

### Supplemental Table S1.

Frequency of viable progeny resulting from crosses between *Ercc1*<sup>+/-</sup>*Ku86*<sup>+/-</sup> and *Ercc1*<sup>+/ $\Delta$</sup> *Ku86*<sup>+/-</sup> mice.

Genotype	Observed	Expected*
wt	17 (8 %)	14 (6 %)
<i>Ku86</i> <sup>-/-</sup>	35 (16 %)	41 (19 %)
<i>Ercc1</i> <sup>-/<math>\Delta</math></sup>	34 (15 %)	41 (19 %)
<i>Ercc1</i> <sup>-/<math>\Delta</math></sup> <i>Ku86</i> <sup>-/-</sup>	0 (0 %)∞	14 (6 %)
<b>Heterozygotes</b> <sup>†</sup>	134 (61 %)	110 (50 %)

\*n=220 offspring from 20 litters.

<sup>†</sup> includes *Ercc1*<sup>+/-</sup>, *Ku86*<sup>+/-</sup>, *Ercc1*<sup>+/ $\Delta$</sup> , *Ercc1*<sup>+/-</sup> *Ku86*<sup>+/-</sup> and *Ercc1*<sup>+/ $\Delta$</sup>  *Ku86*<sup>+/-</sup>

∞ p-value <0.001.

### Supplemental Table S2.

Frequency of *Ercc1*<sup>-/-</sup> *Ku86*<sup>-/-</sup> embryos (E13.5-16.5) resulting from crosses between *Ercc1*<sup>+/-</sup> *Ku86*<sup>+/-</sup> mice.

Genotype	Observed	Expected*
wt	6 (4 %)	8 (6 %)
<i>Ku86</i> <sup>-/-</sup>	19 (14 %)	26 (19 %)
<i>Ercc1</i> <sup>-/-</sup>	14 (10 %)	26 (19 %)
<i>Ercc1</i> <sup>-/-</sup> <i>Ku86</i> <sup>-/-</sup>	7 (5 %)	8 (6 %)
<b>Heterozygous</b> <sup>†</sup>	90 (67 %)	68 (50 %)

\*n=136 offspring from 15 litters.

<sup>†</sup> includes *Ercc1*<sup>+/-</sup>, *Ku86*<sup>+/-</sup> and *Ercc1*<sup>+/-</sup> *Ku86*<sup>+/-</sup>

**Supplementary Table S3.** Nucleotide sequences of junctions from DNA substrates with blunt ends after joining in the wt and *Ercc1*<sup>-/-</sup> cells. Unmodified sequence is shown at the top of each genotype. Red denotes nucleotides deleted and bold denotes sequences of microhomology. n is the number of DNA ends sequenced for each genotype.

Blunt ends	n	size of deletion	size of μhomology	size of insertion
5'GGTACCGCGGGCCC GGGATCCACCGGTCG				
3'CCATGGCGCCCGGG CCCTAGGTGGCCAGC				
<b>wt</b>				
ACTCAGATCT <b>cgag</b> -- <b>accg</b> <b>CG</b> GGCCCCGGA	13	33	2	0
TGAGTCTAGAG <b>CTc</b> -- <b>tggcgc</b> CCGGGCCCT				
TACCGCGGGC <b>ggat</b> -- <b>ttca</b> CCGGGGTGGTG	1	50	0	0
ATGGCGCCCG <b>ccta</b> -- <b>aagt</b> GCCCCACCAC				
TGGCGGTAG <b>gcg</b> t-- <b>cg</b> gATCCACCGGTC	1	127	1	0
ACCGCCAT <b>ccgca</b> -- <b>gcc</b> CTAGGTGGCCAG				
TGTACGGTGG <b>gagg</b> -- <b>gcga</b> CGTAAACGGCC	1	196	0	0
ACATGCCACC <b>ctcc</b> -- <b>cgct</b> GCATTGCGG				
GGAGTTTGT <b>TTtgg</b> -- <b>tttt</b> CACTGCATTCT	1	1134	2	0
CCTCAAAC <b>aaaacc</b> -- <b>aa</b> <b>AA</b> GTGACGTAAGA				
CCGCGGGC <b>CCggga</b> -- <b>cacc</b> ATGGTGAGCAA	1	20	2	0
GGCGCCCG <b>ggccct</b> -- <b>gt</b> <b>GG</b> TACCACCTCGTT				
Blunt ends	n	size of deletion	size of μhomology	size of insertion
5'GGTACCGCGGGCCC GGGATCCACCGGTCG				
3'CCATGGCGCCCGGG CCCTAGGTGGCCAGC				
<b>Ercc1</b>				
ACTCAGATCT <b>cgag</b> -- <b>accg</b> <b>CG</b> GGCCCCGGG	16	33	2	0
TGAGTCTAGAG <b>CTc</b> -- <b>tggcgc</b> CCGGGCCCT				
TACCGGACTC <b>agat</b> -- <b>gcaa</b> GGGCGAGGAG	1	81	0	0
ATGGCCTGAG <b>tcta</b> -- <b>cg</b> ttCCCGCTCCTC				
TCTCGAGC <b>TCaagc</b> -- <b>gatc</b> CACCGGTCGC	1	43	2	0

AGAGCTCG**agttag--ct**AGGTGGCCAGCG

CCACCCATT**gacg--tgga**CGGCGACGTA

3

221

0

0

GGTGGGGTAA**ctgc--acct**GCCGCTGCAT

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**Supplementary Table S4.** Nucleotide sequences of junctions from DNA substrates with compatible ends after joining in the *wt* and *Erccl*<sup>-/-</sup> cells. Unmodified sequence is shown at the top of each genotype. Red denotes nucleotides deleted, bold denotes sequences of microhomology and green represent nucleotides added during the process of ligation. n is the number of DNA ends sequenced for each genotype.

Compatible ends		n	size of deletion	size of $\mu$ homology	size of insertion
5' ATCTCGAGCTCA	AGCTTCGAATTCTGC				
3' TAGAGCTCGAGTTCGA	AGCTTAAGACG				
<b>wt</b>					
TCAGATCT <b>CGagct</b> -- <b>cgcg</b> GGCCCCGGGAT		12	36	2	0
AGTCTAGAg <b>ctcga</b> -- <b>gc</b> GCCCGGGCCCTA					
ATCTCGAGCTCAAGC <b>CTTCGA</b> ATTCTGCAGT		1	0	0	1
TAGAGCTCGAGTTCG <b>GAAGCT</b> TAAAGACGTCA					
TAAGCAGAG <b>Ctgg</b> t-- <b>ggcc</b> CGGGATCCACC		1	90	1	0
ATATCTGGAg <b>acca</b> -- <b>ccg</b> GGCCCTAGGTGG					
TACCGGACTC <b>agat</b> -- <b>agcg</b> TGTCCGGCGAG		1	159	0	0
ATGGCCTGAG <b>tcta</b> -- <b>tcgc</b> ACAGGCCGCTC					
ACCGTCAGAT <b>ccgc</b> -- <b>gacg</b> GTACCGGGGC		1	57	0	0
TGGCAGTCTAg <b>gcg</b> -- <b>ctgc</b> CATGGCGCCCG					
CGGACTCAGAt <b>ctc</b> -- <b>cgac</b> CGTAAACGGCC		1	132	0	0
GCCTGAGTCT <b>agag</b> -- <b>gctg</b> GCATTTGCCGG					
CCACCCATT <b>gacg</b> -- <b>tgga</b> CGGCGACGTAA		1	221	0	0
GGTGGGGTAA <b>ctgc</b> -- <b>acct</b> GCCGCTGCATT					
Compatible ends		n	size of deletion	size of $\mu$ homology	size of insertion
5' ATCTCGAGCTCA	AGCTTCGAATTCTGC				
3' TAGAGCTCGAGTTCGA	AGCTTAAGACG				
<b>Erccl</b>					
TCAGATCT <b>CGagct</b> -- <b>cgcg</b> GGCCCCGGGAT		6	36	2	0
AGTCTAGAg <b>ctcga</b> -- <b>gc</b> GCCCGGGCCCTA					

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ATCTCGAGCTCAAG <b>AGC</b> TTCGAATTCTGCAGT	1	0	0	3
TAGAGCTCGAGTT <b>TCG</b> AAGCTTAAGACGTCA				
ACTCAGATC <b>Tcgag--cgg</b> tACCCGCGGCC	1	33	1	0
TGAGTCTAG <b>agctc--gcc</b> ATGGCGCCCGG				
ACTCAGATC <b>Gtcga--gca</b> GGGCGAGGGC	1	162	0	0
TGAGTCTAG <b>agct--cgct</b> CCCGCTCCCG				
AGGCGTGTAC <b>ggtg--ccct</b> GGCCCACCCT	1	308	2	0
TCCGCACAT <b>GCCac--gggacc</b> GGGTGGGA				
GCGGTAGG <b>CGtgta--gacg</b> GTACCGCGGG	1	108	2	0
CGCCATCC <b>gcacat--ct</b> GCATGGCGCCC				
TCAGATC <b>TCGagct--gtcg</b> CCACCATGGT	1	57	3	0
AGTCTAG <b>agctcga--AGC</b> cGGTGGTACCA				
GGCGGTAGG <b>Cgtgt--gttc</b> ACCGGGGTGG	1	170	1	0
CCGCCATCC <b>gcaca--caa</b> GTTGGTCCTACC				
TCAGATCCG <b>ctagc--cact</b> CTCGGCATGG	1	779	0	0
AGTCTAGG <b>Catcg--gtga</b> GAGCCGTACC				
CCGCCCCATT <b>gacg--tgga</b> CGGCGACGTA	1	221	0	0
GGCGGGGTA <b>actgc--acct</b> GCCGCTGCAT				
GAACCGTCAG <b>tccg--ccat</b> GGTIGAGCAAG	1	93	0	0
CTTGGCAGTC <b>aggc--ggt</b> aCCACTCGTTC				
AATGGGAGTT <b>tggt--ggca</b> TCGACTTCAA	1	595	1	0
TTACCCTCAA <b>Acaa--ccgta</b> GCTGAAGTT				

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**Supplementary Table S5.** Nucleotide sequences of junctions from DNA substrates with non compatible ends after joining in the *wt* and *Ercc1*<sup>-/-</sup> cells. Unmodified sequence is shown at the top of each genotype. Red denotes nucleotides deleted, bold denotes sequences of microhomology and green represent nucleotides added during the process of ligation. n is the number of DNA ends sequenced for each genotype.

Non-compatible ends		n	size of deletion	size of μhomology	size of insertion
5' TCAGATCTCGAGCT	CGCGGGCCCG				
3' AGTCTAGAGC	CATGGCGCCCGGGC				
<b>wt</b>					
TCAGATCTCG <b>agct</b>	CGCGGGCCCG	1	8	0	0
AGTCTAGAGC	<b>catg</b> GGCGCCCGGGC				
TCAGATCT <b>CGagct</b>	<b>cgcg</b> GGCCCG	6	12	2	0
AGTCTAGAG <b>c</b>	<b>catggc</b> GCCCGGGC				
TCAGATCTCG <b>agct</b>	<b>c</b> GGCGGGCCCG	1	9	0	0
AGTCTAGAGC	<b>catgg</b> CGCCCGGGC				
TCAGATCT <b>CGagct</b>	<b>cg</b> CGGGCCCG	1	10	2	0
AGTCTAGAG <b>c</b>	<b>catg</b> GCCCGGGC				
TCAGATCTCG <b>Agct</b>	<b>TAC</b> CGCGGGCCCG	4	3	1	4
AGTCTAGAG <b>T</b>	<b>CAT</b> GGCGCCCGGGC				
TCAGATCT <b>Tcgagct</b>	<b>AC</b> CGCGGGCCCG	2	8	1	2
AGTCTAGAG <b>c</b>	<b>cA</b> TGGCGCCCGGGC				
TCAGATCTCG <b>agct</b>	<b>GTAC</b> CGCGGGCCCG	1	4	0	4
AGTCTAGAGC	CATGGCGCCCGGGC				
TCAGATCTCG <b>Agct</b>	<b>CC</b> CGGGCCCG	1	3	1	2
AGTCTAGAGC	<b>caT</b> GGCGCCCGGGC				
TCAGATCTCGAGCT	<b>CC</b> CGGGCCCG	1	4	0	7
AGTCTAGAGC <b>TCGA</b>	<b>cat</b> GGCGCCCGGGC				
TCAGATCTCG <b>agct</b>	<b>CC</b> CGGGCCCG	1	7	0	1
AGTCTAGAGC	<b>cat</b> GGCGCCCGGGC				
CGCTAC <b>CGA</b> ctca-- <b>gga</b> TCCACCGGTTCG		1	28	3	0

CGGATGGcctgagt--CCTAGGTGGCCAGC				
TACCGGACTCagat--gccGGGATCCACC	1	21	1	0
ATGGCCTGAgctcta--cggGCCCTAGGTGG				
TCAGATCTCagact--gatcCACCGGTCGC	1	20	2	0
AGTCTAGagctcga--ctAGGTGGCCAGCG				
GTCAGATCCGctag--accgGTCGCCACCA	1	49	3	0
CAGTCTAggcgatc--tGGCCAGCGCTGGT				
TCCGCTAGCGctac--ggcgAGGAGCTGTT	1	68	3	0
AGGCGATcgcgatg--cCGCTCCTCGACAA				
GACTCAGATCtcta--gatcCACCGGTCGC	1	22	4	0
CTGAGTctagagct--CTAGGTGGCCAGCG				
CAGATCTCGAGCTC--caccGGGGTGGTGC	1	59	1	6
GTCTAGAGCTCGAg--gtgGCCCCACCACG				
TCCAAGTCTCacc--ttcaCCGGGGTGGT	1	274	1	0
AGGTTCAGAGGtgg--aagtGCCCCACCA				
GTTTTGGCACcaaa--ctacGGCAAGCTGA	1	333	2	0
CAAAACCGtggttt--gaTGCCGTTCGACT				
CCGGCCCCATTgacg--tggaCGGCGACGT	1	104	0	0
GGCCGGGGTAActgc--acctGCCGCTGCA				
GCGTGTACGtgg--ccgGGGTGGTGCCCA	1	136	1	0
CGCACATGCcacc--ggCCCCACCAGGGT				

Non-compatible ends		n	size of deletion	size of μhomology	size of insertion
5' TCAGATCTCGAGCT	CGCGGGCCCG				
3' AGTCTAGAGC	CATGGCGCCCGGGC				

Erccl		n	size of deletion	size of μhomology	size of insertion
TCAGATCTCgagct	cgcgGGCCCG	8	12	2	0
AGTCTAGAgc	catggcGCCCGGGC				
TCAGATCTCgagct	cgcGGGCCCCG	1	11	0	0
AGTCTAGAGC	catggcgCCCGGGC				
TCAGATCTCgagct	cgcGGGCCCCG	5	10	2	0
AGTCTAGAgc	catgGCCCGGGC				
TCAGATCTCgagct	CGCGGGCCCCG	4	8	0	0
AGTCTAGAGC	catgGCGCCCGGGC				
TCAGATCTCgAgct	CCCGGGCCCCG	1	6	1	2

AGTCTAGAGC	<b>caT</b> GGCGCCCGGGC				
TCAGATCTCGAG <b>Ct</b>	CGCGGGCCCG	1	5	1	3
AGTCTAGAG <b>CTC</b>	<b>cat</b> GGCGCCCGGGC				
GTGAAC <b>Cgtcag--ccgg</b>	GATCCACCGTC	1	50	1	0
CACTTGG <b>cagtc--ggc</b>	CCTAGGTGGCAG				
GTCAGAT <b>Ccgct--gccc</b>	GGGATCCACCG	1	40	1	0
CAGTCTA <b>ggcga--cgg</b>	GCCCTAGGTGGC				
GTTTAG <b>GAaccg--gtga</b>	GCAAGGGCGA	1	78	4	0
CAAAT <b>cacttggc--CACT</b>	CGTTCCCGCT				
ACCGTCAGAT <b>ccg--cggg</b>	ATCCACCGGT	1	45	0	0
TGGCAGTCT <b>aggc--gccc</b>	TAGGTGGCCA				
AGATCCGCT <b>agcg--aggg</b>	CGAGGAGCTG	1	70	0	0
TCTAGGCGAT <b>cg--tccc</b>	GCTCCTCGAC				
CAGATCTCG <b>AGCTC--agct</b>	GCCGACCA	1	566	5	2
GTCTAGAG <b>ctcga --TCGAG</b>	CGGCTGGT				
TAGCGCTACCG <b>actc--gttc</b>	GAGGGCGA	1	419	0	0
ATCGCGATGG <b>ctgag--caag</b>	CTCCCGCT				
TCTC <b>GAGCTaagct--gagct</b>	ACCAGTCCGC	1	668	5	0
AGAG <b>ctcgattcga--CTCGA</b>	TGGTCAGGCG				
CGCAAATGG <b>gcgg--tggt</b>	GCCATCCTG	1	159	2	0
GCGTTTACCG <b>cc--acca</b>	GGTAGGAC				
TTTTGGCA <b>Caaa--gtgc</b>	CCATCCTGGT	1	220	1	0
AAAACCGT <b>ggttt--cac</b>	GGTAGGACCA				
GGTAGGCGT <b>gtacg--ccat</b>	GGTGGAGCAGC	1	113	0	0
CCATCCGCAC <b>atgc--ggta</b>	CCACTCGTTC				