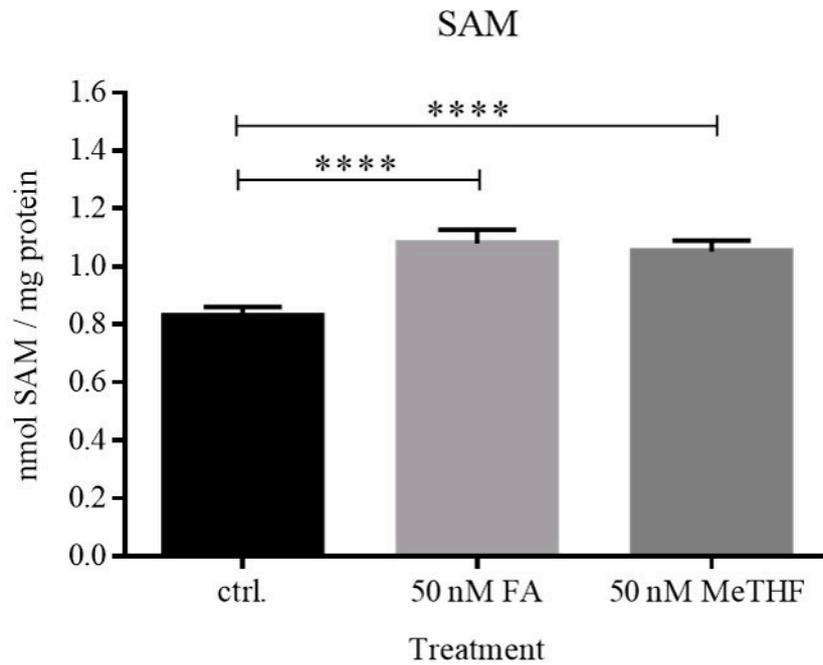
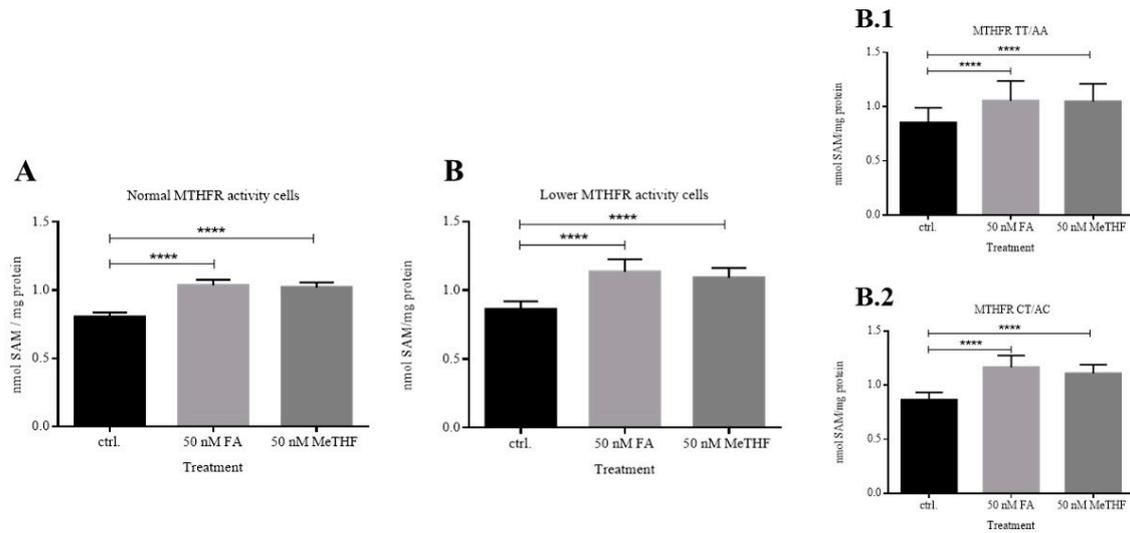


Supplementary Figure 1: Intracellular 5-Me-THF concentrations in (A) NORMAL MTHFR activity cells (genotype 677CC/1298AA, 677CT/1298AA, 677CC/1298AC, and 677CC/1298CC) (N=12) and in (B) LOW MTHFR activity cells (genotype 677TT/1298AA and 677CT/1298AC) (N=15). (B.1) LCLs with 677TT/1298AA genotype (N=5) and (B.2) LCLs with 677CT/1298AC genotype (N=10). Statistical differences were determined by one-way ANOVA with post-hoc Tukey's multiple comparisons test. Values are means \pm SD. * $p \leq 0.05$, ** $p \leq 0.01$, ** $p \leq 0.0001$, compared to untreated control (ctrl.).**

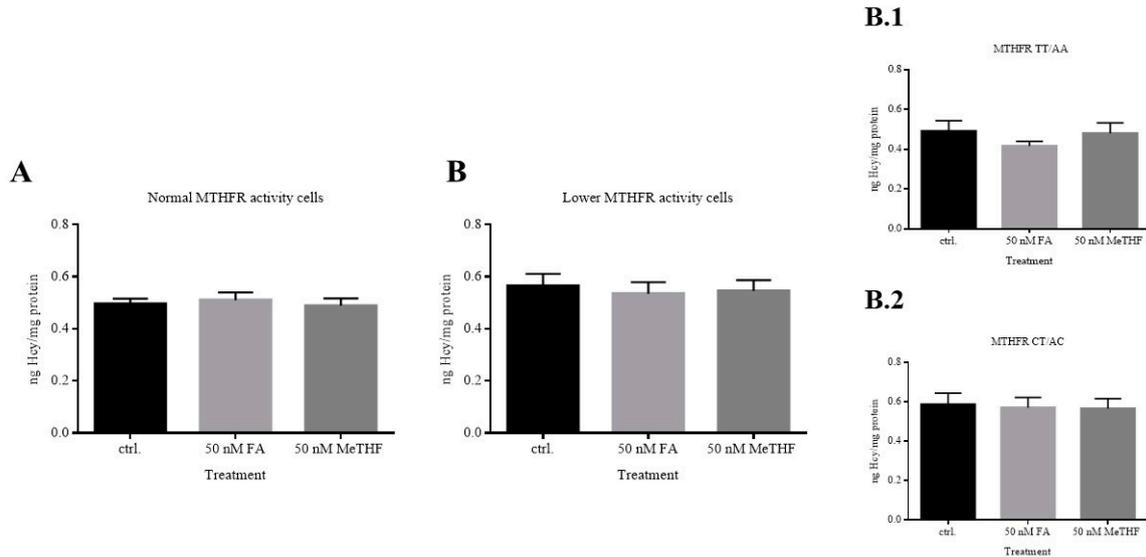


Intracellular concentration of SAM [ngmol SAM / mg protein]		
Ctrl. (mean ± SD)	50 nM FA (mean ± SD)	50 nM 5-Me-THF (mean ± SD)
0.829 ± 0.180	1.080 ± 0.263	1.052 ± 0.213

Supplementary Figure 2: Intracellular SAM concentration in folate-depleted cells (ctrl.) and after FA or 5-Me-THF treatment in LCLs. LCLs (N=35) were treated with equimolar concentration of folate supplements for 72h, then they were lysed and the concentration of SAM was measured with HPLC-UV/vis. Statistical differences were determined by one-way ANOVA with post-hoc Tukey's multiple comparisons test. Values are means ± SD. **** p ≤ 0.0001, compared to control.



Supplementary Figure 3: Intracellular SAM concentrations in (A) NORMAL MTHFR activity cells (genotype 677CC/1298AA, 677CT/1298AA, 677CC/1298AC, and 677CC/1298CC) (N=12) and in (B) LOW MTHFR activity cells (genotype 677TT/1298AA and 677CT/1298AC) (N=15). (B.1) LCLs with 677TT/1298AA genotype (N=5) and (B.2) LCLs with 677CT/1298AC genotype (N=10). Statistical differences were determined by one-way ANOVA with post-hoc Tukey's multiple comparisons test. Values are means \pm SD. ** $p \leq 0.0001$, compared to untreated control (ctrl.).**



Supplementary Figure 4: Intracellular Hcy concentrations in (A) NORMAL MTHFR activity cells (genotype 677CC/1298AA, 677CT/1298AA, 677CC/1298AC, and 677CC/1298CC) (N=12) and in (B) LOW MTHFR activity cells (genotype 677TT/1298AA and 677CT/1298AC) (N=15). (B.1) LCLs with 677TT/1298AA genotype (N=5) and (B.2) LCLs with 677CT/1298AC genotype (N=10). Statistical differences were determined by one-way ANOVA with post-hoc Tukey's multiple comparisons test. Values are means \pm SD. There were no statistical significant changes on intracellular Hcy after the addition of folate supplements, compared to untreated control (ctrl.).

Supplementary Table 1: Genotype of the ten common polymorphisms of genes involved in folate uptake and metabolism in LCL cells.

ID (LCL)	Gene (polymorphism)									
	SLC19A1 (rs105266)	FPGS (rs1544 105)	DHFR (rs16776 93)	MTHFD1 (rs2236225)	MTHFR 677 (rs1801133)	MTHFR 1298 (rs1801131)	MTRR (rs18013 94)	BHMT (rs37338 90)	GNMT (rs10948 059)	DNMT3B (rs2424913)
1112	GA	CT	CC	AA	TT	AA	AG	GG	CT	CC
1122	GA	CC	CA	GG	CC	AC	AG	GG	TT	CC
1515	GA	CT	CA	GA	CT	AC	AG	GA	TT	TT
1516	GG	TT	CA	AA	TT	AA	GG	GG	CC	CT
1570	AA	CT	CA	GG	CC	AC	AA	GA	CT	TT
1728	GA	CC	CC	GA	CT	AC	AA	GA	TT	CC
1754	AA	CC	CC	AA	CT	AA	AG	GG	CT	CT
1801	/	CC	CC	AA	CC	AA	AA	AA	CT	CC
1823	GG	CT	CC	GA	CT	AC	AG	GA	CC	CC
1976	GG	CT	CC	GG	CT	AC	AG	GG	CC	CT
4973	AA	CT	CC	GA	CT	AA	AG	GG	CC	CT
4995	AA	CT	CC	GG	CT	AA	AA	GG	CC	CT
5876	GG	CT	CC	AA	CT	AC	AA	GG	CT	TT
6037	GA	CC	CC	AA	CT	AA	AG	GG	TT	TT
6127	GA	CC	CA	GA	CT	AC	GG	GA	CC	CC
6153	GA	CC	CC	GA	CT	AC	AG	GA	CC	CC
6159	GG	CC	CC	AA	TT	AA	AG	GG	CC	CT
6203	GA	CT	CC	AA	CT	AA	AG	GG	CC	CT
6333	GA	CT	CC	AA	CT	AC	AG	GG	CT	CC
6417	GA	CT	CC	GG	CT	AA	AG	GG	CC	CC
6423	GG	CC	CA	AA	TT	AA	AA	GG	CT	CC
6425	AA	CT	AA	GA	TT	AA	GG	GG	CT	TT
6429	GG	CT	CC	GA	CT	AC	GG	GG	CC	TT
6430	GA	TT	CA	GA	CT	AC	GG	GA	CT	CC
380	AA	CC	CC	AA	CC	AA	AG	GG	CT	TT
381	AA	CT	CC	GA	CC	AA	AG	GA	TT	TT
382	GA	TT	CC	AA	CT	AA	AG	GA	CC	CC
383	GA	TT	CA	AA	CT	AC	GG	GG	CT	CT
384	GA	CT	CC	AA	CC	AC	AG	GG	CC	TT
385	GA	CT	AA	AA	CC	AA	AG	GG	CT	CT
386	GG	CT	CC	GG	CT	AA	AG	GG	CT	CT
387	GA	CC	CC	GG	CT	AA	AG	GG	CT	CT
388	GA	CT	CA	GA	CC	CC	AG	GA	CT	TT
389	GG	CT	CA	GA	CC	AA	AA	GG	CT	CT
390	GG	CT	CC	AA	CC	AC	GG	GG	CT	CT

