Supplementary Material and Methods

Bioinformatics

Information relative to RBM47 sequence, A1CF sequence, Rbm47-wt locus and Rbm47-gt locus has been obtained from ENSEMBL [1] and Sanger sequencing. Protein alignment has been done using method from Pearson et al. [2]. Motif search has been done using PROSITE [3].

Secondary antibodies

Secondary antibodies conjugated to peroxidase or Alexa Fluor 594 are specific for Immunoglobulins (Ig) from: rabbit (Jackson Immunoresearch laboratories, 711-035-152; Invitrogen, A21207), mouse (Jackson Immunoresearch laboratories, 715-035-150) and goat (Jackson Immunoresearch laboratories, 705-035-003; Invitrogen, A11058).

Molecular cloning and plasmids

We obtained mouse Rbm47 cDNA from the I.M.A.G.E. Consortium (Clone ID # 4240441) [4]. Plasmids pNF-4 (pCMV-Rbm47) and pNF-63: Mouse Rbm47 coding sequence (CDS) was amplified by PCR from I.M.A.G.E. clone with primers NF32.1 and NF40.1 (See supplementary Table S1) and cloned between SalI and NotI restriction sites in pCMV-SPORT6 plasmid (I.M.A.G.E.) and pET-28b plasmid (Novagen) respectively. pNF-40 (pCMV-Rbm47-HA) and pNF-41 (pCMV-Rbm47-GFP): Human RBM47 CDS without stop codon was amplified from HEK 293 T cells cDNA with NF32.3 and NF29.1 and cloned between KpnI and XbaI in pCMV-SPORT6 in frame with respectively HA Tag CDS (NF36.1 and NF36.2) or muGFP (amplified from pCMX-GFP plasmid [5] with NF31.2 and NF32.4) cloned between XbaI and Xhol. pNF-20 (pCMV-ΔRRM-Rbm47-HA): Second half of human RBM47 CDS (bp #970 to bp #1779) was amplified from pNF-40 with NF34.4 and NF29.1 and cloned between KpnI and Xbal in pCMV-SPORT6 in frame with HA Tag CDS (NF36.1 and NF36.2) cloned between Xbal and Xhol. pNF-45 (pCMV-3RRM-Rbm47-HA): First half of human RBM47 CDS (bp #1 to bp #969) was amplified from pNF40 with NF32.3 and NF28.3 and cloned between KpnI and Xbal in pCMV-SPORT6 in frame with
HA Tag CDS (NF36.1 and NF36.2) cloned between XbaI and XhoI. pNF-95 (pCMV-Apobec1-FLAG):
Human APOBEC1 CDS in frame with FLAG Tag CDS in 3’ was amplified from small intestine cDNA
(RNA from Clontech) with NF31.8 and NF57.1 and cloned between Sall and NotI in pCMV-SPORT6.

pNF-140 (pCMV-Apobec1-V5): Human APOBEC1 CDS in frame with V5 Tag CDS in 3’ was amplified
from pNF-95 with NF31.8 and NF75.3 and cloned between Sall and NotI in pCMV-SPORT6. pNF-88
(pCMV-A1cf-V5): Human A1CF CDS in frame with V5 Tag CDS in 3’ was amplified from Caco-2 cells
cDNA with NF33.6 and NF75.2 and cloned between Sall and NotI in pCMV-SPORT6. pNF-153
(pGADT7-Rbm47): Human RBM47 CDS was amplified from pNF-40 with NF49.2 and NF50.6, cloned in
the intermediate pDONR 221 plasmid (Invitrogen) by BP recombination then in pGADT7-Gateway [6]
by LR recombination. pNF-154 (pGADT7-ΔRRM-Rbm47): Second half of human RBM47 CDS (bp #970
to bp #1779) was amplified from pNF-40 with NF50.7 and NF50.6, cloned in pDONR 221 by BP
recombination then in pGADT7-Gateway by LR recombination. pNF-155 (pGADT7-3RRM-Rbm47):
First half of human RBM47 CDS (bp #1 to bp #969) was amplified from pNF40 with NF49.2 and
NF49.4, cloned in pDONR 221 by BP recombination then in pGADT7-Gateway by LR recombination.

pNF-151 (pGBK7-Apobec1): Human APOBEC1 CDS was amplified from pNF-95 with NF51.1 and
NF50.8, cloned in pDONR 221 by BP recombination then in pGBK7-Gateway [6] by LR
recombination. pNF-152 (pGBK7-A1cf): Human A1CF CDS was amplified from pNF-88 with NF52.3
and NF50.9, cloned in pDONR 221 by BP recombination then in pGBK7-Gateway by LR
recombination. pNF-5: muGFP was amplified from pCMX-GFP plasmid [5] with NF34.1 and NF32.2
and cloned between Sall and XbaI in pCMV-SPORT6. pNF-90: Mouse Apobec1 CDS was amplified
from intestine cDNA with NF32.11 and NF32.12 and cloned between Sall and NotI in pET-28b. pNF-
89: Mouse A1cf CDS was amplified from intestine cDNA with NF35.3 and NF33.7 and cloned
between Sall and NotI in pET-28b. pNF-104 (pCMV-Apob): A fragment 469 base-pair-long of mouse
Apob CDS containing C 6666 was amplified from genomic DNA with NF30.10 and NF29.8 and cloned
between Sall and NotI in pCMV-SPORT6. pNF-1: A 594 bp fragment of Rbm47 cDNA was cut at KpnI
and BamHI from I.M.A.G.E. clone and inserted into pBlueScript SK(-) using same restriction sites.
pNF-2: A 996 bp fragment of Rbm47 cDNA was cut at EcoRV and NotI from I.M.A.G.E. clone and inserted into pBlueScript SK(-) using same restriction sites. The sequence of the cloned fragments obtained by PCR was verified by Sanger sequencing before experiments.

Isolation of epithelial cells from the small intestine

The small intestine of an adult mouse was collected, washed, everted and cut into pieces 5 cm-long in Hank's balanced salt solution (HBSS; with Ca$^{2+}$ and Mg$^{2+}$). The pieces were washed five times 10 s in 50 mL HBSS (with Ca$^{2+}$ and Mg$^{2+}$) containing 1% foetal calf serum, then once 10 s in 50 mL HBSS (without Ca$^{2+}$ and Mg$^{2+}$) containing 2% glucose and 2% bovine serum albumin. The pieces where then incubated 30 min at 37°C under moderate shaking in 25 mL pre-warmed isolation buffer (HBSS [without Ca$^{2+}$ and Mg$^{2+}$], Edetic Acid [EDTA] 1.5 mM, Dithiothreitol [DTT] 0.5 mM). The pieces were then removed and the epithelial cells in suspension pelleted by centrifugation at 1000 g for 5 min at 4°C. The pellet of epithelial cells was used for RNA extraction or protein immunoprecipitation experiments.

Production and purification of recombinant proteins

Prokaryotic expression plasmids pNF-63 (His$_6$-RBM47), pNF-89 (His$_6$-A1CF) or pNF-90 (His$_6$-Apobec1) were transfected in BL21 (DE3) Escherichia coli bacteria (Invitrogen; Bioline). Bacteria were grown at 37°C in 500 mL Luria Broth (LB) media with 10 µg.mL$^{-1}$ kanamycin until the optical density measured at a wavelength of 600 nm was 0.6-0.7. Temperature was then changed to 25°C. 30 min later, Isopropyl β-D-1-thiogalactopyranoside (IPTG) was added to the media at a final concentration of 0.5 nM. Bacteria were collected by centrifugation 4 h later.

Recombinant proteins were purified at 4°C. Bacteria were resuspended in 15 mL lysis buffer (Phosphate Buffer Saline [PBS] 2X, glycerol 10%, imidazole 50 mM, NaCl 500 mM, DTT 1 mM, Complete protease inhibitor [Roche] 1X) and sonicated for 1 min. Triton X-100 was added at a final concentration of 1%. Lysate was rotated for 30 min and centrifuged at 12000 g for 30 min.
Supernatant was collected and rotated with 250 µL of Nickel-Nitroacetic acid (Ni-NTA) agarose beads (Qiagen) for 1 h. Beads were then loaded on column (Biorad). Column was washed three times with wash buffer (PBS 2X, Triton X-100 1%, imidazole 50 mM, NaCl 500 mM, DTT 1 mM, Complete protease inhibitor [Roche] 1X) before the recombinant protein was eluted with elution buffer (PBS 2X, Triton X-100 0.1%, imidazole 200 mM, NaCl 500 mM, DTT 1 mM, Complete protease inhibitor [Roche] 1X) in 10 fractions of 0.5 mL each. Quantity and purity of the recombinant protein in each fraction was assessed by SDS polyacrylamide gel electrophoresis (PAGE) and coomassie staining. The best fractions were pooled and the recombinant protein was transferred in the buffer for in vitro editing assay overnight by dialysis. Recombinant protein was then concentrated using Amicon Ultra-4 concentrators (Millipore) as specified by manufacturer. Final concentration was measured using bicinchoninic acid (BCA) protein assay kit (Pierce). Purified protein was visualised by SDS-PAGE (NuPAGE 4-12 % bisacrylamide gel, Novex) followed by coomassie staining or western blot analysis with anti-RBM47 (1:100), anti-A1CF (1:500) or anti-Apobec1 (1:200) antibody according to standard protocols. Aliquots were kept at -80°C.

CLIP

Caco-2 cells (five 10 cm dishes, 90-95% density) were exposed to Ultra Violet (UV; 100mJ.cm−2) light which generates covalent bounds (Cross-link) between RNA binding proteins and the RNA molecules they interact with. Following UV-cross linking, Caco-2 cells were scrapped and centrifuged at 15000 g for 1 min at 4°C. For “No Cross-link” control, the same quantity of cells were scrapped and centrifuged but not exposed to UV beforehand. Cell pellet was then resuspended and rotated for 30 min at 4°C in 1 mL lysis buffer (Tris-HCl pH 7.4 50 mM, NaCl 100 mM, MgCl2 1 mM, CaCl2 0.1 mM, NP-40 1%, SDS 0.1%, Sodium Deoxycholate 0.5%, protease inhibitor cocktail set III [Calbiochem] 1%, Anti-RNase 20 U.mL−1). RNA was partially digested by adding 20 U of RNase I (Ambion) to the mix. 10 U of Turbo-DNase (Ambion) was also added and the blend was incubated for 3 min at 37°C with moderate shaking (1000 rpm in thermomixer, eppendorf). Cell lysate was then centrifuged at 18000
g for 10 min at 4°C. Supernatant was collected and rotated for 2 h at 4°C with 50 µL beads pre-coated with antibody: 50 µL protein G dynabeads (Invitrogen) had been washed twice with 1 mL lysis buffer then resuspended and rotated in 200 µL lysis buffer with 10 µg anti-RBM47 antibody for 1 h at room temperature before to be washed again twice with 1 mL lysis buffer and finally be resuspended in 50 µL lysis buffer. For “non-specific” control, the beads were incubated with 10 µg anti-GFP antibody while for “hnRNPC1/C2” control, they were incubated with 10 µg hnRNPC1/C2 antibody. After incubation with the lysate, the beads were washed twice with 1 mL high salt buffer (Tris-HCl pH 7.4 50 mM, NaCl 1 M, EDTA 1 mM, SDS 0.1%, Sodium Deoxycholate 0.5%, NP-40 1%), once with 1 mL PNK1 buffer (Tris-HCl pH 7.4 20 mM, MgCl\(_2\) 10 mM, Tween-20 0.2%) and once with 50 µL PNK2 buffer (T4 Polynucleotide kinase [PNK] buffer 1X [New England biolabs], Tween-20 0.1%) before to be incubated in 8 µL PNK mix (T4 PNK buffer 1X [New England biolabs], T4 PNK 1 U [New England biolabs], \(^{32}\)P-\(\gamma\)-ATP 5 pmol, Tween-20 0.1%), for 3 min at 37°C with moderate shaking to radiolabel RNA. Beads were then isolated with magnetic stand and resuspended and incubated in 20 µL LDS sample buffer 1X (NuPAGE) for 10 min at 70°C with moderate shaking. Eluate was collected, run on SDS-PAGE (NuPAGE 4-12 % bisacrylamide gel, Novex) and transferred on membrane according to standard protocol. Membrane was exposed with X-ray film to detect radioactivity.

Protein Immunofluorescence

For the analysis of exogenous protein localisation, Caco-2 or 3T3 cells were transfected 48 h before immunostaining using Lipofectamine LTX (Invitrogen) according to manufacturer instructions with the following combinations of plasmids: pNF-41 (pCMV-Rbm47-GFP) only, pNF-41 + pNF-95 (pCMV-Apobec1-FLAG) or pNF-41 + pNF-88 (pCMV-A1cf-V5).

Cells were washed twice 5 min with PBS, incubated 5 min in paraformaldehyde (PFA) 4% with Triton X-100 0.5% then 25 min in PFA 4% at room temperature. After fixation, cells were washed three times 5 min with PBS, incubated 15 min at room temperature with CAS-Block (Invitrogen) then overnight at 4°C with anti-RBM47 (1:50), anti-FLAG (1:1000) or anti-V5 (1:1000) antibody diluted in
CAS-Block. The day after, cells were washed three times 5 min with PBS and incubated 40 min at room temperature with Alexa Fluor 594 anti-rabbit or anti-goat Ig antibody (1:400) and 4',6-diamidino-2-phenylindole (DAPI; Sigma-Aldrich; 1:1000) diluted in CAS-Block. Cells were finally washed four times 5 min with PBS at room temperature before to be embedded in Fluoromount-G (Invitrogen) for confocal microscopy analysis.

**Protein Immunoprecipitation**

For the analysis of exogenous protein interaction, Caco-2 cells (10 cm dish, 60-70% density) were transfected 48 h before immunoprecipitation experiment using Lipofectamine LTX (Invitrogen) with the following equimolar (5 µg each) combinations of plasmids: pNF-40 (pCMV-Rbm47-HA) + pNF-140 (pCMV-Apobec1-V5), pNF-20 (pCMV-ΔRRM-Rbm47-HA) + pNF-140, pNF-45 (pCMV-3RRM-Rbm47-HA) + pNF-140, pNF-40 + pNF-88 (pCMV-A1cf-V5), pNF-20 + pNF-88 or pNF-45 + pNF-88.

For Caco-2, cells were washed with PBS, collected by scraping in PBS and spined down at 1000 g for 5 min at 4°C.

Cell pellet (from one 10cm dish of Caco-2 cells at 80-90% density or from one quarter of the epithelial cells isolated from one adult mouse) was resuspended and rotated in 0.5 mL lysis buffer (Hepes-KOH pH 7.9 20 mM, KCl 150 mM, MgCl₂ 2 mM, Triton X-100 0.1%, Glycerol 10%, DTT 1 mM, Complete protease inhibitor [Roche] 1X) for 30 min then centrifuged at 15000 g for 10 min at 4°C. 10 μL of the supernatant was saved for “input” control. The rest of the supernatant was rotated with 2 μg anti-RBM47, anti-HA tag, anti-V5 tag or anti-A1CF antibody for 30 min at 4°C. For “non-specific IgG” control, supernatant was incubated with 2 μg anti-GFP antibody. 50 μL of protein-G agarose beads (Roche) was then added and the sample rotated for 2 h at 4°C. The slurry was loaded on Illustra MicroSpin column (GE Healthcare) and washed with 10 mL washing buffer (Hepes-KOH pH 7.9 20 mM, KCl 150 mM, MgCl₂ 2 mM, Triton X-100 1%, Glycerol 10%, DTT 1 mM, Complete protease inhibitor [Roche] 1X) before to be resuspended on the column in 20 μl of SDS-PAGE buffer 2X (Tris...
pH 6.8, 8mM, SDS 0.8%, Glycerol 4%, 2-mercaptoethanol 2%, Bromophenol blue 0.1%) and incubated for 10 min at 90°C. The column was then spined down at 15000 g for 1 min. Half the eluate was loaded on SDS-PAGE with half the “input” controls for western blot analysis with anti-RBM47 (1:100), anti-HA tag (1:1000), anti-V5 tag (1:1000) or anti-A1CF (1:200) antibody.

**Protein extraction**

For extraction of the whole cell content, pellet of cells or organs collected from adult mice (60 days old) were lysed and rotated in RIPA buffer (PBS 1X, Triton X-100 1.5%, Igepal 1%, Sodium Deoxycholate 0.5%, SDS 0.1%, DTT 1 mM, Complete protease inhibitor [Roche] 1X) for 45 min at 4°C. Samples were then centrifuged at 15000 g for 10 min at 4°C and supernatant collected for western blot analysis.

For independent extraction of the cytoplasmic and the nuclear content, Caco-2 cells (10 cm dish, 90-95% density) were centrifuged at 1000 g for 5 min at 4°C. Cell pellet was resuspended in 300 µL buffer A (Hepes pH 7.9 10 mM, MgCl₂ 1.5 mM, KCl 10 mM, DTT 1 mM, Complete protease inhibitor [Roche] 1X) and incubated for 5 min at 4°C. Sample was homogenised and centrifuged at 228 g for 5 min at 4°C. Supernatant that contains proteins from the cytoplasm (the cytoplasmic fraction) was collected for western blot analysis while pellet composed of nuclei was resuspended in 200 µL S1 buffer (Sucrose 250 mM, MgCl₂ 10 mM, Complete protease inhibitor [Roche] 1X) and slowly layered over 200 µL S3 buffer (Sucrose 880 mM, MgCl₂ 0.5 mM, Complete protease inhibitor [Roche] 1X) before to be centrifuged at 2800 g for 10 min at 4°C. Nuclei Pellet was then resuspended in 60 µL RIPA buffer, sonicated and centrifuged at 2800 g for 10 min at 4°C. Supernatant that contains proteins from the nucleus (the nuclear fraction) was collected for western blot analysis.

For each extraction, protein concentration was measured using BCA protein assay kit (Pierce) or Direct Detect spectrometer (Millipore). 3 to 30 µg of proteins was loaded on SDS-PAGE and analysed by western blot according to standard protocol using anti-RBM47 (1:100), anti-PGK1 (1:500), anti-
Histone H3 (1:1000), anti-HA (1:1000), anti-V5 (1:1000), anti-FLAG (1:1000), anti-APOB (1:2000) or anti-α-tubulin (1:1000) antibody.

RIP

RIP was performed from Caco-2 cells (two 10 cm dishes; 90-95% density) with 10 µg anti-RBM47 antibody using Magna RIP Kit (Millipore) and according to manufacturer instructions. For “non-specific” control, 10 µg anti-GFP antibody was used.

After precipitation, RNA was reverse transcribed using SuperScript III First-Strand kit (Invitrogen). PCR was performed from 2 µL cDNA with Biomix Red (Bioline), primers NF19.89 and NF19.90 and following conditions: 94°C for 30 s, 60°C for 30 s, 72°C for 30 s for 30 cycles. The PCR product was run on 1% agarose gel according to standard protocol.

Yeast two-hybrid

Yeast *Saccharomyces cerevisiae* tester strain AH109 was transformed using a protocol adapted from Gietz and Woods [7] with the following combination of plasmids: pNF-153 (pGADT7-Rbm47) + pNF-151 (pGBK7-Apobec1), pNF-153 + pNF-152 (pGBK7-A1cf), pNF153 + pGBK7-Gateway, pNF-154 (pGADT7-ΔRRM-Rbm47) + pNF-151, pNF-154 + pNF-152, pNF154 + pGBK7-Gateway, pNF-155 (pGADT7-3RRM-Rbm47) + pNF-151, pNF-155 + pNF-152, pNF155 + pGBK7-Gateway, pNF-151 + pGADT7-Gateway or pNF-152 + pGADT7-Gateway. After transformation, yeasts were spread on SD/-Leu/-Trp plates (Bacteriological agar 20 g.L⁻¹, Yeast Nitrogen Base 1.7 g.L⁻¹, Ammonium Sulfate 5 g.L⁻¹, Glucose 2%, Adenine hemisulfate 20 mg.L⁻¹, L-histidine 20 mg.L⁻¹) and incubated for 5-6 days at 30°C until the colonies reached a diameter of 1-2 mm. Individual colonies were then picked for each condition of transformation and resuspended in 100 µL water. 5 µL of the suspension was spotted on SD/-Leu/-Trp plate and SD/-Leu/-Trp/-Ade/-His plate (Bacteriological agar 20 g.L⁻¹, Yeast Nitrogen Base 1.7 g.L⁻¹, Ammonium Sulfate 5 g.L⁻¹, Glucose 2%). Plates were incubated for 6 days at 30°C before the growth of the yeasts was assessed.
Editing experiments and primer extension assay

For the editing experiments in 3T3 cells, the cells (3.5 cm dish, 60-70% density) were transfected 48 h before RNA extraction with the following combinations and quantity of plasmids: pNF-104 (pCMV-Apob; 0.2 µg) + pNF-5 (pCMV-GFP; 3.6 µg), pNF-104 (0.2 µg) + pNF-5 (2.4 µg) + pNF-95 (pCMV-Apobec1-FLAG; 1.2 µg), pNF-104 (0.2 µg) + pNF-5 (2.4 µg) + pNF-88 (pCMV-A1cf-V5; 1.2 µg), pNF-104 (0.2 µg) + pNF-5 (2.4 µg) + pNF-40 (pCMV-Rbm47-HA; 1.2 µg), pNF-104 (0.2 µg) + pNF-5 (1.2 µg) + pNF-95 (1.2 µg) + pNF-40 (1.2 µg), pNF-104 (0.2 µg) + pNF-40 (pCMV-Rbm47-HA; 1.2 µg), pNF-104 (0.2 µg) + pNF-5 (1.2 µg) + pNF-40 (1.2 µg), pNF-104 (0.2 µg) + pNF-88 (1.2 µg) + pNF-95 (1.2 µg) + pNF-40 (1.2 µg), pNF-104 (0.2 µg) + pNF-5 (1.2 µg) + pNF-45 (pCMV-3RRM-Rbm47-HA; 1.2 µg).

For the editing experiments in vitro, a fragment 469 nucleotide-long of Apob RNA containing C 6666 was produced in vitro according to standard protocol with SP6 RNA polymerase (Roche) from pNF-104 plasmid linearised by NotI restriction enzyme. 10 fmol of the Apob RNA fragment was then incubated by itself or with the following combinations and quantity of purified recombinant proteins: APOBEC1 (36 nmol), A1CF (15 nmol), RBM47 (15 nmol), APOBEC1 (36 nmol) + A1CF (15 nmol), APOBEC1 (36 nmol) + RBM47 (15 nmol) or APOBEC1 (36 nmol) + A1CF (15 nmol) + RBM47 (15 nmol) in 20 µL editing buffer (Hepes pH 8.0 20 mM, KCl 100 mM, EDTA 40 mM, DTT 0.25 mM) for 3 h at 37°C.

The Apob RNA fragment from in vitro editing experiments was then purified according to standard protocol while RNA from transfected cells or mouse organs was extracted using RNeasy Mini Kit (Qiagen). RNA was reverse transcribed using SuperScript III First-Strand kit (Invitrogen). A 145 bp region of Apob that contains the editing site was amplified by PCR from 2 µL cDNA with Biomix Red (Bioline), primers NF21.28 and NF21.29 and the following conditions: 94°C for 30 s, 60°C for 30 s, 72°C for 30 s for 35 cycles. The PCR product was run on 1% agarose gel and purified with Wizard SV Gel and PCR Clean-Up System (Promega) for the primer extension assay.
For the primer extension assay, 150 ng of the purified 145 bp Apob PCR product was incubated with 0.5 ng NF35.2 primer (labelled beforehand with $^{32}$P according to standard protocol) in 7 µL annealing buffer (Tris-HCl pH 7.5 57 mM, MgCl$_2$ 28 mM, NaCl 71 mM) for 3 min at 94°C then for 1h at 42°C. Following incubation, 3 µL extension mix (Sequenase V2.0 [Affymetrix] 1.5 U, dTTP [Affymetrix] 0.33 mM, dCTP [Affymetrix] 0.33 mM, dATP [Affymetrix] 0.33 mM, ddGTP [Biolog] 0.83 mM, DTT 333 mM) was added to the annealing buffer and the blend was incubated for 10 min at 42°C. Reaction was terminated by the addition of 10 µL loading buffer (formamide 95%, EDTA 20 mM, Bromophemol blue 0.05%, xylene cyanol 0.05%) and incubation for 5 min at 94°C. Samples were loaded on 15% acrylamide TBE-Urea gel (Invitrogen). After migration, gel was dried and exposed with phosphor-screen to detect radioactivity.

**Rbm47 gene trap mutant mouse**

The modified ES cell line contained a *Rbm47* allele, referred as *Rbm47*$_{gt}$ allele, that had been randomly targeted by a Gene Trap (GT) cassette. Among other features, the GT cassette was composed of an adenoviral splice acceptor (AdSA) followed by a βGeo (LacZ + Neo) coding sequence and a bovine growth hormone polyadenylation (bgHPA) signal. The GT cassette had inserted downstream of the eight transcription start sites reported in databases and upstream of the first coding exon of *Rbm47* ([supplementary Fig S4A](#)). While transcribing the *Rbm47* locus, the RNA polymerase is stopped by the exogenous bovine bgHPA signal before it can reach the *Rbm47* coding exons, which consequently prevents the production of RBM47 protein. Conversely, because of the AdSA, βGeo which activity can be detected by 5-bromo-4-chloro-3-indolyl-β-D-galactopyranoside (X-Gal) staining, is expressed in lieu of *Rbm47*.

*Rbm47* wild type and mutant mice were collected at different ages. For embryonic stage, the day of vaginal plug was taken at E0.5. Genotyping by PCR was done on genomic DNA extracted from tail tissues of adult mice or the yolk sac of embryos with Biomix Red (Bioline), primers NF19.20, NF18.13
and NF21.10 and the following conditions: 94°C for 30 s, 60°C for 30 s, 72°C for 30 s for 35 cycles. The PCR product was visualised on 2% agarose gel.

**In situ hybridisation**

For whole mount in situ hybridisation, two different Rbm47 RNA antisense probes showing the same results were used: A 594 nucleotide probe produced with T3 RNA polymerase (Roche) from pNF-1 plasmid linearised by KpnI restriction enzyme and a 996 nucleotide probe produced with T3 RNA polymerase (Roche) from pNF-2 linearised by EcoRV. Two equivalent Rbm47 RNA sense probes were used as controls: A 594 nucleotide probe produced with T7 RNA polymerase (Roche) from pNF-1 linearised by BamHI and a 996 nucleotide probe produced with T7 RNA polymerase (Roche) from pNF-2 linearised by NotI. Probes were synthesized in vitro according to standard protocol.

**RT-PCR**

For non-quantitative PCR, experiment was performed from cDNA with Biomix Red (Bioline) and the following conditions: 94°C for 30 s, 60°C for 30 s, 72°C for 30 s for 30 cycles. Primers used were NF19.11 and NF18.9 for human RBM47, NF20.287 and NF20.288 for human APOBEC1, NF20.289 and NF20.290 for human A1CF, NF18.14 and NF19.33 for human POLR2A, NF18.13 and NF19.6 or NF19.12 and NF19.13 for mouse Rbm47, NF20.102 and NF20.103 for mouse Apobec1, NF19.95 and NF20.104 for mouse A1cf, NF18.11 and NF19.15 for mouse β-Actin and NF18.3 and NF19.21 for chimeric Rbm47-βGeo. The PCR product was visualised on 1% agarose gel.

For quantitative PCR, cDNA was generated from the small intestine of three independent mice of each genotype and same age (60 days old). Real time PCR was performed in triplicate from 1:5 dilution of cDNA of each mouse using the Rotorgene 6000 thermal cycler (Corbett Research), SYBR Green I (Molecular probes) and Platinum Taq DNA polymerase (Invitrogen). Primers used were NF18.11 and NF19.15 for β-Actin, NF20.95 and NF20.96 for Apob, NF21.19 and NF20.90 for edited Apob, NF21.17 and NF20.129 for Sult1d1, NF23.8 and NF19.110 for edited Sult1d1, NF20.128 and NF19.109 for
Serinc1, NF23.7 and NF20.127 for edited Serinc1, NF19.108 and NF20.126 for Casp6, NF23.6 and NF19.107 for edited Casp6, NF20.124 and NF20.125 for 2010106e10Rik, NF23.5 and NF21.26 for edited 2010106e10Rik. Conditions were similar for all the PCR: 94°C for 30 s, 60°C for 30 s, 72°C for 20 s for 40 cycles. The fluorescence was read at the end of every cycle. We checked that only the fragment of interest had been amplified by plotting a melting curve at the end of every run.

Supplementary references