Jane Sample, DOB 01/01/1964
Review by: Salena Rothenberger, D.PSc, CFMP, CHC
Review on: 08/25/2019
Genomic Data: 23&Me V4

Nutrigenomic Consult Notes

Overview: The key variants are listed below, however it should be noted the synergy and multiplying effect of multiple snps in adjoining pathways lead to greater expression in a negative manner. Jane's genomic report suggests severe difficulty in estrogen metabolism, with multiple challenges in folate, methionine, transsulfuration, and biopterin pathways. In addition, significant snps regarding digestion, iron, immune response, and choline pathways. (***BOLD indicates most severe presence of variants)***

- Estrogen Variants (See attached pathway chart)
  - **CYP19A1; CYP1B1; CYP17; CYP19; CYP1A1; COMT; GST; GSTM; GSTP**; ESR1; **SULT1B1; SULT**; AKR1C3; UGT2B15
- Digestive & Nutrition Variants
  - **Multiple FUT 2** - Non-Secretor, Imbalance B12, Potential Immune to Norovirus
  - GIF – Vit B12 Synthesis
  - MTRR – Vit B12
  - IL2-21 – Increased risk towards gluten/celiac issues
  - BCMO1 – Beta-carotene/Vit A Synthesis
  - **HNMT** – Histamine
  - **NAT2** – Histamine
  - **ABP1** – DAO
  - HFE – Iron
  - VDR – Vit D
  - PANK – Pantethine, Fatty Acids
  - SLC22A5 - Carnitine
- Methylation Variants
  - **DHFR; MTHFS; MTHFR; SHMT1; SHMT2** -- Folate
  - MTRR – B12
  - Others: MAT (methionine); CBS; **PEMT***(indirectly related to Methionine Cycle)
- Transsulfuration Variants
  - CBS; **GSS; GST; GSM; GSTP**; CAT; SOD; CTH
- Biopterin Variants
  - **COMT** (Dopamine, Norepinephrine, Epinephrine, Estrogen)
  - **MAOA**
  - **TYR** (Tyrosine)
- OTHERS:
  - ***PEMT** – Choline
  - ACAT – ATP, ACOA
  - GAD – Glutamate –> GABA
  - **CD14** – Innate immune response – can result in difficulty mounting response to LPS

Summary

It is important to remember that our genes are not our destiny and that we influence our genes through our diet, lifestyle, experiences (Including what our parents and grandparents experienced!), toxic exposures, etc. It is vital to note that: ***All our genes are susceptible to behaving****(expressing)* ***as a 'one-lane highway' whether there is a variant or not due to the influences on those genes.***

A simple illustration to remember this concept is a single lane highway in west Texas and a four-lane highway in Los Angeles. Rush hour traffic in LA is going to be far slower than the one-lane highway in Texas on a regular day. Which leads to the flipside: ***Just because we have a variant does not mean that pathway cannot work in an optimal and efficient fashion. We must look at the entire picture.*** Therefore, the goal should be to support ***all*** our genes with the foundations found in nutrition and stress management as it relates to the individual (this encompasses far more than typically thought of).

When looking at Jane's biochemical pathway's I look at the genomics, symptoms, and lab results. Her lab results show significant dysregulation in tyrosine, steroid hormones, methylation, detoxification, and thyroid imbalances. (Summary on following pages) Her symptoms, as shown on below pyramid graphic, show chronic systemic stress throughout the body, noted by the color red in all categories. This is an important indicator of unresolved trauma and stress which leads to a vital need for supporting resolution of trauma and toxic burdens (whether chemical, pathogen, or emotional). One thing noted is she shows symptoms in her entire Tyrosine pathway – Neurotransmitter, Thyroid, and Skin symptoms.

As for Jane's genomics, there are three core challenges which show up – her "One-Lane Highways". Challenges in Estrogen, Histamine, and Tyrosine (Thyroid/Neurotransmitter/Melanin) pathways. These three are closely related with bi-directional effects, most in a negative way when one or more of those is out of balance. In addition to hormone regulation, the immune response has genetic predisposition to low immune response. Furthermore are challenges with the body supporting: detoxification, a healthy microbiome with FUT2 and other digestion related snps. This creates a vicious cycle between all the above pathways and systems which becomes greatly magnified under times of stress, whether acute or chronic, perceived or real.

When these pathways are not supported with nutritional co-factors it can lead to worsening and/or manifestation of symptoms. Thus, it is extremely important to first address challenges with the core basics of nutrition rather than replacing something in a pathway which is clogged. This why it is also vital to look at both upstream and downstream affects prior to supplementing and why it is vital to start with building blocks found in food.

With that, it is just as vital to ensure any past trauma has been fully resolved from a biochemical standpoint otherwise, one can remain in a situation of attempting to force a clogged pathway to work. Perceived stress has as much of an impact, if not greater, as realized stress on the body's ability to heal. If there is ongoing threat the body is in a constant uphill battle and will be unable to reach a resolution phase. Thus, on ***Page 6 is a list of recommendations*** for supporting and working with Jane's body chemistry to move towards resolution of her pathways which are expressing negatively.

Lab Overview

The majority of Jane's labs point to significant dysregulation in Methylation, Transsulfuration, Biopterin, Steroid Hormone, Thyroid, and Digestion pathways and systems. Some of the key things to note are markers suggesting significant lack of tyrosine with multiple pathways involved, isoleucine imbalance, cortisol imbalance, histamine elevations, hormone dysregulation . In addition, elevation in enzymes prior to methionine which makes me highly suspicious of toxins impeding conversion to methionine. The following is a general summary:

- ***General Labs***
  - CBC – history of elevated EOS, current mild elevation EOS and elevated BASO
  - B12 – continues to rise latest >2000
  - Homocysteine in good functional range, however history of lower end of functional range
  - Iron – history of elevated iron however has improved
  - Thyroid – history of thyroid imbalances – on thyroid replacement
  - Female hormones – imbalanced with history of dysregulated Estrone – on BHRT Estradiol continues to rise
  - SHBG – (APRIL 2019) Double the reference range
  - Inflammatory markers wnl
- ***Stool Testing***
  - GI Effects – decreased SCFA
- ***Nutritional***
  - NutrEval (MAY 2019) – Extremely elevated Taurine & 5HIAA, Elevated IAA, PAA, Glutaric Acid, Isovalerylglycine, Significant need for Tyrosine and Isoleucine. Excessive EPA, Yeast, B12 imbalances with multiple markers suggesting toxic exposure
  - AIBA – Significant amount of histamine, DAO 'normal' however DAO/Histamine ratio strongly favors histamine
  - Dietary Antigen – Dunwoody – relatively mild number reactions considering magnitude of symptoms.
- ***ZRT Hormone Panel***
  - ZRT - Elevated testosterone, PM cortisol, Low estradiol. (Note, cortisol can impede immune response if chronically elevated)
- ***DUTCH***
  - Waiting on results – Doing ZRT rather than DUTCH???
- ***Methylation Panel***
  - Genova - Two panels in 2019 – Shift in methylation ratios however methionine significantly low and B12 continues to show signs of great dysregulation. Taurine wnl. Homocysteine was in lower end of functional range and has increased. Choline elevated.

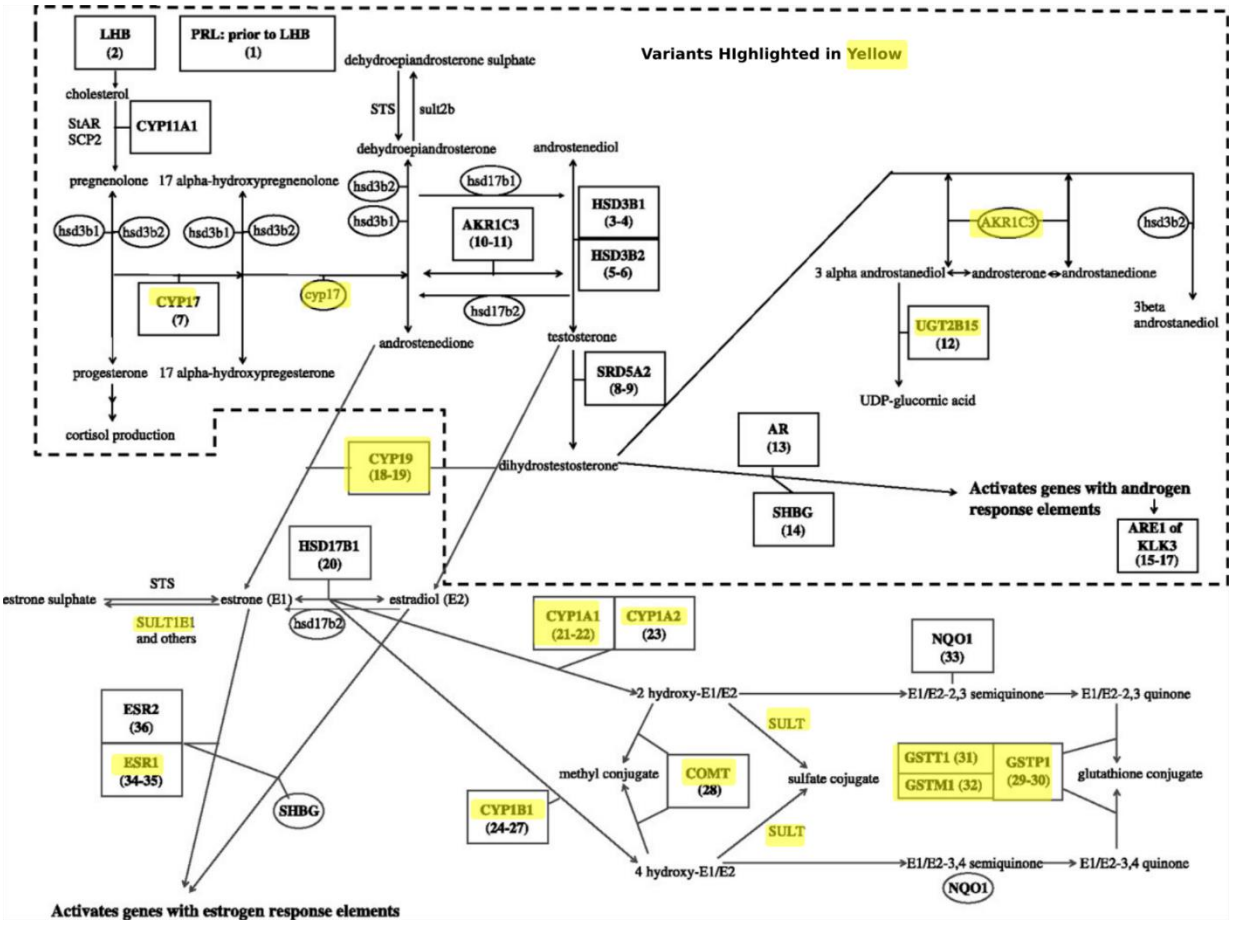
Symptoms Overview

The majority of Jane's symptoms fall under Methylation, Transsulfuration, Biopterin, Steroid Hormone, and Digestion pathways and systems. The following were most notable complaints:

- Chronic excessive fatigue
- Chronic pain
- Chronic brain fog
- Insomnia
- Histamine reactions
- Low pain tolerance
- History of amalgams
- Chemical exposures
- Dizziness if meals skipped or prolonged between eating
- SOB w/moderate exercise
- History of miscarriages
- Stools pellet consistency (occasional)
- Anxiety & Depression
- B12 Imbalances
- Unrestful sleep
- Phobias
- Tend to have low blood pressure
- White spots on skin

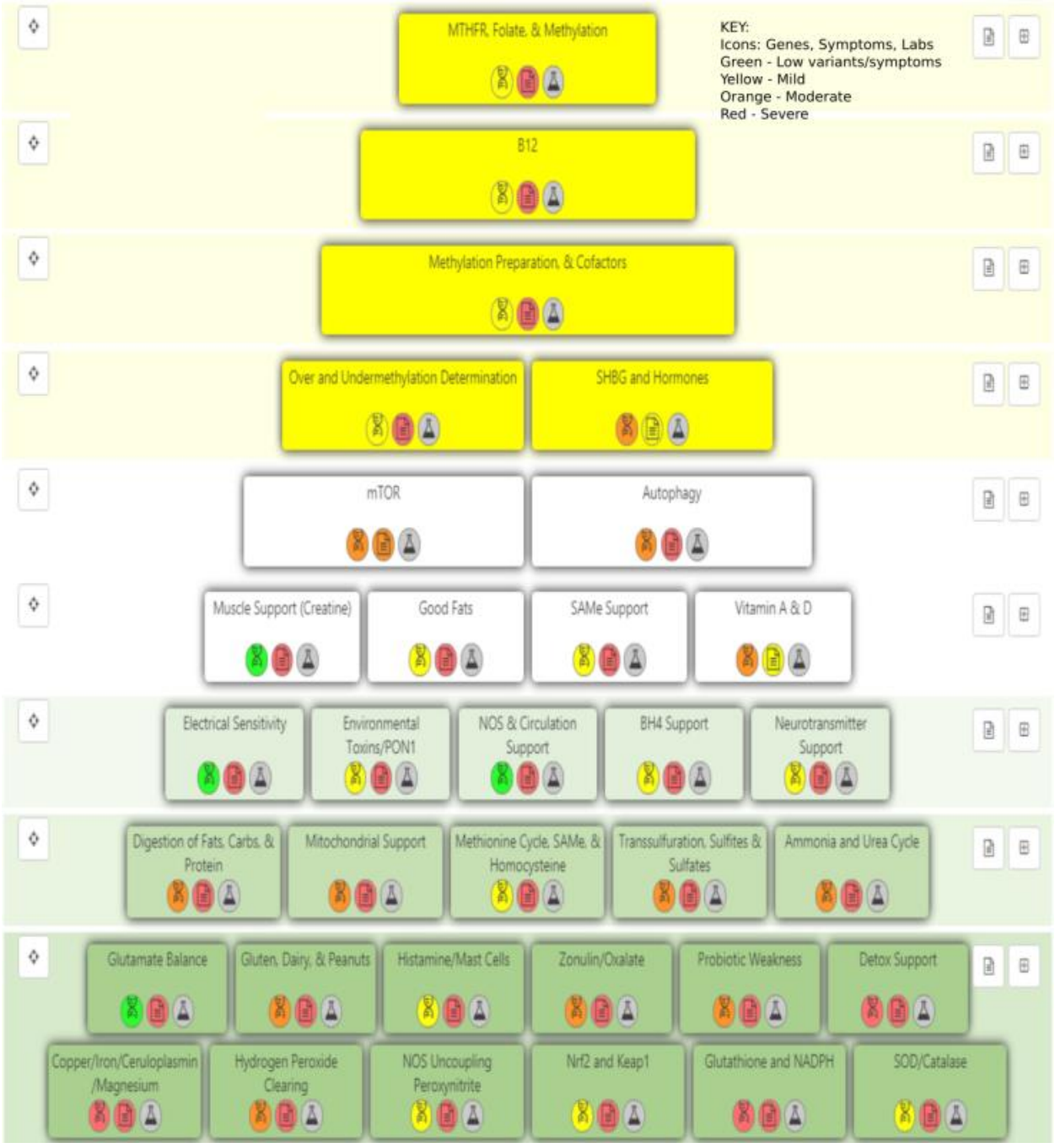
Charts

Steroid – Estrogen Metabolism Pathway



Nutrigenomic Pyramid (Note Labs are NOT reflected on this graphic)

In general the foundation contains the areas to focus on prior to pushing methylation cycle.



Recommendations

Recommendations to consider and discuss with your Primary Care Provider and Dietician:

- ***First priority is to gain skills for emotional healing***
    - Make an inventory of past/current traumas, no matter how 'insignificant' both physical and emotional
    - Consider EMDR (Eye Movement Desensitization and Reprocessing) There are 2 certified practitioners in Lufkin https://emdr.com
    - Consider EFT (Emotional Freedom Technique, aka Tapping) https://www.emofree.com/ Mary Pellcier, MD is a highly skilled EFT practitioner https://nourishnurtureheal.com/
- ***Second priority is to identify any underlying pathogens, toxins, burdens*** on the body which are self-perpetuating biochemical imbalances
    - Heavy Metal & Toxin Testing – Several toxins known to slow down methionine cycle
    - Rule out Lyme and Co-Infections – When there are chronic states of poor immune function the body has greater susceptibility to environmental pathogens. This is compounded with Jane's genetic variants which predispose to inadequate immune response.
    - Ensure previous Yeast issues have resolved
- ***Must ensure a large variety of foods*** with FUT2 – will need to avoid histamines as much as possible in initial healing **however**, ***long-term goal consider a low-histamine food plan***
- Will be vital to ***rotate probiotics*** and prebiotics with a strong emphasis in Bifido strains and avoidance of histamine related strains
    - I have seen good results with D-Lactate-Free Probiotic from Custom Probiotics, there are many others to choose from.
- ***Support co-factors while Avoiding over supplementing*** – would encourage getting a daily snapshot of food intake here: https://nutritiondata.self.com to identify potential nutrient deficiencies, especially: B1, B2, B3, B6, B12, Folate, Selenium, Zinc, Molybdenum & Manganese as these are co-factors for the key processes in Methylation, Transsulfuration, Biopterin cycles as well as for mounting an adequate immune response. Would be extremely cautious with B12 and Folate supplementation. Potentially Hydroxy or Adenysl B12, however in low dosing.
- ***Monitor female hormone levels*** – would currently suggest DUTCH from Precision Analytical
- Consider monitoring the following general blood panels:
    - Iron, Ferritin, Iron Sat, TIBC
    - Zinc, Copper, Ceruloplasmin
    - CBC w/Diff
    - CMP
    - Thyroid – FT3, FT4, TSH, and antibodies
    - Omega 3/6 panel from LabCorp/Quest

Jane researches her health symptoms and had many questions regarding various aspects of her genetics and symptoms and how they are related. We discussed them during the consult.

References:

1. **Estrogen effects in allergy and asthma**; Division of Allergy/Immunology, Department of Internal Medicine, University of Texas Medical Branch, Galveston, Texas 77555, USA. https://www.ncbi.nlm.nih.gov/pubmed/23090385
2. **Incorporation and binding of estrogens into melanin: comparison of mushroom and mammalian tyrosinases.** Jacobsohn GM1, Jacobsohn MK. Biochim Biophys Acta. 1992 Apr 22;1116(2):173-82. Department of Biological Chemistry, Hahnemann University, Philadelphia, PA 19102. https://linkinghub.elsevier.com/retrieve/pii/0304-4165(92)90114-A
3. **Role of Estrogen in Thyroid Function and Growth Regulation;** Journal of Thyroid Research Volume 2011, Article ID 875125, 7 pages http://dx.doi.org/10.4061/2011/875125
4. **Histamine induces microglia activation and dopaminergic neuronal toxicity via H1 receptor activation**. Sandra M. Rocha, et. Al., Journal of Neuroinflammationvolume 13, Article number: 137 (2016) https://jneuroinflammation.biomedcentral.com/articles/10.1186/s12974-016-0600-0
5. **Histamine induces tyrosine phosphorylation of endothelial cell-to-cell adherens junctions.** Arterioscler Thromb Vasc Biol. 1999 Oct;19(10):2286-97. Andriopoulou P1, Navarro P, Zanetti A, Lampugnani MG, Dejana E. https://www.ncbi.nlm.nih.gov/pubmed/10521356
6. **Strategene Pathway Planners; Ben Lynch** https://www.seekinghealth.com/products/pathway-planner-download-strategene-version
7. **Textbook of Biochemistry with Clinical Correlations**; Thomas M. Devlin – 7th Edition, 2010, ISBN 978-0-470-28173-4 https://amzn.to/3237S8y
8. **How eye movements in EMDR work: changes in memory vividness and emotionality.** Leer, A., Engelhard, I. M., & van den Hout, M. A. (2014). https://www.sciencedirect.com/science/article/pii/S0005791614000287?via%3Dihub