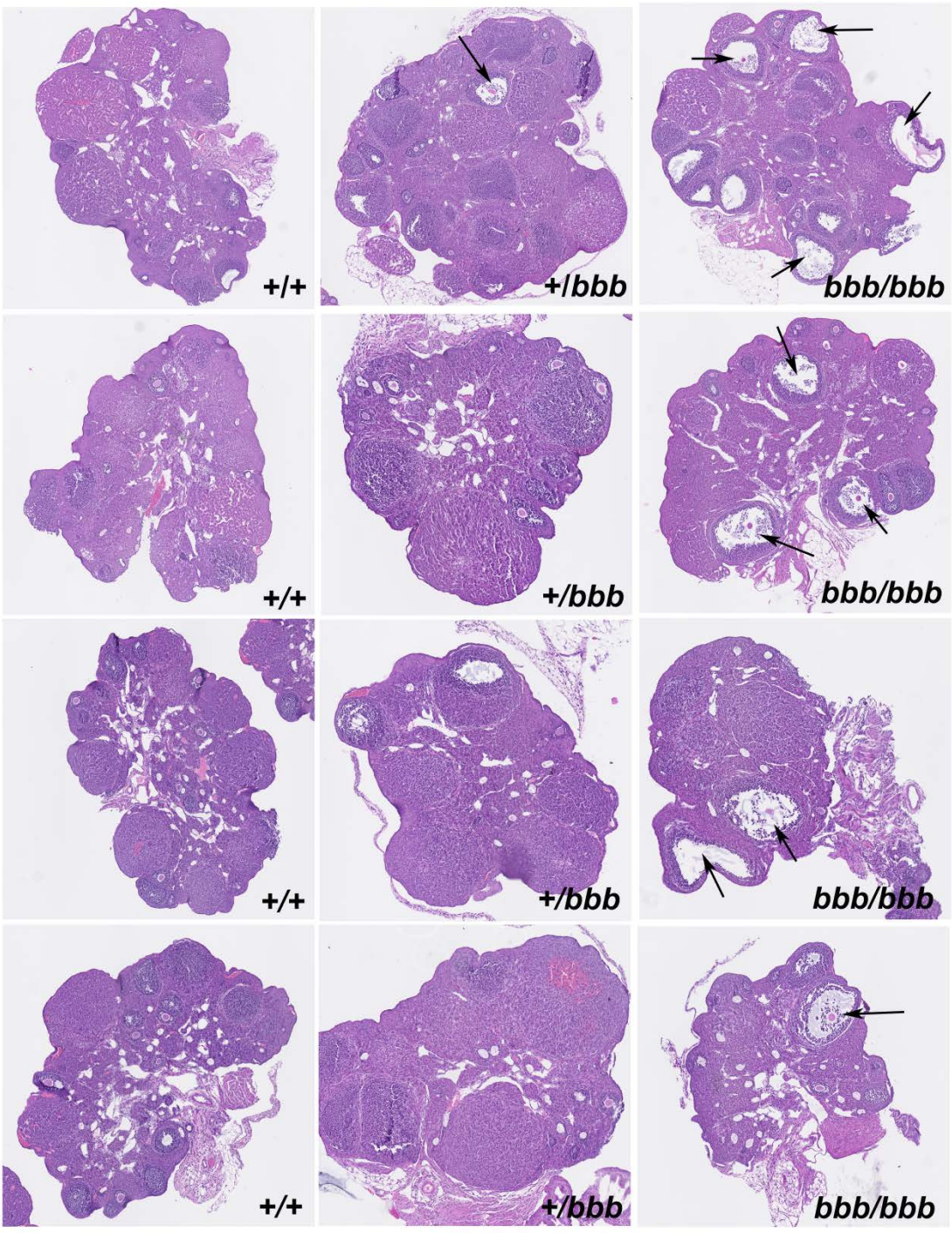
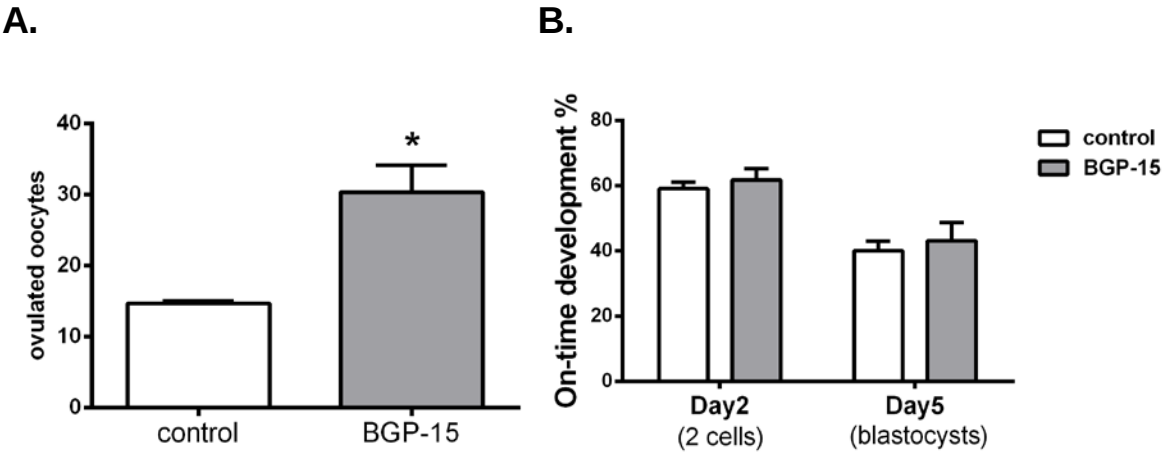
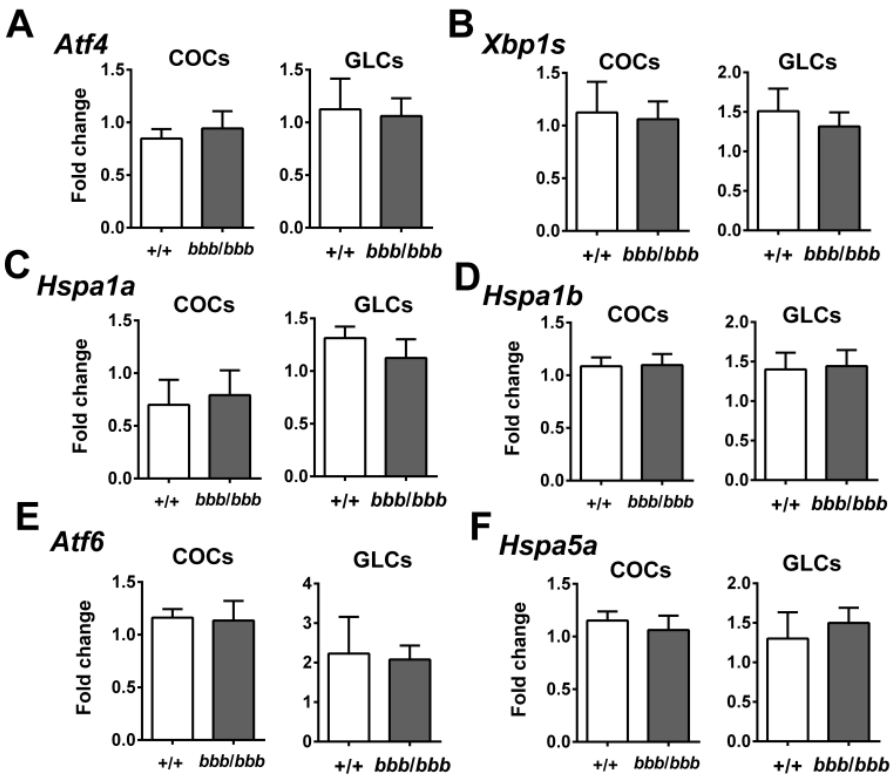


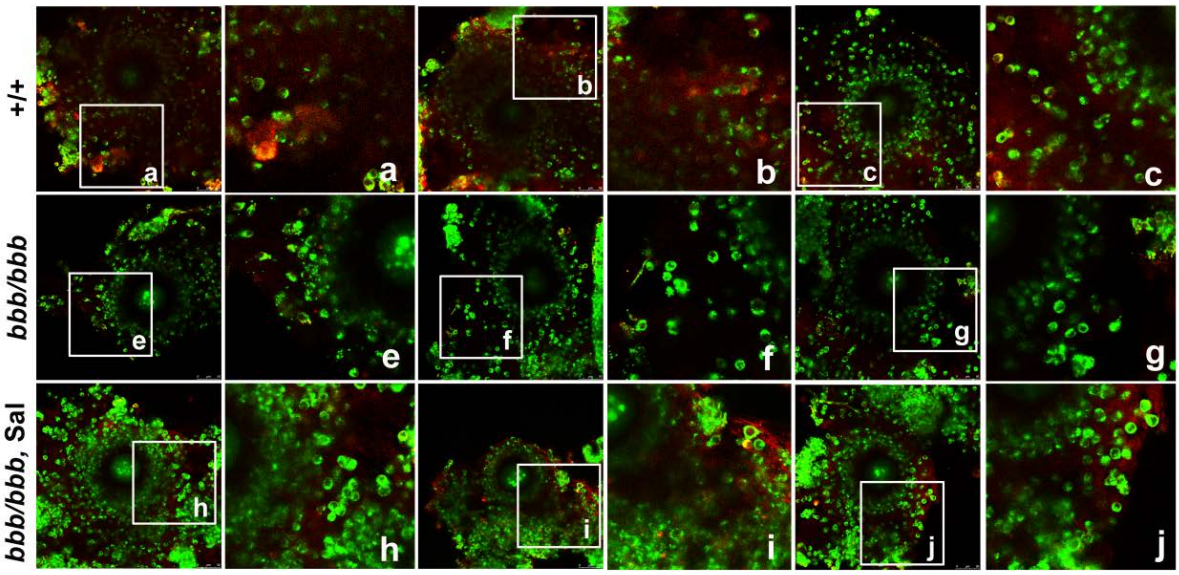
Supplemental Figure 1: Lean (+/+ or +/bbb) and obese Blobby (bbb/bbb) mice at 14 weeks of age were treated with gonadotropins as in Methods. Ovaries were collected at 16h post-hCG, fixed, sectioned and H&E-stained as in Methods. Arrows indicate unruptured follicles which are apparent in ovaries from obese mice.



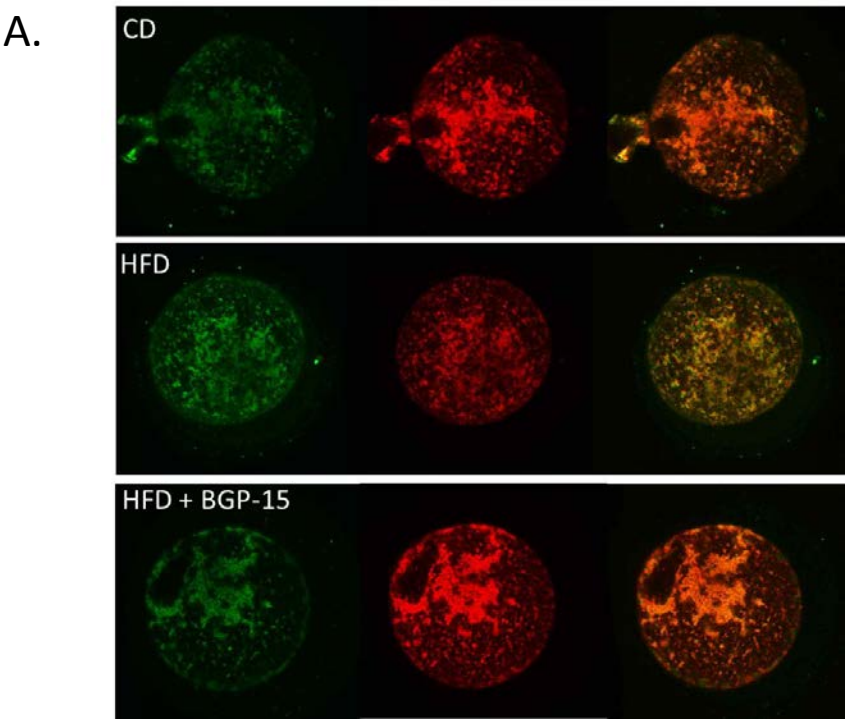
Supplemental Figure 2: Female C57 mice (8 weeks of age) were treated with BGP-15 (or were untreated (control) for 4 days concurrent with eCG and hCG as in Methods. N=3 mice per group. A. Number of ovulated oocytes was counted 16h post-hCG. B. Ovulated oocytes were subjected to IVF as in Methods and on-time development assessed at Day 2 (2-cell embryo stage) and Day 5 (blastocyst stage). BGP-15 treatment significantly increased ovulation rate (* p=0.015) but did not affect embryo development.

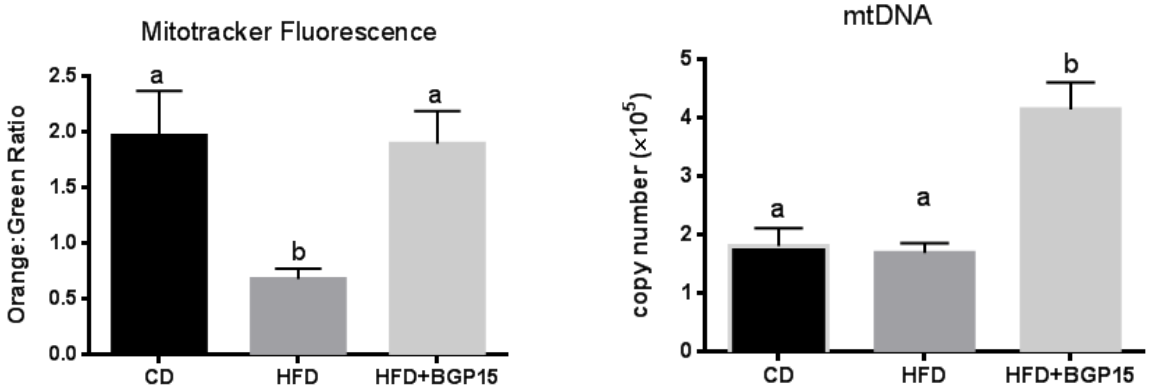


Supplemental Figure 3: Ovulated COCs were collected from oviducts of +/+ or bbb/bbb mice at 6-8 weeks of age following treatment with gonadotropins as in Methods. Expression of ER stress/ UPR marker genes and heat shock chaperone genes (A: Atf4, B: Xbp1s, C: Hspa1a, D: Hspa1b, E: Atf6, and F: Hsp5a), were determined by RT-PCR as Methods. N=7-8 mice per genotype. There were no significant differences detected between groups.



Supplemental Figure 4: Ovulated cumulus-oocyte complexes COCs obtained from oviducts 13h after ovulatory gonadotropin treatment were stained with neutral lipid dye BODIPY 493/503 (green fluorescence) and for cumulus extracellular matrix protein PTX3 by immunocytochemistry (red fluorescence) as in Methods. Lettered panels are higher magnification of respective boxed areas. Images are representative of 10-15 COCs from 2-3 mice per group. COCs from obese mice have increased lipid content but reduced matrix protein PTX3 that is normalized by salubrinal treatment.





Supplemental Figure 5: Female C57 mice were fed a control diet (CD) or high fat diet (HFD; Chen et.al Diabetes 2014 63:3189) from 6 to 14 weeks of age. BGP-15 was administered for 4 days concurrent with eCG/hCG as in Methods. A. Ovulated oocytes were collected, hyaluronidase-treated and stained with MitoTracker Green FM (Molecular Probes) at 100nM in αMEM supplemented with 1% fetal calf serum for 15 min in the dark followed by MitoTracker Orange CM-H2TMRos (Molecular Probes) at 500nM for 30 min in the dark. Oocytes were then washed once in PBS/PVP followed by confocal microscopy imaging. B. Total fluorescence was determined for each stain and expressed as a ratio. N=5-12 oocytes per group. Different letters significantly different by ANOVA; $p<0.01$. C. Oocytes were snap frozen, DNA isolated and mtDNA copy number determined as in Methods. N= 4-10 per group; $p<0.0001$.

SUPPLEMENTAL METHODS

Mice and genotyping

The C57BL/6JSfdAnu-Alms1bbb/Apb mouse strain (named 'Blobby') was sourced from the Australian Phenome Bank (APB ID 31; MGI:3611799). The 'Blobby' mutation (*bbb/bbb*) is an ENU-induced T to A mutation at position 6507 (exon 10) on the Alms 1 gene that results in a truncated Alms1 protein (Li et al., 2007). Blobby mice are a phenocopy of the Alms1 knockout mouse (Collin et al., 2005) and the "Fat Aussie" (*foz/foz*) strain which has a spontaneous 11-bp deletion in exon 8 of the Alms 1 gene causing a frame-shift, premature termination and elimination of the C-terminal two thirds of the Alms1 protein (Arsov et al., 2006). Each of the three existing Alms1 mutant mouse lines exhibits hyperphagia and profound obesity even when maintained on a standard mouse chow diet (Collin et al., 2005; Arsov et al., 2006; Li et al., 2007).

Experimental mice were generated by heterozygous mating pairs and were genotyped using tail DNA and mutation-specific PCR primers (forward: 5'-AAAGCCCCACATGTAGATCG-3', reverse: 5'-TGAGGTATATGCTGAACCTCATAT-3') to screen for the *Alms1* (*bbb*) gene mutation. PCR conditions were 94ºC for 2 min, followed by 38 cycles of 94ºC 30 seconds, 59ºC 1 min, 72ºC 2 min, and 72º C 5min. PCR products were digested by PsiI (BioLabs) restriction enzyme and products visualized on 4% agarose gel. Wildtype DNA produced a single 190bp band, heterozygous mice produced 190 and 200 bp bands and homozygous mice produced a single 200bp band. All mice were maintained on a 12-h light, 12-h dark cycle with standard mouse diet (4.8% total fat, digestible energy 14.0 MJ / Kg, Specialty Feeds, Glen Forrest, Australia) and water available *ad libitum*.

Next generation sequencing of fetal liver mtDNA

MtDNA sequence was examined in fetal liver samples by next generation sequencing. Two overlapping fragments, each spanning 50% of the mitochondrial genome, were produced by long PCR to generate templates. Reactions consisted of 50 ng total DNA, 1x High Fidelity PCR buffer, 100 mM $MgSO_4$, 1 mM dNTPs (Bioline, London, UK), 1U of Platinum Taq High Fidelity (Invitrogen, Carlsbad, CA, USA) and 10μM each of the forward and reverse primer (A forward CCGTGCTACCTAAACACCTTATC and A reverse CGTCCGTACCATCATCCAATTA; B forward CCCTTCATCCTTCTCTCCCTAT and B reverse GTGGGATCCCTTGAGTTACTTC). Reaction conditions were 94°C for 2:00, 94°C for 0:15, 57°C for 0:30, 68°C for 10:00 (34 cycles), 68°C for 10:00, held at 4°C. Products were purified using the QIAquick PCR purification kit (Qiagen). Purified pairs of amplicons from long PCR from the same sample were combined at equal concentrations. Libraries were generated using the Ion Fragment Library Kit and Ion Xpress™ Template kit (Life Technologies). MtDNA was sheared using the Covaris Adaptive Focused Acoustics (AFA™) system. Fragments of ~ 200 bp were selected following electrophoretic separation with the E-gel system (Life Technologies). Product size and quality were assessed using the Agilent High Sensitivity DNA Kit (Agilent, Santa Clara, CA) by the Agilent Bioanalyzer. Each library was barcoded through different ligation adaptors. Libraries were pooled at equal concentrations and loaded onto 316 chips for sequencing on the Ion Torrent Personal Genome Machine (PGM)™.

Variant selection was performed using the CLC Genomics Workbench (v7.0.3). Sequences were mapped to a mouse reference genome (AP013031). Only reads with a Phred quality score of >15 were accepted; reads of <15 bp were excluded and one nucleotide was trimmed from each end. For inclusion, reads had a minimum of 80 % identity to the reference

sequence; a mismatch cost of 2 and an insertion/deletion cost of 3 were set; and duplicate reads were excluded. A minimum mutation threshold of 3 % was set for variant calling.

Supplemental Table S1

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