Genetic Analysis Report (Summary Sheet)
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This handout is intended to give you a brief explanation for some of the major areas of genetic mutation points that are analyzed from Dr. Yasko's "Economy Basic SNP III Panel." This panel can be ordered from www.testing4health.com. For a more in depth explanation about your/or your child's panel results you can order a genetic analysis report directly from Dr. Yasko's office. For more information about Dr. Yasko's work with respect to genetic profiling and their biochemical relationships to autistic-spectrum disorders go to www.holistichealth.com and www.autismanswer.com. Also, Dr. Yasko's book "The Puzzle of Autism: Putting It All Together" is a must read.

This overview sheet can be used to help analyze you/or your child's genetic panel. Place a check mark (√) or circle the mutation defect that fits you/or your child's test results.

NOTE: Mutations in these enzymes listed below occur at multiple points in their amino acid sequences. For our purposes what you need to know is whether a mutation is homozygous, heterozygous or neither. Because we receive genes from both parents (+/+, +/-, or - -) this is the reason for two different mutation categories:

Homozygous Mutation = both genes affected.
Heterozygous Mutation = one gene affected.

****One thing to remember when looking at these enzyme markers is that function and/or dysfunction are not absolute. Just because you/your child carries a specific mutation does not mean that particular enzyme is not working correctly 100%. These markers are indicators of potential problem areas and through environmental influences, ie. toxins, the enzyme system issues become manifest. For instance, mercury toxicity, especially thimerosal significantly impairs the methionine synthase (MTR) enzyme.**

CBS (Cystathione-Beta-Synthase) – helps to convert homocysteine into glutathione (major antioxidant in the body). If a defect exists it will affect ammonia detoxification because excess sulfur in the body (endogenous or exogenous sources, ie. supplements like MSM, Epsom Salt or medications such as DMPS) can be converted to ammonia. Also, this defect can affect an enzyme called G6PDH which has negative effects on blood sugar metabolism and red blood cell formation and blood vessel stability (easy bruising, bleeding, broken blood vessels).

- **CBS C699T (-/-)** = no mutation. Lower potential for ammonia detoxification issues.

- **CBS C699T** (+/-) = heterozygous defect. Partial defect. Higher risk for ammonia detoxification issues.

- **CBS C699T (+/+) =** homozygous defect. Both genes affected. Significant propensity for ammonia detoxification issue. Will need to be careful with sulfur containing supplements, ie. MSM and medications, ie. DMPS.

COMT (Catechol-O-Methyltransferase) – helps to methylate dopamine, serotonin, norepinephrine. Essentially slows down or regulates production of these neurochemicals.

- **COMT V158M (-/-)** = no mutation – indicates that the enzyme works **too efficiently** and will use up resources of methyl groups (CH3), ie. available chemical currency.

- **COMT V158M (+/-)** = heterozygous. Partial defect in system = partial ability to use up CH3 groups. Will be able to handle some methylating supplements, ie. Methyl-12, SAMe, Theanine, DMG.

- **COMT V158M (+/+) =** homozygous mutation. Both genes are affected. Significant defect in system**.** This indicates that the enzyme works sluggishly. Essentially slows down methylation of above listed brain chemicals. In some situations is a better scenario for an autistic child because they will tend not to use up excess methyl groups (chemical currency). Will need to be careful with too many methylating supplements, ie, Methyl-B12, SAMe, Theanine, DMG/TMG. The overuse of these supplements could cause over stimulating leading to hyperactivity, irritability, erratic behavior, etc.

MTHFr C667T (Methylene Tetrahydrofolate Reductase) – helps to convert homocysteine to methionine in the methylation pathway. This enzyme pathway has global effects for immune function, muscle metabolism, neurochemical production and regulation, and detoxification.

- **MTHFr C667T (-/-)** = no mutation – enzyme works efficiently to convert homocysteine to methionine.

- **MTHFR C677T (+/-)** = heterozygous mutation. Partial defect in system, ie. one gene is affected.

- **MTHFr C677T (+/+) =** homozygous mutation. Both genes affected. The enzyme systems works very sluggishly which significantly impairs the process of methylation.

MTHFr A1298C (Methylene Tetrahydrofolate Reductase) – helps to convert BH2 to BH4 for serotonin and dopamine production. Also, has an assistance effect on ammonia detoxification, and protects against too much histamine (stimulates allergic reactions, over-production of stomach acid).

- **MTHFr A1298C (-/-)** = no mutation – enzymes works efficiently to help with the balance of dopamine and serotonin production, as well as its related ammonia detoxification and histamine lower effects.

- **MTHFr A1298C (+ -) =** heterozygous mutation. Partial defect system. This translates into a partial problem with A1298C's function – particularly important when considering the balance of dopamine and serotonin which can increase the propensity for mood swings and non-yeast, non-clostridia (intestinal bacteria) stimming behavior from too much ammonia.

- **MTHFr A1298C (+/+)** = homozygous mutation. Both genes affected. The enzymes system works very sluggishly which significantly impairs the conversion of BH2 to BH4 and it related effects.

MTR (Methionine Synthase – MS) – is necessary to help produce methionine from homocysteine. It needs Methyl-B12 to do this! **Defect = INCREASED enzyme activity which is not ideal because it will cause methyl (CH3) group depletion similar to COMT (-/-)**

- **MTR A2756G (-/-)** = no mutation.

- **MTR A2756G (+/-) =** heterozygous mutation. Partial defect in system.

- **MTR A2756G (+/+)** = homozygous mutation. Both genes affected. This defect causes an INCREASE in enzyme function which increases the risk for methylation or methyl group depletion. Will be better able at handling a variety of methylating substances such as Methyl-B12, DMG, Theanine, SAMe, etc.

MTRR (Methionine Synthase Reductase – MSR) – is necessary to regenerate Methyl-B12 so a constant supply of homocysteine can be converted to methionine. **Defect = DECREASED enzyme activity which is not ideal.**

- **MTRR A66G (-/-)** = no mutation.

- **MTRR A66G (+/-) =** heterozygous mutation. Partial defect in system **–** will need to be cautious with too many methylating substances. – Alec shows homozygous (both genes affected) mutation in this enzyme complex. This translates into decreased ability to regenerate Methyl-B12.

- **MTRR A66G (+/+)** = homozygous mutation. Both genes are affected. This mutation **DECREASES** function of enzyme. Definitely need Methyl-B12 – even if COMT ++ (which usually indicates a possible intolerance to methylating supplements).

VDR Bsm/Taq (Vitamin D Receptor) – helps support COMT in the regulation of dopamine levels – think behavior issues! It uses methyl groups to do this.

- **VDR Bsm/Taq** (-/-) = no mutation.

- **VDR Bsm/Taq (+/-)** = heterozygous mutation. Partial defect in system. Will be somewhat sensitive to methyl donor supplements.

- **VDR Bsm/Taq (+/+)** = homozygous mutation. Both genes affected. If mutation is present will be more sensitive to methyl donor supplements, ie. Methyl-B12, SAMe, DMAE, Theanine, DMG, TMG. Also, will need to watch for behavior issues related to fluctuations in dopamine production – mood swings!

NOTE: a VDR (+/-) and a VDR (+/+) together with a COMT (+/-**)** can behave like a COMT (+/+) **=** increased sensitivity to methylating supplements, ie. Methyl-B12, SAMe, DMAE, Theanine, DMG, TMG. Need to watch for propensity for mood swings, hyperactivity, irritability.

NOS (Nitric Oxide Synthase) – helps in the formation of nitric oxide which has a role in oxidative stress and chemical production. If NOS mutation is present it can affect the urea cycle with respects to ammonia detoxification (hand-flapping, over-stimulatory behavior).

- **NOS D298E (-/-)** = no mutation.

- **NOS D298E (+/-) =** heterozygous mutation. Partial defect in system.

- **NOS D298E (+/+)** = homozygous mutation. Both genes affected. Major issue with NOS effects. Primarily related to ammonia detoxification issues in association with CBS mutation.

ACE Deletion (Angiotensin Converting Enzyme) – This enzymes leads to high levels of angiotensin II which causes an increase in aldosterone. High aldosterone leads to increase potassium loss in the urine and increased sodium retention. Animal studies show a correlation between high angiotensin II with increased anxiety and decreased learning and memory. Decreased potassium can lead to fatigue and decreased energy production as cellular membrane activation, particularly for the brain and peripheral nervous system is dependent upon sodium:potassium balance. ACE deletion are more completed correlated to a marker called AHCY enzyme.

NOTE: More information about ACE and its relationship to body hormone, ie. aldosterone, sodium/potassium, etc. can be performed by a more advanced profile by Dr. Yasko called the "Complete Basic SNP Panel 1." **However, from a well-rounded a basic assessment of the major players with respects to mutation points for autism the above listed mutations: CBS, COMT, MTHFr, MTR, MTRR, NOS, VDR is an excellent place to start.**

- **ACE Del 16** (-/-) = no mutation

- **ACE Del 16 (+/-)** = heterozygous mutation. Partial defect in system

- **ACE Del 16** (+/+) = homozygous mutation. Both genes affected.

Additional Information – this section is not meant to replace the more detailed information you can get from a Dr. Yasko genetic analysis report (GAR) or from her book (listed above). The items below are to highlight some additional information when assessing your child's genetic analysis test results and specific issues they may have. Remember, these are basic recommendations and each person reacts differently to supplements or to the need for supplements. Individuality is Key!

Heavy Metals and Viral Load:

We know because of various genetic tendencies and biochemical imbalances in autistic-spectrum children their ability to detoxify and eliminate heavy metals such as mercury and lead, as well as endogenous (ie., ammonia) and exogenous (environmental chemicals) toxins can significantly impair their immune, hormone, nervous and metabolic systems. In looking at immune and toxicity issues this alternation increases an autistic child's propensity to develop chronic infections from yeast, bacteria, parasites and viruses. Some general trends have been seen with many children with respects to viral load and the presence of heavy metals and their relationship to the various genetic enzymes defects and their corresponding biochemical capacities:

- Aluminum toxicity increases the propensity for bacteria in the body – particularly the gut. The inability to clear gut bacteria can be a sign of aluminum load, as gut bacteria are known to hold onto aluminum.

- An increased viral load can tie up available metallothionein. Metallothionein is our reservoir for sequestering heavy metals such as mercury, lead and cadmium. The majority of metallothionein in found in the digestive system. If there has been damage to the intestinal tract from long-standing food sensitivities and inflammation environmental heavy metal binding can be compromised.

- Viruses many times create an inability to detoxify heavy metals adequately.

- Generally, children (or adults) who are good methylators will have less viral and heavy metal toxins in their body, in contrast to poor methylators who will have more viral load and heavy metal toxins. Another way of saying this is that the child (or adult) who does not carrying increase mutations in the MTHFr, CBS, MTR, and MTRR enzyme pathways may be more capable of excreting heavy metals. COMT is one of those curious mutations were the mutation actually slows down the enzyme function potentially offering some protection against methyl group depletion (which is a favorable thing for a person on the autistic-spectrum). However, the bottom side is that the COMT enzyme complex is sluggish which compromises other functions such as neurotransmitter (brain chemical) deactivation.

General Considerations:

Ammonia Detoxification Protocol:

- **Activated Charcoal** – ½ to 2 capsules at bedtime.
- **Magnesium Citrate** – 250 to 500mg (magnesium flush) following the activated charcoal to assist with bowel movements.
- **Yucca (herbal remedy)** – ½ to 1 capsule per day.

NOTE: Elevated Ammonia and a High (Arginine) and Low (Citrulline) from a Doctor's Data and/or Great Plains Laboratory Urine Amino Acid Test can indicated ammonia detoxification issues. May need to watch protein intake if ammonia is a problem. The specific carbohydrate diet is one diet that is very beneficial for many autistic children because of its effects on inflammatory bowel conditions. However, over time ammonia sensitive children can have problems.

***Mood Swings:* A definite potential if your child has a CBS, COMT (+/-, +/+) VDR, and or NOS mutations.**

- **Liquid Lithium (nutritional lithium) –** 500 to 1000mcg daily
- May need to decrease or discontinue other methylating supplements such theanine, MSM, methyl-B12, SAMe, melatonin, curcumin.

Streptococcal Bacteria:

- **Neem, Goldenseal, Cranberry, Oregon Grape, Bayberry, Uva Ursi, Myrrh** – are all herbal supplements which have a positive effect against chronic strep in the body. The use of these herbs is generally for 30 days – ½ to 1 capsule or ½ to 1 dropperful tincture taken 3x/day.

****Heavy Metal Testing:***

- Dr. Yasko encourages everyone who is following her program of methylation support, viral elimination and heavy metal detoxification to collect weekly urine tests. These are called spot urines and are collected on the same day, at the same time roughly every week, ie. Tuesdays at 3pm. This helps to track heavy metal excretion throughout your child's healing program. You can also visualize your child's urine which will normally darken as viruses are being excreted and then lighten as heavy metals begin to be excreted.

  The idea that viral unloading takes place before heavy metal excretion can occur is based on the scientific evidence that viruses can cause metal trapping in the body. Behaviorally, your child may develop exhibit issues such as irritability, tantrums, stimming, etc. during the time of heavy metal dumping. This is generally seen as an increase in metal excretion on the Urine Toxic Metals test from Doctors Data (and/or Great Plains) and a drop in creatinine concentration. This can be a very helpful way of determining what is causing your child's behavioral changes while undergoing detoxification therapy.

For more information about Dr. Yasko's articles, books and DVD's contact www.holistichealth.com. Supplement purchases for her RNA and other remedies can be ordered from www.holisticheal.com.