deficient, but not wild type, intestinal crypts. Surprisingly, although protein synthesis is increased in Apcfl/fl crypts, it is translation elongation and not initiation that is the rate limiting step. Mechanistically, the inhibition of eukaryotic elongation factor (eEF2) kinase, to increase eEF2 activity downstream of mTORC1 and S6K is required for Wnt-mediated proliferation after IR irradiation. Treatment of established Apcfl/fl adenomas with rapamycin (which inhibits the mTORC1-S6K-eEF2k-eEF2 axis) arrests tumour growth and prolongs life. Furthermore, rapamycin treatment of mice immediately following homozygous Apc loss prevents the onset of symptoms.

Conclusion These data show that intestinal adenoma formation and growth requires an mTOR mediated increase in translation elongation. Treatment of patients at high risk of developing CRC, such as those with Familial Adenomatous Polyposis, with Rapalogs may therefore be of therapeutic value.

Disclosure of Interest None Declared.