## Supplementary Table 2: Studies investigating associations between nutrition-sensitive candidate genes and phenotypes (Search 2).

Reference	Study design	Genes Implicated	Phenotype investigated	Summary of results
Azzi S, et al. <i>Epigenetics</i> . 2014; <b>9:</b> 338–45 <sup>1</sup>	Nested cohort study in France. 254 mother-infant pairs. Healthy infants from the 'EDEN' cohort. Tissue: Cord blood Platform: Allele-specific methylated multiplex real-time quantitative PCR.	PLAGL1 (ZAC1)	Pre- and post-natal growth	ZAC1 methylation index was positively correlated with estimated fetal weight at 32 weeks gestation (r=0.15, p=0.01). It was positively correlated with weight (r = 0.14, p=0.03) and BMI z-scores (r = 0.15, p=0.01) at age 1 year.
Bens S, et al. <i>Eur J Hum Genet</i> . 2013; <b>21</b> :838-43 <sup>2</sup>	Case-control study. 98 SGA infants and 50 AGA controls from centres of the BMBF consortium, Germany (range 0-18 years).  Tissue: Whole blood Platform: Pyrosequencer ID	PLAGL1, IGF2R, GRB10, H19, IGF2, MEG3, NDN, SNRPN, NESP, NESPAS	Size at birth	Cases showed hypomethylation at <i>GRB10</i> (n=1) and <i>H19</i> 2CTCF-binding site (n=1), and hypermethylation at <i>NDN</i> (n=1) and <i>IGF2</i> (n=1). Note case study approach therefore not included in main narrative Table 2.
Bouwland-Both MI, et al. PLoS One. 2013;8:e81731 <sup>3</sup>	Nested cohort study ('Generation R' cohort subset). 69 small-for-gestational age (SGA) vs. 471 controls (appropriate-for-gestational-age; AGA). Tissue: Cord blood Platform: EpiTYPER, Sequenom	IGF2, H19, MTHFR	Birthweight and anthropometry. Weight gain at 3 months	Methylation at the <i>MTHFR</i> locus did not vary significantly between SGA and AGA infants. An inverse association was found between SGA and <i>IGF2</i> DMR0 methylation ( $\beta$ =-1.07, p=0.015). SGA was not significantly associated with <i>H19</i> promoter DMR methylation. <i>IGF2</i> DMR0 methylation was inversely associated with birth-three months weight gain ( $\beta$ =-0.46, p=0.022).
Burris HH, et al., <i>Epigenomics</i> . 2013; <b>5:</b> 271–281 <sup>4</sup>	Cohort study. 219 infants, Mexico. Tissue: Cord blood. Platform: Pyrosequencing	IGF2/H19, KCNQ1OT1, GCR, NR3C1, LINE-1, Alu	Birthweight	No significant methylation-birthweight associations were found for the studied loci.
Córdova-Palomera A, et al. PLoS One. 2014; <b>9:</b> e103639 <sup>5</sup>	Nested cohort study. 34 monozygotic twin pairs of European descent, Spain. Age 22-56 years. Tissue: Whole blood Platform: Illumina Infinium HumanMethylation450 (450K) Bead-Chip.	IGF2, IGF2BP1, IGF2BP2, IGF2BP3	Birthweight, working memory	Mean methylation at 2 CpG sites in <i>IGF2BP1</i> was associated with birthweight ( $\beta$ =83.3 x 10 <sup>-3</sup> , p=0.033) and working memory ( $\beta$ = -4.4 x 10 <sup>-3</sup> , p=0.009). No variation in methylation was observed in other loci studied.
Deodati A, et al. <i>Horm Res</i> Paediatr. 2013; <b>79</b> :361-7 <sup>6</sup>	Cross-sectional study. 85 children, Italy. Mean age 11.6 years. Tissue: Whole blood Platform: Methyl-Profiler DNA Methylation qPCR Assay	IGF2	Lipid profile	Children with intermediate methylation at <i>IGF2</i> had significantly higher levels of triglycerides (107.6 $\pm$ 41.99 vs. 76.6 $\pm$ 30.18 mg/dl, p < 0.005) and higher triglyceride:high-density lipoprotein-cholesterol ratio (2.23 $\pm$ 0.98 vs. 1.79 $\pm$ 0.98, p < 0.02) in comparison with children showing hypomethylation at <i>IGF2</i> .
Drake AJ, et al. <i>Clin Endocrinol</i> . 2012; <b>77:</b> 808-15 <sup>7</sup>	Retrospective cohort study ('Motherwell'). 34 offspring at 40 years of age.	IGF2, H19 ICR, HSD2, NR3C1	Birthweight, current height, weight, waist	There was an inverse association between methylation at specific CpGs in <i>HSD2</i> and neonatal ponderal index (Region

Reference	Study design	Genes Implicated	Phenotype	Summary of results
			investigated	
	Tissue: Whole blood		circumference,	2- CpG14 r=-0.38, CpG19 r=-0.34, p<0.05) and H19 ICR
	Platform: Pyrosequencing using PSQTM HS-96A (Qiagen)		blood pressure	methylation and birth length (r=-0.36, p<0.05). HSD2
				methylation was positively associated with birthweight
				(r=0.49, p<0.05), adiposity measures and blood pressure in
				adulthood. H19 ICR methylation was not significantly
				associated with birthweight but was positively associated
				with weight in adulthood ( $\beta$ =0.37,p=0.03). Both <i>H19</i> and
				NR3C1 Exon methylation were associated with waist
				circumference, BMI and blood pressure at age 40.
Dunstan J, et al., Clin	431 adolescents, USA. Age 10-15 years.	LEP, ICAM-1, CRH,	BMI, waist	In obese boys, LEP methylation was inversely associated
Epigenetics. 2017; <b>29:</b> 29 <sup>8</sup>	Tissue: Saliva	LINE-1	circumference,	with the obesity. No significant associations were found
	Platform: Pyromark Q24, Qiagen		percent body fat	for ICAM-1, CRH and LINE-1.
García-Cardona MC, et al. <i>Int J</i>	Cross-sectional study, n=106 divided into lean and obese	LEP, ADIPOQ	BMI, insulin	No significant variation in overall methylation of LEP,
Obes 2014; <b>38:</b> 1457-65 <sup>9</sup>	adolescents, Mexico. Age 10-16 years.		resistance, glucose,	ADIPOQ. Lower methylation at both genes in obese
	Tissue: Whole blood		cholesterol and	subjects with insulin resistance.
	Platform: Methylation-specific PCR		triglycerides levels	
Godfrey KM, et al. Diabetes.	Cohort study, UK (78 mother-child pairs from Princess Anne	RXRA, eNOS	Adiposity at age 9	RXRA methylation was associated with sex-adjusted
2011; <b>60:</b> 1528–1534 <sup>10</sup>	Hospital (PAH) and 239 mother-infant pairs in replication		years	childhood fat mass (exponentiated regression coefficient
	cohort - Southampton Women's Study(SWS)). Childhood			[β] 17% per SD change in methylation, p=0.009) and % fat
	adiposity measurements were made using dual energy X-ray			mass ( $\beta$ =10%, p=0.023) at age 9 in the PAH cohort and also
	absorptiometry DEXA (PAH study, age 9 years; SWS, age 6			had similar association in the SWS cohort (Fat mass- $\beta$ =6%,
	years).			p=0.002; %fat mass- β=4%, p=0.002).
	Tissue: Cord blood			Methylation at eNOS was associated with fat mass
	Platform EpiTyper software v1.0 (Sequenom)			(β=20%, p<0.001) and %fat mass (β=12%, p=0.002) in the
				PAH cohort only.
Harvey, NC et al. J Bone Miner	Cohort, UK (230 Southampton Women's Study and 64	RXRA	Bone mineral	Methylation at four of six RXRA CpG sites inversely
Res. 2014; <b>29.3:</b> 600–607 <sup>11</sup>	Princess Anne Hospital mother-infant pairs)		content at age 4	correlated with % bone mineral content. Note that
	Tissue: Cord blood		years	maternal free 25(OH)-vitamin D index inversely associated
	Platform: Sequenom MassARRAY Compact System			with methylation at one RXRA CpG site (β=-3.3 SD/unit,
				p=0.03).
Houde AA, et al. BMC Med	Cross-sectional study. 73 severely obese adults, Canada.	LEP, ADIPOQ	BMI,	Higher ADIPOQ methylation levels in SAT were associated
Genet. 2015; <b>16:</b> 29 <sup>12</sup>	Mean age 34.7 years.		anthropometry,	with higher BMI and waist circumference. Lower LEP
	Tissue: Blood, subcutaneous (SAT) and visceral adipose		blood pressure,	methylation in blood was associated with higher BMI. A
	tissues (VAT).		lipid profile	positive correlation was found between fasting LDL-C
	Platform: Pyrosequencing			

Reference	Study design	Genes Implicated	Phenotype investigated	Summary of results
				levels and <i>LEP</i> in blood and SAT, and with <i>ADIPOQ</i> in <i>SAT</i> and VAT.
Hoyo C, et al. <i>Cancer Causes Control.</i> 2012; <b>23:</b> 635-45 <sup>13</sup>	Cohort study (NEST cohort), USA. 300 mother-infant pairs. Tissue: Cord blood Platform: Pyromark Q96 MD (Qiagen)	IGF2, H19	Birthweight	IGF2 DMR0 methylation was inversely associated with IFG2 protein concentrations in cord blood ( $\beta$ = -9.87, p<0.01), having stronger associations in infants of obese women ( $\beta$ =-20.21, p<0.0001). Higher concentrations of IGF2 were related to higher birth weight (p<0.001). No associations found with H19 DMR.
Hoyo C, et al. Epigenetics.	Cohort study ('NEST' cohort). 438 mother-infant pairs, USA.	H19, PEG10/SGCE,	Birth weight	Higher methylation at H19, PEG10/SGCE and PLAGL1
2014; <b>9</b> : 1120–30 <sup>14</sup>	Tissue: Cord blood leukocytes Platform: Pyromark Q96 MD Pyrosequencer (Qiagen).	PLAGL1, MEG3		DMRs, and lower <i>MEG3</i> methylation, associated with higher birth weight.
Huang RC, et al. <i>Clin</i>	Cohort study ('Raine' Study). 315 children, Australia.	IGF2/H19	BMI,	No association was noted between IGF2/H19 ICR1 and
Epigenetics. 2012; <b>4:</b> 21 <sup>15</sup>	Anthropometric parameters measured at birth and follow		anthropometry,	anthropometric measures at birth. A 3.4% increase in
	ups taken at 8 time points after birth.		birthweight	methylation at 2 specific CpGs in the IGF2/H19 ICR was
	Tissue: Whole blood at age 17			associated with 18 mm decrease in head circumference at
	Platform: EpiTyper, Sequenom.			age 17 (p= 0.006).
Kappil MA, et al. Epigenetics.	Cohort study (Rhode Island Child Health Study (RICHS), USA).	108 imprinted	Size at birth	Increased methylation of MEST observed in SGA infants.
2015; <b>10:</b> 842-9 <sup>16</sup>	677 mother-infant pairs, subset of n=211 for methylation	genes		The paper focuses on gene expression data.
	analysis.			
	Tissue: Placenta			
	Platform: Infinium HumanMethylation450 BeadChip.			
Kuehnen, P. et al. <i>PLoS</i>	Case-control study, Germany. Normal weight controls (mean	POMC	Obesity at age 11	Increased methylation score at POMC in obese children
genetics. 2012; <b>8:</b>	age 17.9 years, N=90), obese cases (mean age 11 years,		years	compared to controls. Overall CpG methylation score from
p.e1002543 <sup>17</sup>	N=171).			position -4 to +6 was 40% in cases and 25% in controls
	Tissue: Peripheral blood			(p<0.001).
	Platform: Direct sequencing of bisulfite-converted DNA			
Kühnen P, et al. Cell Metab.	Case-control study in German adults: 103 normal-weight	POMC	BMI	Positive correlation of average POMC VMR methylation
2016; <b>24</b> :502–509 <sup>18</sup>	and 125 obese, mean age 48.2 years.			with BMI (r = 0.18, p = 0.006).
	Tissue: Peripheral blood			
	Platform: Pyromark Q24 (Qiagen)			
Lesseur C, et al. Mol Cell	Nested cohort study, USA. Rhode Island Child Health Study	LEP	Size at birth	Higher LEP methylation levels were observed in SGA
Endocrinol. 2013; <b>381:</b> 160-7 <sup>19</sup>	'RICHS' cohort, 81 mother-infant pairs, categorised by birth			children (p= $4.6 \times 10^{-3}$ ). Infants born to pre-pregnancy obese
	size.			mothers had lower cord blood methylation levels (p=0.03).
	Tissue: Cord blood, placenta			There was an interaction between placental LEP
	Platform: Pyromark MD (Qiagen)			methylation and sex (p=0.05).

Reference	Study design	Genes Implicated	Phenotype investigated	Summary of results
Lesseur C, et al.  Psychoneuroendocrinology. 2014; <b>40</b> :1-9 <sup>20</sup>	Nested cohort study, USA. Rhode Island Child Health Study 'RICHS' cohort. N=444. NICU Network Neurobehavioral Scales (NNNS) used for neurobehavior testing. Tissue: Placenta Platform: Pyromark MD (Qiagen)	LEP	Neurobehavior	In male infants increased <i>LEP</i> methylation a was associated with membership in the profile of increased lethargy and hypotonicity (OR = 1.9; 95% CI: 1.07–3.4), and reduced risk of membership in the profile of decreased lethargy and hypotonicity (OR = 0.54; 95% CI: 0.3–0.94).
Lester BM, et al. <i>Epigenomics</i> . 2015; <b>7:</b> 1123-36 <sup>21</sup>	Cross-sectional study of 67 preterm infants, USA. Tissue: Buccal cells Platform: Pyrosequencing	HSD2 and NR3C1	Neurobehaviour	Infants with a high-risk neurobehavioral profile showed increased NR3C1 methylation and decreased HSD2 methylation compared to infants with a low-risk neurobehavioral profile.
Lin, X, et al. <i>BMC Med</i> . 2017 Mar 7; <b>15:</b> 50 <sup>22</sup>	Cohort study ('GUSTO' cohort), 987 mother-infant pairs, Singapore. Tissue: Cord blood. Platform: Illumina Infinium HumanMethylation450 BeadChip	ANK3, CDKN2B, IGDCC4, P4HA3, MIRLET7BHG, CACNA1G and ZNF423	Birthweight, size and adiposity at 4 years	Methylation at ANK3, CDKN2B, IGDCC4, P4HA3, MIRLET7BHG, CACNA1G and ZNF423 were associated with birth weight. MIRLET7BHG was the only 'nutritionsensitive' loci considered in this review, however.
Murphy R, et al. <i>BMC Med Genet</i> . 2014; <b>15</b> :67 <sup>23</sup>	Cohort study (Auckland Birthweight Collaborative ('ABC') study) following 153 children out of which 80 were SGA. Age 11 years Tissue: whole blood Platform: Methylation-specific multiplex-ligation-dependent probe amplification assay and pyrosequencing.	IGF2, H19, KCNQ10T1	Size at birth	IGF2 DMR0 methylation was 2.7% lower in SGA children.  Methylation did not vary at H19 and KCNQ10T1 ICRs.
Paquette AG, et al.  Epigenomics. 2015; <b>7:</b> 767-79 <sup>24</sup>	Rhode Island Child Health Study 'RICHS' cohort . N=547 infants. NICU Network Neurobehavioral Scales (NNNS) used for neurobehavior testing. Tissue: Placenta Platform: Pyromark MD (Qiagen)	NR3C1, HSD11B2, FKBP5, ADCYAP1R1	Neurobehaviour	Using maximum likelihood factor analysis, 3 factors were identified as explaining the maximum variability in DNA methylation. NR3C1 loaded strongly onto a factor that was associated with decreased quality of movement and self-regulation, increased arousal and excitability, and increased non-optimal refluxes and stress abstinence scores, also referred to as a 'poorly regulated' profile. HSD11B2 methylation loaded onto factor associated with reducing risk of being in the poorly regulated profile.
Qian YY, et al. <i>J Hum Nutr Diet</i> . 2016; <b>29</b> :643-51 <sup>25</sup>	Case-control study. 39 small-for-gestational age (SGA) infants and 49 appropriate-for-gestational-age (AGA) controls, China. Tissue: Umbilical cord blood Platform: EpiTYPER, Sequenom.	MEST,H19	Size at birth	Methylation in SGA children was higher (p<0.05) than controls at 3 sites in the <i>H19</i> DMR. Six sites in the <i>H19</i> DMR had higher methylation in SGA compared to AGA, but only in only males born to mothers who supplemented in pregnancy with folic acid.

Reference	Study design	Genes Implicated	Phenotype investigated	Summary of results
Rijlaarsdam J, et al. <i>J Child</i> Psychol Psychiatry. 2017; <b>58:</b> 19-27 <sup>26</sup>	Nested cohort study ('ALSPAC' cohort). 164 youth with low conduct problems (CP) and early onset persistent (EOP) ADHD.  Tissue: Cord blood, peripheral blood at age 7 Platform: Illumina Infinium HumanMethylation450 BeadChip	IGF2	ADHD	In the case of EOP individuals, <i>IGF2</i> methylation was positively associated with ADHD symptoms.
Souren NY, et al., <i>Obesity</i> . 2011; <b>19:</b> 1519-22 <sup>27</sup>	Monozygotic (MZ) twins study. 16 BMI discordant MZ twin pairs recruited from the East Flanders Prospective Twin Survey (EFPTS), Belgium. Mean age 30.9 years.  Tissue: Saliva Platform: PCR amplification followed by a single-nucleotide primer extension reaction	KvDMR1, H19, IGF2, GRB10, MEST, SNRPN, GNAS	ВМІ	Methylation differences of the studied imprinted genes in salivary DNA did not account for the discordance in BMI between twins in this cohort.
St-Pierre J, et al. <i>Epigenetics</i> . 2012; <b>7</b> :1125-32 <sup>28</sup>	Cohort study. 50 mother-infant pairs, French-Canadian origin, Canada. Tissue: Placenta Platform: Pyromark Q24 (Qiagen)	IGF2, H19	Birthweight	IGF2 DMR2 mean methylation on the fetal placental side was positively correlated with birthweight (Spearman rank correlation=0.44, p< 0.01), height (r=0.40, p< 0.01), head (r=0.32, p< 0.05) and thorax (r=0.32,p< 0.05) circumference. 31% variance in birth weight could be accounted for by IGF2/H19 genotype and epigenotype jointly.
Steegers-Theunissen RP, et al. PLoS One. 2009;4: e784 <sup>29</sup>	Cross sectional study amongst controls for another study ('HAVEN'). 120 mother-infant pairs, The Netherlands. Tissue: Infant blood taken at 17 months. Platform: Epityper, Sequenom	IGF2	Birth weight	IGF2 methylation was inversely associated with birthweight (-1.7% methylation per SD birthweight; p=0.034).
Tobi EW, et al. <i>Epigenetics</i> . 2011; <b>6:</b> 171-6 <sup>30</sup>	Cohort study (The Dutch Project on Preterm and Small for Gestational Age Infants ('POPS')). 38 small for gestational age (SGA) and 75 appropriate for gestational age (AGA) individuals studied.  Tissue: Whole blood at age 19. Methylation analysis by Platform: Epityper, Sequenom.	IGF2, GNASAS, INSIGF, LEP	Size at birth	Methylation levels of <i>IGF2</i> DMR0, <i>GNASAS</i> , <i>INSIGF</i> and <i>LEP</i> did not significantly vary between SGA and AGA individuals at 19 years of age.
Wijnands KP, et al. <i>Nutr Metab Cardiovasc Dis.</i> 2015; <b>25</b> :608- 14 <sup>31</sup>	Cohort study. 120 healthy children at 17 months of age, Netherlands. Tissue: Whole blood Platform: EpiTyper, Sequenom.	TNFa, LEP	Lipid profile	High-density lipoprotein-cholesterol levels in the children were inversely associated with <i>TNFa</i> methylation (-6.1%, p =0.058) and <i>LEP</i> (-3.4%, p=0.021)

**Abbreviations:** ADHD, attention-deficit/hyperactivity disorder; BMI, body mass index; CI, confidence interval; DMR, differentially methylated region; ICR, imprinting control region; LDL-c, low-density lipoprotein cholesterol; OR, odds ratio; SD, standard deviation; VMR, variably methylated region.

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