

Supplementary Table to Giusti et al. “Early-onset ischaemic stroke: Analysis of 58 polymorphisms in 17 genes involved in methionine metabolism” (Thromb Haemost 2010; 104.2)

Table A. Haplotype Interaction Analysis: list of the combinations of haplotypes of two different genes with a combination frequency in patients or controls higher than 0.001.

BHMT region1	CBS region2	Stoke	CTR	OR	p
:	C C G G	0,079	0,079	1	0.0296
C C A A	C C G C	0,013	0,011	1,21	
C C T A	C C G G	0,244	0,241	1,02	
C C T A	C C G C	0,045	0,036	1,26	
C C A T	C C G G	0,134	0,113	1,21	
C C A T	C C G C	0,016	0,018	0,87	
T T A A	C C G G	0,219	0,268	0,76	
T T A A	C C G C	0,044	0,038	1,15	
C T A A	C C G G	0,020	0,019	1,05	
T C T A	C C G G	0,075	0,083	0,9	
T C T A	C C G C	0,015	0,011	1,43	
T C A T	C C G G	0,032	0,051	0,62	
BHMT region1:	FOLH1 region2				
C C A A	A T	0.049	0.067	0.72	
C C A A	A A	0.021	0.004	5.99	
C C A A	G A	0.014	0.012	1.23	
C C T A	A T	0.193	0.215	0.87	
C C T A	A A	0.057	0.017	3.54	
C C T A	G A	0.044	0.042	1.06	
C C A T	A T	0.098	0.105	0.93	
C C A T	A A	0.019	0.008	2.47	
C C A T	G A	0.024	0.019	1.26	
T T A A	A T	0.167	0.246	0.61	
T T A A	A A	0.054	0.020	2.82	
T T A A	G A	0.041	0.048	0.84	
C T A A	A T	0.027	0.028	0.94	
T C T A	A T	0.054	0.056	0.96	
T C T A	A A	0.017	0.006	2.97	
T C T A	G A	0.019	0.013	1.56	
T C A T	A T	0.036	0.049	0.71	
BHMT region1	MTR region2				0.0071
:	G A C A A	0.035	0.032	1.08	
C C A A	C A T C C	0.031	0.027	1.13	
C C A A	C G T C C	0.01	0.015	0.66	
C C T A	G A C A A	0.133	0.109	1.25	
C C T A	C A T C C	0.111	0.097	1.17	
C C T A	C A T A A	0.01	0.012	0.8	

C C T A	C G T C C	0.051	0.039	1.31
C C A T	G A C A A	0.067	0.046	1.49
C C A T	C A T C C	0.047	0.044	1.08
C C A T	C G T C C	0.017	0.024	0.71
C T A A	G A C A A	0.011	0.013	0.86
C T A A	C A T C C	0.01	0.012	0.87
T C T A	G A C A A	0.048	0.027	1.85
T C T A	C A T C C	0.03	0.03	0.99
T C T A	C G T C C	0.022	0.016	1.41
T T A A	C A C A A	0.005	0.011	0.41
T T A A	G A C A A	0.114	0.13	0.86
T T A A	C A T C C	0.059	0.112	0.5
T T A A	C A T A A	0.018	0.011	1.64
T T A A	C G T C C	0.044	0.041	1.06
T C A T	G A C A A	0.026	0.026	1.02
T C A T	C A T C C	0.018	0.022	0.84
T C A T	C G T C C	0.011	0.01	1.07

BHMT
region1:

C C A A
C C A A
C C A A
C C T A
C C T A
C C T A
C C T A
C C A T
C C A T
C C A T
C T A A
C T A A
C T A A
T C A T
T C A T
T C A T
T T A A
T T A A
T T A A
T T A A
T T A A
T C T A
T C T A
T C T A

TCNII
region2

:	G C T A	0.009	0.018	0.53
	A G T G	0.022	0.022	0.98
	G C T G	0.023	0.024	0.99
	G G T G	0.014	0.017	0.86
	G C T A	0.053	0.059	0.89
	A G T G	0.087	0.093	0.94
	G C T G	0.097	0.093	1.05
	G C T A	0.039	0.032	1.23
	A G T G	0.059	0.043	1.38
	G C T G	0.047	0.041	1.14
	G C T A	0.003	0.012	0.27
	A G T G	0.011	0.009	1.17
	G C T G	0.011	0.012	0.92
	G C T A	0.02	0.01	1.94
	A G T G	0.022	0.019	1.19
	G C T G	0.023	0.019	1.21
	G G T G	0.019	0.021	0.87
	G C T A	0.07	0.072	0.96
	A G T G	0.072	0.109	0.64
	G C T G	0.121	0.108	1.14
	A C T G	0.003	0.013	0.23
	G C T A	0.031	0.014	2.27
	A G T G	0.024	0.017	1.44
	G C T G	0.041	0.023	1.86

0.0074

BHMT
region1:

C C A A
C C A A
C C A A
C C T A
C C T A
C C T A
C C A T
C C A T
C C A T

TYMS
region2

:	T C A	0.049	0.041	1.21
	C C A	0.005	0.014	0.38
	C A C	0.032	0.037	0.87
	T C A	0.154	0.123	1.3
	C C A	0.041	0.036	1.17
	C A C	0.098	0.113	0.86
	T C A	0.064	0.054	1.2
	C C A	0.017	0.021	0.83
	C A C	0.052	0.047	1.11

0.0119

C T A A	T C A	0.018	0.012	1.49
T C T A	T C A	0.046	0.041	1.12
T C T A	C C A	0.016	0.018	0.91
T C T A	C A C	0.035	0.032	1.11
T T A A	T C A	0.114	0.14	0.79
T T A A	C C A	0.032	0.047	0.67
T T A A	C A C	0.081	0.112	0.7
T C A T	T C A	0.026	0.03	0.86
T C A T	C A C	0.02	0.03	0.65

CBS
region1

FOLH1
region2

0.0006

:	C C G G	:	A T	0.527	0.661	0.57
	C C G G		A A	0.171	0.051	3.87
	C C G G		G A	0.133	0.147	0.89
	C C G C		A T	0.106	0.097	1.1
	C C G C		A A	0.03	0.006	5.07
	C C G C		G A	0.026	0.019	1.37

CBS
region1

PON2
region2

0.0197

:	C C G G	:	C C	0.653	0.668	0.94
	C C G G		G G	0.163	0.199	0.78
	C C G C		C C	0.156	0.092	1.83
	C C G C		G G	0.018	0.029	0.62

FOLH1
region1:

MTR
region2

0.0026

A T	:	C A C A A	0.011	0.021	0.52
A T		G A T C C	0.001	0.015	0.08
A T		G A C A A	0.261	0.307	0.8
A T		C A T C C	0.203	0.27	0.69
A T		C A T A A	0.019	0.028	0.68
A T		C G T C C	0.1	0.119	0.82
A A		G A C A A	0.097	0.022	4.7
A A		C A T C C	0.075	0.021	3.72
A A		C A T A A	0.014	0.001	9.87
A A		C G T C C	0.039	0.012	3.49
G A		G A C A A	0.065	0.057	1.15
G A		C A T C C	0.057	0.056	1.02
G A		C G T C C	0.031	0.024	1.33

FOLH1
region1

TCNII
region2

0.0304

:	A T	:	A C T A	0.012	0.016	0.74
	A T		G G T G	0.036	0.05	0.7
	A T		G C T A	0.198	0.181	1.12
	A T		A G T G	0.24	0.242	0.99
	A T		G C T G	0.261	0.258	1.02
	A T		A C T G	0.014	0.027	0.52
	A A		G C T A	0.014	0.014	1
	A A		A G T G	0.011	0.022	0.47
	A A		G C T G	0.019	0.024	0.78
	G A		G C T A	0.027	0.032	0.85
	G A		A G T G	0.059	0.045	1.35
	G A		G C T G	0.067	0.045	1.53

FOLH1

region1

:

A T
A T
A T
A T
A A
A A
A A
G A
G A
G A

TYMS

region2:

T C A
T A C
C C A
C A C
T C A
C C A
C A C
T C A
C C A
C A C

0.297 0.335 0.84
0.015 0.013 1.18
0.09 0.109 0.81
0.219 0.313 0.62
0.089 0.025 3.8
0.036 0.008 4.57
0.072 0.015 4.94
0.073 0.081 0.89
0.023 0.023 0.97
0.064 0.058 1.11

0.0004**MTR**

region1

:

C A C A A
G A T C C
G A C A A
G A C A A
C A T C C
C A T C C
C A T A A
C A T A A
G A C C C
C G T C C
C G T C C

PON2

region2:

C C
C C
C C
G G
C C
G G
C C
G G
C C
C C
G G

0.016 0.022 0.73
0 0.015 0.02
0.311 0.316 0.98
0.058 0.076 0.76
0.253 0.272 0.91
0.084 0.073 1.17
0.037 0.026 1.45
0.018 0.009 1.95
0.025 0 291.48
0.129 0.128 1.01
0.046 0.029 1.58

0.0053**MTR**

region1:

C A C A A
C A C A A
G A C A A
G A C A A
G A C A A
G A C A A
C A T C C
C A T C C
C A T C C
C A T C C
C A T C C
C A T C C
C A T A A
C A T A A
C A T A A
C G T C C
C G T C C
C G T C C

TCNII

region2:

:

A G T G
G C T G
G G T G
G C T A
A G T G
G C T G
G G T G
G C T A
A G T G
G C T G
A C T G
G C T A
A G T G
G C T G
G C T A
A G T G
G C T G

0.009 0.011 0.79
0.007 0.012 0.57
0.018 0.015 1.17
0.095 0.099 0.95
0.103 0.113 0.9
0.16 0.132 1.25
0.014 0.019 0.71
0.075 0.073 1.03
0.093 0.118 0.77
0.109 0.104 1.05
0.004 0.011 0.36
0.003 0.012 0.21
0.013 0.009 1.53
0.016 0.008 1.97
0.042 0.024 1.76
0.078 0.049 1.64
0.061 0.047 1.34

0.0114**PON2**

region1:

C C
C C
C C
C C
G G
G G

TYMS

region2:

T C A
T A C
C C A
C A C
T C A
C C A

0.362 0.344 1.08
0.011 0.014 0.74
0.116 0.112 1.04
0.29 0.307 0.92
0.096 0.102 0.93
0.032 0.03 1.05

0.0054

G G

C A C

0.05

0.082

0.59

*= multiple testing correction has been applied via the minP approach (the p value of the best marker/region configuration is corrected via Monte-Carlo simulations) [20, 21].