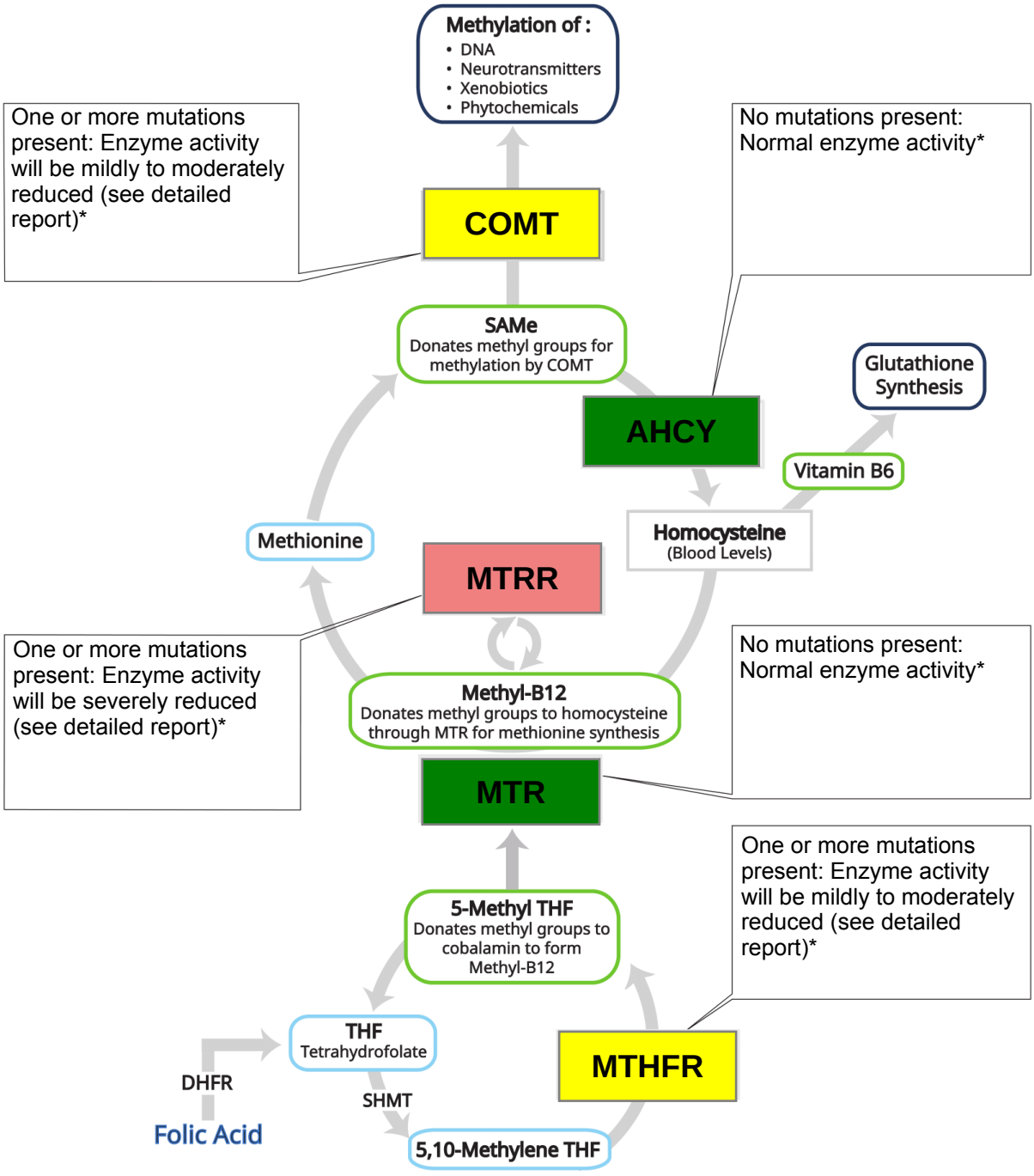
Advanced Methylation Detoxification Profile

GENOMIC INSIGHTS ™

Patient Information

Name:	SAMPLE PATIENT	Physician:	SAMPLE PHYSICIAN
Date Of Birth:	XX/XX/XXXX	Clinic ID:	XXXXX
Gender:	M	Date Drawn:	02/01/2016
Lab ID:	XXXXXX	Date Reported:	02/09/2016
Date Received:	2/2/2016	Page:	1 of 6 Pages

Methylation Detoxification Cycle:



** Note that mutations other than those tested may contribute to the decrease in the enzyme activity.*

Patient Information

Name:	SAMPLE PATIENT	Physician:	SAMPLE PHYSICIAN
Date Of Birth:	XX/XX/XXXX	Clinic ID:	XXXXX
Gender:	M	Date Drawn:	02/01/2016
Lab ID:	XXXXXX	Date Reported:	02/09/2016
Date Received:	2/2/2016	Page:	2 of 6 Pages

Personalized Genomic Commentary:

MTHFR C677T	Heterozygous	A gene inherited from one parent has a mutation while the other gene is normal. Enzyme activity tends to be mildly to moderately reduced regarding the investigated mutation site.
MTHFR A1298C	Homozygous Negative	Genes inherited from both parents have no mutations. Enzyme activity tends to be normal regarding the investigated mutation site.

Summary of results regarding the investigated mutation sites:

1. **Enzyme effectiveness tends to be mildly to moderately reduced (see page 4 for genomic recommendations)**
2. **Mild tendency towards elevated homocysteine levels.**

Important:

1. **If individual is being treated with antifolates and homocysteine levels are elevated, supporting literature strongly suggests supplementation with 5-MTHF.**
   Examples of antifolates include:
   Methotrexate (Rheumatrex, Trexall), Pyrimethanine (Daraprim) , Premetrezed (Alimta), Trimethoprim, Proguani.
2. **Use caution with individuals previously diagnosed with serotonin syndrome.**

MTR C3518T (Pro1173Leu)	Homozygous Negative	Genes inherited from both parents have no mutations. Enzyme activity tends to be normal regarding the investigated mutation site.
MTR A2756G (Asp856Gly)	Homozygous Negative	Genes inherited from both parents have no mutations. Enzyme activity tends to be normal regarding the investigated mutation site.

Summary of results regarding the investigated mutation sites:

1. **Enzyme effectiveness tends to be normal.**
2. **No tendency towards elevated homocysteine levels due to the investigated mutation site.**

MTRR A66G (Ile49Met)	Homozygous Positive	Genes inherited from both mother and father have mutations. Enzyme activity tends to be reduced regarding the investigated mutation site.

Summary of results regarding the investigated mutation sites:

1. **Enzyme effectiveness tends to be significantly reduced (see page 4 for genomic recommendations)**

Important:

1. **In combination with the C677T polymorphism in MTHFR, MTRR genotypes AG (heterozygous) and GG (homozygous positive) influence total plasma homocysteine levels. Additionally, the combination of the genetic polymorphisms in MTRR and MTHFR is linked to an increase in DNA damage as measured by micronucleus frequency (MN). Use caution with individuals previously diagnosed with serotonin syndrome.**

Patient Information

Name:	SAMPLE PATIENT	Physician:	SAMPLE PHYSICIAN
Date Of Birth:	XX/XX/XXXX	Clinic ID:	XXXXX
Gender:	M	Date Drawn:	02/01/2016
Lab ID:	XXXXXX	Date Reported:	02/09/2016
Date Received:	2/2/2016	Page:	3 of 6 Pages

Personalized Genomic Commentary:

AHCY g.G32878481C	Homozygous Negative	Genes inherited from both parents have no mutations. Enzyme activity tends to be normal regarding the investigated mutation site.
AHCY C112T (Arg10Trp)	Homozygous Negative	Genes inherited from both parents have no mutations. Enzyme activity tends to be normal regarding the investigated mutation site.
AHCY G367A (Gly95Arg)	Homozygous Negative	Genes inherited from both parents have no mutations. Enzyme activity tends to be normal regarding the investigated mutation site.

Summary of results regarding the investigated mutation sites:

1. **Enzyme effectiveness tends to be normal.**

Important:

1. **Relevant mutations are associated with decreased enzyme presence and/or impaired function leading to elevated AdoHcy (s-adenosylhomocysteine) concentrations which may impair methylation potential. Studies show that association between mutations resulting in poor methylation potential may lead to severe myopathies, developmental delays, and hypermethionemia.**

COMT G472A (Val108/158Met)	Heterozygous	A gene inherited from one parent has a mutation while the other gene is normal. Enzyme activity tends to be mildly to moderately reduced regarding the investigated mutation site.
COMT G304A (Ala52/102Thr)	Homozygous Negative	Genes inherited from both parents have no mutations. Enzyme activity tends to be normal regarding the investigated mutation site.

Summary of results regarding the investigated mutation sites:

1. **Enzyme effectiveness tends to be mildly to moderately reduced (see page 4 for genomic recommendations)**
2. **Degradation of the following substances by methylation tends to be mildly to moderately reduced:**
   - **catechol estrogens**
   - **catechol xenobiotics**
   - **catechol estrogens**
   - **nucleotides**
   - **catechol amines (neurotransmitters)**
   - **nucleotides**

Important:

1. **Physician should be aware of this genetic test result should the patient be taking COMT inhibitors such as:**
   - **entacapone (Comtan)**
   - **tolcapone (Tasmar)**
   - **nitecapone**
2. **Consumption of COMT inhibitors like tea catechins (green and black tea) and quercetin should be limited in the case of reduced COMT enzyme activity. Both are natural inhibitors of COMT, which can result in further inhibition of COMT activity. Quercetin is found in the following fruits and vegetables:**
   - **capers**
   - **radish leaves**
   - **dill**
   - **fennel leaves**
   - **radicchio**
   - **buckwheat**
   - **chokeberry**
   - **lingonberry**
   - **cow peas**
   - **blueberry**
   - **rowanberry**
   - **prickly pear cactus fruits**
   - **broccoli**
   - **dock like sorrel**
   - **carob fiber**
   - **cilantro**
   - **red onion**
   - **watercress**
   - **cranberry**
   - **kale**
   - **black plum**
   - **sea buckthorn berry**
   - **sweet potato**
   - **crowberry**
   - **apples**
   - **bilberry**
3. **Caution: Review past medical history for prior evidence of serotonin syndrome or use of anti-Parkinson's medication before supplementing S-Adenosylmethionine (SAMe).**

Patient Information

Name:	SAMPLE PATIENT	Physician:	SAMPLE PHYSICIAN
Date Of Birth:	XX/XX/XXXX	Clinic ID:	XXXXX
Gender:	M	Date Drawn:	02/01/2016
Lab ID:	XXXXXX	Date Reported:	02/09/2016
Date Received:	2/2/2016	Page:	4 of 6 Pages

Genomic Recommendations:

Gene	Recommendation	Dosage†
COMT	SAMe (s-Adenosyl Methionine)	Oral dosage: 200mg – 600mg (No known side effects)
MTHFR	5-MTHF [(6s) 5-methyltetrahydrofolate]	Oral dosage: 0.1mg – 1.0mg (see product recommendations)
MTRR	SAMe (s-Adenosyl Methionine)	Oral dosage: 200mg – 600mg (No known side effects)

†Recommended daily allowances

Additional Information:
If homocysteine levels are still elevated after targeted supplementation, additional vitamin B6, L-cysteine, L-glycine and L- glutamic acid are recommended.

Patient Information

Name:	SAMPLE PATIENT	Physician:	SAMPLE PHYSICIAN
Date Of Birth:	XX/XX/XXXX	Clinic ID:	XXXXX
Gender:	M	Date Drawn:	02/01/2016
Lab ID:	XXXXXX	Date Reported:	02/09/2016
Date Received:	2/2/2016	Page:	5 of 6 Pages

References:

Daijun Zhou et al.: The Polymorphisms in Methylenetetrahydrofolate Reductase, Methionine Synthase, Methionine Synthase Reductase, and the Risk of Colorectal Cancer. *Int. J. Biol. Sci.* 8(6):819-830, 2012

David Watkins et al.: Hyperhomocysteinemia due to Methionine Synthase Deficiency, cblG: Structure of the MTR Gene, Genotype Diversity, and Recognition of a Common Mutation, P1173L. *Am. J. Hum. Genet.* 71:143-153, 2002.

David Watkins & David S. Rosenblatt. Update and new concepts in vitamin responsive disorders of folate transport and metabolism. *J Inherit Metab Dis*, DOI 10.1007/s10545-011-9418-1, 2011

Ercole L.Cavalieri et al.: Catechol ortho-quinones: the electrophilic compounds that form depurinating DNA adducts and could initiate cancer and other diseases. *Carcinogenesis* vol.23 no 6 pp.1071-1077, 2012.

Gaughan DJ et al.: The methionine synthase reductase (MTRR) A66G polymorphism is a novel genetic determinant of plasma homocysteine concentrations. Atherosclerosis. 2001 Aug;157(2):451-6.

Jamerson B.D. et al.: Folate Metabolism Genes, Dietary Folate and Response to Antidepressant Medications in Late-Life Depression. Int J Geriatr Psychiatry, 2013 September; 28(9).

Jane C. Figueiredo et al.: Global DNA Hypomethylation (LINE-1) in the Normal Colon and Lifestyle Characteristics, Dietary and Genetic Factors. *Cancer Epidemiol Biomarkers Prev.*, 18(4): 1041-1049, April 2009.

Mojgan Hosseini: Role of Polymorphism of Methyltetrahydrofolate-Homocysteine Methyltransferase (MTR) A2756G and Breast Cancer Risk. POL. J. PATHOL 2013; 64 (3): 191-195

Qiping Feng et al.: Human S-adenosylhomocysteine hydrolase: common gene sequence variation and functional genomic characterization. J. Neurochem. (2009) 110, 1806-1817.

Sheila Dawling et al.: Catechol-O-Methyltransferase (COMT)-mediated Metabolism of catechol Estrogens: Comparison of Wild-Type and variant COMT Isoforms. *CANCER RESEARCH* 61, 6716-6722, September 15, 2001.

Seong-Gene Lee et al.: Association of Ala72Ser polymorphism with COMT enzyme activity and the risk of schizophrenia in Koreans. *Hum Genet*, 116: 319-328, 2005.

Xiang Tan and Minhwu Chen. Association between Catechol-O-methyltransferase rs4680 (G>A) polymorphism and lung cancer risk. *Diagnostic Pathology*, 9:192, 2014

Advanced Methylation Detoxification Profile

GENOMIC INSIGHTS ™

Patient Information

Name:	SAMPLE PATIENT	Physician:	SAMPLE PHYSICIAN
Date Of Birth:	XX/XX/XXXX	Clinic ID:	XXXXX
Gender:	M	Date Drawn:	02/01/2016
Lab ID:	XXXXXX	Date Reported:	02/09/2016
Date Received:	2/2/2016	Page:	6 of 6 Pages

Homocysteine (serum) : **11.81** (µmol/L) **Age: 35**

Reference Ranges*:

Normal (µmol/L)	Mildly Elevated (µmol/L)	Moderately Elevated (µmol/L)	Severely Elevated (µmol/L)
< 15	**15 - 30**	**30 - 60**	**> 60**

* The reference ranges represent a mean value based on recommendations in literature (see references).

Result Comment:

Elevated homocysteine levels are associated with coronary artery disease, stroke, aortic aneurym, atherosclerosis, deep vein thrombosis, schizophrenia, depression, dementia, autoimmune diseases, hypothyroidism, kidney diseases, and others.

References:

Moll S., et al.: Homocysteine and MTHFR Mutations. Circulation. 132:e6-e9, 2015.

Cotton F., et al.: Reference Intervals for Plasma Homocysteine by the AxSYM Immunoassay after Collection in Fluoride tubes. Clinical Chemistry 49, No.2, 2003.

Rasmussen K., et al.: Age- and gender- specific reference intervals for total homocysteine and methylmalonic acid in plasma before and after vitamin supplementation. Clinical Chemistry 42:4, 630-636, 1996.

Faure – Delanef L., et al.: Methylenetetrahydrofolate Reductase Thermolabile variant and Human Longevity. Am. J. Hum. Genet., 60:999 -1001, 1997.

M.R Nehler, L.M Taylor Jr, J.M Porter. Homocysteinemia as a risk factor for atherosclerosis: a review.Cardiovascular Surgery Volume 5, Issue 6, December, Pages 559–567, 1997