METHYLATION PANEL

GENOVA DIAGNOSTICS
63 Zillicoa Street
Asheville, NC 28801

Patient: **Sample Patient**

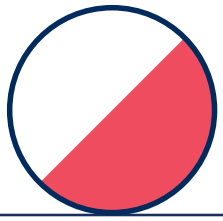
DOB:
Sex:
MRN:

3534 Methylation Panel - Plasma & Whole Blood

Interpretation At-a-Glance

Methylation

- Homocysteine ▲
- SAH ▲
- Methionine ▲
- Choline ▲
- Sarcosine ▲

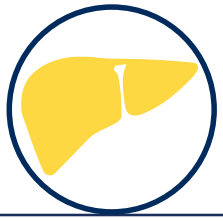


Genetic Polymorphism

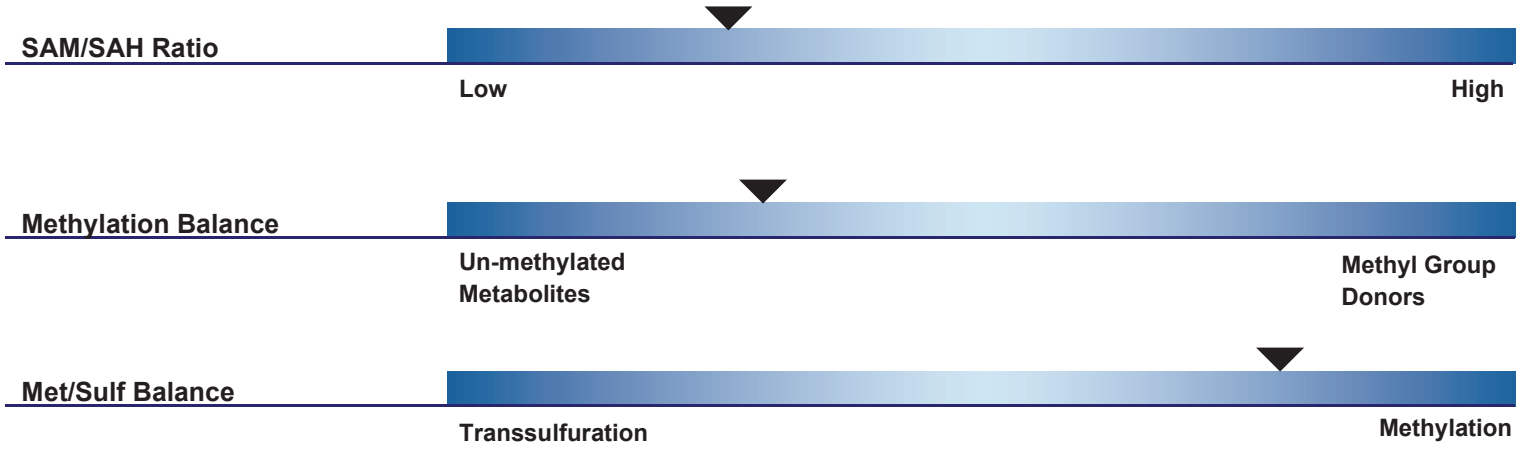
DOWNREGULATING SNPS		UPREGULATING SNPS	
MTHFR		**MTR**	
C677T	−/+	A2756G	−/−
A1298C	−/+	**CBS**	
COMT		C699T	−/+
V158M	+/+	**BHMT**	
MTRR		G742A	−/−
A66G	−/+	**GNMT**	
MAT1A		C1289T	−/−
D18777A	−/−		
SHMT1			
C1240T	−/+		

Transsulfuration

- Serine ▲



Methylation Status



3534 Methylation Panel - Plasma & Whole Blood

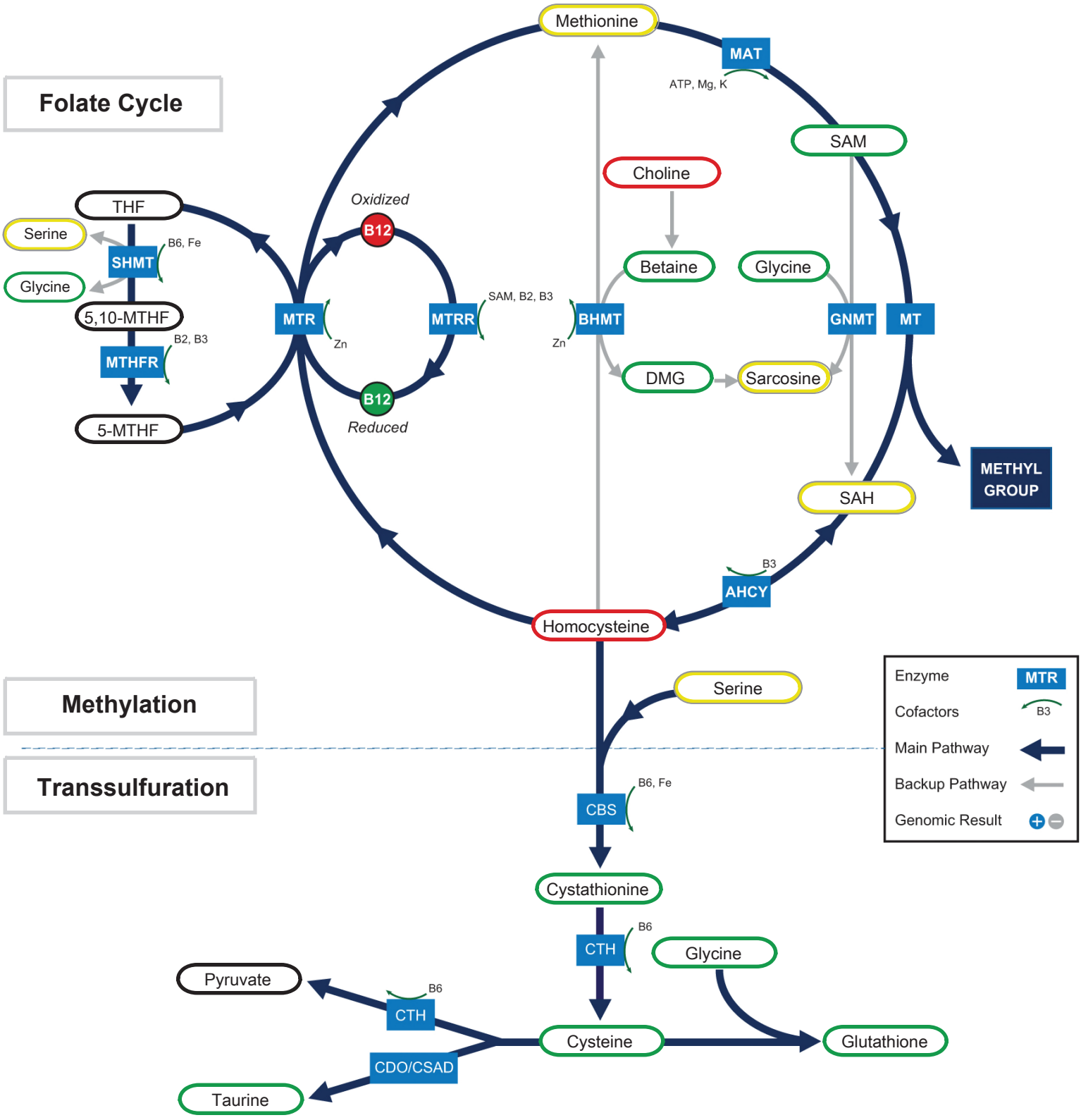
Methodology: LCMSMS & Colorimetric

	Results micromol/L		QUINTILE DISTRIBUTION 1st 2nd 3rd 4th 5th	Reference Range
Methylation Capacity				
Ratios				
1. Methylation Index (SAM/SAH Ratio)	3.3			2.2-6.4
2. Methylation Balance Ratio	1.08			1.03-1.20
3. Met/Sulf Balance Ratio	0.62			0.55-0.64
4. Betaine/Choline Ratio	2.3	L		2.6-7.7
Methyl Group Donors				
5. S-adenosylmethionine (SAM)	109			65-150 nanomol/L
6. Methionine	36			23-38
7. Choline	19.1	H		5.2-13.0
8. Betaine	44			21-71
9. Serine	147			91-161
Methyl Group Metabolites				
10. S-adenosylhomocysteine (SAH)	33			16-41 nanomol/L
11. Homocysteine †	11.3	H		3.7-10.4
12. Dimethylglycine (DMG)	2.9			1.6-5.0
13. Sarcosine	6,368			3,670-6,743 nanomol/L
14. Glycine	267			181-440
Transsulfuration Metabolites				
15. Cystathionine	216			74-369 nanomol/L
16. Cyst(e)ine	323			271-392
17. Taurine	83			50-139
18. Glutathione †	1,577			>=669

†These results are not represented by quintile values.

Tests were developed and their performance characteristics determined by Genova Diagnostics. Unless otherwise noted with ◆, the assays have not been cleared by the U.S. Food and Drug Administration.

Methylation / Transsulfuration Pathway



3535 Add-on Methylation Genomics - Buccal sample

Methodology: DNA Sequencing

MTHFR C677T — 5,10-methylenetetrahydrofolate reductase

Your Genotype:

Allele 1	Allele 2
C	T

Wild Type - Variant +

Potential Impact:

Downregulation

Genotypes	Amino Acid
C C	Ala Ala
C T	Ala Val
T T	Val Val

Amino Acid Position: 222

Alanine to Valine

GCC → GTC

DNA Position: 894

SNP

TCTGCGGGA G(C or T) C GATTTCATC

Amino Acid Codon

Rs Number: rs1801133

Location: Chromosome 1p36.22

Methylenetetrahydrofolate reductase (MTHFR) is a key regulatory enzyme which converts 5,10-methylenetetrahydrofolate to 5-methyltetrahydrofolate (5-MTHF). This step activates folate to be used for homocysteine (Hcy) conversion to methionine, instead of nucleotide synthesis.

Health Implications

- The C677T polymorphism downregulates enzymatic activity, which can limit Amethylation reactions in the body. The C677T polymorphism results in an increased risk of high homocysteine and an increased tendency for lower folate levels.[1,2]
- Homozygosity for 677 (+/+) results in 60-70% reduction in MTHFR enzyme activity. Heterozygosity for 677 (-/+) results in 30-40% reduction in MTHFR enzyme activity.[3]
- Lower levels of B-vitamin and folate increase the risk of elevated homocysteine related to MTHFR SNPs.[2]
- Homozygous C677T subjects have higher Hcy levels, while heterozygous subjects have mildly raised Hcy levels compared to controls.[4]
- MTHFR C677T SNPs have been associated with many disease processes including:
  - Cardiovascular disease [5-7]
  - Depression and schizophrenia [8,9]
  - Increased risk of birth defects and Down's syndrome [10]
  - Psoriasis
  - Diabetes
  - Parkinson's disease

Clinical Considerations

- Ensure adequate intake of dark-green leafy vegetables and other B vitamin-rich foods.
- Evaluate homocysteine, SAM, and SAH levels.
- Supplementation with methylated folate and folate-rich foods may help lower Hcy and mitigate risk.[11]
- Evaluate the status of vitamin B-2 and B-3 (MTHFR enzyme cofactors).

* Frequency:

Population Category	CC	CT	TT
EUR	47%	44%	9%
EAS	37%	47%	16%
AFR	81%	91%	<1%
AMR	32%	52%	16%
SAS	68%	30%	2%

References

1. Yang Q, et al. *Am J Clin Nutr*. 2012;95(5):1245-1253.
2. Garcia-Minguillan CJ, et al. *Genes Nutr*. 2014;9(6):435.
3. Weisberg IS, et al. *Atherosclerosis*. 2001;156(2):409-415.
4. Liew S-C, et al. *Eur J Med Genet*. 2015;58(1):1-10.
5. Zhang P, et al. *Angiology*. 2015;66(5):422-432.
6. Yang KM, et al. *Biomed Rep*. 2014;2(5):699-708.
7. Cui T. *Int J Neurosci*. 2015.
8. Wu YL, et al. *Prog Neuropsychopharmacol Biol Psychiatry*. 2013;46:78-85.
9. Hu CY, et al. *J Neural Transm (Vienna)*. 2015;122(2):307-320.
10. Yadav U, et al. *Metab Brain Dis*. 2015;30(1):7-24.
11. Zhao M, et al. *Stroke*. 2017;48(5):1183-1190.

*Population frequency data is from 1000 GENOMES project as sourced from NCBI dbSNP. The population categories are listed below:
EAS (East Asian): Han Chinese (Beijing), Japanese (Tokyo), Southern Han Chinese, Chinese Dai, Kinh (Vietnam)
EUR (European): Americans with Northern and Western European Ancestry, Toscani, Finnish, British, Spanish
AFR (African): Nigerian, Kenyan, Gambian, Mendi (Sierra Leone), African Americans, African Caribbeans
AMR (Ad Mixed American): Mexican, Puerto Rican, Colombian, Peruvian
SAS (South Asian): Americans of Gujarati descent (India), Punjabi (Pakistan), Bengali (Bangladesh), Sri Lankan/Indian in UK