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Data Article

Transcriptome datasets of gonadotropin-induced ESR2-regulated genes in rat oocytes

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Disruption of estrogen receptor beta (ESR2) dysregulates oocyte maturation, which leads to failure of ovulation. We investigated ESR2-regulated genes during gonadotropin-induced oocyte maturation using RNA-sequencing. Through the administration of pregnant mare's serum gonadotropin (PMSG), synchronized follicle development was initiated in four-week-old wildtype and Esr2-null female rats. Forty-eight hours after the PMSG injection, human chorionic gonadotropin (hCG) was used for further maturation. Oocytes were collected from the ovaries 4 h after hCG injection. The total RNA was isolated from the oocytes and the whole oocyte transcriptome was determined by RNA-sequencing on the Illumina HiSeq4000 sequencer. RNA-sequencing data of wildtype and Esr2-null oocytes were analyzed, and differentially expressed genes were identified using the CLC Genomics Workbench. Whole oocyte transcriptome data of wildtype and Esr2-null oocytes were compared to identify the differentially expressed genes. Raw data are deposited to the NCBI Sequence Read Archive (SRA) and analyzed data are presented in this data article. These datasets can be utilized to identify the gonadotropin-induced genes in oocytes that are ESR2-regulated and important to oocyte maturation.

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Specifications Table

Subject	Biology
Specific subject area	Reproductive biology
Type of data	Transcriptomic data, table
How data were acquired	High-throughput RNA sequencing using Illumina HiSeq4000 sequencer
Data format	Raw (FASTQ) and analyzed (Excel table)
Parameters for data collection	RNA sequencing was performed on oocytes collected from gonadotropin-treated wildtype and *Esr2*-null rats.
Description of data collection	Four-week-old wildtype and *Esr2*-null Holtzman rats were treated with 30IU of pregnant mare's serum gonadotropin (PMSG). Forty-eight hours after the PMSG administration, 30IU of human chorionic gonadotropin (hCG) was injected into the rats. Four hours after the hCG injection, oocytes were collected from the ovaries. RNAs were purified and analyzed by mRNA-sequencing. Differentially expressed gonadotropin-induced genes in Esr2-null oocytes were identified through analyses of the transcriptome data using CLC Genomics Workbench.
Data source location	University of Kansas Medical Center, Kansas City, KS 66160, USA
Data accessibility	Repository name: Raw data are available in SRA Data identification number: PRJNA562521 Direct URL to data: https://www.ncbi.nlm.nih.gov/bioproject/PRJNA562521

Value of the Data

- This article provides the whole oocyte transcriptome data of gonadotropin-treated rats.
- These datasets also represent the differentially expressed gonadotropin-induced genes in Esr2-null rat oocytes.
- These data will help understand the role of ESR2 signaling and ESR2-regulated genes during gonadotropin-stimulated oocyte maturation.
- These data will be useful to the researchers who study the biology of oocyte maturation.

1. Data

Transcriptome data generated by RNA-sequencing of wildtype and Esr2-null oocytes were compared to identify the differentially expressed genes. Analyzed data are presented in Excel format and the raw data are deposited to the NCBI SRA (SRR10024657-10024662, included under PRJNA562521). SRR10024660, SRR10024661 and SRR10024662 are the raw data obtained from wildtype oocytes, while SRR10024657, SRR10024658 and SRR10024659 are the raw data obtained from Esr2-null oocytes. The corresponding experiment numbers are SRX6761695, SRX6761696, SRX6761697, SRX6761698, SRX6761699 and SRX6761700. Analyzed data are presented in the following tables: (see Tables 1 and 2)

Transcriptome analyses of gonadotropin-induced genes in Esr2-null rat oocytes were compared to that of wildtype. Of the 933 differentially expressed genes, 535 were $\geq$2 fold upregulated, whereas the 398 were $\leq$2 fold downregulated.

2. Experimental design, materials and methods

2.1. Experimental animals

Four-week-old wildtype and Esr2-null female Holtzman Sprague-Dawley (HSD) rats were included in these RNA-sequencing analyses. Holtzman Sprague-Dawley (HSD) *Esr2*-mutant rat models were generated by the targeted deletion of exon 3 in the *Esr2* gene as described previously [3]. Deletion of exon 3 caused a frameshift and null mutation in the ESR2 coding sequence [3].

All animals were screened for mutation by PCR-based genotyping that uses tail-tip DNA samples (RED extract-N-Amp Tissue PCR Kit, Sigma-Aldrich) and primers targeting the flanking intron sequences [3]. All procedures performed and precautions taken were in accordance with the protocols approved by the University of Kansas Medical Center Animal Care and Use Committee. Each sample in

Table 1
Top 50 upregulated genes in gonadotropin treated Esr2 null rat oocytes. This data-table shows the top 50 upregulated genes selected from the differentially expressed genes.

Name	Chr.	Region	Max gr. mean	Log_2 fold change	Fold change	P-value	FDR P-value	Bon-ferroni	ENSEMBL
AABR07001512.1	1	complement(48565160..48565711)	4.190	8.670	408.400	0.000	0.003	1.000	ENSRNOG00000017412
Ms4a6bl	1	227240383..227252250	1.200	8.250	304.330	0.001	0.007	1.000	ENSRNOG00000050395
Tsen34l1	1	complement(64024240..64030175)	1.640	8.160	285.430	0.001	0.010	1.000	ENSRNOG00000055179
LOC108348062_2	6	108745895..108756130	1.710	7.940	245.090	0.002	0.010	1.000	ENSRNOG00000040153
Myh9	7	complement(118741110..118792625)	3.020	6.460	88.180	0.000	0.000	0.000	ENSRNOG00000004860
RGD1561661	X	13441558..13443470	3.840	6.220	74.450	0.000	0.000	0.000	ENSRNOG00000023094
Serpinc1	13	78805347..78833192	3.610	5.150	35.420	0.000	0.000	0.000	ENSRNOG00000002783
Cpa2	4	57855416..57879239	53.310	4.870	29.300	0.000	0.000	0.000	ENSRNOG00000028092
Cma1	15	complement(34601037..34603819)	1.070	4.830	28.480	0.000	0.000	0.040	ENSRNOG00000020563
Ces1d	19	15033108..15239821	8.570	4.570	23.830	0.000	0.000	0.000	ENSRNOG00000015519
Ifit1	1	252944103..252946170	1.920	4.530	23.080	0.000	0.000	0.000	ENSRNOG00000019050
RT1-Bb	20	4039413..4049711	55.030	4.170	17.980	0.000	0.000	0.000	ENSRNOG00000032708
AABR07043407.1	19	complement(28142561..28148135)	2.920	4.140	17.670	0.000	0.000	0.020	ENSRNOG00000060719
Cga	5	50381244..50393367	201.520	4.120	17.390	0.000	0.000	0.000	ENSRNOG00000009269
Mcpt1l1	15	complement(34609776..34612432)	1.600	4.070	16.740	0.000	0.000	0.000	ENSRNOG00000053494
Rgs13	13	complement(60970247..61003744)	1.120	3.940	15.400	0.000	0.000	0.000	ENSRNOG00000003888
Qrfpr	2	complement(122891321..122949241)	1.410	3.860	14.500	0.000	0.000	0.000	ENSRNOG00000014414
Aqp11	1	complement(162703442..162713610)	1.030	3.760	13.520	0.000	0.000	0.000	ENSRNOG00000013358
Amtn	14	complement(21286510..21299068)	1.090	3.710	13.130	0.000	0.000	0.003	ENSRNOG00000003776
AABR07027872.1	17	47870611..47878555	1.970	3.650	12.560	0.000	0.000	0.000	ENSRNOG00000055197
Lrrc17	4	complement(10108192..10138652)	9.790	3.640	12.440	0.000	0.000	0.000	ENSRNOG00000012817
Spag4	3	151609602..151613942	1.200	3.640	12.430	0.000	0.000	0.000	ENSRNOG00000048056
Shisal2b	2	complement(34946797..34963207)	9.710	3.520	11.430	0.000	0.000	0.000	ENSRNOG00000013372
Cst8	3	143129248..143156177	1.380	3.450	10.930	0.000	0.000	0.004	ENSRNOG00000004989
Myorg	5	complement(57876498..57881944)	1.550	3.370	10.350	0.000	0.000	0.000	ENSRNOG00000023208
Oit3	20	complement(29009330..29029905)	13.220	3.240	9.480	0.000	0.000	0.000	ENSRNOG00000046365
Lrp2	3	complement(55665145..55822551)	2.020	3.230	9.370	0.000	0.000	0.000	ENSRNOG00000056184
Cd70	9	9842585..9845728	2.030	3.120	8.700	0.000	0.000	0.000	ENSRNOG00000051015
LOC100364500	20	complement(2704148..2707120)	12.940	3.110	8.640	0.000	0.000	0.000	ENSRNOG00000048951
Cx3cl1	19	complement(10644244..10653800)	22.930	3.110	8.610	0.000	0.000	0.000	ENSRNOG00000016326
RT1-A1	20	5351605..5421098	169.660	3.030	8.140	0.000	0.000	0.000	ENSRNOG00000038999
Higd1b	10	90929423..90931639	1.130	2.980	7.870	0.000	0.000	0.200	ENSRNOG00000002814
AABR07042609.1	19	275531..277005	1.230	2.920	7.590	0.002	0.010	1.000	ENSRNOG00000051666
Ptgds	3	complement(2686123..2689084)	19.660	2.920	7.570	0.000	0.000	0.000	ENSRNOG00000015550
Tnfsf13b	16	complement(85275678..85306366)	3.470	2.890	7.420	0.000	0.000	0.000	ENSRNOG00000014464
Aard	7	91588458..91593297	7.240	2.860	7.250	0.000	0.000	0.000	ENSRNOG00000004708
Atp6ap1l	2	complement(19781408..19808937)	12.450	2.840	7.160	0.000	0.000	0.000	ENSRNOG00000040201
AABR07046778.1	5	6373583..6373849	1.390	2.830	7.130	0.005	0.030	1.000	ENSRNOG00000058589

(*continued on next page*)

Table 1 (*continued*)

Name	Chr.	Region	Max gr. mean	Log_2 fold change	Fold change	P-value	FDR P-value	Bon-ferroni	ENSEMBL
AABR07058124.4	7	complement(101138549..101138860)	21.080	2.830	7.130	0.000	0.000	0.000	ENSRNOG00000055178
Actc1	3	complement(105507403..105512939)	1.290	2.820	7.080	0.000	0.000	0.000	ENSRNOG00000008536
AABR07043200.1	19	26416818..26417597	1.140	2.800	6.970	0.002	0.010	1.000	ENSRNOG00000058276
Fcgr3a	13	89385859..89396051	3.080	2.800	6.940	0.000	0.000	0.000	ENSRNOG00000024382
Synpo2	2	complement(227255902..227411964)	2.160	2.740	6.670	0.000	0.000	0.000	ENSRNOG00000014867
Calca	1	complement(184184020..184188911)	2.750	2.720	6.610	0.000	0.000	0.000	ENSRNOG00000011130
AABR07049499.1	5	124442293..124542156	2.560	2.710	6.550	0.000	0.000	0.000	ENSRNOG00000030938
Cntn3	4	complement(134784668..135069970)	3.130	2.690	6.460	0.000	0.000	0.000	ENSRNOG00000006144
Hp	19	42097995..42100804	22.850	2.690	6.440	0.000	0.000	0.000	ENSRNOG00000014964
Aldob	5	complement(64805773..64818824)	3.070	2.680	6.400	0.000	0.000	0.000	ENSRNOG00000006807
Smpx	X	complement(40030248..40086870)	8.320	2.640	6.240	0.000	0.000	0.000	ENSRNOG00000007495
Uchl3_1	3	complement(171092946..171134655)	3.530	2.620	6.130	0.009	0.050	1.000	ENSRNOG00000046120

Chr. Chromosome; Max gr. mean, Maximum group mean.

Table 2
Top 50 downregulated genes in gonadotropin treated Esr2-null rat oocytes. This data-table shows the top 50 downregulated genes selected from the differentially expressed genes.

Name	Chr.	Region	Max gr. mean	Log_2 fold change	Fold change	P-value	FDR P-value	Bonfe-rroni	ENSEMBL
Impad1_1	5	complement(17633766..17663589)	1.210	−8.690	−413.81	0.000	0.001	1.000	ENSRNOG00000027079
Ncbp2_2	11	complement(72921282..72929003)	4.010	−8.370	−329.92	0.000	0.003	1.000	ENSRNOG00000048589
LOC103690018	3	57286892..57300840	1.300	−8.260	−307.35	0.000	0.003	1.000	ENSRNOG00000023386
LOC100361898	1	248402980..248403399	2.890	−7.740	−214.50	0.001	0.006	1.000	ENSRNOG00000033038
Kiss1	13	complement(50529510..50535389)	27.18	−7.180	−144.59	0.000	0.000	0.000	ENSRNOG00000047481
Spp1	14	complement(6673686..6679901)	231.1	−6.450	−87.560	0.000	0.000	0.000	ENSRNOG00000043451
Car14	2	complement(198010349..198016898)	9.110	−6.380	−83.380	0.000	0.000	0.000	ENSRNOG00000023162
Lce1m	2	complement(193333800..193335002)	1.220	−5.640	−49.730	0.000	0.000	0.250	ENSRNOG00000009581
Vstm2l	3	154395187..154424625	1.590	−4.920	−30.190	0.000	0.000	0.040	ENSRNOG00000034031
Myh15	11	complement(54204775..54344615)	28.32	−4.870	−29.300	0.000	0.000	0.000	ENSRNOG00000061038
Npr3	2	complement(61888950..61949926)	3.600	−4.550	−23.370	0.000	0.000	0.000	ENSRNOG00000019184
Ptgs2	13	67351087..67359335	294.8	−4.210	−18.560	0.000	0.000	0.000	ENSRNOG00000002525
Kcnk12	6	complement(11373917..11494459)	3.450	−4.180	−18.150	0.000	0.000	0.000	ENSRNOG00000016110
AABR07052431.1	3	53316026..53316481	2.030	−4.170	−18.050	0.000	0.000	0.030	ENSRNOG00000038559
Adcyap1	9	complement(121706979..121725716)	504.6	−4.080	−16.910	0.000	0.000	0.000	ENSRNOG00000049882
Heatr9	10	complement(70726071..70735742)	2.570	−3.980	−15.810	0.000	0.000	0.000	ENSRNOG00000037100
Olr154	1	169575656..169576609	2.310	−3.960	−15.620	0.000	0.000	0.000	ENSRNOG00000059092
Wnt16	4	49369296..49379703	2.520	−3.950	−15.490	0.000	0.000	0.000	ENSRNOG00000005781
Lif	14	84482674..84500642	10.81	−3.920	−15.180	0.000	0.000	0.000	ENSRNOG00000007002
LOC108348130	11	33845463..33847793	83.93	−3.910	−15.010	0.000	0.003	1.000	ENSRNOG00000049693
Olfr656	1	169616178..169617571	1.570	−3.890	−14.780	0.000	0.000	0.000	ENSRNOG00000017252
Fam25a	16	complement(10702263..10706073)	3.800	−3.850	−14.440	0.000	0.000	0.000	ENSRNOG00000055025
Gal	1	complement(218652917..218657925)	169.4	−3.810	−13.990	0.000	0.000	0.000	ENSRNOG00000015156
Kcnk2	13	complement(107690087..107886476)	5.400	−3.680	−12.800	0.000	0.000	0.000	ENSRNOG00000002653
Rpl10l	6	complement(88231611..88232252)	9.090	−3.630	−12.350	0.000	0.000	0.000	ENSRNOG00000032720
Olr155	1	169590308..169591279	7.040	−3.570	−11.840	0.000	0.000	0.000	ENSRNOG00000017234
Fndc9	10	31324512..31325192	4.410	−3.560	−11.810	0.000	0.000	0.000	ENSRNOG00000006549
Igsf9	13	complement(90815562..90832469)	30.57	−3.540	−11.660	0.000	0.000	0.000	ENSRNOG00000008054
Hamp	1	complement(89368021..89369960)	38.27	−3.510	−11.380	0.000	0.000	0.000	ENSRNOG00000021029
Dok6	18	complement(86420361..86878142)	7.510	−3.480	−11.140	0.000	0.000	0.000	ENSRNOG00000038190
.	1	complement(22649081..22661377)	10.74	−3.460	−11.000	0.000	0.000	0.000	ENSRNOG00000039865
Mt1m	20	3677474..3677847	1.010	−3.410	−10.640	0.001	0.009	1.000	ENSRNOG00000028841
LOC102555453	X	complement(1345684..1346181)	54.65	−3.370	−10.340	0.000	0.000	0.000	ENSRNOG00000028993
Ms4a4c	1	227640680..227661311	3.460	−3.320	−9.990	0.000	0.000	0.000	ENSRNOG00000020997
Snap25	3	129599353..129788400	23.03	−3.320	−9.980	0.000	0.000	0.000	ENSRNOG00000006037
Sult1e1	14	22072024..22089248	71.00	−3.290	−9.770	0.000	0.000	0.000	ENSRNOG00000001957
AABR07044900.1	20	complement(25064702..25826658)	14.22	−3.250	−9.490	0.000	0.000	0.000	ENSRNOG00000000373
Fam124a	15	45712821..45780405	2.12	−3.210	−9.240	0.000	0.000	0.000	ENSRNOG00000009802

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Table 2 (*continued*)

Name	Chr.	Region	Max gr. mean	Log_2 fold change	Fold change	P-value	FDR P-value	Bonfe-rroni	ENSEMBL
Gdf1	16	complement(20845576..20860767)	2.95	−3.170	−9.020	0.000	0.000	0.050	ENSRNOG00000020142
Adtrp	17	22619891..22688307	4.640	−3.140	−8.810	0.000	0.000	0.000	ENSRNOG00000014481
Nup62cl	X	complement(111334252..111365849)	1.740	−3.040	−8.250	0.000	0.000	0.000	ENSRNOG00000057753
Tdh	15	complement(46667926..46681467)	6.230	−3.010	−8.030	0.000	0.000	0.000	ENSRNOG00000011342
Il13ra2	X	complement(118443823..118513061)	11.52	−2.990	−7.960	0.000	0.000	0.000	ENSRNOG00000032973
Adgrf5	9	complement(20091099..20195566)	7.240	−2.820	−7.070	0.000	0.000	0.000	ENSRNOG00000011154
Sfmbt2	17	complement(71723620..71897972)	3.820	−2.790	−6.900	0.000	0.000	0.000	ENSRNOG00000029235
Xpnpep2	X	134940615..134969996	10.73	−2.760	−6.790	0.000	0.000	0.000	ENSRNOG00000004009

Chr., Chromosome; Max gr. mean, Maximum group mean.

the data represents the RNA obtained by pooling oocytes from three different animals of the same genotype. So, a total of 9 wildtype and 9 Esr2-null rats were used in the present study.

2.2. Gonadotropin treatment

Synchronized follicular growth was initiated through the administration of gonadotropins to four-week-old wildtype and *Esr-2* null female rats [1–3]. First, 30 IU of PMSG (Lee Bioscience, MO) was intraperitoneally injected into the rats. Forty-eight hours after this PMSG treatment, 30 IU of hCG (Lee Bioscience, MO) was injected (Fig. 1A).

2.3. Sample collection and processing

Four hours after the hCG injection to PMSG-treated rats, Esr2-null and wildtype rats were sacrificed, and their ovaries were collected (Fig. 1B). Cumulus oocyte complexes (COCs) were isolated from the large antral ovaries by needle puncture under microscopic examination (Fig. 1B) [1,2]. All cumulus cells were removed from the oocytes by pipetting followed by repeated washings into fresh media using capillary suction. The total RNA was extracted from the cumulus-free oocytes using TRI Reagent (Sigma-Aldrich, St. Louis, MO) following the manufacturer's instruction. RNA quality was assessed by a Bioanalyzer and samples with a RIN value over 9 were selected for mRNA-sequencing library preparation. Approximately 500 ng of the total RNA was used for the RNA-sequencing library preparation using a TruSeq Standard mRNA kit (Illumina, San Diego, CA) following the manufacturer's instruction [4]. The cDNA libraries were evaluated for quality and then sequenced on an Illumina HiSeq 4000 sequencer (Novogene Corporation, Sacramento, CA).

2.4. RNA-seq data analyses

RNA-sequencing data were demultiplexed, trimmed, aligned and analyzed using CLC Genomics Workbench 12.2 (Qiagen Bioinformatics, Germantown, MD). Through trimming, low-quality reads were removed, and good-quality reads were aligned with *Rattus norvegicus* genome (Rnor_6.0) using default guidelines: (a) maximum number of allowable mismatches = 2, (b) minimum length and similarity fraction = 0.8, and (c) minimum number of hits per read = 10. Gene expression values were measured in transcripts per million (TPM). Differentially expressed genes were identified with an absolute fold change of TPM values ≥ 2 showing a false discovery rate (FDR) p-value of ≤ 0.05.

2.5. Statistical analysis

Each RNA-sequencing library was prepared using pooled RNA samples from three or more individual wildtype or *Esr2*-null rats. Each group for RNA-sequencing consisted of three libraries. Differentially expressed genes were identified by CLC Genomics Workbench as described previously [4].

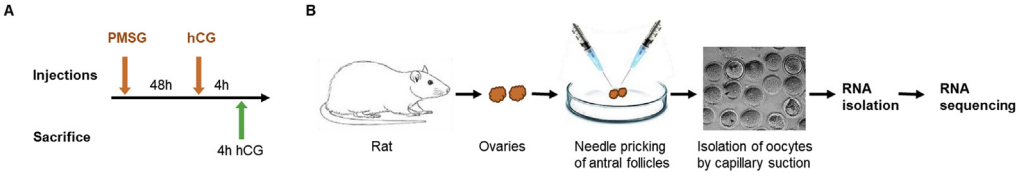

Fig. 1. Schematic presentation of the experimental design. A) Four-week-old wildtype or *Esr2*-null female rats were injected intraperitoneally with 30IU of PMSG, and 48 h after the PMSG injection, with 30IU of hCG. **B**) Rats were sacrificed 4 h after hCG injection, and the ovaries were collected for oocyte isolation. COCs were isolated from the ovaries by needle puncturing under stereoscope. Cumulus cells were removed by pipetting followed by repeated washings using capillary suction under microscope. The total RNA was extracted, quality assessed, and used for mRNA sequencing.

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Conflict of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.dib.2019.104786.

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