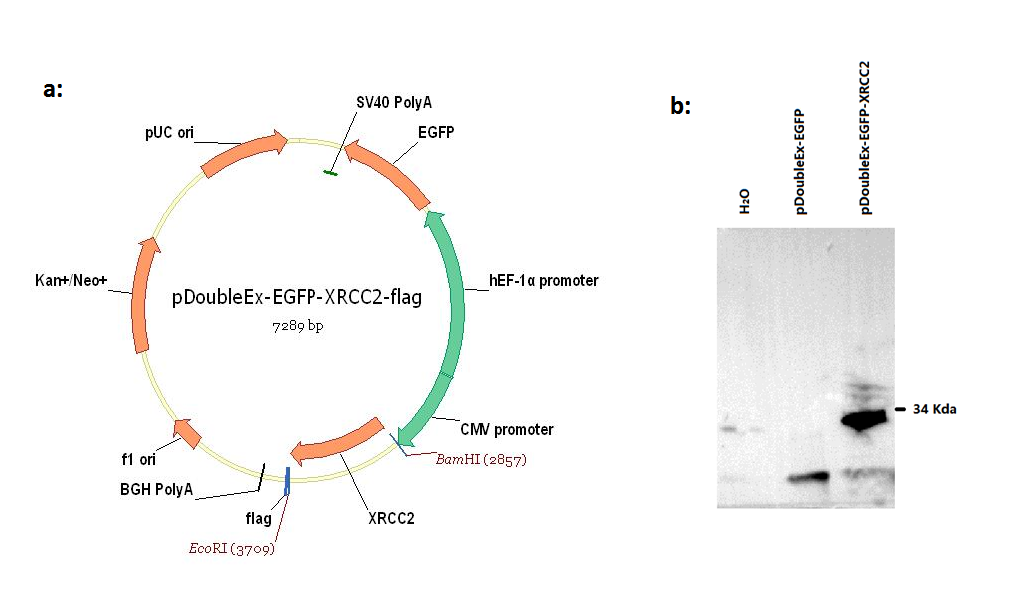
**Table S1: Primers and PCR conditions of the present study.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Gene/Exon：** | **Forward (5’-3')** | **Reverse (5’-3')** | **Product size** | **Anealing temperature** |
| Human XRCC2-EXON1 | AGGCCCGCACACCCTATT | GGCCTTGTTCCCATCTCC | 249 bp | 63℃ |
| Human XRCC2-EXON2 | ACAGCACCCAGCCTAAAGTT | TTGTCTGACACCGATGAGGA | 378 bp | 63℃ |
| Human XRCC2-EXON3-1 | TGCATTTTGTAACCTACCCTTG | TCTCTAAGCACTGAGAACATTTCC | 485 bp | 61℃ |
| Human XRCC2-EXON3-2 | tgttttgtagtcacccatctctctg | cacacataggaggatcccttgag | 575 bp | 60℃ |
| Mouse XRCC2-EXON2 | GCCTCAGTCGCCTCTGTACACAT | CATGGCTATGCAGGAGATCAAGTAAC | 364 bp | 59℃ |
|
| Mouse 5'UTR -3'UTR | TGCTGGCGGGTAGGTTGA | ATCCAGTAAAAAGACGACAGGC | 509 bp | 60℃ |
| Human 5'UTR -3'UTR | GGCGGGAAAGTTGAGTCTCT | CTTTCTCCTCCATTGACGCG | 536 bp | 59℃ |
| *β*-actin | CCAGCCTTCCTTCTTGGGTAT | GTTGGCATAGAGGTCTTTACGG | 103bp | 60℃ |

**Figure s1: The XRCC2 antibody affinity assay.** The mice *XRCC2* cDNA sequence was amplified and linked to the pDoubleEx-EGFP-flag-N plasmid, the predicted molecular size of the fusion protein is 33 Kda (a). The plasmid purified and then transfect to COS-7 cells. Transfection efficiency was assessed by cellular immunofluorescence. After the cell cultured for 48 hours, the cell was harvested and subject to Western blot assay (b).



**Table S2. Recent semen analyses for two infertile brothers.**

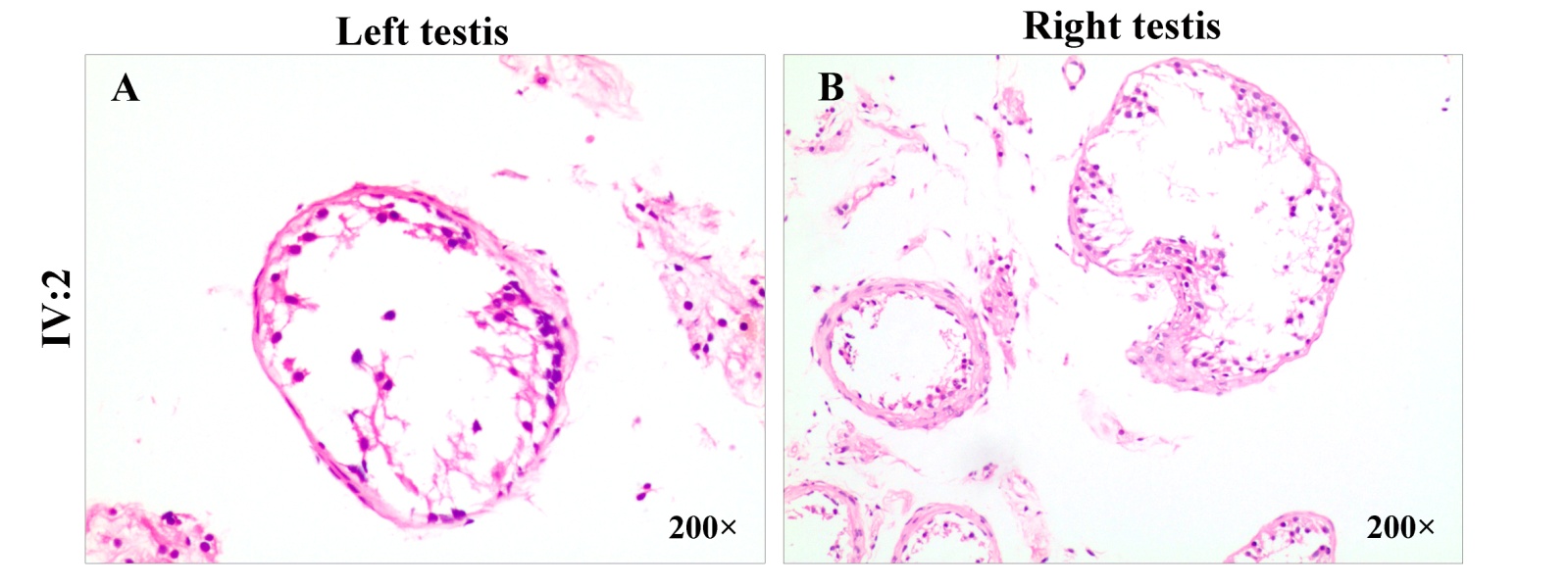
|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **sperm volume（ml）** | **PR (Forward motion)** | **NP (Non forward motion)** | **IM (Inactive sperm)** | **PR+NP (Total vitality)** | **Sperm concentration （Million/ml）** |
| **Control case** | 2.2 | 47.6 | 1.5 | 50.9 | 49.1 | 91.8 |
| **IV:2** | 2.8 | 0 | 0 | 0 | 0 | 0 |
| **IV:3** | 2.6 | 0 | 0 | 0 | 0 | 0 |
| **Normal range** | ≧1.5 | ≧32 | \ | \ | ≧40 | ≧15 |

**Table S3. General clinical data for two infertile men.**

Intelligence Quotient(IQ) is based on the Wechsler Adult Intelligence Scale in Chinese.

Birth weight, weight, height and other clinical scores are based on a local Hospital Standard

|  |  |  |  |
| --- | --- | --- | --- |
| Subjects | IV:2 | IV:3 | REFERENCE |
| Age (years) | 31.5 | 29 | **-** |
| Weight(Kg) | 68.5 | 68.5 | **～**50 centile |
| Height(cm) | 169 | 171 | **～**50 centile |
| Birth Weight (g) | 3050 | 2900 | **～**50 centile |
| IQ | 100 | 110 | - |
| Karyotype | 46,XY | 46,XY | - |
| AZF(a,b,c region) | (+) | (+) | (+) |
| Follicle-stimulating hormone(mIU/ml) | 8.23 | 9.12 | 1.5-12.5 |
| Luteotropic hormone (mIU/ml) | 7.9 | 8.6 | 1.7-8.6 |
| [Estradiol](http://www.baidu.com/link?url=czD8HJilI7NxIib659ixJjIGnaSYdE1OYFO4iwnFY48K4znXMl9HHrZJ8kaz9vN6kJWwl4stX-SZyowjIOuSWxyj3WwSTEGkGXdHW82FNhm) (pg/ml) | 38 | 35 | 25.8-60.7 |
| P[rogesterone](http://www.baidu.com/link?url=ASi5pe1SWVwZzVFf_nMlX8LTuMjyUZsjqLrtNmbftEuWkRbUslhFdEAHzDKA3sB2LLfsCQ6ouSZ-CJYb4L36jiCR5unC6uXmnPfbOlVgfYy) (pg/ml) | 1.1 | 0.4 | 0.2-1.4 |
| Prolactin (pg/ml) | 12 | 7.91 | 1.6-21.4 |
| Testosterone (pg/ml) | 7.4 | 8.25 | 2.49-8.36 |

**Figure S2**. **Histology of IV:2.** H&E staining revealed no sperm in the seminiferous tubules. Magnification: AB=200×. 

**Figure S3. Details of homozygositymapping for two patients in the family.** Homozygous intervals for IV:2 and IV:3 were labeled with blue and red frames, respectively. Note: All homo-intervals are more than 3Mb. 

**Table S4: Quality control data of whole exome sequencing for the investigated family.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Sample | IV:2 | III:5 | M0951 | IV:3 |
| Clean reads (Read Count) | 44675216 | 40787158 | 60051812 | 55648360 |
| Mapped reads (Read Count) | 39880494 (89.27%) | 36445660 (89.36%) | 53272753 (88.71%) | 49425059 (88.82%) |
| Fraction of effective bases on target | 61.75% | 60.61% | 62.82% | 62.50% |
| Fraction of effective bases on or near target | 92.35% | 92.28% | 92.27% | 92.26% |
| Average sequencing depth on target | 55.91x | 45.67x | 78.06x | 72.1x |
| Average sequencing depth near target | 14.94x | 12.86x | 19.73x | 18.51x |
| Coverage of target region | 97.90% | 97.65% | 97.90% | 97.93% |
| Fraction of target covered at least 4x | 97.52% | 97.09% | 97.52% | 97.56% |
| Fraction of target covered at least 10x | 96.60% | 95.83% | 96.76% | 96.74% |
| Fraction of target covered at least 20x | 92.92% | 91.03% | 94.23% | 93.76% |
| Fraction of target covered at least 50x | 54.86% | 38.25% | 73.47% | 69.68% |

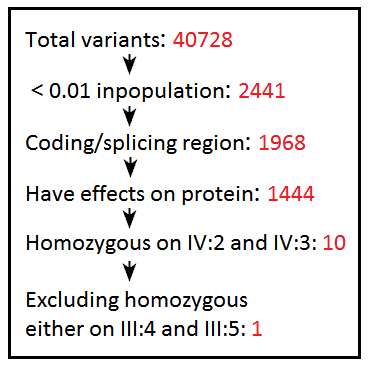
**Table S5: The candidate homozygous variants identified in the family.**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Chr** | **Position** | **Ref** | **Alt** | **Gene** | **Func.** | **ExonicFunc.refGene** | **IV:2** | **IV:3** | **III:4** | **III:5** |
| 1 | 24296088 | G | T | SRSF10 | UTR3 | . | 1/1 | 1/1 | 1/1 | 1/1 |
| 17 | 72889676 | - | GGC… | FADS6 | exonic | nonframeshift insert | 1/1 | 1/1 | 1/1 | 1/1 |
| 21 | 14982886 | G | A | POTED | exonic | nonsynonymous SNV | 1/1 | 1/1 | 0/1 | 1/1 |
| 21 | 14982952 | A | G | POTED | exonic | nonsynonymous SNV | 1/1 | 1/1 | 1/1 | 1/1 |
| 21 | 15013735 | A | G | POTED | exonic | nonsynonymous SNV | 1/1 | 1/1 | 1/1 | 1/1 |
| 3 | 75787726 | G | A | ZNF717 | exonic | nonsynonymous SNV | 1/1 | 1/1 | 1/1 | 1/1 |
| 3 | 100170600 | - | TCC… | LNP1 | exonic | nonframeshift insert | 1/1 | 1/1 | 1/1 | 1/1 |
| 6 | 32796456 | - | ACC… | TAP2 | UTR3 | . | 1/1 | 1/1 | 1/1 | 0/1 |
| 7 | 152357866 | A | G | XRCC2 | exonic | nonsynonymous SNV | 1/1 | 1/1 | 0/1 | 0/1 |

**Table S6: Candidate pathogenic gene (MAF<0.01).**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Gene | Variant | Chr | Coord inate | Variant Type | Allelic Depths | Geno type | Transcript | CDS | Amine Acid | Consequ ence | MAF |
| XRCC2 | A>G/G | 7 | 15235 7866 | snv | 16/16 | homoz ygous | NM\_0054 31.1 | c.41T>C | p.Leu1 4Pro | missense variant, splice region variant | 0% |

**Figure S4: Filtering strategy for variants obtained from the whole exome sequencing**.

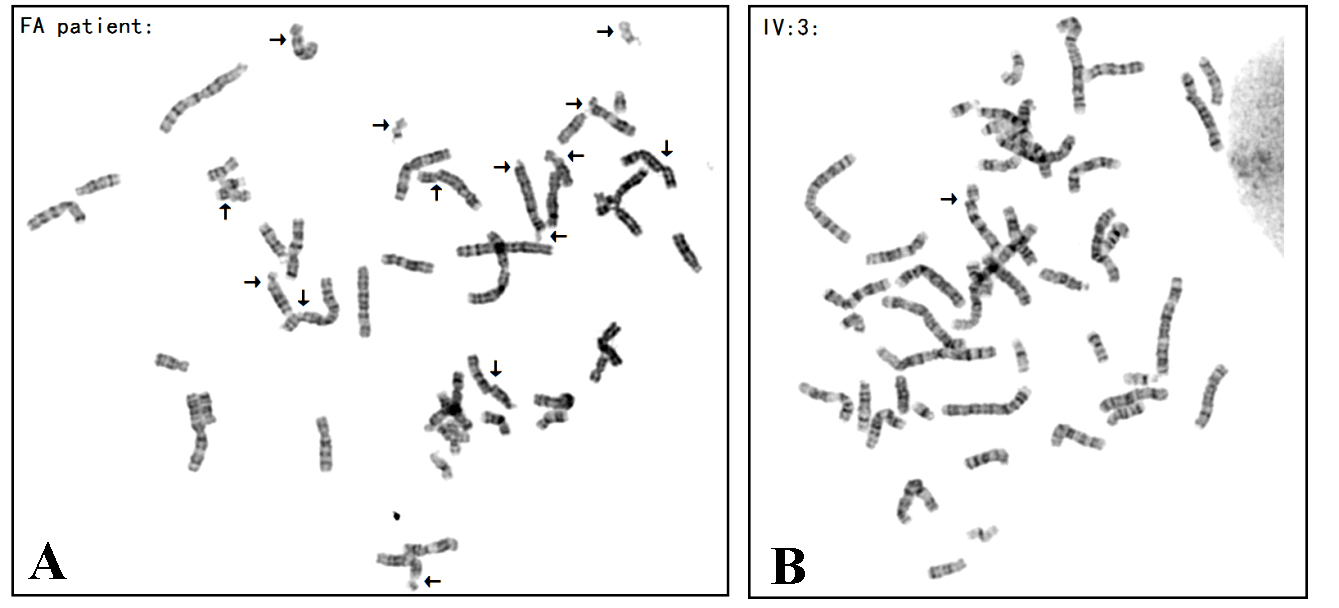
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**Table S7: Frequencies of chromosomal breaks induced by DNA-breaking agents mitomycin C (MMC) or cisplatin (DDP).**

Samples: C1384, lymphocytes of a healthy 35-year-old man; FA, lymphocytes of a 7.5-year-old girl affected by Fanconi anemia and recessive *FANCA* mutations; IV:2 and IV:3, lymphocytes of two infertile brothers with the *XRCC2* c.41 T>C/p.Leu14Pro mutation of this study.

|  |  |  |  |
| --- | --- | --- | --- |
| Break agents (dose) | Sample | Mean breaks/cell | Analyzed cells |
| PBS | C1384 | 0 | 100 |
| FA | 0.07 | 100 |
| IV:2 | 0.01 | 100 |
| IV:3 | 0 | 100 |
| MMC （50ng/ml） | C1384 | 0.26 | 86 |
| FA | 1.72 | 40 |
| IV:2 | 0.23 | 78 |
| IV:3 | 0.19 | 84 |
| MMC （100ng/ml） | C1384 | 0.61 | 46 |
| FA | 3.74 | 23 |
| IV:2 | 0.66 | 53 |
| IV:3 | 0.69 | 61 |
| DDP（3.75ug/ml） | C1384 | 1.22 | 27 |
| FA | 7.4 | 5 |
| IV:2 | 1.19 | 21 |
| IV:3 | 1.27 | 19 |

**Figure S5: Representative of chromosomal breaks (arrow) in *XRCC2*-mutated cells (IV:3) and *FANCA*-mutated cells (FA).** Note: Chromosomal double-strand breaks were induced by 3.75 µg/ml cisplatin. Magnification: 1000×.

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**Table S8. Data of 21 litters transmitted from heterozygote (Xrcc2WT/L14P) intercrosses and the data of body weight of the offspring.** Total offspring=171, ♀=78,♂=93; WT=42, Heterozygote=90, Homozygote=39.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Litters | ID | Sex | Genotype | Weight(7 days) (g) | Weight (30 days) (g) | Weight (60 days) (g) |
| 1 | F1 | ♂ | het | 5.91 | 15.67 | 26.05 |
| F2 | ♂ | hom | 5.06 | 15.09 | 23.83 |
| F3 | ♂ | hom | 5.64 | 15.41 | 23.56 |
| F4 | ♂ | het | 5.53 | 16.28 | 24.05 |
| F5 | ♂ | wt | 5.39 | 15.86 | 23.16 |
| F6 | ♂ | wt | 5.16 | 13.69 | 22.69 |
| F7 | ♀ | hom | 5.26 | 12.21 | 17.5 |
| F8 | ♂ | het | 4.49 | 12.22 | 23.91 |
| F9 | ♀ | het | 5.38 | 14.1 | 21.15 |
| F10 | ♂ | het | 5.75 | 15.54 | 25.15 |
| F11 | ♀ | het | 5.66 | 13.39 | 17.65 |
| F12 | ♂ | wt | 5.67 | 14.99 | 24.99 |
| 2 | G1 | ♀ | het | 4.98 | 12.58 | 20.42 |
| G2 | ♀ | wt | 5.04 | 12.88 | 19.83 |
| G3 | ♀ | wt | 4.99 | 13.88 | 18.87 |
| G4 | ♂ | wt | 4.98 | 15.63 | 25.02 |
| G5 | ♂ | het | 5.24 | 14.38 | 23.87 |
| G6 | ♀ | het | 3.74 | 9.68 | 17.51 |
| G7 | ♂ | hom | 5.38 | 13.92 | 23.5 |
| G8 | ♂ | hom | 3.8 | 8.17 | 23.18 |
| 3 | L1 | ♂ | hom | 3.78 | 12.42 | 22.77 |
| L2 | ♂ | wt | 4.5 | 12.39 | 24.72 |
| L3 | ♂ | hom | 3.95 | 12.57 | 23.56 |
| L4 | ♀ | hom | 4.33 | 10.85 | 17.7 |
| L5 | ♂ | hom | 3.67 | 11.36 | 23.74 |
| L6 | ♀ | hom | 4.06 | 10.37 | 17 |
| 4 | O1 | ♂ | het | 7.96 | 17.05 | 24.85 |
| O2 | ♂ | het | 7.67 | 15.77 | 24.64 |
| O3 | ♀ | het | 7.22 | 14.32 | 18.16 |
| O4 | ♀ | hom | 6.86 | 13.93 | 18.66 |
| O5 | ♂ | hom | 6.88 | 13.18 | 21.92 |
| O6 | ♂ | het | 7.52 | 15.69 | 24.88 |
| O7 | ♀ | het | 4.45 | 13.96 | 18.24 |
| 5 | P1 | ♀ | het | 3.12 | 13.72 | 18.26 |
| P2 | ♂ | het | 3.9 | 17.96 | 27.35 |
| P3 | ♀ | wt | 3.54 | 15.75 | 19.37 |
| P4 | ♂ | het | 3.66 | 16.5 | 27.98 |
| P5 | ♀ | wt | 3.74 | 15.75 | 19.08 |
| P6 | ♂ | wt | 2.72 | 12.41 | 23.06 |
| 6 | Q1 | ♀ | het | 2.17 | 11.68 | 17.8 |
| Q2 | ♀ | het | 2.6 | 11.43 | 16.89 |
| Q3 | ♀ | het | 2.61 | 11.78 | 18.02 |
| Q4 | ♂ | wt | 2.56 | 12.46 | 23.31 |
| Q5 | ♂ | het | 2.58 | 10.83 | 21.6 |
| Q6 | ♀ | wt | 2.78 | 11.64 | 18.67 |
| Q7 | ♂ | het | 2.51 | 10.25 | 11.33 |
| Q8 | ♂ | het | 2.71 | 12.03 | 18.39 |
| Q9 | ♂ | hom | 2.75 | 13.51 | 23.28 |
| Q10 | ♀ | het | 2.54 | 11.94 | 18.35 |
| Q11 | ♀ | wt | 1.61 | 8.58 | 17.79 |
| 7 | R1 | ♂ | hom | 2.53 | 15.75 | 23.62 |
| R2 | ♀ | het | 2.68 | 16.22 | 20.15 |
| R3 | ♂ | het | 2.96 | 8.94 | 23.22 |
| R4 | ♀ | wt | 2.86 | 14.28 | 21.6 |
| R5 | ♂ | wt | 2.16 | 15.76 | 26.48 |
| R6 | ♂ | hom | 2.81 | 12.32 | 22.18 |
| R7 | ♀ | wt | 2.12 | 12.89 | 19.08 |
| R8 | ♂ | het | 3.56 | 11.56 | 28.78 |
| 8 | T1 | ♀ | hom | 5.32 | 9.97 | 17.2 |
| T2 | ♂ | wt | 5.37 | 11.2 | 22.3 |
| T3 | ♀ | het | 5.55 | 10.67 | 18.22 |
| T4 | ♂ | het | 5.51 | 11.51 | 23.83 |
| T5 | ♂ | wt | 4.88 | 8.99 | 19.57 |
| T6 | ♀ | het | 5.65 | 11.29 | 18.54 |
| 9 | U1 | ♂ | het | 4.6 | 14.82 | 26.05 |
| U2 | ♂ | het | 4.96 | 15.22 | 22.69 |
| U3 | ♂ | wt | 4.19 | 15.47 | 25.77 |
| U4 | ♂ | het | 4.6 | 12.86 | 23.34 |
| U5 | ♂ | het | 4.78 | 17.37 | 22.86 |
| U6 | ♀ | wt | 4.37 | 12.21 | 20.63 |
| 10 | V1 | ♀ | wt | 6.12 | 9.82 | 18.49 |
| V2 | ♀ | het | 6.35 | 12.6 | 17.17 |
| V3 | ♂ | wt | 7.25 | 15.23 | 26.77 |
| V4 | ♀ | hom | 6.57 | 13.43 | 17.75 |
| V5 | ♀ | het | 6.57 | 12.99 | 18.62 |
| V6 | ♀ | wt | 6.5 | 12.67 | 16.21 |
| V7 | ♂ | hom | 6.81 | 14.23 | 24.99 |
| V8 | ♀ | hom | 6.25 | 12.6 | 18.98 |
| V9 | ♂ | het | 6.36 | 12.83 | 21.84 |
| V10 | ♂ | wt | 6.94 | 15.01 | 26.15 |
| 11 | W1 | ♂ | het | 4.92 | 11.5 | 23.66 |
| W2 | ♀ | het | 5.8 | 12.53 | 21 |
| W3 | ♂ | wt | 5.58 | 13.13 | 21.42 |
| W4 | ♂ | hom | 5.62 | 12.62 | 26.08 |
| W5 | ♂ | wt | 5.66 | 13.86 | 28.65 |
| W6 | ♂ | wt | 4.52 | 11.53 | 25.02 |
| W7 | ♂ | het | 5.27 | 11.69 | 26.7 |
| W8 | ♀ | het | 4.93 | 10.98 | 20.06 |
| 12 | Z1 | ♂ | het | 3.53 | 13.86 | 23.14 |
| Z2 | ♀ | het | 3.55 | 14.31 | 18.18 |
| Z3 | ♀ | wt | 3.72 | 14.23 | 17.8 |
| Z4 | ♀ | het | 4 | 14.52 | 17.44 |
| Z5 | ♀ | wt | 3.66 | 12.04 | 17.12 |
| Z6 | ♂ | het | 4.02 | 13.47 | 23.52 |
| Z7 | ♂ | het | 3.99 | 13.7 | 21.06 |
| Z8 | ♀ | wt | 3.54 | 12.6 | 17.02 |
| Z9 | ♀ | wt | 3.76 | 13.37 | 19.29 |
| 13 | AA1 | ♀ | het | 6.14 | 12.93 | 17.86 |
| AA2 | ♀ | het | 5.93 | 15.18 | 18.14 |
| AA3 | ♂ | het | 6.11 | 18.77 | 24.33 |
| AA4 | ♀ | hom | 6.26 | 13.16 | 18.33 |
| AA5 | ♀ | het | 5.98 | 13.21 | 16.36 |
| AA6 | ♂ | het | 6.21 | 15.16 | 25.14 |
| AA7 | ♂ | het | 5.98 | 18.23 | 25.22 |
| 14 | AB1 | ♂ | het | 3.93 | 14.64 | 22.12 |
| AB2 | ♂ | het | 3.49 | 11.61 | 18.93 |
| AB3 | ♀ | wt | 4.1 | 13.27 | 19.62 |
| AB4 | ♂ | het | 4.4 | 14.79 | 23.44 |
| AB5 | ♀ | het | 3.73 | 13.01 | 20.32 |
| AB6 | ♂ | hom | 4.06 | 14.9 | 22.86 |
| AB7 | ♀ | het | 3.91 | 11.72 | 18.37 |
| AB8 | ♂ | het | 3.01 | 12.81 | 23.36 |
| AB9 | ♂ | het | 4.4 | 15.1 | 23.3 |
| AB10 | ♂ | het | 3.66 | 16.8 | 22.82 |
| AB11 | ♂ | het | 4.3 | 15.62 | 23.45 |
| AB12 | ♀ | het | 4.12 | 12.44 | 18.42 |
| 15 | AC1 | ♀ | wt | 4.45 | 11.31 | 16.41 |
| AC2 | ♀ | hom | 4.83 | 11.36 | 16.8 |
| AC3 | ♀ | het | 3.82 | 11.01 | 17.92 |
| AC4 | ♂ | hom | 3.67 | 12.08 | 23.07 |
| AC5 | ♂ | hom | 4.8 | 12.79 | 22.55 |
| AC6 | ♀ | hom | 4.59 | 14.52 | 18.56 |
| AC7 | ♂ | wt | 5 | 15.02 | 21.79 |
| AC8 | ♂ | wt | 4.9 | 14.27 | 22.46 |
| AC9 | ♂ | hom | 5.08 | 15.28 | 21.88 |
| AC10 | ♀ | het | 4.73 | 13.51 | 19.95 |
| AC11 | ♀ | het | 4.64 | 12.51 | 18.79 |
| AC12 | ♂ | het | 4.98 | 15.04 | 23.62 |
| 16 | AD1 | ♂ | hom | 4.94 | 13.57 | 21.8 |
| AD2 | ♂ | hom | 6.18 | 14.65 | 25.44 |
| AD3 | ♂ | het | 5.22 | 13.46 | 22.22 |
| AD4 | ♀ | het | 5.9 | 14.43 | 18.5 |
| AD5 | ♂ | het | 4.61 | 15.41 | 23.48 |
| AD6 | ♂ | het | 5.98 | 15.15 | 24.49 |
| 17 | AE1 | ♀ | het | 4.38 | 16.02 | 19.69 |
| AE2 | ♀ | hom | 4.29 | 15.8 | 17.56 |
| AE3 | ♀ | het | 4.26 | 11.18 | 18.23 |
| AE4 | ♂ | hom | 3.83 | 15.37 | 22.69 |
| AE5 | ♀ | wt | 4.38 | 15.22 | 18.97 |
| 18 | AF1 | ♀ | hom | 4.16 | 13.26 | 19.1 |
| AF2 | ♂ | het | 3.89 | 15.55 | 22.74 |
| AF3 | ♂ | het | 4.16 | 15.98 | 23.5 |
| AF4 | ♀ | hom | 4.24 | 14.57 | 20.06 |
| AF5 | ♀ | het | 4.01 | 11.85 | 16.75 |
| AF6 | ♂ | hom | 4.34 | 16.06 | 25.13 |
| AF7 | ♂ | wt | 4.34 | 14.9 | 25.12 |
| AF8 | ♂ | het | 4.33 | 14.19 | 24.31 |
| AF9 | ♀ | het | 3.38 | 10.36 | 18.67 |
| 19 | AG1 | ♂ | het | 5.96 | 16.01 | 24.94 |
| AG2 | ♂ | het | 5.7 | 13.75 | 22.88 |
| AG3 | ♀ | hom | 5.82 | 13.76 | 19.17 |
| AG4 | ♂ | hom | 6.25 | 15.95 | 22.1 |
| AG5 | ♀ | het | 5.73 | 14.12 | 18.85 |
| 20 | AH1 | ♂ | hom | 4.64 | 16.3 | 21.25 |
| AH2 | ♀ | wt | 5.41 | 13.69 | 19.67 |
| AH3 | ♀ | hom | 5.33 | 13.78 | 18.11 |
| AH4 | ♀ | wt | 5.67 | 15.02 | 18.58 |
| AH5 | ♂ | het | 5.7 | 17.52 | 23.19 |
| AH6 | ♀ | het | 4.9 | 13.19 | 16.62 |
| AH7 | ♀ | het | 4.61 | 13.22 | 16.61 |
| 21 | AI1 | ♀ | het | 4.25 | 10.7 | 18.66 |
| AI2 | ♀ | hom | 4.2 | 11.26 | 17.98 |
| AI3 | ♀ | wt | 3.91 | 11.58 | 17.65 |
| AI4 | ♂ | het | 4.55 | 12.1 | 24.21 |
| AI5 | ♂ | wt | 4.39 | 12.94 | 23.98 |
| AI6 | ♂ | het | 4.19 | 13.35 | 21.65 |
| AI7 | ♀ | het | 4.04 | 12.26 | 17.85 |
| AI8 | ♀ | wt | 4.27 | 12.66 | 16.92 |
| AI9 | ♀ | het | 4.03 | 12.65 | 17.23 |
| AI10 | ♂ | het | 4.38 | 11.61 | 23.8 |
| AI11 | ♂ | het | 3.83 | 11.86 | 24.31 |

**Table S9.Statistics in body weight between the *Xrcc2*WT/WT and *Xrcc2*WT/L14P male mice.**

|  |  |  |  |
| --- | --- | --- | --- |
| **Groups** | **7d** | **30d** | **60d** |
| Het♂（n=46） | 4.79±1.29 | 14.46±2.23 | 23.77±3.20 |
| WT♂（n=19） | 4.83±1.30 | 13.78±1.88 | 24.32±2.28 |
| t | -0.10 | 1.17 | -0.60 |
| p | 0.92 | 0.25 | 0.55 |

**Table S10:Statistics in body weight between the *Xrcc2*WT/WT and *Xrcc2*L14P/L14P male mice.**

|  |  |  |  |
| --- | --- | --- | --- |
| **Groups** | **7d** | **30d** | **60d** |
| Hom♂（n=23） | 4.63±1.24 | 13.80±1.91 | 23.55±1.08 |
| WT♂（n=19） | 4.83±1.30 | 13.78±1.88 | 24.32±2.28 |
| t | -0.51 | 0.04 | -1.11 |
| p | 0.61 | 0.97 | 0.28 |

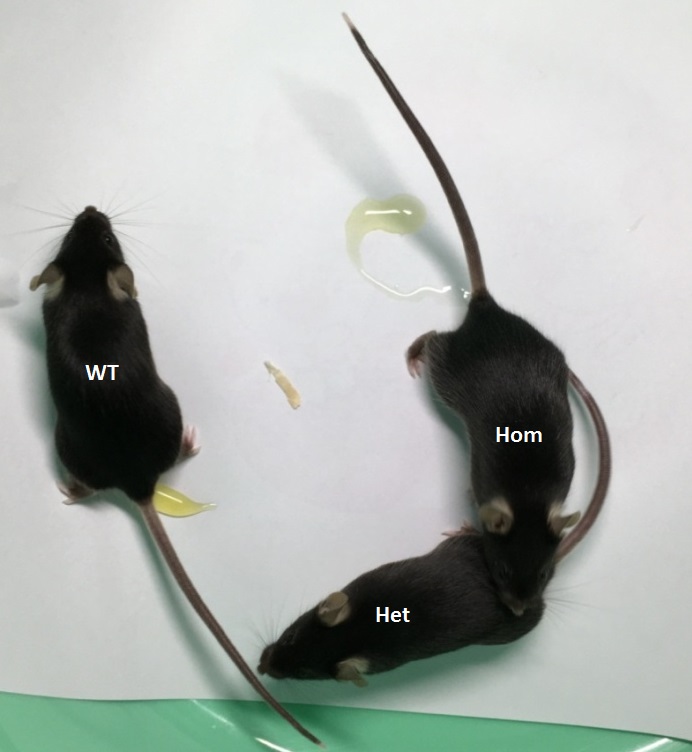
**Table S11:Statistics in body weight between the *Xrcc2*WT/WT and *Xrcc2*WT/L14P female mice.**

|  |  |  |  |
| --- | --- | --- | --- |
| **Groups** | **7d** | **30d** | 60d |
| Het♀（n=44） | 4.52±1.18 | 12.71±1.46 | 18.44±1.27 |
| WT♀（n=25） | 4.22±1.19 | 12.94±1.71 | 18.72±1.41 |
| t | 1.01 | -0.59 | -0.64 |
| p | 0.32 | 0.56 | 0.53 |

**Table S12.Statistics in body weight between the *Xrcc2*WT/WT and *Xrcc2*L14P/L14P female mice at 30 and 60 days.**

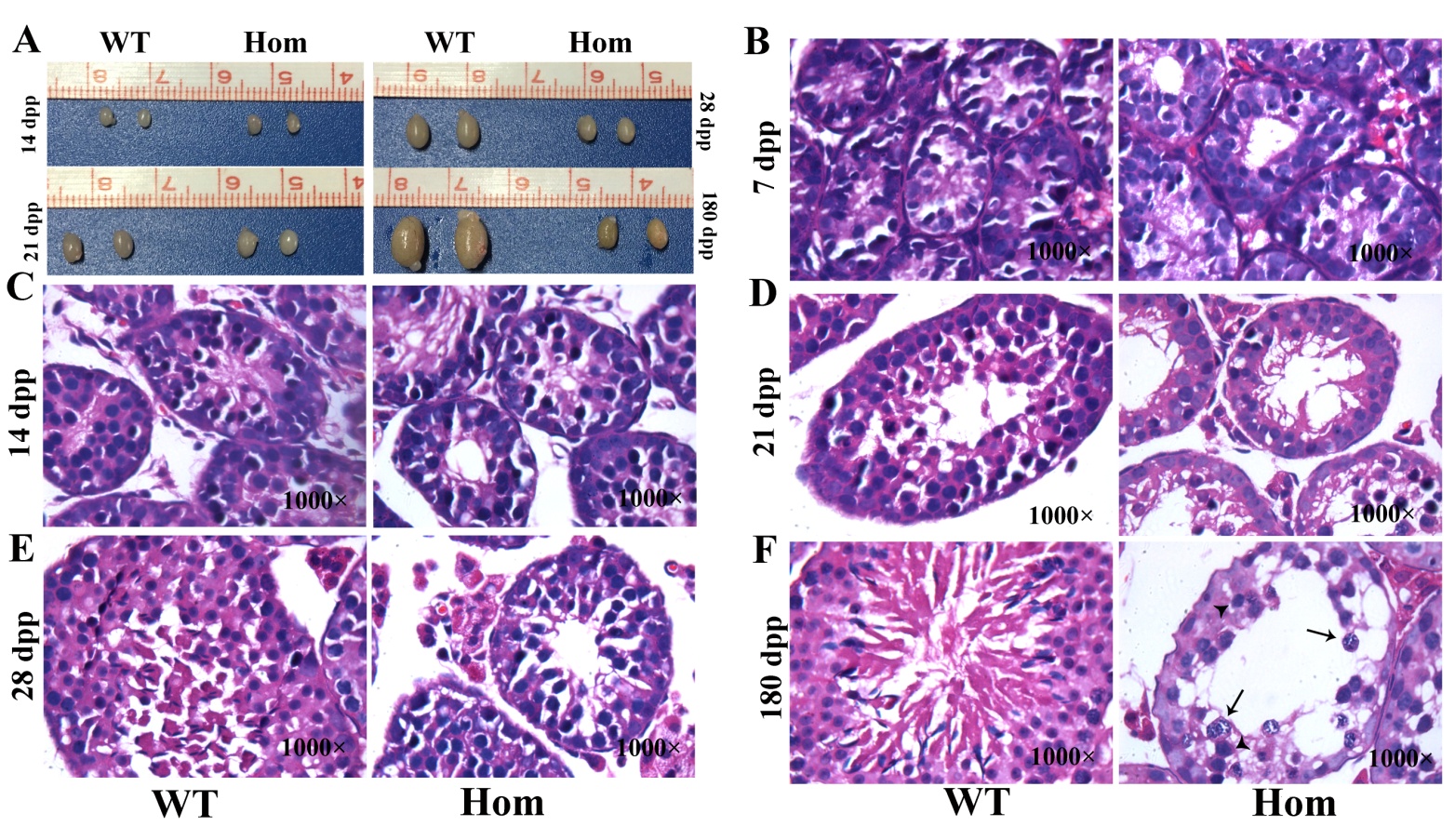
|  |  |  |  |
| --- | --- | --- | --- |
| **Groups** | **30d** | **60d** |  |
| Hom（n=14） | 12.84±1.72 | 17.89±0.70 |  |
| WT（n=25） | 12.94±1.71 | 18.72±1.41 |  |
| t | -0.17 | -1.56 |  |
| p | 0.86 | 0.13 |  |

**Figure S6: Physical characteristics of three males with different genotypes at 28 days post-partum.**

****

**Figure S7: Testis characteristics of homozygotes or WT mice from 7 days to 180 days post-partum (dpp).** A: Testis size; BCDEF: H&E staining ofseminiferous tubule, magnification=1000×.

Note: In 28 dpp tubules, multiple layers of spermatocytes were arrested at the zygotene stage of prophase I for homozygotes; in 180 dpp tubules, cells were arrested in the zygotene (arrow head) or pachytene stage (arrow).



**Table S13: Fertility of male homozygous mice.** Data of 17 (8-week old) ***Xrcc2***L14P/L14P males mated with wild-type or heterozygousfemales for 60–90 days.

|  |  |  |  |
| --- | --- | --- | --- |
| **Male ID** | **Female ID** | **Mating days** | **Giving birth status** |
| ♂ 0721 25（hom) (L1） | ♀ 0714 11(het) (L3) | 90 days | no birth |
| ♂ 0714 13（hom) (L2） | ♀ 0721 21(wt)(L2) | 90 days | no birth |
| ♂ 0714 13(hom) (L3) | ♀ 160917 B3(wt) (F3) | 90 days | no birth |
| ♂ 161101 C2(hom) (L2) | ♀ 160907 A5(wt) (R1) | 90 days | no birth |
| ♂ 161107 D1(hom) (L1) | ♀ 161101 C4(het) (L4) | 90 days | no birth |
| ♂ 161107 D7(hom) (R3) | ♀ 161101 C6(het) (R2) | 60 days | no birth |
| ♂ 161127 F2(hom) (L2) | ♀ 161127 G2(wt) (L2) | 60 days | no birth |
| ♂ 161127 F3(hom) (L3) | ♀ 161127 G3(wt) (L3) | 60 days | no birth |
| ♂ 161127 G8(hom) (R4) | ♀ 161127 F9(het) (FL1) | 60 days | no birth |
| ♂ 161201 H3(hom) (L3) | ♀ 161204 I1(wt) (L1) | 60 days | no birth |
| ♂ 161229 K5(hom) (R1) | ♀ 161204 R4(wt) (L4) | 60 days | no birth |
| ♂ 170110 L4(hom) (L4) | ♀ 161204 I5(wt) (R1) | 60 days | no birth |
| ♂ 170111 M6(hom) (R2) | ♀ 161204 I2(wt) (L2) | 60 days | no birth |
| ♂ 170111 M7(hom) (R3) | ♀ 161127 G2(wt) (L2) | 60 days | no birth |
| ♂ 170110 L5(hom) (R1) | ♀ 170111 M4(wt) (R4) | 60 days | no birth |
| ♂ 170110 L1(hom) (L1) | ♀ 170111 M8(wt) (R4) | 60 days | no birth |
| ♂ 170110 L3(hom) (L3) | ♀ 170111 M1(wt) (L1) | 60 days | no birth |

**Table S14.Fertility of female homozygote mice.** Data of 17 (8-week old) Xrcc2L14P/L14P females continually mated with WT or heterozygote males for 60 days.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Male ID** | **Female ID** | **Mating days** | **Fertility** | **Litter size** |
| ♂ 0410 25(het) | ♀ 0714 10(hom) | 41 days | yes | 7 |
| ♂ 071414 L1(wt) | ♀ 0721 20(hom) | 45 days | yes | 5 |
| ♂ 161107 D4(het)(L4) | ♀ 161101 C5(hom)(R1) | 24 days | yes | 5 |
| ♂ 161127 F12(wt)(FL4) | ♀ 170110 L6(hom)(R2) | 52 days | yes | 4 |
| ♂ 161127 F6(wt)(R2) | ♀ 170111 M3(hom)(L3) | 46 days | yes | 4 |
| ♂ 161204 I5(wt)(R1) | ♀ 170110 L4(hom)(L4) | 46 days | yes | 5 |
| ♂ 160907 A7 (wt)(R3) | ♀ 161101 C8(hom)(R4) | 53 days | yes | 2 |
| ♂ 161107 D4(het)(L4) | ♀ 161101 C5(hom)(R1) | 47 days | yes | 1 |
| ♂ 170121 P6(wt)(R2) | ♀ 170120 O4(hom)(L4) | 46 days | yes | 8 |
| ♂ 0405 22(het) | ♀ 160907 A1(hom)(F1) | 60 days | no birth | - |
| ♂ 161107 D4(het)(L4) | ♀ 161101 C7(hom)(R1) | 60 days | no birth | - |
| ♂ 161127 G4(het)(L4) | ♀ 161127 F7(hom)(R3) | 60 days | no birth | - |
| ♂ 160907 A6(het)(R2) | ♀ 161201 H1(hom)(L1) | 60 days | no birth | - |
| ♂ 161204 I6(wt)(R2) | ♀ 161201 H5(hom)(R1) | 60 days | no birth | - |
| ♂ 170111 M2 (wt)(L2) | ♀ 170213 T1(hom)(L1) | 60 days | no birth | - |
| ♂ 170205 S2 (wt)(L2) | ♀ 170214 V4(hom)(L4) | 60 days | no birth | - |
| ♂ 170213 T5 (wt)(R1) | ♀ 170222 X4(hom)(L4) | 60 days | no birth | - |

**Table S15**. **Statistics of litter size and mating time between fertile *Xrcc2*L14P/L14P and *Xrcc2*L14P/WT females.**

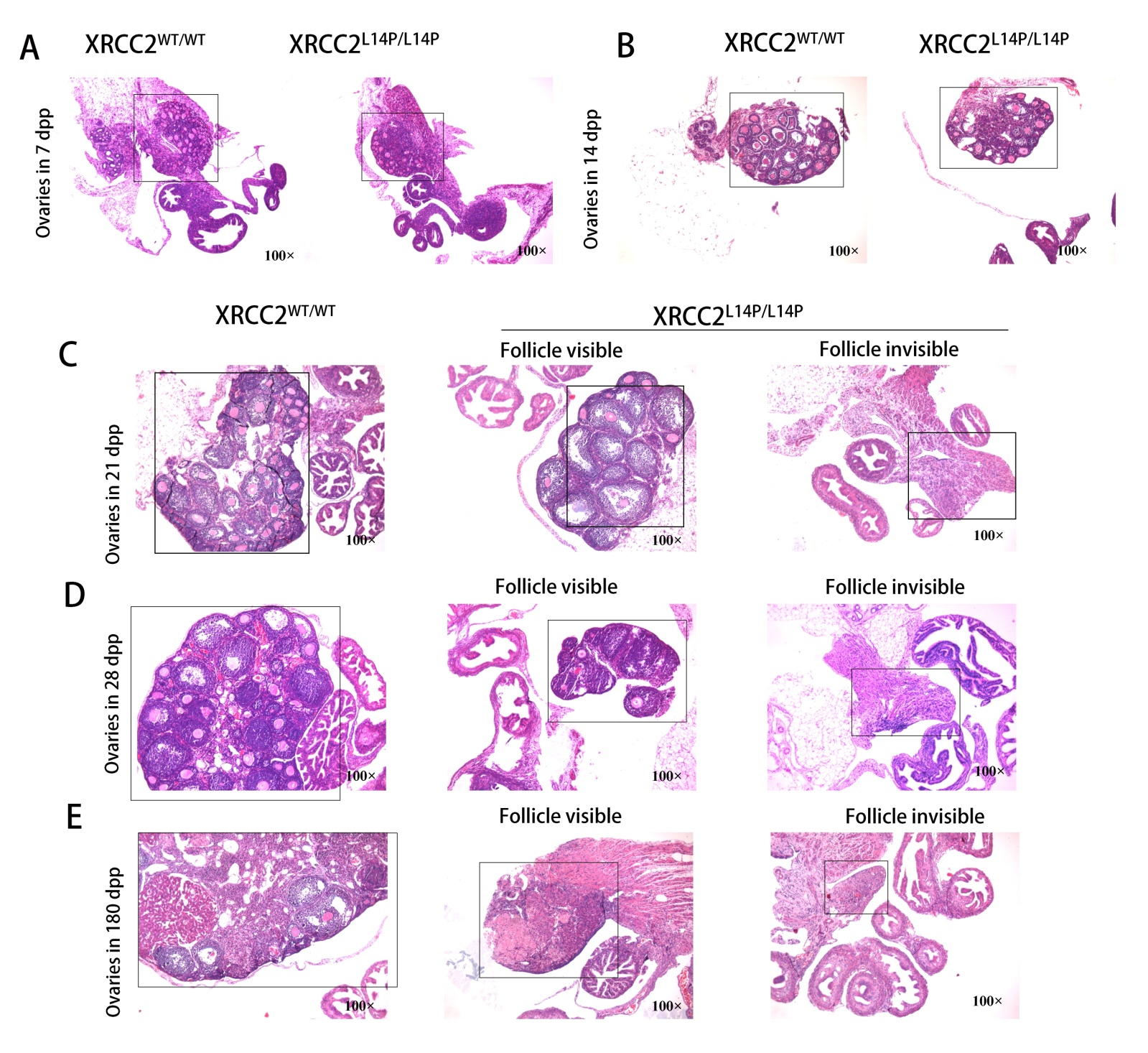
|  |  |  |
| --- | --- | --- |
| Groups | Mating time to give birth | Litter size |
| XRCC2L14P/L14P females（n=9） | 44.44±8.47 | 4.56±2.19 |
| XRCC2L14P/WTfemales（n=27） | 23.41±4.24 | 7.85±2.28 |
| t | 9.87 | -3.79 |
| p | ＜0.0001 | ＜0.001 |

**Table S16**.  **Results of histology of *Xrcc2*L14P/L14P mice ovaries from 7 days to 180 days post-partum (dpp).**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Mice age** | **7 dpp** | **14 dpp** | **21 dpp** | **28 dpp** | **90 dpp** | **180 dpp** |
| **Number of ovaries** | 10 | 10 | 10 | 10 | 10 | 10 |
| **Follicle visiable** | 10 | 10 | 8 | 7 | 5 | 2 |
| **Follicle invisiable** | 0 | 0 | 2 | 3 | 5 | 8 |

**Figure S8: Representative H&E staining figures of *Xrcc2*-mutated mice ovaries from 7 days to 180 days post-partum.**

Magnification=100. Box: ovary.



**Figure S9: Diagram of models of XRCC2 and other RAD51 paralogs.**

(A) Functional regions are shown for five RAD51 paralogs. Note: XRCC2 shows a special structure, and the asterisk indicates the position of the p.L14P mutation.

(B) Ribbon diagram of XRCC2. Arrow: residue 14-leucine is substituted by proline. The linker regions are encircled. This diagram was created by SWISS-MODEL (https://www.swissmodel.expasy.org) using the template 5h1c.1.

