Increased Genetic Variants Associated with Reduced Autophagy & Increased mTOR in Chronic Lyme Disease Patients *(Phase IV)*

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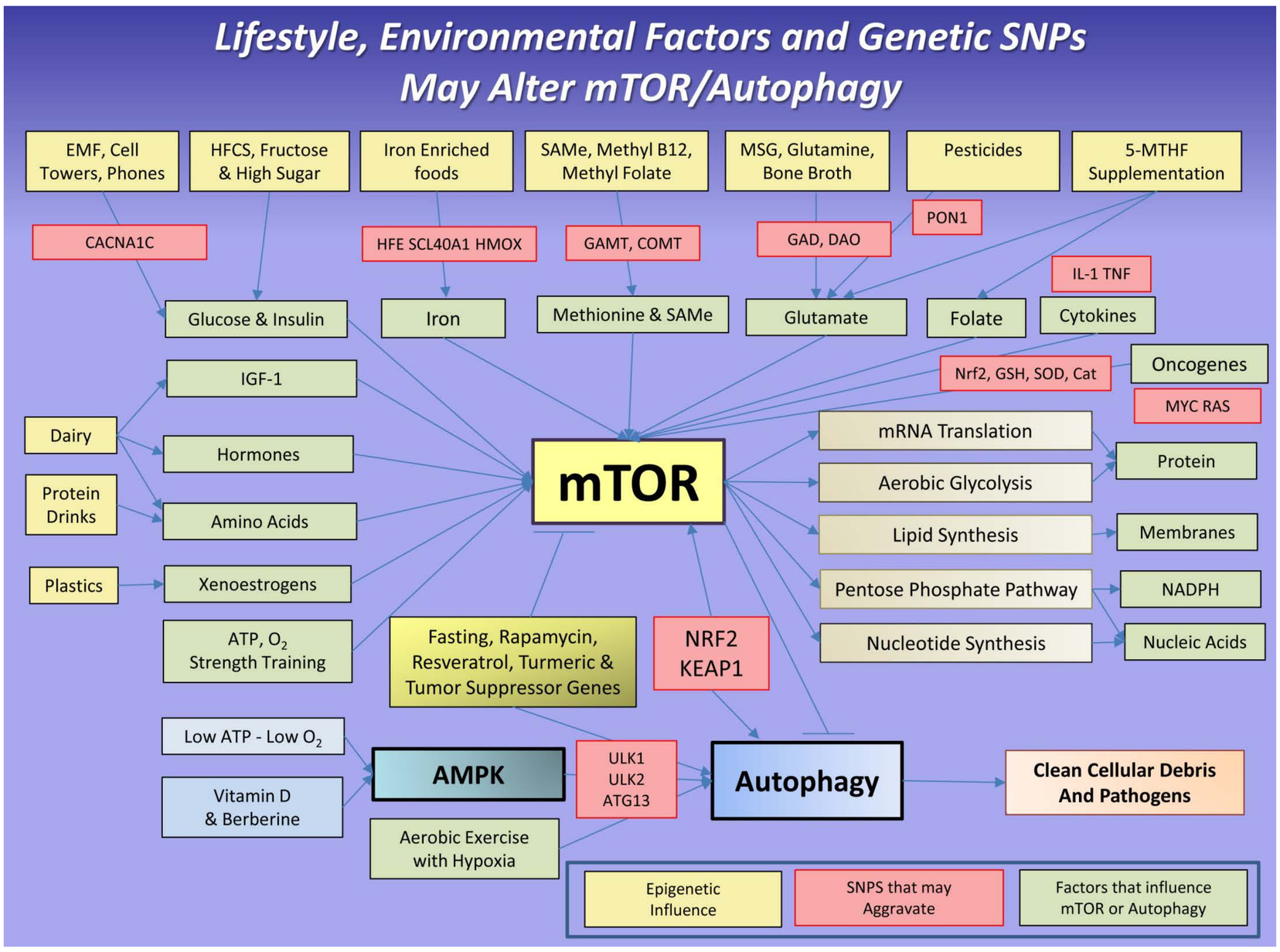
Some patients with Lyme disease do not respond well to treatment due to difficulty with inflammation and detoxification. Autophagy supports detoxification by recycling old cells and clearing viruses, bacteria, mold, and toxic substances [**1**].

The mammalian target of rapamycin (mTOR) coordinates cell growth with the growth factor and nutrient and energy status of the cell. Consequently, it increases energy production, but creates products that need to be cleared. Autophagy contributes to clearing the cells of all irreversibly oxidized biomolecules (proteins, DNA, and lipids). However, autophagy is most active when mTOR is decreased [**2**].

Hormones (xenoestrogens, dairy, and meats), growth factors (dairy, and meats), iron (iron enriched foods), glutamate (MSG & pesticides), insulin (high sugar foods), EMF, leucine, arginine, and folate all stimulate mTOR, which are all now more prevalent in the food supply and environment.

Consequently, environmental factors, endogenous conditions, and genetic variants can contribute to higher mTOR activity and reduced autophagy. It has been projected that increased mTOR and autophagy related genetic variation may be found within individuals diagnosed with Chronic Lyme disease.

To evaluate this hypothesis, 391 participants with Lyme disease submitted their 23andMe supplied genome for a contrast to the 1000 Genome Project [**3**]. We evaluated genes that when variated would stimulate mTOR and inhibit autophagy. The reference and alternate alleles for each of the SNPs were determined using the HaploReg v4.1 database [**4**]. The ratio of SNPs between the Chronic Lyme Group and the Genome Project was calculated. The genetic analysis found increased variants in the genes that would stimulate mTOR from epigenetic factors and the genes that would support autophagy.



Iron

Iron deficiency has been shown to inhibit mTOR signaling [**5**]. The Lyme group showed increased variation within several iron-related genes that would increase iron levels. 10% to 12% in HFE, 10% to 17% in TRF2, 35% to 37% in HMOX, and 22% in SLC40A1.

Antioxidants

Inflammation stimulates mTOR [**6**]. An increased number of variants were found in the antioxidant production genes in the Lyme group: 15% to 18% more variants in SOD, 12% to 33% more in catalase production genes, and a 12% to 44% increase in the GCLC, GLRX, GSS and GSTM1, 3, and 4 that produce and utilize glutathione.

Hydroxyl Radicals from Fenton Reaction

Hydroxyl radicals are formed when hydrogen peroxide combines with copper or iron [**7**]. The Lyme group had 12% to 38% more variants in the GPX3, GPX7, PRDX1, TXNRD1 and ME1 genes that support the clearing of hydrogen peroxide. (See Phase I and III studies for more info on Fenton reaction).

Glutamine and Glutamate

Glutamine stimulates mTOR [**8**]. More variants were found in the Lyme group impacting glutamine. The Lyme group had 13% to 50% more variants in the GRIA1, SLC7A11, SLC1A1, GAD1, GOT1 and GOT2 genes. DAO, that stimulates glutamate, had genes that were increased by 12% to 24% in the Lyme group.

Pesticides and Glutamate

Pesticides increase glutamate, PON1 helps detox pesticides [**9**]. The Lyme group had 32% to 37% more genetic variants in the PON1 gene.

Nrf2

In addition to supporting iron sequestration, the production, recycling and utilization of glutathione, Nrf2 also regulates both mTOR and autophagy [**10**]. The Lyme group had 28% to 32% more variants in NFE2L2.

FOXO

The FOXO genes are involved with the mTOR/Autophagy balance. The FOXO genes control the expression of genes involved in stress resistance, metabolism, cell-cycle arrest and apoptosis [**11**]. The Lyme group had 11% to 35% more variants in the FOXO gene.

Insulin

Insulin will stimulate mTOR [**12**]. Diets higher in sugar and HFCS will stimulate mTOR [**13**]. Additionally, EMF has been shown to increase insulin [**14**]. Compared to the control group, genetic variants in the CLCN6 gene, associated with electrical sensitivity, were increased in the Lyme group by 10%.

Autophagy

The ULK1, ULK2 and ATG13 genes are involved with supporting autophagy [**15-16**]. The Lyme group had 36% to 44% more variants in ATG13, and 12% to 38% more in ULK1 and ULK2.

AMPK

AMPK also stimulates autophagy [**17**]. 21% to 42% more variants were found in PRKAA1 gene that stimulates AMPK in the Lyme group.

Conclusion

Higher levels of genetic variants involved in autophagy and mTOR have been found in individuals with Lyme disease potentially creating a self-perpetuating cycle of inflammation and toxicity favorable to pathogens and treatment resistance.

Personalized supplementation that directly supports autophagy (lithium, berberine) and reduces the stimulation of mTOR (resveratrol, turmeric) along with lifestyle and dietary modifications (intermittent fasting, reduced dairy), cautious supplementation with folate, amino acids, iron and glutamine, and a low carb ketogenic diet may reduce mTOR and stimulate autophagy [**18-25**]. This may be an effective complementary treatment to traditional medical care.

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