Abstract
The oocytes of B6.YTIR sex-reversed female mouse mature in culture but fail to develop after fertilization because of their cytoplasmic defects. To identify the defective components, we compared the gene expression profiles between the fully-grown oocytes of B6.YTIR (XY) females and those of their XX littermates by cDNA microarray. 173 genes were found to be higher and 485 genes were lower in XY oocytes than in XX oocytes by at least 2-fold. We compared the transcript levels of selected genes by RT-PCR in XY and XX oocytes, as well as in XO oocytes missing paternal X-chromosomes. All genes tested showed comparable transcript levels between XX and XO oocytes, indicating that mRNA accumulation is well adjusted in XO oocytes. By contrast, in addition to Y-encoded genes, many genes showed significantly different transcript levels in XY oocytes. We speculate that the presence of the Y-chromosome, rather than the absence of the second X-chromosome, caused dramatic changes in the gene expression profile in the XY fully-grown oocyte.

Introduction
The cytoplasm of the oocyte (ooplasm) exerts pivotal and long-lasting effects on not only the meiotic cell cycle progression but also fertilization and preimplantation embryonic development [1,2]. In the ovary, most of the oocytes are arrested at the end of meiotic prophase until they are recruited into the growth phase accompanied by follicular development. The oocytes are active in transcription during their growth but cease transcription entirely by the end of growth phase [3,4,5,6], and subsequent events are carried out by translation of the stored mRNAs and their post-translational modifications [7,8,9]. One of the most critical events in the oocyte is the segregation of homologous chromosomes at the first meiotic division and that of sister chromatids at the second meiotic division. A failure in the proper chromosome/chromatids segregation results in aneuploidy in embryos, the major cause of infertility in women over 35 years old [10,11]. It is conceivable that some ooplasmic components are required for the proper assembly of meiotic spindles and consequent chromosome segregations. Several molecules have been identified for such roles based on their knock-out or knock-down experiments. However, their phenotypes are often severe and unlikely to occur in the oocytes under physiological conditions such as in older women.

The B6.YTIR female mouse provides an excellent animal model for investigating the influence of ooplasmic components on the second meiotic spindle assembly and subsequent cell cycle progression under physiological conditions. Sex-reversal occurs when the YTIR-chromosome of a local Mus. Musculus domesticus variant in Tirano, Italy (TIR) is placed on the C57BL/6J (B6) genetic background [12,13]. We have previously shown that the XY female mouse is anatomically normal at young ages, and its oocytes reach the second meiotic metaphase in culture [14]. However, these oocytes contain aberrant second meiotic spindles, which fail at chromosome segregation after fertilization. Furthermore, these meiotic errors can be prevented by transferring the XY nucleus into an enucleated XX oocyte, thereby enabling the production of healthy offspring from the XY oocyte nucleus [15]. The offspring carry various combinations of sex chromosomes such as XO, XXY, and XYY, reflecting the lack of pairing between X- and Y-chromosomes during the meiotic prophase [16,17]. Thus, sex chromosome aneuploidy per se does not block oocyte maturation or embryonic development while inadequate sex chromosomes appear to render the ooplasm defective.

The XY female also provides a great opportunity to study the role of sex chromosomes in gametogenesis. It is well known that the behavior and transcriptional activity of sex chromosomes in the germ-line are very different between the two sexes. In the female germ-line, the second X-chromosome is reactivated prior to the onset of meiosis and remains active throughout oogenesis [18]. In the male germ-line, on the other hand, both the X- and Y-chromosomes are placed in a compartment, named XY or sex body, and transcriptionally repressed at the pachytene stage of meiotic prophase, named meiotic sex chromosome inactivation (MSCI) [19]. It is, therefore, informative to examine the behavior of sex-chromosomes in the XY oocyte. Our previous studies have shown that the X- and Y-chromosomes do not pair and the majority of single X-chromosomes are silent, as evident by the coating with γH2AX, at the pachytene stage of meiotic prophase.
The single Y-chromosome is rarely coated with H2A.X and at least one Y-encoded gene, Ube1y1, is transcribed in the XY fetal ovary. The transcriptional activity of sex chromosomes in XY oocytes during the resting stage or growth phase has not yet been examined.

In the present study, we compared gene expression profiles between XX and XY oocytes at the GV-stage collected from antral follicles by cDNA microarray. We evaluated the transcript levels of selected genes by semi-quantitative RT-PCR (sqRT-PCR) in XX and XY oocytes, as well as XO oocytes, in which the paternal X-chromosome is absent like XY oocytes. Such XO female mice can be produced from the XY male mouse carrying a Psf mutation on its X-chromosome, which results in a high frequency of X-Y non-disjunction [21,22]. Our results suggest that the expression of Y-encoded genes, rather than the haploinsufficiency of X-encoded genes, makes the XY oocyte defective in its cytoplasm.

Results and Discussion

Differentially expressed genes between XX and XY oocytes identified by microarray

In order to identify the cytoplasmic components responsible for the developmental incompetence of XY oocytes, we compared the gene expression profiles in the fully-grown oocytes from XY females with those from XX littersmates by microarray analysis. The Affymetrix Mouse Expression 430v2.0 GeneChip contains 45,037 probe sets that represent 14,484 full-length genes, 9450 non-ESTs and 21,103 ESTs, according to the manufacturer. The results showed that 4 Y-encoded, 8 X-encoded, and 161 autosomal genes had significantly higher transcript levels, whereas 77 X-encoded and 408 autosomal genes had lower transcript levels in XY oocytes than in XX oocytes by at least 2-fold (P<0.05 by students t-test) (Tables S1 and S2). Of these, 65 genes appeared with two or more probe sets which were available in the microarray, suggesting that results were highly reproducible. The differentially expressed genes include those involved in apoptosis, mitochondrial functions, posttranslational modifications, cellular gap junctions, carbohydrate metabolism, and ubiquitination.

mRNAs of most Y-encoded genes were detectable in XY oocytes

Microarray data showed that the transcript levels of Y-encoded genes, Ddx3y, Eif2s3y, Ube1y1, and Zfy2 were significantly higher in XY oocytes than in XX oocytes by at least 2-fold. We examined the transcript levels of these genes by linear-range sqRT-PCR by using random hexamers for cDNA synthesis. We also examined Y-encoded genes Rbmy1, Sry, Ssty1, Usp9y, Uty, and Zfy1, which were not included as being differentially expressed in the microarray data. Examples of agarose gel electrophoresis are shown in Figure 1. The transcript levels of Eif2s3y, Ddx3y, Ube1y1, and Uty (not shown) were high, those of Rbmy1, Ssty1, Usp9y, and Zfy1 (not shown) were near the detection limit, and those of Zfy2 or Sry (not shown) were undetectable in XY oocytes. The transcript levels of Zfy1 were similar to those of Rbmy1 after the same 36 amplitifcation cycles (not shown), but increased after 4 more cycles (Figure 1). On the other hand, none of the examined genes was detectable in XX oocytes. Results were consistent in three repeated experiments. These results suggest that the Y-chromosome is transcriptionally active in XY oocytes during the growth phase. Since Rbmy1, Ssty1, and Zfy2 are located near the centromere, their low or undetectable levels can be attributed to the heterochromatinization of this region.

Figure 1. RT-PCR detection of Y-encoded gene transcripts in XY and XX oocytes. Agarose gel electrophoresis stained with ethidium bromide. High transcript levels of Eif2s3y, Ddx3y, and Ube1y1 and lower levels of Romb1 were visible in XY oocytes but not in XX oocytes. The transcript levels of Zfy1 was similar to those of Rbmy1 after the same amplification cycles, but increased, as shown here, by adding 4 more cycles. For each RT-PCR experiment, β-actin was included as an internal control. S, 100 bp ladders.

Eif2s3y and Ddx3y encode highly conserved eukaryotic translation initiation factor subunit and RNA helicase, respectively, and are known to be essential for spermatogenesis in the mouse [23,24,25,26]. Ube1y1 encodes a ubiquitin-activating enzyme and may be involved in protein degradation during the metaphase to anaphase transition [27,28]. Romb1 encodes a RNA-binding protein, repeated over 50 times, and is known to be expressed in a germ-cell-dependent manner in both fetal and adult testes [29]. Zfy1 and Zfy2 are transcription factors encoding zinc-finger proteins, highly homologous but differentially regulated in males; Zfy2 is predominantly expressed in the germ cells of adult testes [30,31] whereas Zfy1 is expressed, in addition, in various embryonic tissues [30,31,32]. Although the microarray data included Zfy2, sqRT-PCR indicated that Zfy1 was expressed at much higher levels than Zfy2 in XY oocytes. It is conceivable that the microarray probe set may have hybridized with Zfy1 in the nearly absence of Zfy2. It was recently suggested that both Zfy1 and Zfy2 play a role in the elimination of asynapsed spermatocytes [33].

We do not know if any of these Y-encoded gene products exerts direct detrimental effects on the oocyte. However, it is conceivable that the expression of Y-encoded genes, which does not occur in normal oocytes, may cause dynamic changes in the expression of other genes in XY oocytes. For example, the expression of Y-encoded genes may influence the expression of their homologous X-encoded genes. To test this possibility, we compared the transcript levels of Ube1x (Uba1), Usp9x, and Eif2as3x normalized to those of β-actin in XX and XY oocytes by sqRT-PCR. No difference was found for Ube1x or Eif2as3x whereas the transcript levels of Usp9x was significantly lower in XY oocytes than in XX oocytes (n=3 each) (Figure 2). Since we found that the transcript levels of Ube1x and Eif2as3y were high (Figure 1) while those of Usp9y were near the detection limit (not shown), there was no direct correlation between the expression of Y-encoded genes and that of their homologous X-encoded genes in the fully-grown oocyte. It is intriguing that the transcript levels of most X-encoded genes in XY oocytes were no less than in XX oocytes despite their carrying single X chromosomes. Therefore, we also examined XO oocytes, but did not find any difference (Figure 2).

Accumulation of X-encoded gene mRNAs in XX, XO, and XY oocytes

The microarray data showed that the transcript levels of seven X-encoded genes were higher in XY oocytes than in XX oocytes.
levels of in XY oocytes than in XX or XO oocytes (n = 3, P<0.05). Microarray analysis also showed that the transcript levels of Bub1b, Brca1, Gja1, and Ggta1 were significantly higher in XY oocytes than in XX or XO oocytes (n = 3, P<0.01). The levels of Brca1 and Whip5 were also higher but did not reach a significant difference (n = 3). Microarray analysis also showed that the transcript levels of Atrx and Xiap were significant lower in XY oocytes than in XX oocytes by at least 2-fold. sqRT-PCR analysis confirmed that the transcript levels of Atrx and Xiap were lower in XY oocytes than in XX oocytes by at least 2-fold, sqRT-PCR analysis confirmed that the transcript levels of Atrx and Xiap were lower in XY than in XX oocytes (n = 6, P<0.05). No difference was found for Bub1b (n = 4). We added two X-encoded housekeeping genes, Pkg-1 and Hprt, but again found no difference between XX, XO, and XY oocytes (Figure 2). We used transcript levels of beta-actin for normalizing the results in each pool of oocytes. No difference was found in the beta-actin transcript levels in the same number of fully-grown oocytes from XX, XO, or XY females (n = 3) (not shown).

It is known that the second X-chromosome in the XX oocyte is activated prior to the onset of meiosis and remains active throughout oogenesis [10]. This is in agreement with our data that no Xist mRNAs were detectable in XX oocytes at the GV-stage (Figure 3). Consequently, we anticipated the expression of X-encoded genes in XO and XY oocytes to be half of those in XX oocytes. Therefore, we were surprised that the transcript levels of most X-encoded genes were comparable in XX, XO, and XY oocytes. The discrepancy between the microarray data and sqRT-PCR results can be attributed to the choice of primers, oligo-d(T) and random hexamers, respectively, for cDNA synthesis. Oligo-d(T) primers are less efficient in the reverse transcription of mRNAs with short poly(A) tails, which are common in the fully grown oocyte. We speculate that we detected the accumulation of mRNAs, not the steady-state transcription, in the fully-grown oocyte [34,35]. Therefore, our results suggest that the maximum storage of mRNAs is adjusted in XX and XO oocytes. In this light, significantly higher or lower transcript levels of some X-encoded genes in XY oocytes, namely Im2a, Atrx, and Xiap, are remarkable and may be associated with the cytoplasmic defects of XY oocytes.

Im2a encodes a type II integral membrane protein that is involved in osteo- and chondrogenic differentiation [36]. Its expression or role in germ cells is unknown. Since it contains consensus binding sites for various transcription factors, its transcript levels may have been altered by a change in certain transcription factors in XY oocytes. ATRX, a member of the SNF2 family of helicase/ATPase, is required for the second metaphase (MII) chromosome alignment and meiotic spindle assembly in mouse oocytes [37]. It was also reported that ATRX deficiency results in centromere instability and a high incidence of aneuploidy in oocytes and preimplantation embryos [38]. In the XY oocyte matured in vitro, we have observed an aberrant MII-spindle with chromosome misalignment, leading to a failure in the second meiotic division after fertilization [17]. We speculate that the lower Atrx transcript levels may be, at least partially, responsible for the meiotic defects in the XY oocyte. Xiap encodes a dominant endogenous inhibitor of apoptosis [39]. The direct role of XIAP in protecting oocytes from apoptosis is unlikely since XY oocytes within follicles rarely undergo apoptosis [40]. However, the majority of follicles undergo atresia under physiological conditions, and high expression of XIAP in follicular cells is associated with the prevention of follicular atresia [41,42,43]. Therefore, lower Xiap transcript levels in the XY oocyte may reflect the status in its neighbouring cumulus cells.

Transcript levels of autosomal genes in XX, XO, and XY oocytes

The results of microarray analysis showed that the transcript levels of 179 genes spread over all autosomes were higher in XY oocytes than in XX oocytes by at least 2-fold. sqRT-PCR analysis confirmed that, from the list of differentially expressed genes, Agtr1a, Amy2a1/2a5/2b, and Vas were significantly higher in XY oocytes than in XX or XO oocytes in the range of 10–15 fold (Figure 4). Stx19 transcript levels were higher but did not reach a statistical significance (n = 3). The microarray data also showed that the transcript levels of Acen1, Dub2, and Epsa1 were higher in XY oocytes but they were eliminated from the final list because signals of some samples were not within the acceptable range. However, sqRT-PCR confirmed that they were significantly higher in XY oocytes (Figures 3 and 4). We tested more genes, such as Bub1b, Boca1, Gja1, and Ggt1, which were not included in the microarray data as differentially expressed genes, and sqRT-PCR confirmed that their transcript levels were similar in XY and XX oocytes. Transcript levels of all genes examined were comparable between XX and XO oocytes. These results are consistent with our hypothesis that the storage of mRNAs for most genes was well adjusted in the fully grown oocyte, but those for specific genes were abnormally higher in XY oocytes.

The higher transcript levels of Amy2a3 and Epsa1 may reflect the poor supply of energy source into the XY oocyte from its surrounding cumulus cells.
neighboring cumulus cells. *Amy2a5* encodes pancreatic α-amylase, which is involved in the metabolism of carbohydrate and fatty acids such as starch, glycogen, and oligosaccharides. α-glucosidase, a resultant metabolite, further degrades disaccharides into simpler sugars [44], which are readily available for ATP production. It is known that *Amy2a5* is upregulated in the absence of glucose in certain cell types [45]. Since oocytes cannot directly use glucose, the surrounding cumulus cells must provide oocytes with glucose metabolites [46]. Therefore, our present results may indicate that either the oocyte-cumulus cell communication is impaired or cumulus cells are malfunctioning in the XY ovary.

*Epas1* encodes a transcription factor, Hypoxia-Inducible Factor 2α (HIF-2α), and plays key roles in the Krebs cycle and fatty acid oxidation [47]. Its upregulation in XY oocytes may reflect a limited energy supply from the cumulus cells. Unlike *Amy2a5*, however, *Epas1* transcript levels were significantly higher in the growing oocytes isolated from XY ovaries as early as 10 dpp (Figure 5). It is conceivable that the altered gene expression profile in XY oocytes may not be cell-autonomous but involve interaction with the surrounding somatic cells.

*Agr1a*, *Eps1*, and *Vasn* are known to play roles in ovulation [48,49,50,51,52]. We have previously reported that follicular development is largely normal up to the antral stage but rarely reaches the preovulatory stage in the XY ovary [40], and very few or no oocytes are ovulated by XY females by gonadotropin treatment [53]. The higher transcript levels of the above three genes in XY oocytes may reflect the conditions which are essential for ovulation. *Dub2* encodes a deubiquitinating enzyme involved in proteolysis, which has been implicated in the control of mammalian gametogenesis and fertilization [54,55,56]. *Acer1* encodes alkaline ceramidase 1, which catalyzes hydrolysis of ceramides to generate sphingosine (SPH), which in turn is phosphorylated to form sphingosine-1-phosphate (S1P). Ceramide, SPH, and S1P are bioactive lipid second messengers associated with cell proliferation and apoptosis [57,58,59,60,61]. The higher transcript levels of *Acer1* in XY oocytes may influence the proliferation of cumulus cells. This is consistent with our previous finding that the number of cumulus cells in the antral follicles is smaller in the XY ovary than in the XX ovary by 40% [62].

Figure 3. RT-PCR detection of additional X-encoded (in rectangular boxes) and autosomal gene transcripts in XX, XO and XY oocytes. A. Agarose gel electrophoresis stained with ethidium bromide. S, 100 bp ladders. B and C. Relative transcript levels of X-encoded (A) and autosomal (C) genes. In each set of experiment, the transcript levels were normalized against the mean of two β-actin controls. Each column indicates the mean ± SEM (n = 6 for *Atrx* and *Xiap*, n = 4 for *Atp2g5* and *Dub2*, n = 3 for others). Different low case and capital letters above columns denote statistical differences at P < 0.05 and 0.01, respectively, by one-way ANOVA.
doi:10.1371/journal.pone.0040481.g003
Conclusion

The present results show that similar levels of mRNAs were accumulated in XO and XX oocytes by the end of growth phase despite the different dosages of X-encoded genes. By contrast, mRNA levels of certain X-encoded and autosomal genes were significantly different in XY oocytes. We speculate that the accumulation of mRNAs was adjusted despite the absence of the second X-chromosome, but altered by the expression of Y-encoded genes in the fully-grown oocyte. We need further studies to provide evidence for supporting this hypothesis. Nonetheless, the list of genes in the present study provides an opportunity to identify the ooplasmic components which have critical effects on the second meiotic spindle assembly in the oocyte.

Materials and Methods

Mouse

All animal experiments were conducted in accordance with the Guide to the Care and Use of Experimental Animal issued by the Canadian Council on Animal Care and with the approval by Animal Research Committee of McGill University. The C3H/HeJ.B6.YTIR male mice (N45–50 backcross generations) were crossed with B6 females (Jackson Laboratory, Bar Harbor, ME) to produce XY females and their XX littermates. A Paf carrier mutant male on the C3H/HeJ genetic background was purchased from the Jackson Laboratory and backcrossed to B6 females in our mouse colony. Paf carrier males (8–10 backcross generations) were crossed with B6 females to produce XO females carrying maternal X-chromosomes. The day of delivery was defined as 0 dpp.

Genotyping

Upon weaning of pups at 20–25 dpp, their ear punches were taken and used for determining their genotypes. For the offspring from the cross between B6 females and B6,YTIR males, ear punches were digested overnight in a lysis buffer and the heat-inactivated lysate was subjected to PCR amplification of the Y-encoded Zfy gene as described previously [63]. For the offspring from the cross between B6 females and Paf carrier males, total RNA was extracted from ear punches by using TRIzol (Invitrogen, Burlington, ON) and dissolved in RNase-free water. The RNA sample was then subjected to cDNA synthesis and subsequent PCR amplification of the Xist transcript, using the conditions and primers previously described [64].

Collection of oocytes

XX, XY and XO females at 25–29 dpp were injected intraperitoneally each with 5 IU equine chorionic gonadotropin (Sigma, St Louis, MO), and sacrificed 45–47 hours later. Fully grown GV-stage oocytes surrounded by cumulus cells were isolated by puncturing large antral follicles with a pair of 26-gauge needles, and then denuded of cumulus cells by repeated pipetting through a fine glass needle. Only the oocytes with an intact GV and no apparent sign of degeneration were collected and stored at 2°C.

Growing oocytes were collected from XX, XY, and XO females at 10 and 17 dpp. Ovaries were treated with 0.5 mg/ml each of testicular hyaluronidase (type IV), collagenase (B grade) and egg white lysozyme (all from Sigma) in M2 medium.
as previously reported [65]. Oocytes with 40–60 μm diameter were collected with a fine glass needle, transferred in a group into a microcentrifuge tube, and stored at −80°C.

Microarray analysis
Total RNA were isolated from 10 oocytes each from 3 XY and 3 XX females using the RNeasy Micro Kit (Qiagen, Valencia, CA) and extracted in 11 μl RNase-free water. The Two-Cycle Eukaryotic Target Labeling Kit (Affymetrix) was used for synthesizing cRNA with oligo(dT) primers starting from 9 μl total RNA in solution. Manufacturers' protocols were optimized for small quantities of total RNA as previously reported [66]. Equal amounts (10 μg) of fragmented and biotin-labeled cRNA from each sample were hybridized to Affymetrix Mouse Genome 430 2.0 GeneChip® arrays for 16 h at 45°C. The GeneChips were then washed and stained with a GeneChip Fluidics Station 460 (Affymetrix) according to the Expression Analysis Technical Manual. An Affymetrix GeneChip Scanner 3000 was used to quantify the signals. The GeneChip Operating Software (GCOS) version 1.3 (Affymetrix) output files were then loaded into GeneSpring v10.1 (Agilent Technologies, Santa Clara, CA) with a normalization shift to the 50th percentile and baseline transformation to the median of all the samples. In the first step of data processing, present (P), marginal (M), or absent (A) calls, based on hybridization intensity with perfect match probes over transcripts with a raw signal intensity greater than 100 for at least two samples in either XX or XY group were selected. In the second step, genes with at least 2-fold differences common in three sample sets were selected. In the resultant list, significant differences (P<0.05) were calculated between XX and XY samples by students t-test. When one sample of the group with higher expression was below 100 (A call), it was excluded, while all three samples of the group with lower expression were included in the statistical analyses.

Semi-quantitative RT-PCR
Total RNA were isolated from 40–80 oocytes in a group using the RNeasy Micro Kit as described above. First-strand cDNA synthesis was carried out by using Moloney Marine Leukemia Virus Reverse Transcriptase (M-MLV, Invitrogen) and random hexamers as described previously [67]. Each cDNA sample was processed for PCR amplification by denaturation at 95°C for 5 min followed by 36 cycles (unless specified in Table S3) at 95°C for 25 sec, 60°C for 25 sec, and 72°C for 40 sec and final extension at 72°C for 10 min with a thermocycler (Biometra, Model T1, Göttingen, Germany). The primers used for RT-PCR are given in Table S3. After PCR amplifications, 15 μl of each reaction mixture was applied to 2% agarose gel electrophoresis in TAE buffer and visualized with ethidium bromide fluorescence labeling. The intensity of each band was quantified and the relative intensity against β-actin in the same lane was calculated using Alphalmager 2000 system (Alpha Innotech Co., San Leandro, CA). Results were analyzed by either one-way ANOVA followed by LSD test or students t-test.

Supporting Information
Table S1 Differentially expressed genes at higher levels in XY oocytes than in XX oocytes, identified by cDNA microarray. This table provides the list of genes which were found to be expressed at higher levels in XY oocytes than in XX oocytes by at least 2-fold (p<0.05, student t-test).

Table S2 Differentially expressed genes at lower levels in XY oocytes than in XX oocytes, identified by cDNA microarray. This table provides the list of genes which were found to be expressed at lower levels in XY oocytes than in XX oocytes by at least 2-fold (p<0.05, students t-test).

Table S3 Primer sequences. This table provides the list of primer sequences used for RT-PCR.

Author Contributions
Conceived and designed the experiments: BX YO TT. Performed the experiments: BX YO FC. Analyzed the data: BX YO TT. Contributed reagents/materials/analysis tools: TT YO. Wrote the paper: BX YO TT.

References
1. Zheng P, Dean J (2007) Oocyte-specific genes affect folliculogenesis, fertilization, and early development. Semin Reprod Med 25: 243–251.
2. Li L, Zheng P, Dean J (2010) Maternal control of early mouse development. Development 137: 859–870.
3. Kaplan G, Abreu SL, Bachvarova R (1982) rRNA accumulation and protein synthetic patterns in growing mouse oocytes. J Exp Zool 220: 361–370.
4. Paynton BV, Rempel R, Bachvarova R (1983) Changes in state of adenylation and time course of degradation of maternal mRNAs during oocyte maturation and early embryonic development in the mouse. Dev Biol 129: 304–314.
5. Rollier RJ, Kinloch RA, Hirschka BY, Li SS, Wassarman PM (1989) Gene expression during mammalian oogenesis and early embryogenesis: quantification of three messenger RNAs abundant in fully grown mouse oocytes. Development 106: 251–261.
6. Potrykus S, Vasenova R, Patel BG, Latham KE (2008) Analysis of polysomal mRNA populations of mouse oocytes and zygotes: dynamic changes in maternal mRNA utilization and function. Dev Biol 298: 155–166.
7. De Leon V, Johnson A, Bachvarova R (1983) Half-lives and relative amounts of maternal mRNA populations of mouse oocytes and zygotes in the mouse. J Biol Chem 258: 2535–2546.
8. Oh B, Hwang S, McLaughlin J, Solter D, Knowles BB (2000) Timely translation of maternal and early development in vitro. Dev Biol 178: 263–275.
9. Ohata Y, Villermue M, Kono T, Takeko T (2008) Transcription of Y chromosomes from XY female mice was made possible by the replacement of cytoplasm during oocyte maturation. Proc Natl Acad Sci U S A 105: 13918–13923.
10. Anleah A, Smith L, Chen H, Taketo T (2000) Both nuclear and cytoplasmic components are defective in oocytes of the B6-YDOM sex-reversed female for maturation, fertilization, and embryonic development in vitro. Dev Biol 219: 263–275.
11. Hassold T, Hunt P (2001) Too err (meiotically) is human: the genesis of human aneuploidy. Nat Rev Genet 2: 289–291.
12. Eicher EM, Washburn LL, Whitney JB 3rd, Morrow KE (1982) Mus poecilavius Y chromosome in the C57BL/6J murine genome causes sex reversal. Science 217: 535–537.
13. Nagamine CM, Takeko T, Koo GC (1987) Studies on the genetics of tda-1 XY sex reversal in the mouse. Differentiation 33: 223–231.
14. Anleah A, Leedie N, Saced T, Taketo T (1996) Competence of oocytes from the B6-YDOM sex-reversed female mouse for fertilization, and embryonic development in vitro. Dev Biol 178: 263–275.
15. Ohata Y, Villermue M, Kono T, Takeko T (2008) Transmission of Y chromosomes from XY female mice was made possible by the replacement of cytoplasm during oocyte maturation. Proc Natl Acad Sci U S A 105: 13918–13923.
16. Anleah A, Smith L, Chen H, Taketo T (2000) Both nuclear and cytoplasmic components are defective in oocytes of the B6-Y(TIR) sex-reversed female mouse. Dev Biol 219: 277–286.
17. Villermue M, Chen HY, Kurokawa M, Fisore RA, Takeko T (2007) The presence of X- and Y-chromosomes in oocytes leads to impairment in the progression of the second meiotic division. Dev Biol 301: 1–13.
18. Mori M, McLaren A (1981) X-chromosome activity in foetal germ cells of the mouse. J Embryol Exp Morphol 63: 73–84.
19. Turner JM, Mahadevaiah SK, Benavente R, Offenberg HH, Heyting C, et al. (2000) Analysis of male meiotic “sex body” proteins during XY female meiosis provides new insights into their functions. Chromosoma 109: 426–432.
20. Alton M, Lau MP, Villermue M, Takeko T (2008) The behavior of the X- and Y-chromosomes in the oocyte during meiotic prophase in the B6-Y(TIR) sex-reversed mouse ovary. Reproduction 135: 241–252.
39. Kawamura K, Sato N, Fukuda J, Kodama H, Kumagai J, et al. (2003) Survivin
37. De La Fuente R, Viveiros MM, Wigglesworth K, Eppig JJ (2004) ATRX, a
36. Pittois K, Wauters J, Bossuyt P, Deleersnijder W, Merregaert J (1999) Genomic
35. Tay J, Hodgman R, Richter JD (2000) The control of cyclin B1 mRNA
34. Huarte J, Stutz A, O'Connell ML, Gubler P, Belin D, et al. (1992) Transient
32. Zwingman T, Erickson RP, Boyer T, Ao A (1993) Transcription of the sex-
31. Nagamine CM, Chan K, Hake LE, Lau YF (1990) The two candidate testis-
30. Koopman P, Gubbay J, Collignon J, Lovell-Badge R (1989) Zfy gene expression
29. Lee J, Hong J, Kim E, Kim K, Kim SW, et al. (2004) Developmental stage-
27. Hendriksen PJ, Hoogerbrugge JW, Themmen AP, Koken MH, Hoeijmakers JH,
25. Ditton HJ, Zimmer J, Kamp C, Rajpert-De Meyts E, Vogt PH (2004) The AZFa
23. Ehrmann IE, Ellis PS, Mazeyrat S, Duthie S, Brockdorff N, et al. (1998) Evidence that meiotic sex chromosome inactivation is essential for male fertility.
22. Burgoyne PS, Evans EP (2000) A high frequency of XO offspring from X(Paf)Y*
21. Lane PW, Davisson MT (1990) Patchy fur (Paf), a semidominant X-linked gene
20. Ehrmann IE, Ellis PS, Mazeyrat S, Duthie S, Brockdorff N, et al. (1998) Determining region genes Sry and Zfy in the mouse preimplantation embryo. PLoS Genet 6: e1001137.
19. Cho Y, Oda T, Akiba M, Yoshikawa Y, Koyama N, et al. (1994) A Y-encoded subunit of the translation initiation factor eIF2 is essential for mouse spermatogenesis. Nat Genet 9: 49–55.
18. Hendriksen PJ, Hoogerbrugge JW, Themmen AP, Koken MH, Hoeijmakers JH, et al. (1995) Postmeiotic transcription of X and Y chromosomal genes during spermatogenesis in the mouse. Dev Biol 170: 730–733.
17. Zwingman T, Bignell C, Erickson RP, Boyer T, Ao A (1993) Transcription of the sex-
16. Pittois K, Wauters J, Bossuyt P, Deleersnijder W, Merregaert J (1999) Genomic
15. Taketo-Hosotani T, Nishioka Y, Nagamine CM, Villalpando I, Merchant-
14. Huarte J, Stutz A, O'Connell ML, Gubler P, Belin D, et al. (1992) Transient
13. Lee J, Hong J, Kim E, Kim K, Kim SW, et al. (2004) Developmental stage-
12. Lee CH, Taketo T (2001) Low levels of Sry transcripts cannot be the sole cause
11. Lightman A, Tarlatzis BC, Guller B, Jellinck H, et al. (1985) The origin of the X chromosome inactivation. Cell 72: 171–182.
10. Ikeda Y, Imai Y, Kumagai H, Nosaka T, Morikawa Y, et al. (2004) Vasorin, a member of the SNF2 family of helicase/ATPases, is required for chromosome alignment and meiotic spindle organization in metaphase II stage mouse oocytes. Dev Biol 272: 1–14.
9. Morita Y, Tilly JL (2000) Sphingolipid regulation of female gonadal cell differentiation, fertilization, and sperm quality control: killing three birds with one stone. Microsc Res Tech 61: 88–102.
8. Larios H (1989) Development and fertility of ovaries in the B6.YDOM sex-reversed female mouse. Development 105: 95–105.
7. Burgoyne PS, Evans EP (2000) A high frequency of XO offspring from X(Paf)Y* male mice: evidence that the Paf mutation involves an inversion spanning the X PAR boundary. Cytogenet Cell Genet 91: 57–61.
6.坑田和, 小林和, 高田和, 萩本道, 藤本道, 他 (2001) 3′重写録子は、大円運動を誘導する。Biochem Biophys Acta 1483: 2732–2740.
5. Baumgarten C, Vincze MM, De La Fuente R (2010) Loss of maternal ATRX results in centromere instability and aneuploidy in the mammalian oocyte and pre-implantation embryo. PLoS Genet 6: e1000741.
4. Kawamura T, Sato N, Fukuda J, Kodama H, Kumagai J, et al. (2003) Survivin
3. Dittum HJ, Zimmerman J, Kamp C, Rajpert-De Meyts E, Vogt PH (2004) The AZFa gene DBY (DIX3Y) is widely transcribed but the protein is limited to the male germ cells by translation control. Hum Mol Genet 13: 2333–2341.
2. Abdelhaleem M (2003) RNA helicases: regulators of differentiation. Clin Biochem 38: 499–503.
1. Hendriksen PJ, Hoogerbrugge JW, Themmen AP, Koken MH, Hoeijmakers JH, et al. (1995) Postmeiotic transcription of X and Y chromosomal genes during spermatogenesis in the mouse. Dev Biol 170: 730–733.

Gene Expression Profiles in the XY Oocyte