Supplemental data and figures

Supplemental Table.

Table1. Primer sequences for qPCR and Southern blot probes.

Gene	Forward primer	Reverse primer
Cox1(probe)	TGCTAGCCGCAGGCATTACT	CGGGATCAAAGAAAGTTGTGTTT
18S rRNA (probe)	ATCCTGCCAGTAGCATATGC	TCTGATCGTCTTCGAACCTC
Cox1	GCCTTTCAGGAATACCACGA	AGGTTGGTTCCTCGAATGTG
18S rRNA	TCGATGCTCTTAGCTGAGT	TCTGATCGTCTTCGAACCTC

Supplemental Figures

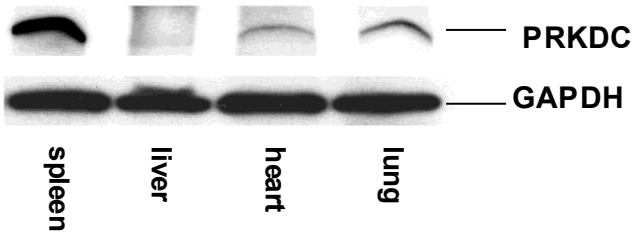

Figure1.

Marked variation in PRKDC protein level in different tissues of B6 strain.

Positions of PRKDC and GAPDH (loading control) are indicated by bars. 100ug of total protein per well were loaded for each tissue.

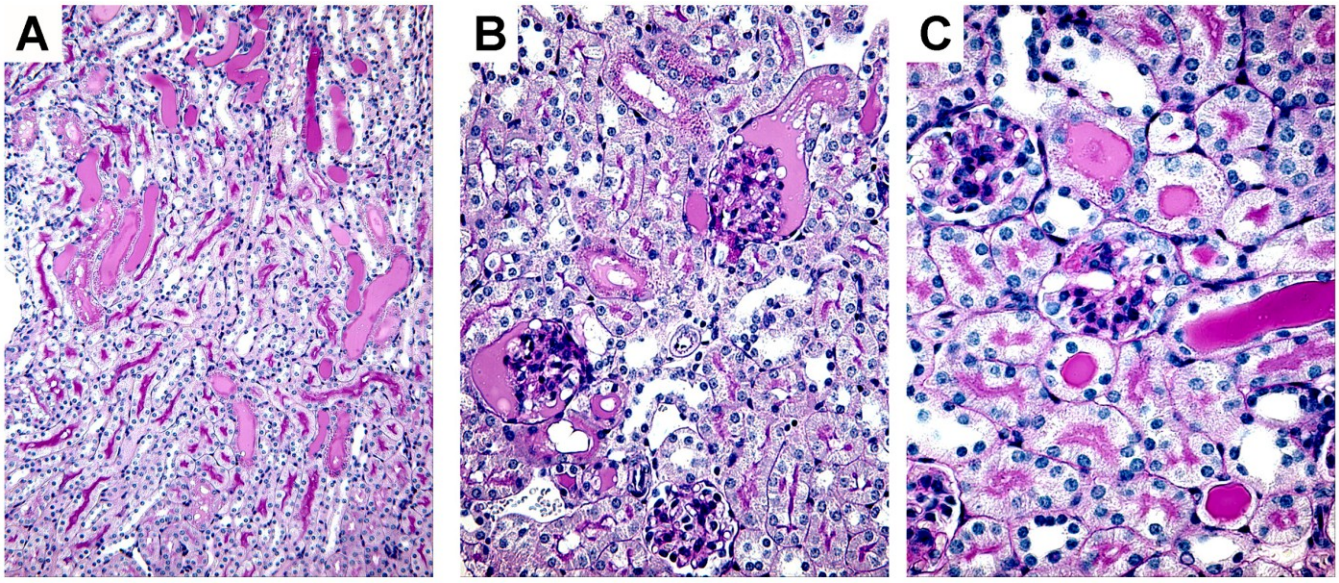

Figure2.

ADR-induced nephropathy in Cb.17 mice, carring Prkdc^{SCID} mutation.

Renal histopathology shows tubular proteinacious casts (**A,C**) and glomerulosclerosis (**B,C**) at 200x (**A,B**) and 600x(**C**) magnifications.

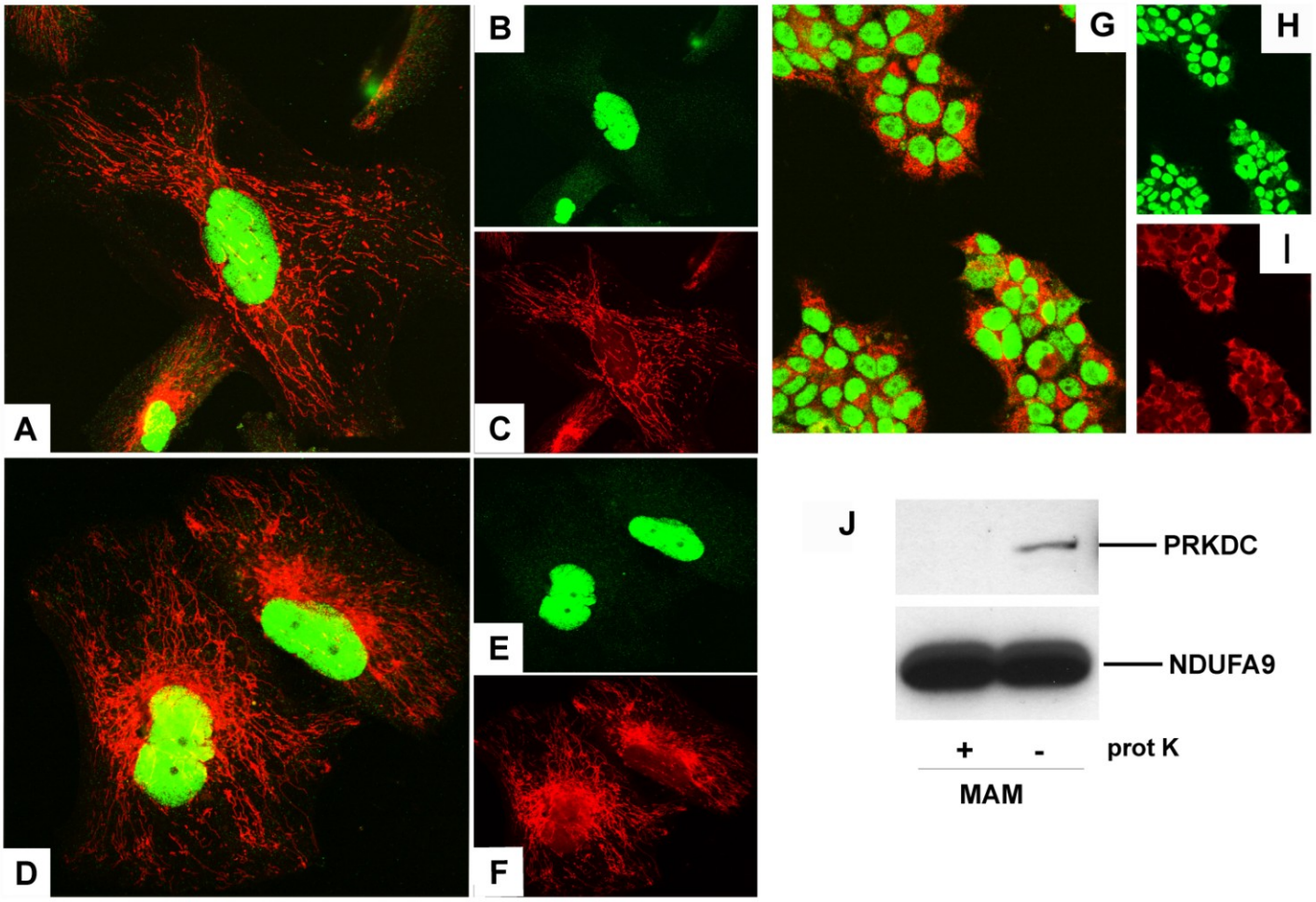

Figure3.

Nuclear and not mitochontrial localization of PRKDC.

A-F. Confocal microscopy shows nuclear localization of PRKDC (green) and absence of its co-localization with mitochondrial marker Mitotraker Red in control (**A-C**) or ADR treated (**D-F)** podocytes and in 293HEK cells (**G-I**). **J.** Western blot of mitochondrial fractions from human kidney shows no PRKDC in the proteinase K treated sample.

"MAM" corresponds to the membrane-associated mitochondria. NDUFA9 (Complex I-39 kD) is an inner mitochondrial membrain protein which was used as a control for mitochondrial integrity and loading. As the detection level of NDUFA9 has not been changed by the Proteinase K treatment, disappearance of PRKDC post treatment could exclude localization of PRKDC inside the mitochonria, which is necessary for its direct function in mtDNA repair.

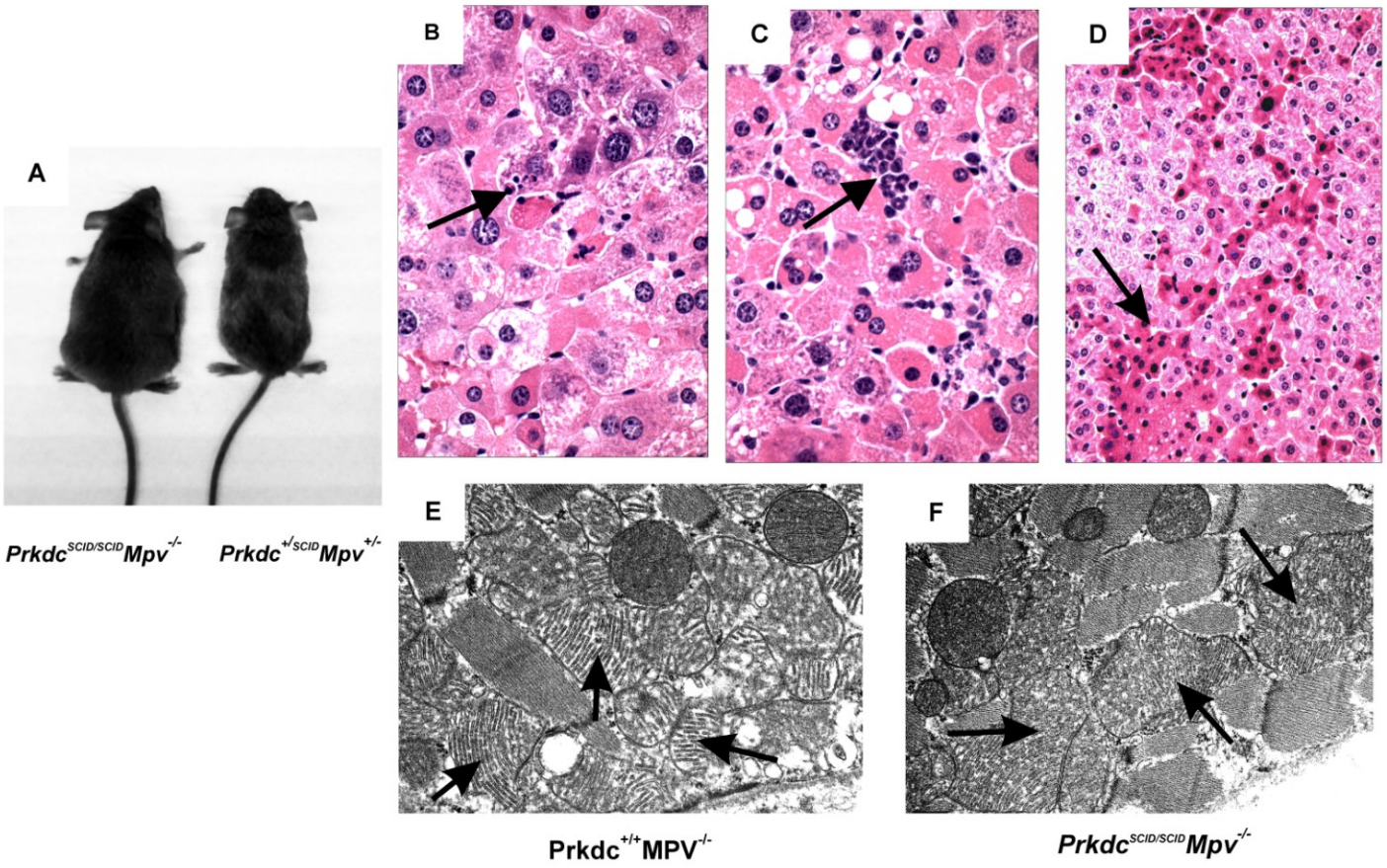

Figure4.

Additional clinical phenotypes observed in the Cb17xMPV17 cross.

A. Ascites, observed in a double null mouse, compared to a normal littermate. **B-D**. Liver histopathology shows a variety of lesions: apoptosis (**B**)**,** inflammation (**C**), hypereosinophylia (**D**)**. E-F.** Electron microscopy of heart tissue shows defects in mitochondrial architecture in double null mice (**E**)**,** but not in Mpv17 null mice (**F**)**.** Mitochondria are indicated by arrows.

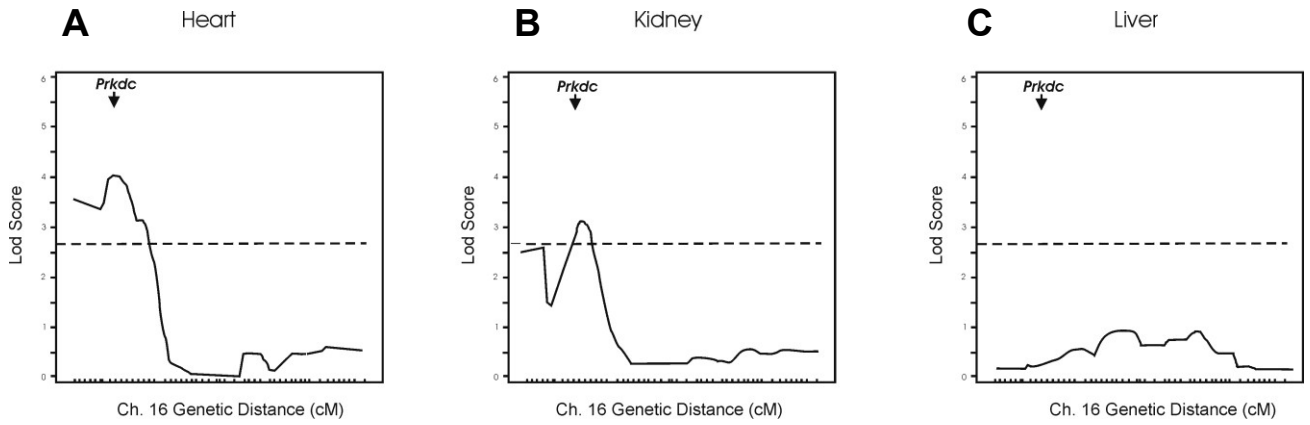

Figure 5.

Lod plots of mouse chromosome 16 show linkage of mtDNA levels to the Prkdc locus in the heart (A), kidney (B), but not liver (C) tissues of mice from the intercross *Mpv17* xCb17 intercross.

The Y axis shows the lod score. The X-axis shows the genetic distance on chromosome 16 (cM). The dashed line represents the lod score of 3, which is the traditional threshold for genome-wide significance.