## Supplemental Table S1: Suboptimal gestational exposures and mitochondrial biology: animal studies

| Authors | Animal model | Age at assessment | Gestational exposure(s) | Cell/tissue type | Mitochondrial biology outcomes |
|---|---|---|---|---|---|
| Igosheva N. et al. 2010[61] | Mouse | Zygote (PC1) | Pre-gestational, conception and early embryonic exposure to obesity induced by HF/HS obesogenic diet | Pre-implantation zygote | no Δ in mitochondrial content (mtDNAcn +TFAM, NRF1 gene expression (GE) indicators of biogenesis))<br>↑mitochondrial membrane potential<br>↑ROS (measured by dihydroethidium (HEt) fluorescence) |
| Wu L.L. et al. 2015[62] | Mouse | Blastocyst (PC5) + Fetal (GD14.5) | Pre-gestational exposure to obesity: Oocytes taken from polygenic obese mice ('Blobby' strain, which overeat and develop severe obesity on standard low-fat mouse chow) and fertilized via IVF - transplanted to lean mice for gestation | Pre-implantation blastocyst + Fetal liver, kidney, heart | ↓ mitochondrial content (mtDNAcn), in blastocyst, and fetal liver and kidney tissue<br>↑ mtDNA damage (e.g. deletions) in liver |
| Shankar K. et al. 2011[63] | Rat | Blastocyst (PC4.5) | Pre-gestational, conception and early embryonic exposure to obesity: Maternal obesity induced through enteric overfeeding prior to conception | Pre-implantation blastocyst | ↓mitochondrial GE (69 transcripts, including TFAM & NRF1- indicate ↓mito content) |
| Andreas E. et al. 2019[44] | Mouse | Blastocyst (PC4) + post-natal PND70 (see[4] for F2, F3 data) | Pre- and gestational exposure to obesity: Maternal obesity induced by HF/HS- IVF fertilization for blastocyst analysis and standard mating for F1 post-natal oocyte analysis | Pre-implantation blastocyst + Post-natal oocyte | Blastocyst: ↓ mitochondrial content (mitotracker red and CS), ↓ATP, ↑mitochondrial membrane potential, ↑ nDNA methylation (lysine-9-methylated histone H3 (H3K9me2))<br>F1 post-natal oocyte: ↓ mitochondrial content (mitotracker red and CS), ↓ATP, ↑ nDNA methylation(5- methyl-cytosine (5mC)) |
| McPherson N.O. et al 2015[64] | Mouse | Fetal (GD18) + placenta | Pre-gestational and conception exposure to obesity: Maternal obesity induced via HFD- transplanted to lean mice for gestation | Fetal liver + placenta | ↓ mitochondrial content (mtDNAcn) in liver<br>↓mitochondrial content (proxy GE measure- NRF1- didn't measure mtDNAcn) in placenta |
| Peterside I.E. et al 2003[48] | Rat | Fetal (GD21) + post-natal (PND1, 14 & 28) | Gestational exposure IUGR: Uteroplacental insufficiency at GD19 induced by surgical uterine arterial ligation | Fetal and post-natal liver | ↑mitochondrial content (mitochondrial protein) at fetal, PND1 & 14, but no change at day28<br>↑OXPHOS substrate oxidation in fetal +PND1, but ↓OXPHOS in PND14 &28<br>↑ ROS at all time points (ROS product, measured by HNE-modified protein) |
| Simmons R.A. et al 2003[59] | Rat | Fetal (GD21) + post-natal (PND7, 49 & 105) | Gestational exposure IUGR: Uteroplacental insufficiency at GD18 induced by surgical uterine arterial ligation. Pups fostered on normal unoperated female rats until weaned. | Fetal and post-natal pancreatic islet cells | ↑mitochondrial content (mtDNAcn) in fetus, but ↓mtDNAcn by day105<br>↓ATP production (all time points, further decrease post-natal)<br>↓ Complex I and III activity (all time points)<br>no Δ in Complex II, IV + CS activity (except ↓CS at day105)<br>↑ mtDNA mutations (only day49+105) ↓mitochondrial GE (all time points)<br>↑ ROS at all time points (measured by $H_2$DCFDA fluorescence + oxidative stress/ROS product measured by HNE) |
| Jones A.K. et al 2019[58] | Sheep | Fetal (~125 GD) | Gestational exposure to IUGR: IUGR created by exposing pregnant ewes to elevated humidity and temperature (40°C for 12h, 35°C for 12h) from ~37 GD to 112~116 GD. In-vivo experiments (liver biopsy) | Fetal liver | Altered mitochondrial nDNA encoded GE<br>↓mitochondrial metabolic intermediates (acetate, citrate, & succinate- suggesting ↓OXPHOS) |
| McCurdy C.E. et al 2016[53] | Primate | Fetal (GD130) | Pre- and gestational exposure to HFD and/or obesity | Fetal skeletal muscle | ↓mitochondrial content (mtDNAcn + CS)<br>↑OXPHOS ETC activity (complex I and IV)<br>↓ OXPHOS capacity & efficiency<br>↑ROS (ROS product (lipid peroxidation), measured by TBARS & HNE- modified protein) |
| Mayeur S. et al 2013[57] | Rat | Placenta (at full term birth- PC21) | Gestational exposure IUGR: Maternal caloric restriction (70% food-restricted) from PC0-PC21 | Placenta | ↑mtDNA content (mtDNAcn +GE indicators PGC-1α, TFAM & NRF1)<br>Altered mtDNA GE: ↓(MT-COX1 (complex IV), MT-ATP6 (complex V); ↑ (MT-COX2 (complex IV))<br>↑mitochondrial inefficiency: ↑OXPHOS ($O_2$consumption: max, basal, RCR)) but ↓ATP production |
| Borengasser S.J. et al 2014[54] | Rat | Placenta + Post-natal (PND35 &130) | Pre- and gestational exposure to obesity: Maternal obesity induced through enteric overfeeding prior to conception with ad libitum feeding during gestation- offspring cross-fostered to lean dams after birth | Placenta & post-natal liver, skeletal muscle | no Δ to mitochondrial content (mtDNAcn)<br>↓mitochondrial GE (regulators of mitochondrial dynamics- varied by tissue) |
| Mdaki K.S. et al. 2016[55] | Rat | At birth (PC-22) | Pregestational exposure to obesity (HF) and gestational exposure to diabetes (DM): Maternal obesity was induced | Post-natal cardiac muscle | Altered mitochondrial content (mtDNAcn):↑HF exposed, but ↓DM exposed |

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| | | | through HF >28 days prior to breeding, and on GD14 maternal diabetes was induced by maternal streptozotocin injection. (4 groups: HF, DM, HF+DM, vs control) | | ↓ OXPHOS (all OCR measures: basal, spare, maximum, ATP-linked and proton leak) and ↓FAO in DM exposed and DM+HF exposed (lowest in DM+HF)<br>↓mitochondrial membrane potential and ↑fission (mito-tracker green) in DM+HF exposed |
| Bruin J.E. et al. 2008[47] | Rat | Post-natal (PND21-28, 105 & 182) | Pre- and gestational exposure to nicotine: Maternal nicotine bitartrate via subcutaneous injection for 2 weeks prior to mating until weaning | Post-natal pancreas | no Δ in mitochondrial content (mitochondrial#/beta cell mass or CS) at any time point<br>↓ OXPHOS ETC complex IV activity at PND182 (no difference before)<br>↑ROS/oxidative stress (measured by $H_2$DCFDA fluorescence + ROS product, measured by OxyBlot), only measured at PND182 |
| Borengasser S.J. et al 2011[66] | Rat | Post-natal (PND21) | Pre- and gestational exposure to obesity: Maternal obesity induced through enteric overfeeding prior to conception with ad libitum feeding during gestation- offspring cross-fostered to lean dams after birth | Post-natal liver | no Δ in mito content (GE indicator- TFAM)<br>↓mitochondrial fatty acid oxidation (GE of PGC-1α)<br>↓ OXPHOS ETC complex protein (II, III and V) |
| Ferreira D.J.S. et al 2016[60] | Rat | Post-natal (PND22) | Gestational exposure to dietary protein restriction: Maternal ad libitum diet of low-protein (8%) post-conception | Post-natal brainstem | ↓mitochondrial content (citrate synthase (CS))<br>↑basal OXPHOS respiration but ↓RCR<br>↑ROS/oxidative stress (measured by $H_2$DCFDA fluorescence + ROS product, measured by protein carbonyls) |
| McMurray F. et al 2019[67] | Mouse | Post-natal (PND~30 & ~90) | Pre- and gestational exposure to obesity: Maternal obesity induced via HF/HS diet | Post-natal skeletal muscle (white & red gastrocnemius) | ↑proton-leak respiration (30&90PND in white muscle, only 30D in red muscle)<br>↓ROS production induced by FAO (measured by Amplex Ultra Red fluorescence) in red muscle 90PND, no Δ in white<br>↓mitoflash activity (indicator of mito metabolism) at 90PND |
| Saben J.L. et al 2016[65] | Mouse | Post-natal (PND56) (see[17] for F2 F3 data) | Pre- and gestational exposure to obesity: Maternal obesity induced by HF/HS diet | Post-natal skeletal muscle & oocyte | ↓mitochondrial content (mtDNAcn) (in the oocyte)<br>↓beta-oxidation & ↓RCR<br>↓ETC complex activity (II, III and V)<br>↑ROS/oxidative stress (ROS product (lipid peroxidation), measured by TBARS) |
| Alfaradhi M.Z. et al 2014[49] | Mouse | Post-natal (PND56) | Pre- and gestational exposure to obesity: Maternal obesity induced by HF/HS diet | Post-natal liver | ↑mitochondrial content (proxy measure GDH)<br>↑ROS/oxidative stress (ROS products, measured by 8-OH-dG + HNE)<br>↓ cytochrome c & ↑ETC complex I & II activity (suggests mitochondrial uncoupling) |
| Aiken C.E. et al. 2016[46] | Mouse | Post-natal (PND84) | Pre- and gestational exposure to obesity: Maternal obesity induced by HF/HS diet (post-natal diet was varied, but had no effect on mitochondrial outcomes) | Post-natal ovary | ↑mitochondrial content (mtDNAcn and Tfam gene expression)<br>↑ROS/oxidative stress (ROS products, measured by gene expression Alox12 & Alox15 ) |
| Fetterman J.L. et al 2013[45] | Mouse | Post-natal (~PND84) | Gestational exposure to second-hand smoke: Maternal exposure from GD1-19 (*in utero*) vs post-natal 1-21 vs control | Post-natal heart- aorta | ↑mitochondrial content (mtDNAcn) (both *in utero* & post natal smoke exposure groups vs control)<br>↑mtDNA damage (# unique deletions) (both)<br>Only ↑mtDNA damage (deletion load) from *in utero* exposure<br>↑ROS/oxidative stress (measured by aconitase enzymatic activity) (both) |
| de Velasco P.C. et al 2017[50] | Mouse | Post-natal (PND110) | Gestational exposure to "poor quality" (trans- and interesterified) dietary fats | Post-natal liver | no Δ mitochondrial content (CS)<br>↓ OXPHOS max and reserve capacity (respirometry)<br>↑ROS (measured by Amplex Red fluorescence) + electron leakage |
| Burgueño A.L. et al 2013[56] | Rat | Post-natal (PND245) | Pre-gestational and conception exposure to obesity: Maternal obesity induced via HFD | Post-natal liver | ↓mitohcondrial content (mtDNAcn) but no Δ in GE indicators of content (TFAM, NRF1) |
| Tarry-Adkins J.L et al 2016[52] | Rat | Post-natal (PND365) | Gestational exposure to dietary protein restriction: Maternal ad libitum diet of low-protein (8%) post-conception- cross-fostered to control dams PND3 | Post-natal skeletal muscle | ↓mitochondrial content (CS)<br>↑ETC activity (complex I, II-III, IV)<br>↑ROS/oxidative stress (measured by gene expression, Gp91phox, P22phox) |

**Supplemental Table S1 Legend:**

*Table 1 focuses on inter-generational transmission (mother to embryo/child) - see following references [44,65,106,107] for trans-generational specific details and F2, F3 evidence

8-OH-dG= 8-hydroxo-2'-deoxyguanosine (marker of oxidative damage to DNA), no Δ= no change, Amplex Red = Amplex Red® (N-acetyl-3, 7-dihydroxy- phenoxazine) (marker of ROS), ATP= Adenosine Triphosphate, CS=citrate synthase (marker of mitochondrial content), ETC= electron transport chain, FAO= fatty acid oxidation, GD=gestation day, GDH= Glutamate dehydrogenase (a marker of intact mitochondria, proxy for mitochondrial content), GE= gene expression, $H_2$DCFDA= 2',7'- dichlorodihydrofluorescein diacetate (marker of ROS), HFD= high fat diet; HF/HS= high fat/high sugar diet; HNE= trans-4-hydroxy-2-nonenal (marker of lipid peroxidation/oxidative stress), IUGR= intra-uterine growth restriction, mtDNAcn= mitochondrial DNA copy number (ratio of mtDNA/nDNA), OXPHOS= oxidative phosphorylation, OxyBlot= OxyBlot™ Protein Oxidation Detection Kit (marker of protein oxidation/oxidative stress), PC=post-conception, PND=post-natal day, RCR=respiratory control ratio (indicator of highly coupled respiration), ROS= reactive oxygen species, TBARS= thiobarbituric acid reactive substance (marker of lipid peroxidation/oxidative stress)

## Supplemental Table S2: Suboptimal gestational exposures and mitochondrial biology: human studies

| Authors | Age at assessment | Gestational exposure(s) | Offspring cell /tissue type | Mitochondrial biology outcomes |
|---|---|---|---|---|
| Leary C. et al 2014[89] | 3-5 days (PC) | Pre-gestational Obesity: Comparison of 150 IVF/ICSI surplus embryos from 29 women with a range of pre-gestational BMI | Embryo/ blastocyst stage | ↓mitochondrial metabolism and impaired substrate oxidation (glucose) in blastocysts from overweight vs normal weight women |
| Lassance L. et al 2015[86] | 7-12 (GW) | Gestational Obesity: Comparison from obese (n=18) vs. lean (n=17) woman in the first trimester (voluntary terminations) | Placenta | ↓mitochondrial and nuclear encoded mitochondrial gene expression in obese vs lean women |
| Janssen B.G. et al 2015[82] | At birth | Gestational air pollution: Calculated maternal $PM_{2.5}$ exposure by address in each trimester (n=381 mother/child pairs) | Placenta | ↓mitochondrial content (mtDNAcn)<br>↑mtDNA methylation (MT-RNR1, D-loop) |
| Clemente D.B.P. et al 2016[77] | At birth | Gestational air pollution exposure: Calculated maternal nitrogen dioxide ($NO_2$) across pregnancy (n=336 mother/child pairs) | Placenta | ↓mitochondrial content (mtDNAcn) |
| Clemente D.B.P. et al 2017[101] | At birth | Gestational air pollution exposure: Calculated maternal nitrogen dioxide ($NO_2$) across pregnancy (n=336 mother/child pairs) | placenta | Follow up study to[77]- Mediation analysis showed that mtDNAcn mediated 5.5% of the inverse association between prenatal $NO_2$ exposure during trimester 1 and infant height at age 6 months |
| Vriens A. at al 2017[96] | At birth | Gestational environmental pollution exposure: Measured cord blood levels of four perfluoroalkyl compounds and nine organochlorine compounds (n=233 infants) | Placenta | Altered mitochondrial content (mtDNAcn) in association with infant pollution exposure (measured in cord blood): ↓mtDNAcn in association with thallium and ↑ mtDNAcn in association arsenic and β-hexachlorocyclohexane |
| Lattuada D. et al 2008[88] | At birth | Gestational intra-uterine growth restriction (IUGR, n=24) vs uncomplicated pregnancies (n=26) | Placenta | ↑mitochondrial content (mtDNAcn) |
| Mando C. et al 2014[90] | At birth | Gestational preeclampsia (PE, n=6) and IUGR (n=8) vs uncomplicated pregnancies (n=8) | Placenta + isolated cytotrophoblast | In IUGR: ↑mitochondrial content (mtDNAcn) placenta but ↓mtDNAcn in cytotrophoblast; ↓mitochondrial gene expression (related to complex II-IV and NRF1 (mito biogenesis)) in cytotrophoblast; ↑OXPHOS/ETC activity (respirometry) in cytotrophoblast<br>In PE: <u>no association</u> with mtDNAcn |
| Wang Y. and S.W. Walsh 1998[97] | At birth | Gestational PE (n=8) vs uncomplicated pregnancy (n=8) | Placenta | ↑mitochondrial content (mitochondrial protein + CS)<br>↑ROS (ROS product (lipid peroxidation), measured by MDA) |
| Bouhours-Nouet N. et al 2005[74] | At birth | Gestational exposure to maternal smoking: Comparison of cigarette smoking (n=19) vs non-smoking (n=19) mothers | Placenta | ↓mitochondrial content (mtDNAcn)<br>↓ETC activity (enzymatic activity complex III)<br><u>No difference</u> in OXPHOS/ETC activity (respirometry) |
| Mele J. et al 2014[91] | At birth | Gestational exposure to maternal obesity: Comparison of obese (n=26), and overweight women (n=21) versus lean (n=28) | Placenta | ↓mitochondrial content (mtDNAcn + CS)<br>↓OXPHOS/ETC function and capacity (ATP levels, complex I-V protein levels, and direct respiratory maximum, basal capacity) in obese vs lean |
| Hastie R. and M. Lappas 2014[81] | At birth | Gestational exposure to maternal obesity and Type I & Type II DM: Comparison of (i) obese (n= 23) and non-obese (n=19) normal glucose tolerant (NGT) pregnant women; (ii) women with type 1 DM (n=14) and BMI-matched NGT women (n =14); and (iii) women with type 2 DM (n=11) and BMI-matched NGT women (n=11) | Placenta | In obese vs non-obese NGT women:↓mitochondrial content (mtDNAcn); ↓ETC activity (complex III); ↑ROS (measured by ferric–xylenol orange)<br>In type I DM vs NGT BMI matched women: ↓ETC activity (complex I, II & III, and III); ↑ROS (measured by ferric–xylenol orange assay)<br>In type II DM vs NGT BMI matched women:<br>↓ETC activity (complex II & III) |
| Lassance L. et al 2015[87] | At birth | Gestational Obesity: Comparison of obese (n=140) versus lean (n=90) women | Placenta | <u>No difference</u> in mitochondrial content (CS + mtDNAcn)<br>↓mitochondrial cholesterol concentrations &membrane cholesterol translocator protein & gene expression |
| Lambertini L. et al 2015[85] | At birth | Gestational psychosocial stress and maternal obesity: Measures of maternal psychosocial stress during pregnancy (e.g. Perceived Stress Scale (PSS-14)) and women with range of weights (n=108) | Placenta | Altered mtDNA gene expression: 1) stress associations: ↑MT-ND2 and ↓MT-ND6 (complex I), ↑MT-CO2 (complex IV); 2) obesity/overweight associations: ↑MT-ND1 and ↓MT-ND6 (complex I), ↑MT-CO2 (complex IV) and ↑MT-ATP6 (complex V) |
| Brunst K.J. et al 2017[75] | At birth | Gestational exposure to maternal chronic and current psychosocial stress (n=147) | Placenta | ↓mitochondrial content (mtDNAcn) |
| Janssen B.G. et al 2012 [83] | At birth | Gestational air pollution: Calculated maternal $PM_{10}$ exposure by address across gestation (stronger association closer to birth); placental tissue (n=174) and fetal cord blood (n=176) | Placenta + cord blood (buffy coat) | ↓mitochondrial content (mtDNAcn) (placenta)<br><u>No association</u> with cord blood mtDNAcn |
| Brunst K.J. et al 2018[76] | At birth | Gestational exposure to air pollution and maternal chronic psychosocial stress: Calculated $PM_{2.5}$ exposure by address across pregnancy and stress by the Life Stressor Checklist-Revised (n=167) | Placenta + cord blood (buffy coat) | ↓ placental mitochondrial content (mtDNAcn) in association with psychosocial stress<br>↓cord blood mtDNAcn in association with $PM_{2.5}$ |
| Rosa M.J. et al 2017[94] | At birth | Gestational air pollution: Calculated maternal $PM_{2.5}$ exposure by address across pregnancy (n=456 mother/child pairs) | Cord blood (whole blood+ RBC lysis) | ↓mitochondrial content (mtDNAcn) in association with late pregnancy $PM_{2.5}$ |

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| Sanchez-Guerra M. et al 2019[95] | At birth | Gestational lead (Pb) exposure: Measured Pb exposure (n=410 mother/child pairs) in maternal blood second and third trimester and at birth in fetal cord blood | Cord blood (whole blood+ mixed methods) | ↑mitochondrial content (mtDNAcn) in association with gestational maternal blood Pb and cord blood Pb levels |
| Xu Y. et al 2019[98] | At birth | Gestational methylmercury (MeHg) and polyunsaturated fatty acids (PUFA) exposure: Measured maternal MeHg and PUFA levels (n= 1488) in maternal blood (28 wk) and at birth in fetal cord blood | Cord blood (whole blood) | ↓mitochondrial content (mtDNAcn) in association with fetal MeHg cord blood<br>No association in mitochondrial content (mtDNAcn) with maternal MeHg or PUFA |
| Grevendonk L. et al 2016[79] | At birth | Gestational air pollution: Calculated maternal $PM_{2.5}$ or $PM_{10}$ exposure by address across pregnancy (n=293 mother/child pairs) | Cord blood (buffy coat) | ↑ROS/oxidative stress (ROS product, measured by 8-OHdG) in cord blood in association with gestational $PM_{10}$ exposure |
| Novielli C. et al 2017[92] | At birth | Gestational IUGR (n=31), 17 PE/IUGR (n=17) and PE (n=17) vs. 35 term and 8 preterm control | Cord blood (whole blood) | In IUGR, PE/IUGR, and PE vs control:<br>↑mitochondrial content (mtDNAcn)<br>↓mtDNA methylated cytosines (%) in D-loop region |
| Reimann B. et al 2019[93] | At birth | Metabolic variation in early life represented by neonatal insulin level (n= 882 with mtDNAcn; n= 176 with mtDNAcn and epigenome data) | Cord blood (buffy coat) | mtDNA content (mtDNAcn) positively correlated with cord blood insulin<br>significant gene expression and epigenome-wide associations with cord blood and mtDNAcn (34 significant DMRs) |
| Vriens A. et al 2018[99] | At birth | Metabolic variation in early life represented by neonatal insulin and leptin levels (n=236) | Cord blood (buffy coat) | mtDNA content (mtDNAcn) positively and independently correlated with cord blood insulin and leptin |
| Breton C.V. et al 2019[100] | At birth | Gestational traffic-related air pollution (TRAP): Calculated TRAP and ambient air pollutant (AAP) exposures, including PM10, PM2.5, O3 and $NO_2$, by address, BaP-tetrol measured in cord blood (n= 82 mother/child pairs) | Cord blood (buffy coat for mtDNA and plasma for mito peptides) | Gestational air pollution associated ↑with mito peptides: (TRAP (+) with MOTS-s, PM10 (+) with HN, BaP-tetrol (+) with SHLP2 and MOTS-c)<br>↑ mtDNA content (mtDNAcn) with BaP-tetrol (no other sig relationships)<br>(+) associations between mito peptides and mtDNA methylation |
| Costa S.M., et al 2016[78] | At birth | Gestational exposure to maternal obesity: Comparison of overweight/obese (n=24) vs normal weight (n=13) | Umbilical vein endothelial cells | Significantly different gene expression pathway analysis in multiple mitochondrial functional and structural genes |
| Boyle K.E. et al 2017[102] | At birth | Gestational exposure to maternal obesity: Comparison of obese (n=14) vs normal weight (n=15) | Umbilical cord mesenchymal stem cells (uMSC) | ↓ Fatty Acid Oxidation rates<br>No difference in ETC measures (CS enzyme activity or ETC complexes I-IV protein levels)<br>↑ in methylation of FAO related mitochondrial genes (CPT1A) and ETC (Complex II-SDHC) that corresponded with ↓ gene expression |
| Kim J. et al 2015[84] | At birth | Gestational GDM: Contrast between cells lines derived from 4 GDM and 3 control pregnancies | uMSC | ↓mitochondrial gene expression: mtDNA ETC genes (MT-ND2 (complex 1) and MT-ATP8 (complex V) & nDNA mito. biogenesis (TFAM, PGC-1α)<br>↓OXPHOS/ETC activity (respirometry)<br>↑ROS (measured by DCF-DA and MitoSOX) |
| Baker P.R. et al 2017[103] | At birth | Gestational exposure to maternal obesity: Comparison of obese (OB, n=12) vs normal weight (NW, n=13) or association with neonatal fat mass (%BF) at birth (measured by air displacement plethysmography), or maternal serum FFA levels | uMSCs differentiated to adipocytes and myocytes | uMSC myocytes: altered Fatty Acid Oxidation metabolism= incomplete β-oxidation (↑LCAC+ LCOH), with compensatory ↑ω-oxidation and anaplerosis in association with ↑neonatal %BF, but no differences when comparing OB vs NW groups (no change in uMSC adipocytes)<br>uMSC adipocytes: altered gene expression indicating ↑OXPHOS/ETC (complexes I-V), but ↑fission and ↓mitochondrial biogenesis and mitophagy in association with ↑neonatal %BF, OB status or maternal FFA exposure |
| Gruzieva O. et al 2017[80] | At birth + 4yrs + 8 yrs | Gestational air pollution: Calculated maternal $NO_2$ air pollution exposure by address across pregnancy; offspring data in newborns (n=1,508) with subsequent look-up analyses in children 4 (n=733) and 8 (n=786) years | Cord blood + venous blood (4 & 8yr) (whole blood- mixed methods) | ↑newborn DNA methylation in three mitochondria-related genes: cg12283362 (LONP1), cg24172570 (HIBADH), and cg08973675 (SLC25A28)<br>↑4yr+8yr DNA methylation cg08973675 (SLC25A28) (matches one of the genes hypermethylated at birth) |
| Abraham M. et al 2018[73] | 1-3 (PND) | Gestational exposure to maternal obesity: Comparison of overweight/obese (n=14) vs lean (n=8) | Endothelial cells (isolated +cultured fibroblasts) | ↑mitochondrial inefficiency (respirometry: ↑$O_2$ consumption but no ↑ATP)<br>↑ROS/oxidative stress (measured by MitoSOX Red + ROS product, measured by protein carbonylation)<br>No difference in mitochondrial content (mtDNAcn) |

**Supplemental Table S2 Legend:**
8-OH-dG=8-hydroxy-2′-deoxyguanosine (marker of oxidative damage to DNA), AGA=average for gestational age, CS= citrate synthase, DCF-DA =2',7'-dichlorofluorescin diacetate (marker of ROS), DMR= differentially methylated regions, ETC= electron transport chain, GDM= gestational diabetes exposure, GW=gestation week, IUGR= intra-uterine growth restriction, IVF/ICSI= in-vitro fertilization/intracytoplasmic sperm injection, LCAC= long-chain acylcarnitines, LCOH= long-chain hydroxy acylcarnitine species, LGA=large for gestational age, MDA= malondialdehyde (marker of lipid peroxidation/oxidative stress), mtDNAcn= mitochondrial DNA copy number, OXPHOS= oxidative phosphorylation, PC=post-conception, PE= preeclampsia, PND=post-natal day, RBC= red blood cell, ROS= reactive oxygen species, SGA=small for gestational age