signalling, in regulating intestinal epithelial apoptosis in vivo have not previously been investigated.

**Aims** To assess susceptibility to intestinal apoptosis and the associated molecular changes in mice with germline deletions of three individual NfkB family members.

**Methods** Intestinal apoptosis was induced in male c-Rel-null, NfkB1-null and NfkB2-null mice and their wild-type (C57BL/6) counterparts by 8Gy γ-irradiation (n=6 per group). Apoptosis was assessed on a cell positional basis from H/E stained sections. The mRNA expression of 10 key apoptotic regulating genes in the small intestine and colon (TRAIL, Caspase12, BAK, FAS-L, FAS, p53, BCL2, BCL-XL, c-IAP2 and XIAP) was assessed by real time PCR (n=4 per group). Statistical comparisons were by ANOVA with Bonferroni post-hoc tests.

**Results** Basal small intestinal crypt apoptosis was significantly increased in NfkB2-null relative to C57BL/6 mice. In addition, small intestinal and colonic crypt apoptotic indices were both significantly increased (up to threefold) in NfkB1-null and NfkB2-null mice 4.5 h after 8Gy γ-irradiation relative to wild-type and c-Rel-null mice. Untreated NfkB1-null and NfkB2-null small intestine showed reduced mRNA expression of the anti-apoptotic genes BCL2, BCL-XL, c-IAP2 and XIAP. Following irradiation, NfkB1-null mice showed significant increases in the mRNA of the pro-apoptotic genes TRAIL, Caspase12 (in both small intestine and colon) and BAK (small intestine only) compared to wild-type mice. Significant increases in the mRNA of the pro-apoptotic genes Caspase12 and FAS-L were also seen in irradiated NfkB2-null small intestine and colon relative to wild-type mice.

**Conclusion** c-Rel expression does not appear to regulate susceptibility to intestinal epithelial apoptosis in vivo. NfkB1 and NfkB2 deletion both caused increased susceptibility to intestinal apoptosis and this was associated with altered expression of TRAIL, Caspase12, BAK and FAS-L. These NfkB family members may therefore also regulate the susceptibility of intestinal epithelia to other consequences of DNA damage such as cancer.

**Competing interests** None declared.

**REFERENCE**