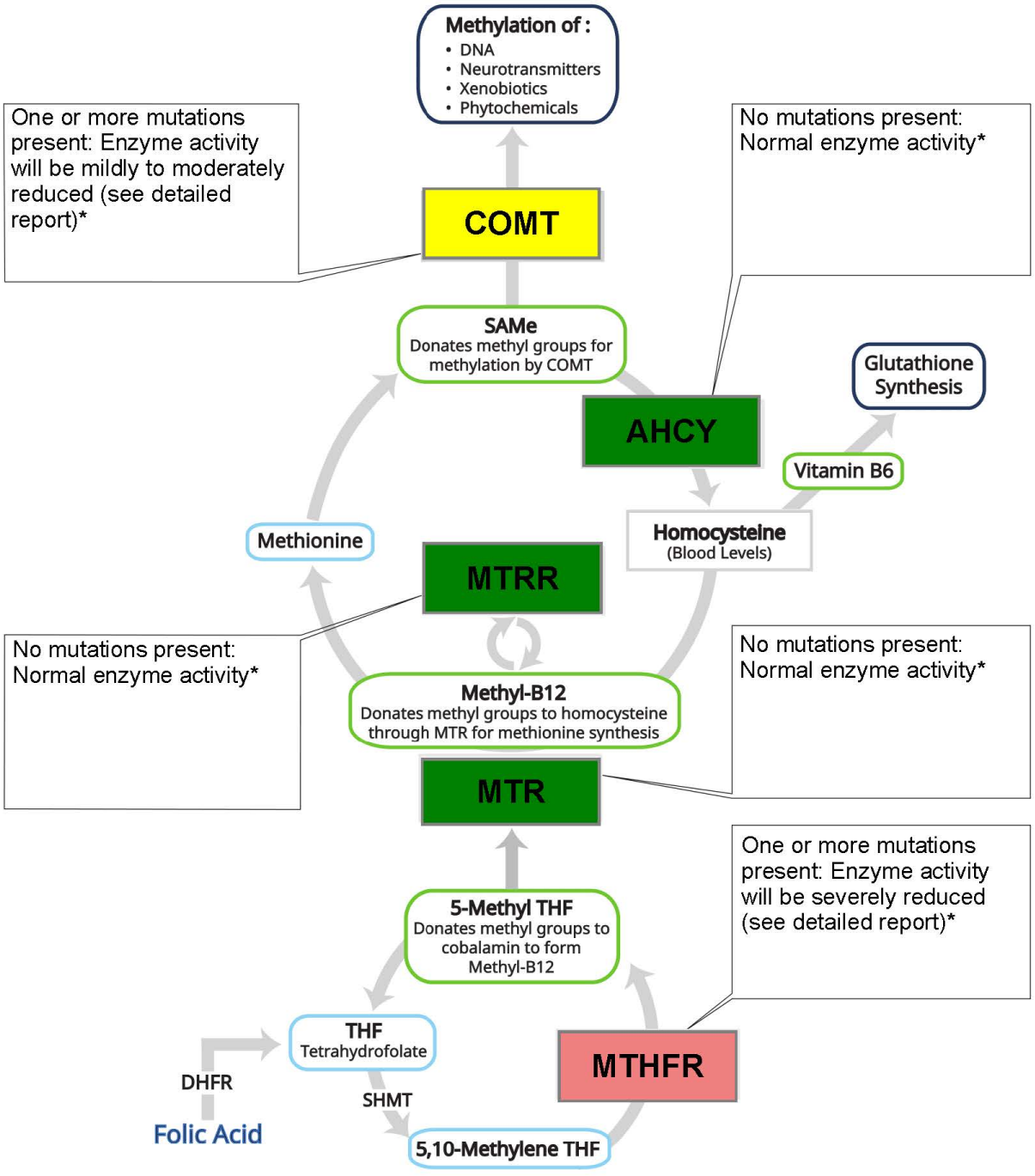
# Methylation Detoxification Profile

GENOMIC INSIGHTS™

| Patient Information | Name: | PATIENT II, PRETEND | | |
|---|---|---|---|---|
| Date of Birth: | 11/04/1977 | Gender: F | Lab ID: | 68220 |
| Date Received: | 02/11/2010 | Date Collected: | Date Reported: | 01/17/2017 |
| Physician: | Sample Physician | | Clinic ID: | 10804 |



## *Methylation Detoxification Cycle:*




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

## *Personalized Genomic Commentary:*

| | | | |
|---|---|---|---|
| MTHFR | C677T | Homozygous Positive | Genes inherited from both mother and father have mutations. Enzyme activity tends to be reduced regarding the investigated mutation site. |
| | A1298C | Homozygous Negative | Genes inherited from both parents have no mutations. Enzyme activity tends to be normal regarding the investigated mutation site. |

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

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

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

2. No tendency towards elevated homocysteine levels due to the investigated mutation site.

| | | | |
|---|---|---|---|
| MTRR | A66G (Ile49Met) | Homozygous Negative | Genes inherited from both parents have no mutations. Enzyme activity tends to be normal regarding the investigated mutation site. |

**Summary:** Enzyme effectiveness tends to be normal.

**Important:** 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.

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

**Summary:** Enzyme effectiveness tends to be normal.

**Important:** 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 | G304A (Ala52/102Thr) | Homozygous Negative | Genes inherited from both parents have no mutations. Enzyme activity tends to be normal regarding the investigated mutation site. |
| | 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. |

**Summary:** 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:

**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. Use CAUTION when providing supplemental nutrients for those :
a. who have a history of serotonin syndrome
b. who take medication for Parkinson's disease
c. who take COMT inhibitors like Entacapone, Tolcapone in connection with L-Dopa (Dopamine).

## *Genomic Recommendations:*

| Gene | Address Need For | Nutrient Applications | RDA | Consider Supplementation With Practitioner Guidance |
|---|---|---|---|---|
| **COMT** | Precursors for body to make SAMe (cofactor for COMT enzyme):L-methionine Cofactor:: magnesium | Food sources of methionine:eggs, fish, turkey, cheese,legumes, nuts/seeds.Green tea and quercetin are COMT inhibitors. Attention to amount consumed may be necessary. Avoid quercetin in supplementation. (**see quercetin content of foods chart included in report) | mg of methioine and cysteine per kg body weight:<br>4-8 years 22 mg<br>9-13 years boys 22 mg<br>9-13 years girls 21 mg<br>14-18 years boys 21 mg<br>14-18 years girls 19 mg<br>19+ years 19 mg<br>Pregnancy 25 mg<br>Lactation 26 mg | Clinical experience suggests an oral dose of<br>500 mg methionine 1-2 times per day, **<br>Address dietary intake. |
| **MTHFR** | 5-MTHF (5-methyltetrahydrofolate)<br>Cofactors: riboflavin, niacin, magnesium, zinc. | Encourage intake of green leafy vegetables, legumes, citrus fruit, beets, whole grains. Avoid folic acid in supplements and fortified foods. | folate:<br>1-3 years 150 ug<br>4-8 years 200 ug<br>9-13 years 300 ug<br>14 + years 400 ug | A daily dose of 100-1000 ug (.1- 1 mg) is typically used in research studies to achieve clinical benefit.**<br>Additional support using vitamin B2, B6, B12, and betaine may also need to be addressed.** |

***Limitations of the Recommended Dietary Allowances** The RDA is defined by The Food and Nutrition Board of the Institute of Medicine as "the average daily dietary nutrient intake level sufficient to meet the nutrient requirement of nearly all (97 to 98 percent) healthy individuals in a particular life stage and gender group." This does not mean that additional nutrients provided via supplementation would not be beneficial.
The RDAs are not meant to apply to those managing inherited metabolic disorders, medical conditions, or those using nutrient depleting medications. It is generally well accepted by nutrition professionals, that higher levels of nutrient intake can help prevent chronic disease and promote optimal health.

****Consult with ordering health care practitioner to assess need for supplementation and proper dosage. Therapeutic dose to be determined by ordering health care provider. (the level of nutrient intake to optimize methylation status varies from individual to individual)**

## FOOD and LIFESTYLE FIRST

An individual's nutrient status depends on many factors. Digestion, absorption, and assimilation impacts the availability of nutrients supporting methylation, so issues potentially interfering with that availability need to be addressed. Further laboratory assessment may be indicated.

For food and lifestyle based support of methylation:

- Address GI function, intestinal permeability, dysbiosis, and food sensitivities. Avoid offending foods and ingredients.
- Consume a variety of organic, whole, colorful plant foods providing fiber, anti-inflammatory and anti-oxidant benefit. Include omega 3 fatty acids. Consume enough protein from lean- antibiotic/hormone free animal sources and/or plant sources- legumes, nuts/seeds.
- Manage weight and regulate blood glucose.
- Hydrate well with filtered water. Overall fluid need = 1 ounce/kg body weight (~½ body weight in fluid ounces, unless fluid restriction prescribed by physician)
- Avoid sugar, refined/fortified grains, conventionally raised animal products, trans fats, charbroiled foods (avoid grilling and deep frying) .
- Avoid air pollutants, pesticides, bisphenol A, phthalates, automobile fumes, jet fuel, benzene, heavy metals, plastic food/beverage containers. Avoid high mercury fish- tuna, shark, swordfish, King mackerel.
- Avoid excessive alcohol consumption.
- Don't smoke.
- Work with a nutrition expert who can tailor the eating pattern to meet individual requirements.
- Lead an active lifestyle. Adopt a moderate exercise routine. Consult an exercise specialist to individualize routine. Avoid over-training.
- Reduce and manage stress. Consider meditation, yoga, prayer, positive thinking, acupuncture, social interaction, journaling. Get adequate sleep.

## Dietary sources of key methylation nutrients

**Folate** - leafy greens- spinach, turnip greens, mustard greens, collard greens, legumes- mung beans, chickpeas , pinto beans, great northern beans, lentils, black beans, fava beans, kidney beans, soybeans, navy beans, pinto beans, black eye peas , split peas, peanuts, leeks, asparagus, broccoli, Brussels sprouts, avocado, citrus fruit, beets, spearmint, rosemary, daikon radishes, basil, cilantro (coriander leaf), marjoram, oregano, sage, tarragon, thyme, peanuts, sunflower seeds, wakame seaweed, quinoa, kelp seaweed, bay leaf, parsley, shitake mushrooms, dill, okra, egg, artichokes.

**Riboflavin** - spirulina, egg, paprika, chives, cilantro, spearmint, tarragon, shiitake mushrooms, parsley, almonds, fish roe, cayenne pepper, chili powder, soybeans, game meat, daikon radish, chervil, goat cheese, mackerel, brie cheese, sesame, liver-lamb, beef, chicken, duck, goose.

**Niacin** - peanuts, sunflower seeds, chicken, shiitake mushrooms, sesame seeds, salmon, spirulina, pork cilantro, mackerel, parsley, beef, game meats, sun-dried tomatoes, tarragon, trout, lamb, chili powder, mustard seed, duck, cod, anchovy, liver- beef, lamb, chicken.

**Magnesium** - Agar seaweed, herbs, spices, bran, pumpkin seeds cocoa flaxseed, Brazil nuts, sunflower seeds, sesame seeds, poppy seeds, almonds, cashews, buckwheat, amaranth, rye, molasses, walnuts, quinoa, great northern beans, mung beans, teff, tofu, chickpeas, oats, daikon radish, bulgur, lambsquarters, hazelnuts, leeks, black beans, kidney beans, horseradish.

**Vitamin B12** - meat- beef, chicken, goose, pork, lamb, game meat , fish- mackerel, whitefish, salmon, cod, herring,snapper, trout, crab, clams, lobster, oysters, mussels, eggs, liver (lamb, beef, turkey, duck, goose, chicken) milk and milk products.

**Zinc** - Oysters, pumpkin seeds, sesame seeds, chervil, beef, game meats, lamb, poppy seed, shiitake mushroom, cardamom, celery seed, crab, bison, turkey, pork, peanuts, pine nuts, cocoa, thyme, parsley, rice bran, basil, agar seaweed, cashews, lobster, mustard seed, dark rye.

**Methionine** - Egg, cod, whitefish, sesame seeds, spirulina, parmesan cheese, sunflower seeds, Brazil nuts, chicken, beef, lamb, salmon, buffalo, turkey, halibut, anchovy, Romano cheese, game meats, gruyere cheese, goat cheese, goose, duck, snapper, tilapia, mackerel, haddock, lobster, pumpkin seeds, sardine, herring, bison.

### Quercetin

*(Quantity -- Quercetin content mg/100 grams)*

| Food | Quantity | Food | Quantity | Food | Quantity |
|---|---|---|---|---|---|
| Capers, canned | 173 | Carob fiber | 58 | Elderberry juice concentrate | 108 |
| Dock, Rumex spp., raw | 86 | Dill weed, fresh | 55 | Fennel leaves, raw (Fennel bulb raw 0.23) | 49 |
| Radicchio | 32 | Onions, red, raw | 39 | Radish leaves, raw (radishes raw 0) | 70 |
| Watercress, raw | 30 | Elderberry, raw | 27 | Kale, raw | 23 |
| Okra, raw | 21 | Bee pollen | 21 | Onions, raw | 20 |

Dietary Sources of Key Methylation Nutrients adapted from: USDA, USDA National Nutrient Database for Standard Reference, Release 27 (revised).*US Department of Agriculture, Agricultural Research Service, Nutrient Data Laboratory. 2015.

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Quercetin chart- Adapted from: USDA Database for the Flavonoid Content of Selected Foods Release 3.1. Prepared by Seema Bhagwat, David B. Haytowitz, and Joanne M. Holden (ret.) Nutrient Data Laboratory Beltsville Human Nutrition Research Center Agricultural Research Service U.S. Department of Agriculture December 2013 Slightly revised, May 2014. http://www.ars.usda.gov/SP2UserFiles/Place/80400525/Data/Flav/Flav_R03-1.pdf Accessed November 3, 2015

## Homocysteine (serum) : 6.47 (µmol/L) Age: 39

**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:**


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