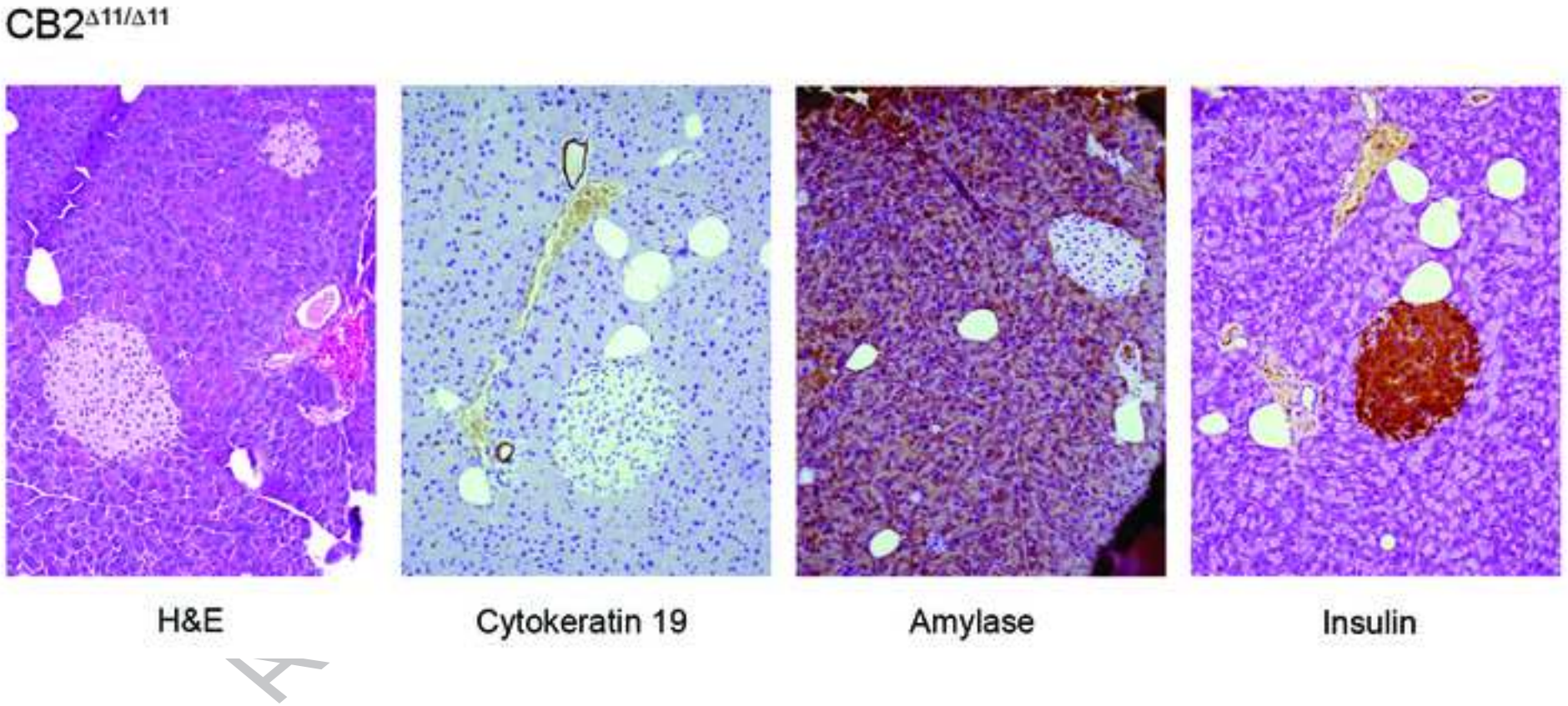
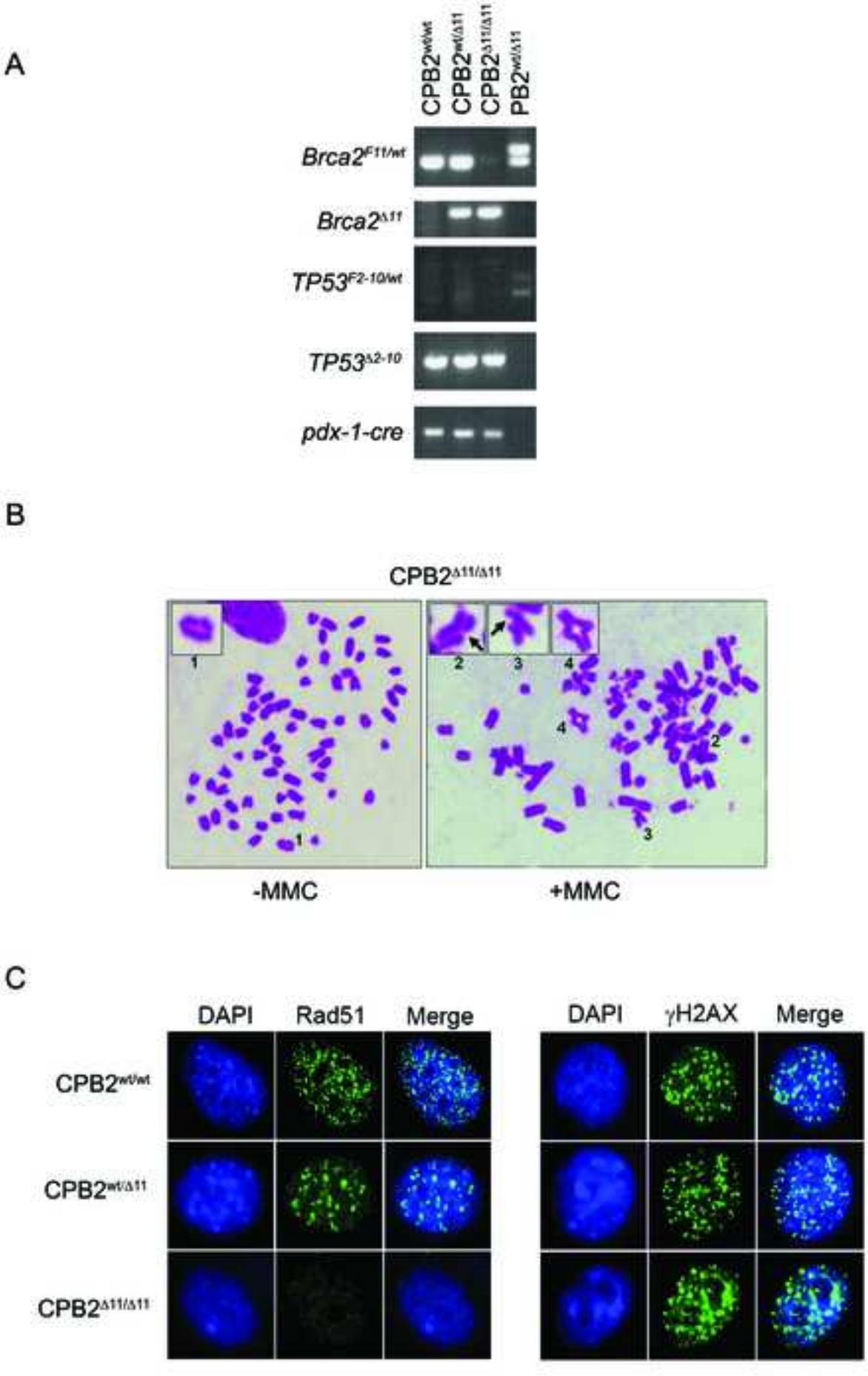
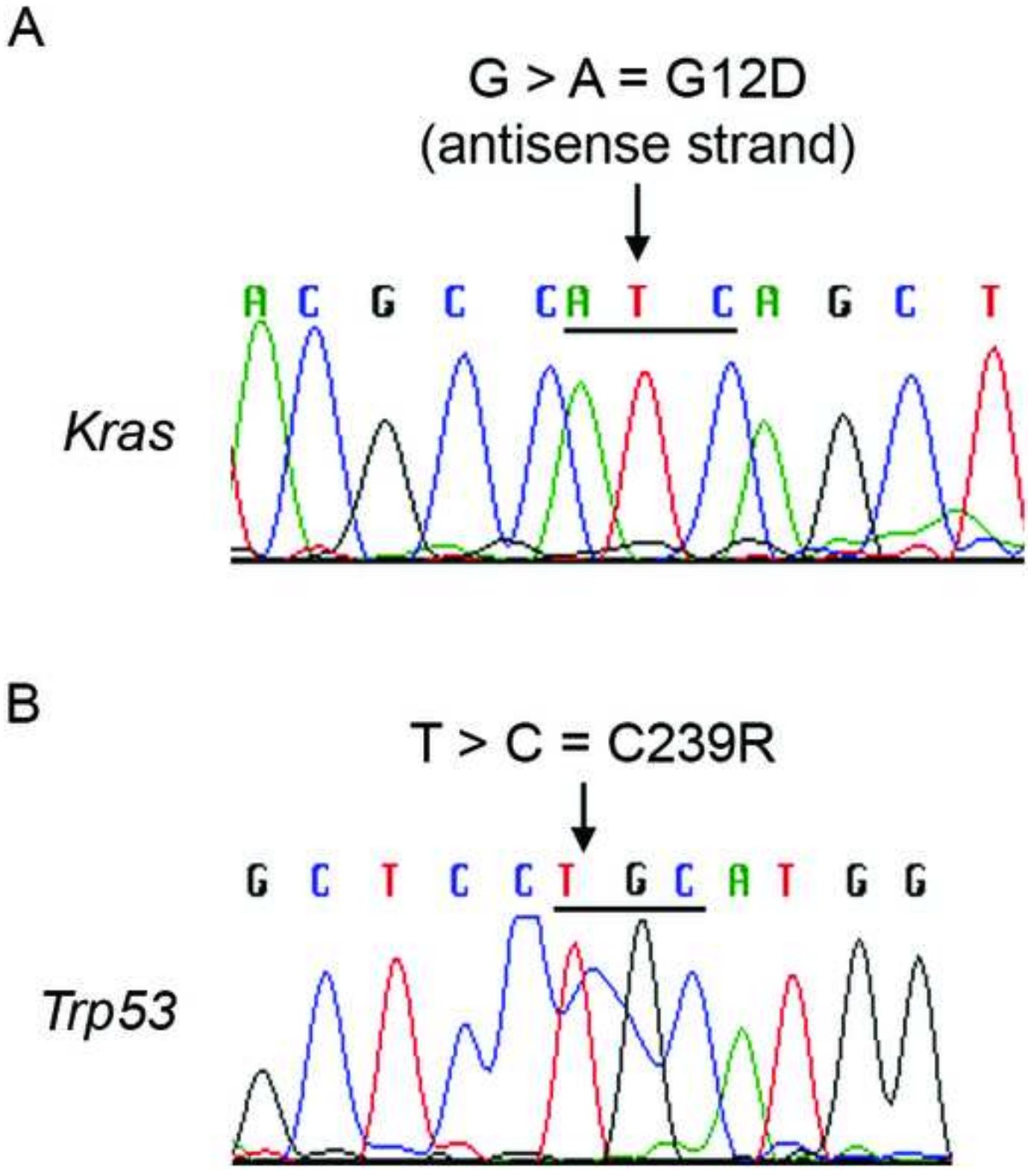
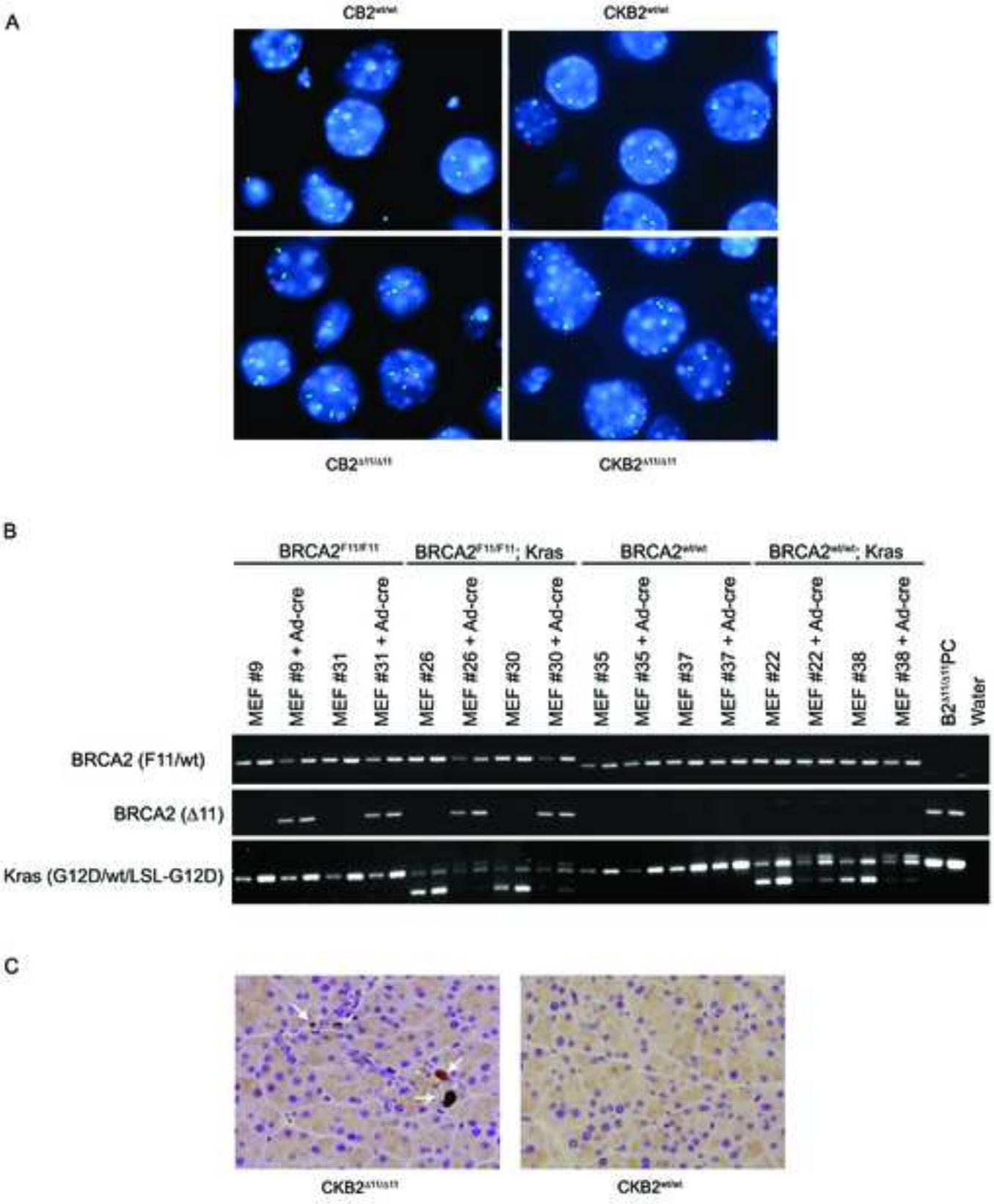
Figure S1









Supplemental information

Genotyping Primers:

BRCA2F: GGCTGTCTTAGAACTTAGGCTG

BRCA2R: CTCCACACATACATCATGTGTC

KrasF: AGCTAGCCACCATGGCTTGAGTAAGTCTGCA

KrasR: CCTTTACAAGCGCACGCAGACTGTAGA

Cre 5': AGATGTTCGCGATTATCTTC

Cre 3': AGCTACACCAGAGACGG

p53F: AAGGGGTATGAGGGACAAGG

p53R: GAAGACAGAAAAGGGGAGGG

Antibodies used for immunofluorescence:

BRCA2: polyclonal antibody against the N-terminus of human BRCA2

CEP-55: polyclonal antibody against the C-Terminus of CEP55

CHMP1B: Novus Biologicals

Endobrevin: Gift from T. Weimbs, Cleveland Clinic, OH

α-Tubulin: Sigma B512 monoclonal antibody

γ-H2AX and Rad51: Gifts from Junjie Chen. MD Anderson Cancer Center

Antibodies used for immunohistochemistry:

Cytokeratin 19 (TROMA-III): Developmental Studies Hybridoma Bank at University of Iowa

Amylase: Sigma

Insulin: DAKO

Cleaved caspase 3: Biocare Medical

p53: Novocastra NCL-p53-CM5p

Ki-67: Dako M7249

Shh: R&D Systems AF445

pERK: Cell Signaling Technologies 9101

Synaptophysin: Chemicon MAB5258

Hes1: Millipore AB5702

β-Catenin: Santa Cruz sc-7963

Kras mutation screen primers:

Kras12/13 F: AGGCCTGCTGAAAATGACTG

Kras12/13 R: ATTAGCTGTATCGTCAAGGC

Kras61 F: GTCTCTTGGATATTCTCGAC

Kras61 R: CCCTCCCCAGTTCTCATGTA

Supplemental Figure Legends

Figure S1. Aged CB2$^{\Delta 11/\Delta 11}$ mice show normal histology in the pancreas. (i) H&E, (ii) cytokeratin 19, (iii) amylase and (iv) insulin staining of a normal pancreas from a CB2$^{\Delta 11/\Delta 11}$ mouse.

Figure S2. Cell lines generated from CPB2$^{\Delta 11/\Delta 11}$ mice have a suppressed DNA damage repair response. (A) PCR analysis demonstrating rearrangement of *Brca2* and *Trp53* alleles in cell lines generated from tumors isolated from CPB2$^{\Delta 11/\Delta 11}$, CPB2$^{wt/\Delta 11}$, and CPB2$^{wt/wt}$ mice. **(B)** Metaphase spreads from a CPB2$^{\Delta 11/\Delta 11}$ pancreatic tumor cell line either untreated or treated with 100nM MMC. Inserts show examples of a ring chromosome (1), chromosome break (2), gaps (3), and radial structures (4). **(C)** Images of Rad51 and γH2AX foci in CPB2$^{\Delta 11/\Delta 11}$, CPB2$^{wt/\Delta 11}$, and CPB2$^{wt/wt}$ tumor cell lines stained by immunofluorescence with Rad51 or γH2AX antibodies 3 hours after 10Gy γ-irradiation.

Figure S3. Sequencing to identify mutations in *Kras* and *Trp53* alleles. (A) Sequence of the *Kras* gene in DNA isolated from pancreatic tumor tissue derived from CPB2$^{\Delta 11/\Delta 11}$ mice. The underlined sequence represents the antisence sequence of codon 12 and the arrow points to the mutation. (B) Sequence of the Trp53 gene in DNA isolated from pancreatic tumor tissue derived from CKB2$^{\Delta 11/\Delta 11}$ mice. The underlined sequence represents codon 239 and the arrow points to the mutation.

Figure S4. Disruption of BRCA2 promotes genomic instability and apoptosis. (A) FISH analysis of normal mouse pancreatic tissues stained with centromeric probes for

chromosome 9 (red) or 12 (green). **(B)** PCR analysis of MEF cell lines with or without adenoviral-cre showing rearrangement of the *Brca2* and *Kras* loci. Top panel shows $B2^{F11}$ or $B2^{wt}$ alleles, middle panel shows the $Brca2^{\Delta 11}$ allele and the bottom panel shows the $Kras^{G12D}$ allele (upper band), $Kras^{wt}$ allele (middle band) and $LSL\text{-}Kras^{G12D}$ allele (lower band). **(C)** Cleaved caspase-3 staining in pancreatic tissue from 4 month old $CKB2^{\Delta 11/\Delta 11}$ and $CKB2^{wt/wt}$ mice. Arrows show cells positive for cleaved caspase 3.