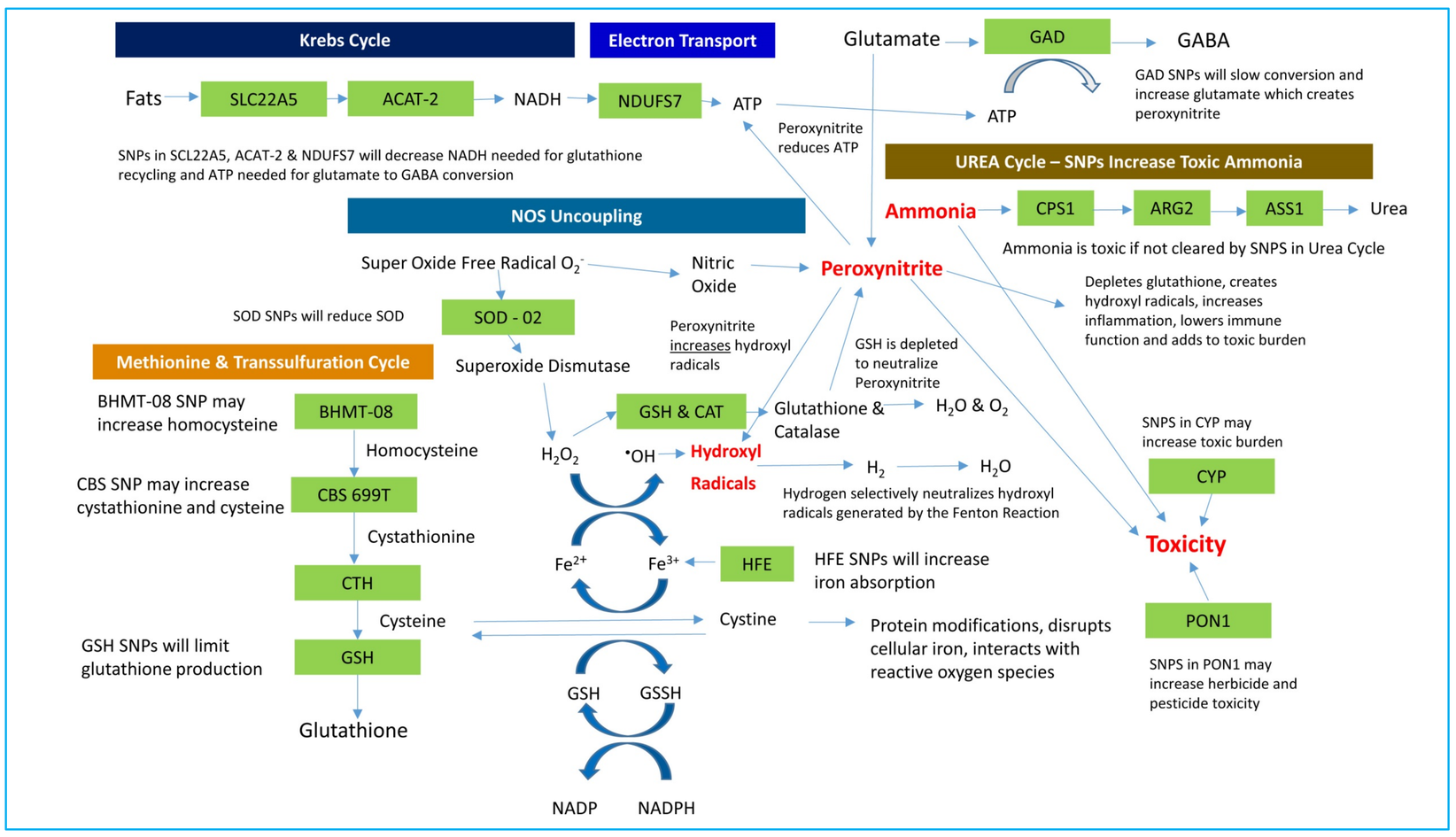
Higher Levels of Genetic Variants (SNPs) Found in those with Chronic Lyme Disease

Robert Miller, CTN

NutriGenetic Research Institute, Ephrata, PA, United States

NutriGenetic RESEARCH INSTITUTE

Genetic mutations (SNPs) can lead to nutrient deficiencies and increased free radicals or other toxic substances that may allow Lyme to be resistant to traditional treatment. To determine if unique genetic patterns exist with chronic Lyme, we examined 350 genes from 192 participants, who submitted their genome for a global contrast to data supplied by the 1000 Genome Phase 3 Project [**1**]. The reference and alternate alleles for each of the SNPs were determined using the HaploReg v4.1 database [**2**]. This data was then compared to data supplied by the 1000 Genome Phase 3 Project. The ratio of SNPs between the chronic Lyme group and the Genome Project study was then calculated. The genes with the most significant increase in the Lyme group were as follows:



Mitochondrial Function

The first step of getting fats into the mitochondria is the production of carnitine from the SLC22A5 genes. If fats are not carried into the mitochondria, beta oxidation may occur, creating inflammation, and lack of ATP production [**3**]. Then, the ACAT genes are responsible for turning fats and proteins into Acetyl-CoA, the first step of the Krebs Cycle [**4**]. NDUFS7 functions in the transfer of electrons from NADH to the respiratory chain [**5**].

Table 1: Mitochondrial Function & SNPs

Gene Name	RS Number	Ratio Between Groups
SLC22A5	rs17622208	2.39
SLC22A5	rs2073643	1.56
SLC22A5	rs1045020	2.17
ACAT-2	rs3465	1.72
ACAT-2	rs3798211	1.70
ACAT-2	rs25683	1.69
NDUFS7	rs1142530	1.45

Long-Chain Fatty Acid coenzyme A Ligase

The protein encoded by the ACSL1 gene is an isozyme of the long-chain fatty-acid-coenzyme A ligase family. This family converts free long-chain fatty acids into fatty acyl-CoA esters, playing a key role in lipid biosynthesis and fatty acid degradation [**6**]. There were 1.82 times more SNPs for ACSL1 rs13120078 in the Lyme group.

Methylation

The Methylation Cycle produces SAMe, the methyl donor that is in 165 processes. The Lyme group has 1.26 times the amount of SNPs in the genes involved in the entire methylation cycle.

Table 2: Methylation Cycle SNPs

Gene Name	RS Number	Ratio Between Groups
MTHFR C677T	rs1801133	1.40
MTHFR A1298C	rs1801131	1.35
Methylation Cycle SNPs	(Appendix A)	1.26

Detoxification Genes

The CYP genes are responsible for phase I liver detoxification and glutathione is responsible for phase II liver detoxification. The CYP1A1 encodes a member of the cytochrome P450 superfamily of enzymes which catalyze many reactions involved in drug metabolism, synthesis of cholesterol, and steroids and other lipids [**7**]. The PON1 gene is responsible for hydrolyzing organophosphate pesticides and nerve gasses. Superoxide dismutase and glutathione are critical antioxidants and weakness in these antioxidants may lead to poor detoxification [**8**].

Table 3: Detoxification SNPs

Gene Name	RS Number	Ratio Between Groups
CYP1A1*4 C2453A	rs1799814	4.09
CYP1B1 N453S	rs1800440	1.72
PON1	rs854561	1.79
SOD2	rs2758331	1.53
GSTP1 A114V	rs1138272	2.80

Excess Glutamate

The enzyme encoded by GAD1 is responsible for catalyzing the production of gamma-aminobutyric acid (GABA) from L-glutamic acid. Studies have shown that glutamate triggers the production of nitric oxide and superoxide. This can lead to the formation of peroxynitrite (ONOO−). High serum levels of total NO, MDA and nitrotyrosine observed in patients with Lyme borreliosis indicate on enhancement of lipid peroxidation and protein nitration. This may increase inflammation in Lyme patients [**9**].

Table 4: Glutamate SNPs

Gene Name	RS Number	Ratio Between Groups
GAD1	rs3791850	1.61
GAD1	rs3828275	1.53
GAD1	rs12185692	1.55
GAD1	rs3791878	1.53

Excess Ammonia

The Urea Cycle is responsible for removing ammonia. The CPS1 gene provides instructions for making the enzyme carbamoyl phosphate synthetase I, the first step of the urea cycle [**10**]. The ASS1 gene provides instructions for making argininosuccinate synthase 1, which is responsible for the third step of the urea cycle [**11**]. A series of additional chemical reactions uses argininosuccinic acid to form urea, which is excreted in urine.

Table 5: Urea Cycle SNPs

Gene Name	RS Number	Ratio Between Groups
CPS1	rs1509821	2.54
CPS1	rs6435580	2.18
CPS1	rs12468557	1.54
CPS1	rs7607205	1.52
ASS1	rs12375699	1.62
ARG2	rs3742879	2.38
ARG2	rs742869	1.74

Fenton Reaction & Iron Oxidation

The gene that was the most significantly elevated in the chronic Lyme group was the HFE C282Y which often results in higher absorption of iron. Increased body stores of iron in various clinical situations may tip the immune regulatory balance unfavorably to allow increased growth rates of infectious organisms, and complicate the clinical management of preexisting acute and chronic diseases [**12**]. The following SNPs may increase the potential of the Fenton Reaction, thus resulting in hydroxyl radicals, toxicity and higher peroxynitrite.

Table 6: HFE & Potential Hydroxyl Radical Production SNPs

Gene Name	RS Number	Ratio Between Groups
HFE C282Y	rs1800562	5.21
HFE H63D	rs1799945	1.53
CBS C699T	rs234706	1.93
BHMT-08	rs651852	1.17
SOD2	rs2758331	1.53
SOD2 A16V	rs4880	1.28
GSTP1 A114V	rs1138272	2.80
GSTP1 I105V	rs1695	1.13
CTH	rs1021737	1.25
PEMT	rs4244593	1.03
PEMT	rs7946	1.71
PEMT	rs4646406	1.78

Impaired DNA Repair

The ATM gene provides instructions for making a protein that is located primarily in the nucleus of cells, where it helps control the rate at which cells grow and divide. ATM assists cells in recognizing damaged or broken DNA strands and coordinates DNA repair by activating enzymes that fix the broken strands [**13**]. The ratio between groups for ATM rs1801516 was found to be 2.33 times higher.

Conclusion

Unique genetic variations have been found in individuals with chronic Lyme Disease. Targeted nutritional therapy to compensate for these SNPs may be helpful for those with chronic Lyme.

References

1. The 1000 Genomes Project Consortium. (2015). A global reference for human genetic variation. *Nature*, *526*(7571), 68–74. http://doi.org/10.1038/nature15393
2. Ward, L. D., & Kellis, M. (2012). HaploReg: a resource for exploring chromatin states, conservation, and regulatory motif alterations within sets of genetically linked variants. *Nucleic Acids Research*, *40*(Database issue), D930–D934. http://doi.org/10.1093/nar/gkr917
3. Genetics Home Reference (2016). SLC22A5. https://ghr.nlm.nih.gov/gene/SLC22A5#sourcesforpage
4. Gene Cards (2016). ACAT2 Gene. http://www.genecards.org/cgi-bin/carddisp.pl?gene=ACAT2
5. Genetics Home Reference (2016). NDUFS7. https://ghr.nlm.nih.gov/gene/NDUFS7
6. NCBI (2016). ACSL1 acyl-CoA synthetase long-chain family member 1 [Homo sapiens (human)]. http://www.ncbi.nlm.nih.gov/gene/2180
7. NCBI (2016). CYP1A1 cytochrome P450 family 1 subfamily A member 1 [Homo sapiens (human)]https://www.ncbi.nlm.nih.gov/gene/1543
8. Primo-Parmo SL, Sorenson RC, Teiber J, La Du BN (May 1996). "The human serum paraoxonase/arylesterase gene (PON1) is one member of a multigene family". *Genomics***33** (3): 498–507
9. Ratajczak-Wrona, W., Jabłońska, E., Pancewicz, A. S., Zajkowska, J., Garley, M., Iżycka-Herman, A., et al. Evaluation of serum levels of nitric oxide and its biomarkers in patients with Lyme borreliosis. *Progress in Health Sciences*, *3*, 26-32
10. Genetics Home Reference (2016). CPS1. https://ghr.nlm.nih.gov/gene/CPS1
11. Genetics Home Reference (2016). ASS1. https://ghr.nlm.nih.gov/gene/ASS1
12. Ann Clin Lab Sci. 2000 Oct;30(4):354-65. Effects of iron overload on the immune system. Walker EM Jr1, Walker SM.
13. Genetics Home Reference (2016). ATM. https://ghr.nlm.nih.gov/gene/ATM