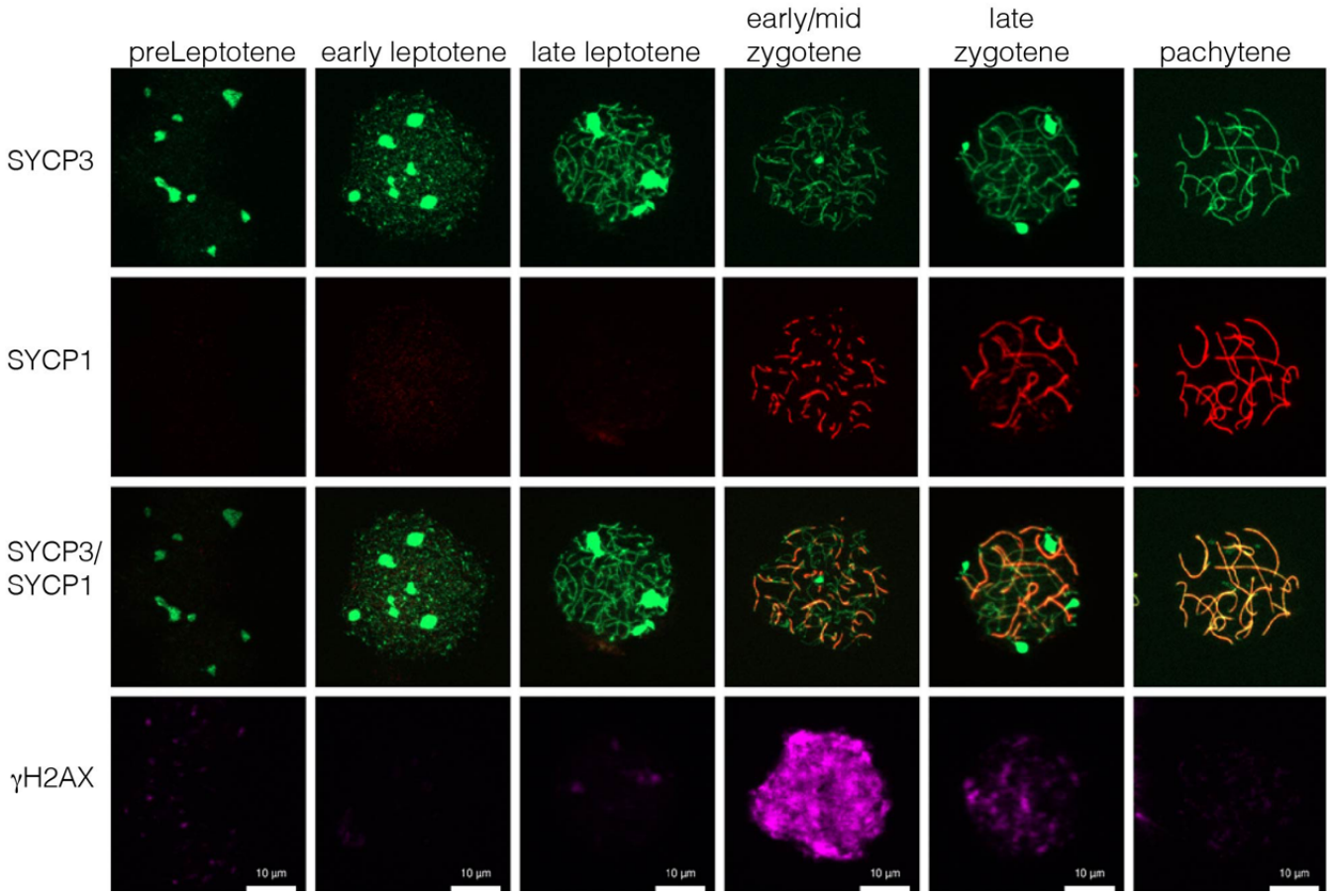
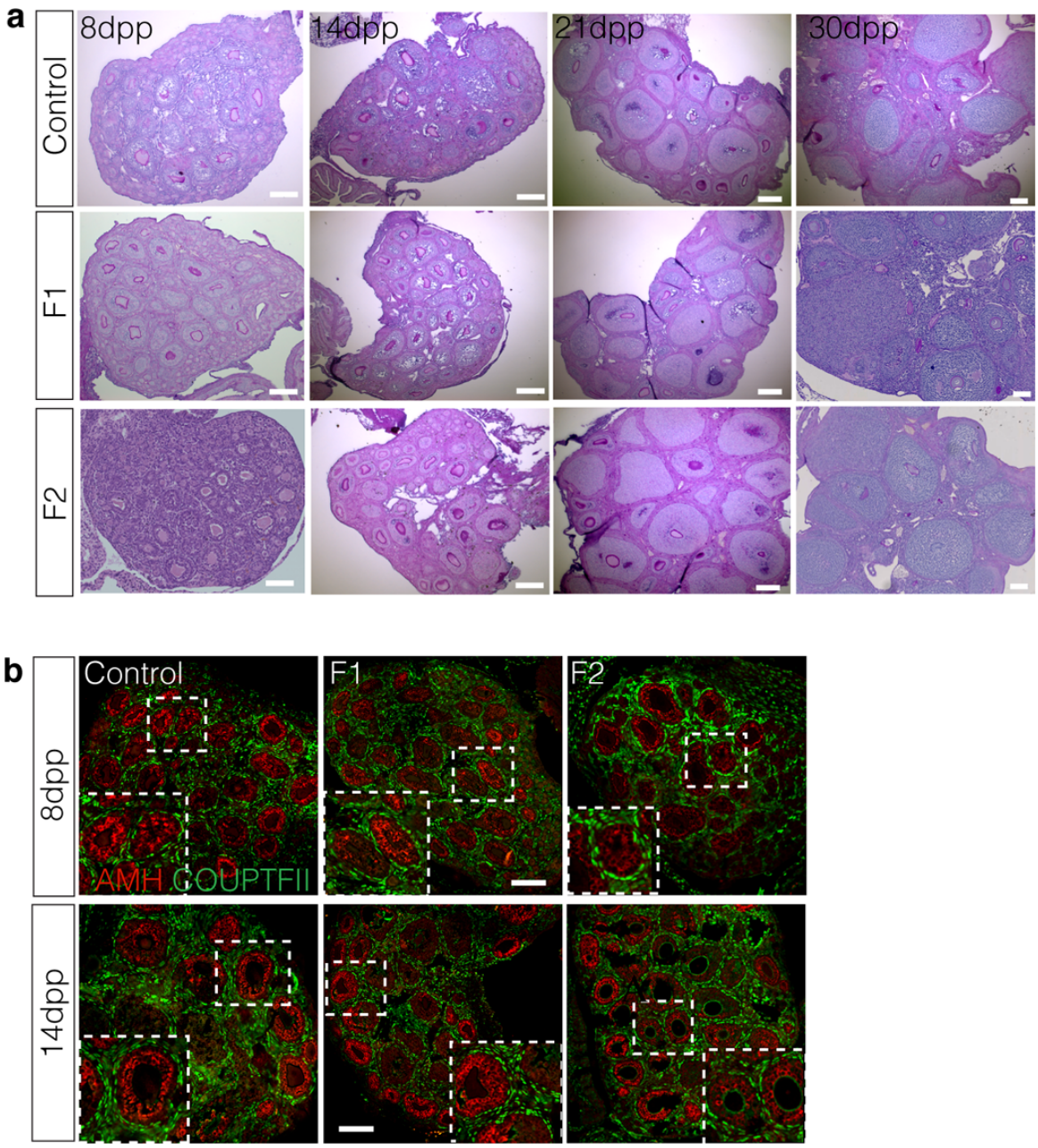
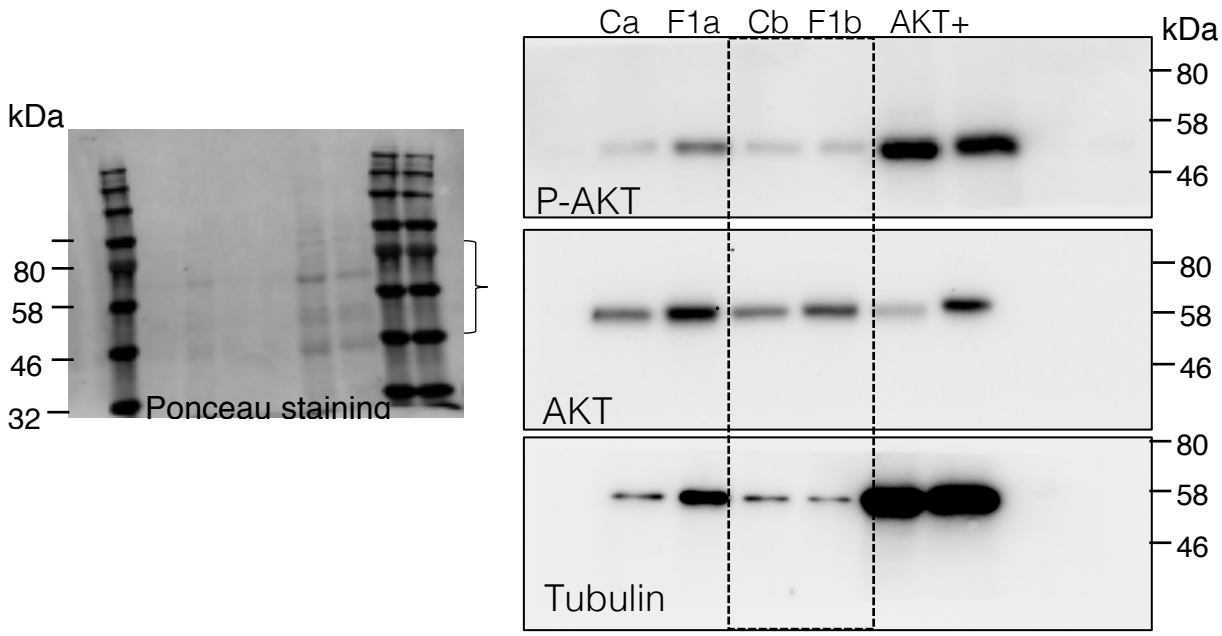
Supplementary Information



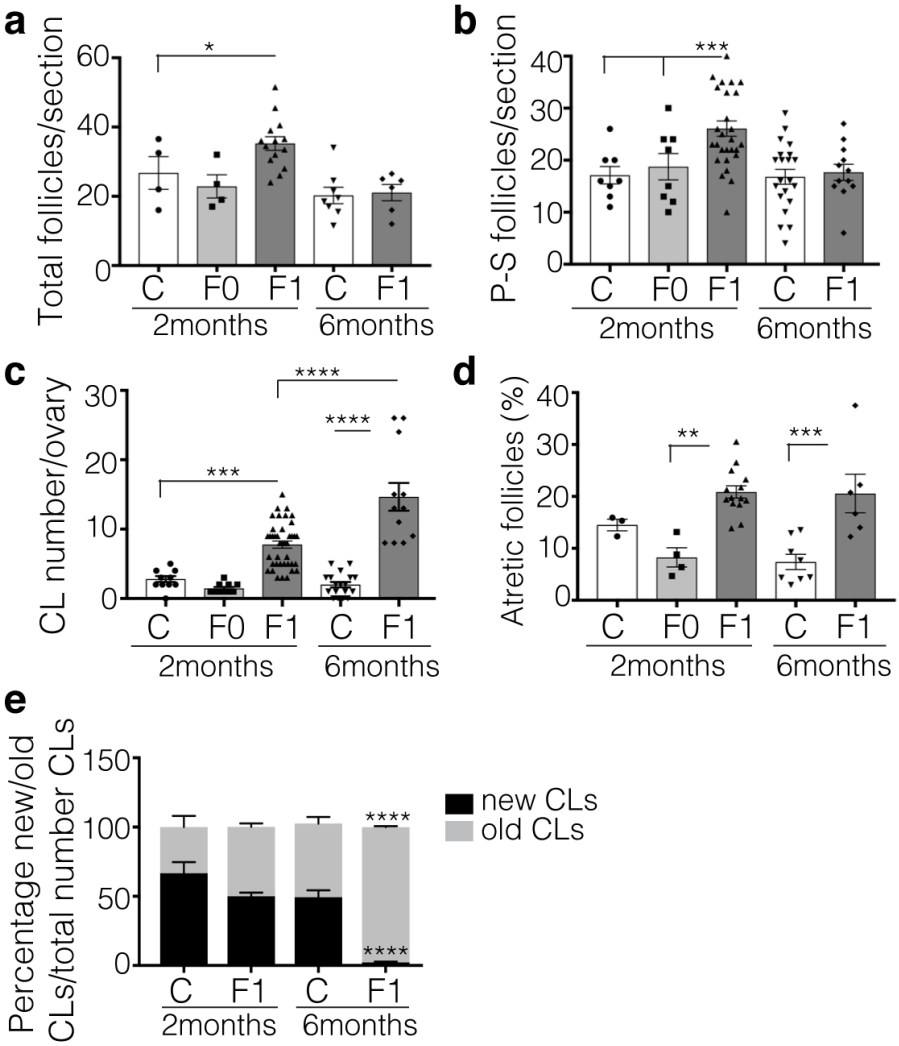
Supplementary Fig. 1. SYCP3, SYCP1 and γH2AX staining changes during meiotic prophase I substages.



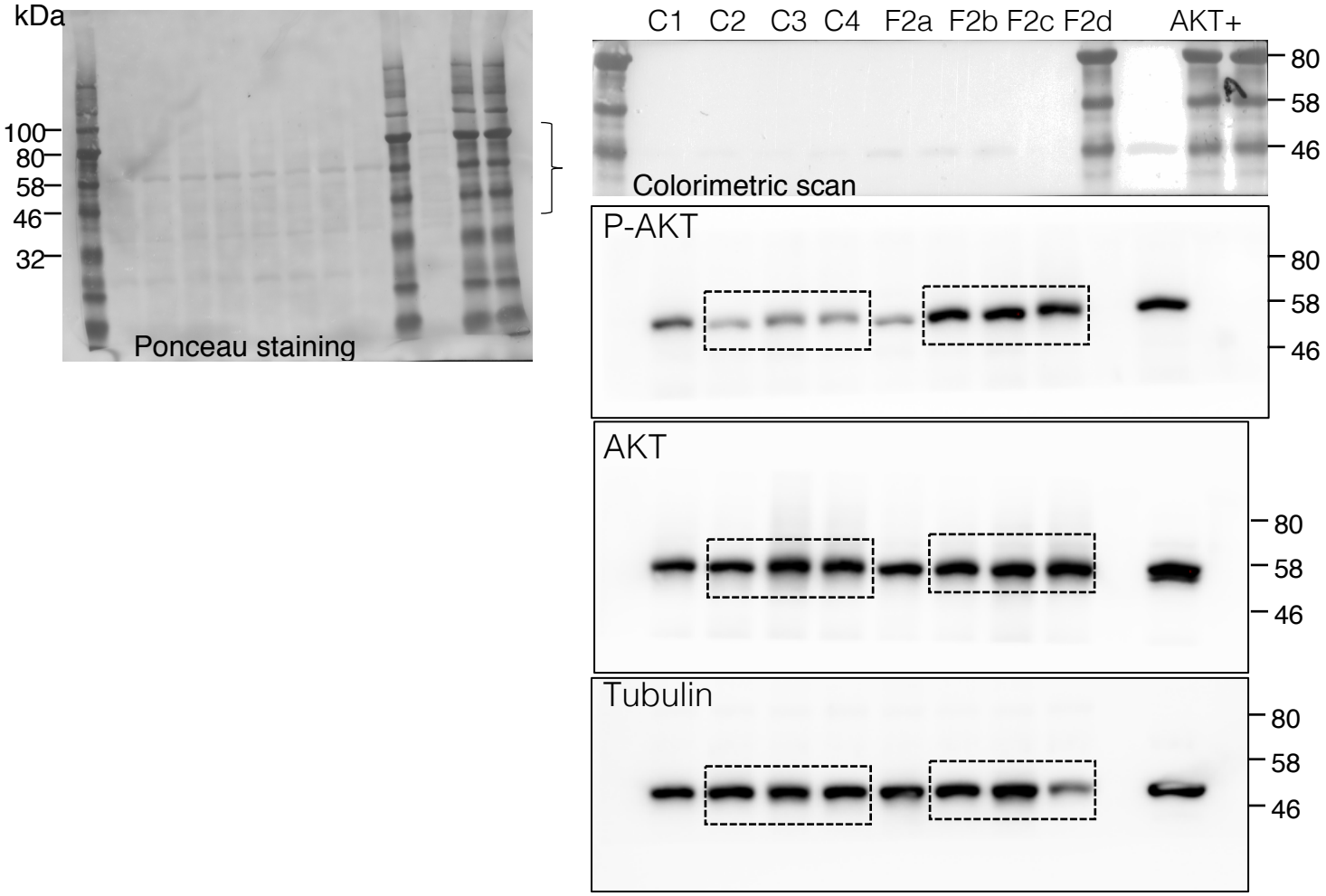
Supplementary Fig. 2. Follicular development in postnatal ovaries of *in utero* exposed animals and their offspring. **a** Representative images of paraffin-embedded tissue sections from 8, 14, 21 and 30dpp control, F1 and F2 ovaries, stained with the Periodic acid-Shiff dye. Scale bars= 80µm. **b** Representative immunofluorescence images for AMH (granulosa cell marker, red) and COUPTFII (interstitial cell marker, green) in tissue sections from 8 and 14dpp control, F1 and F2 ovaries. Enlarged panels show representative growing follicles. Scale bars=80µm.



Supplementary Fig. 3. Full scans of images of Western blot data; C=8jpp control gonads, F1=8dpp F1 gonads; AKT+ is a positive AKT cell extract.



Supplementary Fig. 4. Follicle and corpus luteum (CL) counts in 2-month- and 6-month-old ovaries. **a** Total follicle number per section. **b** Primary (P) and secondary (S) follicle number per section. **c** CL number per section. **d** Percentage of atretic follicles relative to the total number of follicles. **e** Percentage of newly formed CLs (new CL) and CLs formed in previous cycles (old CL) in 2-month- and 6-month-old control and F2 ovaries. **a-e** Data are the mean ± SEM of all follicles and CLs on 3 sections from ovaries (n=6 to 10 animals per group), and *P <0.05, **P <0.01, ***P <0.005, ****P <0.001.



Supplementary Fig. 5. Full scans of images of Western blot data; C1-C4 and F2a-F2d are 6month-old control and F2 ovaries; AKT+ is a positive AKT cell extract.

Supplementary Table 1. Gene ontology analysis of differentially expressed genes in 13.5dpc APAP+IBU exposed ovaries compared with controls.

Down-regulated genes/ GO biological process	**Number of genes**
ribosomal small subunit assembly (GO:0000028)	19
ATP synthesis coupled proton transport (GO:0015986)	21
energy coupled proton transport, down electrochemical gradient (GO:0015985)	21
GTP biosynthetic process (GO:0006183)	10
deoxyribonucleoside monophosphate metabolic process (GO:0009162)	9
protein import into mitochondrial matrix (GO:0030150)	17
positive regulation of protein homooligomerization (GO:0032464)	11
mitochondrial electron transport, ubiquinol to cytochrome c (GO:0006122)	13
guanosine-containing compound biosynthetic process (GO:1901070)	13
cytoplasmic translation (GO:0002181)	62
ribosome assembly (GO:0042255)	70
NADH dehydrogenase complex assembly (GO:0010257)	42
mitochondrial respiratory chain complex I assembly (GO:0032981)	42
purine ribonucleoside biosynthetic process (GO:0046129)	20
cellular detoxification (GO:1990748)	20
purine nucleoside biosynthetic process (GO:0042451)	20
proteasomal ubiquitin-independent protein catabolic process (GO:0010499)	24
cellular response to superoxide (GO:0071451)	13
cellular response to oxygen radical (GO:0071450)	13
pyrimidine deoxyribonucleotide metabolic process (GO:0009219)	13
positive regulation of mitochondrial membrane potential (GO:0010918)	13
purine ribonucleoside triphosphate biosynthetic process (GO:0009206)	83
regulation of ubiquitin protein ligase activity (GO:1904666)	17
Up-regulated genes/ GO biological process	**Number of genes**
chromosome organization involved in meiotic cell cycle (GO:0070192)	71
homologous chromosome segregation (GO:0045143)	61
synaptonemal complex organization (GO:0070193)	25
meiotic chromosome segregation (GO:0045132)	93
male meiosis I (GO:0007141)	22
positive regulation of neuron migration (GO:2001224)	20
microtubule nucleation (GO:0007020)	20
reciprocal meiotic recombination (GO:0007131)	45
homologous recombination (GO:0035825)	45
meiosis II (GO:0007135)	12
negative regulation of translation, ncRNA-mediated (GO:0040033)	12
meiosis II cell cycle process (GO:0061983)	12
miRNA mediated inhibition of translation (GO:0035278)	12
centriole-centriole cohesion (GO:0010457)	12
regulation of translation, ncRNA-mediated (GO:0045974)	12
meiotic chromosome separation (GO:0051307)	23
synaptonemal complex assembly (GO:0007130)	22
DNA synthesis involved in DNA repair (GO:0000731)	28
resolution of meiotic recombination intermediates (GO:0000712)	19
synapsis (GO:0007129)	50
microtubule anchoring (GO:0034453)	25
miRNA metabolic process (GO:0010586)	16

Supplementary Table 2. Meiotic genes that are differentially expressed in 13.5dpc female gonads upon APAP+IBU exposure.

	APAP+IBU downregulated genes	**Fold change**
Stra8	stimulated by retinoic acid gene 8	0.76
Rec8	REC8 meiotic recombination protein	0.65

	APAP+IBU upregulated genes	**Fold change**
Rad51ap2	RAD51 associated protein 2	3.15
Tex16	testis expressed gene 16	2.92
Sycp1	synaptonemal complex protein 1	2.82
Spata22	spermatogenesis associated 22	2.66
Hfm1	HFM1, ATP-dependent DNA helicase homolog	2.47
Sycp2	synaptonemal complex protein 2	2.45
Pet2	plasmacytoma expressed transcript 2	2.43
Rad21l	RAD21-like (S. pombe)	2.41
Fbxo47	F-box protein 47	2.40
Ccnb3	cyclin B3	2.29
Ugt8a	UDP galactosyltransferase 8A	2.21
Ccdc73	coiled-coil domain containing 73	2.11
Pramel1	preferentially expressed antigen in melanoma-like 1	2.08
Spdya	speedy/RINGO cell cycle regulator family, member A	2.02
Prdm9	PR domain containing 9	2.01
Msh4	mutS homolog 4	1.98
Tktl1	transketolase-like 1	1.94
Cdkl2	cyclin-dependent kinase-like 2 (CDC2-related kinase)	1.91
Meioc	meiosis specific with coiled-coil domain	1.89
D1Pas1	DNA segment, Chr 1, Pasteur Institute 1	1.88
Msh5	mutS homolog 5	1.87
Tsga10	testis specific 10	1.80
Usp32	ubiquitin specific peptidase 32	1.79
Sycp3	synaptonemal complex protein 3	1.78
Spo11	SPO11 meiotic protein covalently bound to DSB	1.77
Dmc1	DNA meiotic recombinase 1	1.77
Ddb2	damage specific DNA binding protein 2	1.77
Hormad1	HORMA domain containing 1	1.74
Dennd4a	DENN/MADD domain containing 4A	1.72
Dopey1	dopey family member 1	1.72
Caprin2	caprin family member 2	1.71
Adarb1	adenosine deaminase, RNA-specific, B1	1.67
Poln	DNA polymerase N	1.67
Taf7l	TATA-box binding protein associated factor 7 like	1.62
Cyld	CYLD lysine 63 deubiquitinase	1,62
Setdb2	SET domain, bifurcated 2	1.57
Inca1	inhibitor of CDK, cyclin A1 interacting protein 1	1.55
Crebl2	cAMP responsive element binding protein-like 2	1.50
Tex11	testis expressed gene 11	1.49
Tex12	testis expressed gene 12	1.48
Zfp541	zinc finger protein 541	1.46
Hormad2	HORMA domain containing 2	1.45
Dmrtc2	doublesex and mab-3 related transcription factor like family C2	1.41
Taf9b	TATA-box binding protein associated factor 9B	1.40
Ccdc36	coiled-coil domain containing 36	1.37
Stag3	stromal antigen 3	1.37
Madd	MAP-kinase activating death domain	1.36
Madd	MAP-kinase activating death domain	1.36
Syn2	synapsin II	1.35

Supplementary Table 3. List of antibodies used for immunofluorescence (IF) experiments on tissues, western blotting (WB) and IF on chromosome spreads (SP).

Antigen	Species	Provider	Reference	Dilution WB/IF/SP
FOXL2	Rabbit	Gift from Dagmar Wilhelm	[1]	1/300
AMH	Rabbit	Gift from N. diClemente	[2]	1/400
VASA/MVH	Rabbit	Millipore	AB4330	1/300
VASA/MVH	Mouse	Abcam	ab27591	1/2000
PCNA	Mouse	Sigma-Aldrich	P8825	1/500
FOXO3 (D19A7)	Rabbit	Cell Signaling	12829	1/1000 WB 1/500 IF
COUPTFII (NR2F2)	Mouse	R&D Systems	T9026	1/300
AKT(pan) (C67E7)	Rabbit	Cell Signaling	4691	1/1000 WB
Phosphorylated-AKT (Ser473)	Rabbit	Cell Signaling	9271	1/1000 WB
SYCP3	Rabbit	Abcam	ab15093	1/200 (IF)
SYCP3	Guinea pig	Homemade	[3]	1/1000 (SP)
SYCP1	Rabbit	Abcam	ab15090	1/400 (SP)
γH2AX	Mouse	Sigma-Aldrich	05-636	1/1000 (IF) 1/10000 (SP)

Supplementary Table 4. Oligonucleotides used for qPCR. For each gene, the upper oligonucleotide corresponds to the forward primer and the lower to the reverse primer.

Gene	Sequence 5'-3'	Gene	Sequence 5'-3'
Rps29	tgaaggcaagatgggtcac gcacatgttcagcccgtatt	*Akr1c18 (20αHsd)*	tggccctagccaagagttt gccaattggaaatcaaagacc
18S	gatccattggagggcaagtct ccaagatccaactacgagcttt	*ProgR*	tgcacctgatctaatcctaaatga ggtaaggcacagcgagtagaa
Amh	ggggagactggagaacagc agagctcgggctcccata	*StaR*	ttgggcatactcaacaacca acttcgtccccgttctcc
FoxL2	cggggttcctcaacaactc catctggcaggaggcgta	*Cyp11a1*	aagtatggccccatttacagg tggggtccacgatgtaaact
Wnt4	gcgtagccttctcacagtcc cgcatgtgtgtcaagatgg	*Lhcgr*	gatgcacagtggcaccttc cctgcaatttggtggaagag
Rspo1	cgacatgaacaaatgcatca ctcctgacacttggtgcaga	*Hsd3β*	gaccagaaaccaaggaggaa gcactgggcatccagaat
FoxO1	cttcaaggataagggcgaca gacagattgtggcgaattga	*Pten*	aggcacaagaggccctagat ctgactgggaattgtgactcc
Pou5fl (Oct4)	cctgggggctctatttgg ctcctgaagattttcattgttgtc	*Akt1*	tcgtgtggcaggatgtgtat acctggtgtcagtctcagagg
Ddx4 (Vasa)	cgccaaacccttatgttcag aaaaactctgcagccaacctt	*Akt2*	ataccaggcacccttcct cacaaagcataggcggtca
Dppa4	gctttcccagaacaaatgct ttgtgagctgtcttcaacctg	*PI3K*	ccagacagtgtttttgtaagagga tccatgccctatgcgact
Kitlg	tcaacattaggtcccgagaaa actgctactgctgtcattcctaag	*Pdk1*	tgatgaagactgctatggcaac cgtagacagggagtgggaag
Nobox	acggagaagctctgcaagaa ctgtctccagtgcagcagtc	*MTor*	agaagacagcggggaagg gcatcttgccctgaggttc
Figla	ggaagaagcgaaggtctcag gtcagagggtctgccactgt	*FoxO3*	gctaagcaggcctcatctca ttccgtcagtttgagggtct
Sohlh1	gagcgcgttgtcattcagt ctggctgccatgagtgag	*Lhx8*	gatgggacgatgctgactg ggtcattggatggggtaaca
Bmp15	acacagtaaggcctcccaga tgctacctggtttgatgctaga	*Gdf9*	acccagcaaccaggtgac cgatttgagcaagtgttccat

Supplementary References

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2 Tran, D., Picard, J. Y., Campargue, J. & Josso, N. Immunocytochemical detection of anti-mullerian hormone in Sertoli cells of various mammalian species including human. *J Histochem Cytochem* **35**, 733-743, doi:10.1177/35.7.3295030 (1987).

3 Grey, C., Baudat, F. & de Massy, B. Genome-wide control of the distribution of meiotic recombination. *PLoS Biol* **7**, e35, doi:10.1371/journal.pbio.1000035 (2009).