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Table 1. Number of genes with altered methylation due to an ALL risk exposure (FDR ≤ 0.05) and the overlapping number of genes also observed to have altered methylation in ALL disease.

Exposure	Number of CpGs (hyper/hypo-methylated) with altered methylation in association with exposure (FDR ≤ 0.05)	Number of gene loci with altered methylation in association with exposure (FDR ≤ 0.05)	Number of overlapping gene loci with exposure-associated methylation change and altered methylation in ALL ^a	Number of overlapping gene loci with the same direction of methylation change (i.e. hypo/hypermethylated) for exposure and ALL (% concordance) ^b	Number of overlapping gene loci with exposure-associated methylation change and altered methylation in ALL from all published literature ^{a,c}
<i>In utero exposures</i>					
Radiation exposure	288 (140/148)	239	54 (1.69 x 10⁻⁸)	40 (74%; 0.001)	156 (0.001)
Alcohol intake	192 (158/34)	175	33 (3.98 x 10⁻⁴)	29 (88%; 0.006)	94 (0.702)
Sugary caffeinated drinks	66 (48/18)	54	12 (7.42 x 10⁻³)	10 (83%; 0.045)	30 (0.548)
Smoking throughout pregnancy	22 (10/12)	13	5 (7.11 x 10⁻³)	3 (60%; 0.140)	10 (0.097)
Smoking at 3 months pregnancy	15 (7/8)	7	3 (2.73 x 10⁻²)	1 (33%; 0.530)	5 (0.324)
Smoking pre-pregnancy	7 (4/3)	4	2 (5.45 x 10⁻²)	1 (50%; 0.350)	4 (0.094)
Folic acid supplementation	9 (1/8)	7	2 (0.155)	1 (50%; 0.155)	5 (0.324)
Coffee consumption	15 (9/6)	13	1 (0.754)	0	4 (0.981)
<i>Post-natal exposures</i>					
Reported a cold (6 months)	75 (20/55)	60	9 (0.156)	3 (33%; 0.952)	39 (0.085)

Attended day nursery (8 months)	11 (6/5)	11	6 (2.65 x 10 ⁻⁵)	5 (83%; 0.003)	9 (0.068)
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^a P-value for Hypergeometric probability test for number of overlapping gene loci. ^b P-value for Hypergeometric probability test for number of overlapping gene loci with same direction of methylation change. ^c Published literature identifying ALL disease associated methylation changes (no restrictions on the methods used to measure methylation) [1-7].

Table 2. KEGG pathway which may be altered in response to altered methylation observed in children who were exposed *in utero* to radiation exposure (Total number of genes recognised by DAVID n = 79). - = hypomethylated, + hypermethylated.

KEGG pathway term	Pathway name	Total genes altered on pathway	Genes altered (-/+ methylation)	Total genes on pathway	P-value
hsa05146	Amoebiasis	5	LAMA3 (+), LAMA5 (-), NFKB1 (+), IL12B (+), COL5A1(-)	106	0.031399

Table 3. Number of genes with altered methylation due to ALL risk exposure, reported in published 450K studies (FDR corrected and cell type adjusted) and the overlapping number of genes also observed to have altered methylation in ALL.

Exposure	Study (reference)	Number of CpGs (hyper/hypo-methylated) with altered methylation in association with exposure (FDR ≤ 0.05)	Number of gene loci with altered methylation in association with exposure (FDR ≤ 0.05)	Number of overlapping gene loci with exposure-associated methylation change and altered methylation in ALL*
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<i>In utero exposures</i>				
Smoking throughout pregnancy	[8]	6073 (3185/2888)	3176	431 (4.95 x 10⁻¹¹)
Maternal plasma folate	[9]	443 (27/416)	229	62 (4.32 x 10⁻¹³)

^a P-value for Hypergeometric probability test for number of overlapping gene loci.

Table 4. KEGG pathway which may be altered in response to altered methylation observed in children who were postnatally recorded as having a cold (6 months) (Total number of genes recognised by DAVID n = 12). - = hypomethylated, + hypermethylated.

KEGG pathway term	Pathway name	Total genes altered on pathway	Genes altered (- /+ methylation)	Total genes on pathway	P-value
hsa04010	MAPK signalling pathway	4	MAP3K7 (-), MAPK1 (-), ATF4 (-), ARRB1(-)	267	0.017247

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