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LABORATORY INFORMATIONLab ID:N8C9841Collection Date:01/11/10Test Date:01/21/10Report Date:01/22/10

GENE MARKER				$\rangle$ association		Сом	MENT		
APOE	E3/E4	1		Lipid transportation and Cholesterol levels		Increased risk for cardiovascular disease, elevated triglycerides, total cholesterol and LDL			
APOE	E E3/E4			Late Onset Alzheimer's Disease Risk		People with this variant are at an increased risk for developing Late Onset Alzheimer's Disease			
ASSESSMENT OF RISK TABLE									
RESUL	.T E2/E2		'E2	E2/E3	E2/	E4	E3/E3	E3/E4	E4/E4
CARDIAC	Decrea except for hyperlipop		ed Risk those with oteinemia*	No Increased Risk	No Increa	sed Risk	No Increased Risk	Increased Risk	Significantly Increased Risk
ALZHEIME DISEASE	ALZHEIMER'S Lowe		t Risk	Decreased Risk	Increase	d Risk	No Increased Risk	Increased Risk	Significantly Increased Risk

In the brain, ApoE is a protein involved in clearing harmful plaques that form around nerve cells. These plaques are a hallmark of Alzheimer's disease,<sup>3,4</sup> and consist of damaged proteins called amyloid- $\beta$  (A $\beta$ ) which stick together to form the toxic plaques.

There are three possible types of ApoE protein, called E2, E3 and E4.<sup>5,6</sup> The E2 form is the most effective at removing A $\beta$  plaque from the brain and subsequently is protective against Alzheimer's disease (AD). However, the E4 form of the ApoE protein is not very effective at removing A $\beta$  plaque and carries an increased risk for developing AD.<sup>2,7,8</sup>

\* For the majority of people, the E2 ApoE variant confers a decreased risk of cardiovascular disease and promotes a more optimal cholesterol profile. Having two copies of the E2 variant generally provides the most protection; however, those with two copies of E2 (E2/E2) are at a slightly increased risk (less than 10%) for a rare hereditary condition called hyperlipoproteinemia (III HLP).<sup>10</sup> People with III HLP have high total cholesterol, LDL and triglycerides, putting them at risk for atherosclerosis and cardiovascular disease. Overall, those who carry E2 are likely at a decreased risk for heart disease but should monitor their cholesterol levels yearly to check for III HLP.<sup>9,10</sup>

E4 allele carriers are at an increased risk for cardiovascular disease, elevated triglycerides, elevated total cholesterol and elevated LDL.<sup>11</sup>

### SUGGESTED CARDIOVASCULAR INTERVENTIONS

Regular exercise is linked to a decrease in cardiovascular disease and a healthier lipid profile.

The Mediterranean diet is linked to a lower incidence of heart disease.<sup>1,2</sup>

The Mediterranean diet is a heart healthy eating plan that emphasizes:

- Plant-based foods, such as fruits and vegetables, whole grains, legumes and nuts
- Replacing butter with olive oil
- Using herbs and spices
- Limiting red meat to no more than a few times a month
- Eating fish and poultry at least twice a week, preferably wild or organic
- Drinking red wine in moderation. This means no more than 5 ounces (148 milliliters) of wine daily for women or men age > 65, and no more than 10 ounces (296 milliliters) of wine daily for men under age 65.<sup>3</sup>

#### CARDIOVASCULAR NUTRIENT SUGGESTIONS

#### All Alleles

Regardless of your test results, it is suggested to provide the cardiovascular system with basic support and the following nutrients should be considered. If you have ApoE4, the higher risk allele, or other risk factors for cardiovascular disease, the additional nutrients in the next section should also be considered.

Supplement	Starting Dosage Range	Comments
Omega 3	1400mg EPA and 1000mg DHA/day	Studies have shown that omega-3 fatty acids support healthy vasculature via multiple mechanisms, including, supporting healthy triglyceride levels, supporting a healthy blood pressure and improving the function of the inner lining of blood vessels. <sup>4</sup>
Ubiquinol CoQ10	200-400mg/day	<ul> <li>CoQ10 is critically important for vascular health, as it is directly involved in the production of ATP, the "energy currency" of the human body. CoQ 10 is also a potent antioxidant.</li> <li>CoQ10 is the first line of defense against LDL oxidation; oxidized LDL is a major contributor to endothelial dysfunction and atherosclerosis.<sup>5</sup></li> </ul>
Vitamin K	2200mcg/day; providing K1, MK-4 and MK-7	<ul> <li>Vitamin K supports healthy blood vessels by directing calcium away from the arteries and into the bones.<sup>6</sup></li> <li>A large study of more than 4,800 subjects followed for 7-10 years in the Netherlands demonstrated that people in the highest one-third of vitamin K2 intake had a 57% reduction in risk of dying from vascular disease, compared to those with the lowest intake.<sup>7</sup></li> </ul>

## ApoE4 Homozygous or Heterozygous

If you carry ApoE4 the following nutrients are suggested in addition to the nutrients listed above. The higher your risk, the more we suggest using all of the scientifically supported nutrients below to pro-actively support cardiovascular health.

## **Arterial Support:**

Supplement	Starting Dosage Range	Comments
Pomegranate Extract	400-1,500mg/day	<ul> <li>Pomegranate blocks the ACE enzyme, helping to support healthy blood pressure.<sup>8</sup></li> <li>Pomegranate maintains optimal artery thickness and flexibility.<sup>9</sup></li> <li>Pomegranate is a powerful antioxidant and supports healthy interactions between arterial walls and lipids by protecting LDL from oxidation.<sup>10</sup></li> </ul>
<b>Pycnogenol</b> (French Maritime Pine Extract)	100mg/day	Pycnogenol has been shown to support healthy arterial blood flow <sup>11</sup> and, when combined with Gotu Kola, was shown to support the body's ability to control plaque formation compared to a control group. <sup>12</sup>
<b>Gotu Kola</b> (Centella) Extract	250mg/day	Gotu kola supports arterial stability and strength. <sup>13</sup>

### **Cholesterol Support:**

Supplement	Starting Dosage Range	Comments
<b>Amla</b> (Indian Gooseberry) Extract	500 - 1000mg/day	In human studies, extracts of amla have been shown to support healthy LDL, total cholesterol, triglycerides, and protective HDL. <sup>14</sup>
<b>Black Tea Extract</b> (Theaflavins)	350 - 700mg /day	<ul> <li>Black tea flavonoids are strong antioxidants and can mitigate oxidative damage to cells and tissues from free radicals.</li> <li>Theaflavins can regulate key inflammatory mediators, thus helping to preserve endothelial integrity.<sup>15,16</sup></li> </ul>
Artichoke Leaf	500 - 1000mg/day	Clinical studies demonstrate that artichoke leaf extract's polyphenolic compounds support optimal HDL/LDL ratios. <sup>17,18</sup>
Pantethine (B5)	600 - 1200mg/day	Pantethine is the biologically active form of pantothenic acid or vitamin B5. Clinical trials show pantethine safely maintains healthy levels of LDL and total cholesterol. <sup>19</sup>

### SUGGESTED COGNITIVE INTERVENTIONS

Regular aerobic exercise is linked to a decrease in cognitive decline and Alzheimer's.<sup>1-4</sup>

A healthy diet protects against cognitive decline.

- Foods to include in your diet: Green Leafy vegetables, other vegetables, nuts, berries, beans, whole grains, fish, poultry, olive oil, wine.<sup>5</sup>
- Foods to avoid include: Red meats, butter and margarine, cheese, pastries and sweets, fried/fast food.<sup>5</sup> The Mediterranean diet is a good option and it has been shown to support healthy cognition.<sup>6</sup>

### **COGNITIVE NUTRIENT SUGGESTIONS**

### **All Alleles**

Regardless of your test results, it is suggested to provide the brain with basic cognitive support and the following nutrients should be considered. If you have higher risk alleles, the additional nutrients in the next section should also be considered.

Supplement	Starting Dosage Range	Comments
Omega 3 Fatty Acids	1400mg EPA and 1000mg DHA/day	<ul> <li>Omega 3 fatty acids, especially DHA are a prominent component of nerve cell makeup.</li> <li>In a randomized study involving 485 individuals with age-related cognitive decline, 900 mg of DHA daily for six months resulted in a marked improvement in learning and memory tests.<sup>7</sup></li> <li>In a small cross-sectional study of cognitively healthy older adults, higher serum DHA levels were associated with less cerebral amyloidosis, better memory scores, and less regional brain atrophy.<sup>8</sup></li> <li>Docosahexaenoic acid (DHA) supplements may support healthy cognition in people who carry the APOE4 allele.<sup>9</sup></li> </ul>
Phosphatidylserine	100mg/day	<ul> <li>Phosphatidylserine (PS) is a naturally occurring component of cell membranes.</li> <li>In a study conducted in Japan on 78 elderly people, supplementation with PS for six months resulted in significant improvements in memory functions.<sup>10</sup></li> <li>In another study, 18 elderly subjects with age-related memory decline took 100 mg of PS 3 times daily for 12 weeks. Tests at 6 and 12 weeks showed cognitive gains compared to baseline measurements.<sup>11</sup></li> </ul>

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Supplement	Starting Dosage Range	Comments
Glyceryl Phosphoryl Choline	• 600mg/day	Glyceryl Phosphoryl Choline (GPC) is a structural component of brain cell membranes and a precursor to the neurotransmitter acetylcholine. Acetylcholine is needed for learning and memory and declines in Alzheimer's disease.
Vinpocetine <u>or</u> Ginkgo biloba	Vinpocetine: 20mg / day Ginkgo: 120mg standardized extract/ day	Vinpocetine, derived from the periwinkle plant, has neuroprotective properties and increases cerebral circulation. <sup>12-14</sup> Ginkgo, if effectively combined with other brain- supporting nutrients, appears to offer a synergistic cognitive effect, resulting partly from its ability to improve cerebrovascular function. <sup>15</sup>

## **Higher Risk Alleles:**

If you carry one or more higher-risk alleles (E3 or especially E4) the following nutrients are suggested in addition to the nutrients listed above. The higher your risk, the more we suggest using all of the scientifically supported nutrients below to pro-actively support brain health and cognition.

Supplement	Starting Dosage Range	Comments
Lithium	300mcg/day	<ul> <li>Lithium promotes autophagy, the healthy breakdown of tau and abeta proteins through natural processes.<sup>16</sup></li> <li>In animal studies, lithium helped maintain memory health and cognitive performance.<sup>17</sup></li> <li>In a human study, lithium stabilized cognitive measurements.<sup>18</sup></li> </ul>
Colostrinin	100mcg/day	<ul> <li>Colostrinin polypeptide complex promotes cognition, memory, and helps inhibit inflammatory factors in the brain.</li> <li>Colostrinin encourages production of enzymes which support the natural breakdown of a-beta proteins, and it encourages learning and memory in animal studies.<sup>19</sup></li> <li>In human studies, individuals given colostrinin over 16-28 months showed an improvement on cognitive test scores.<sup>20</sup></li> </ul>

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Supplement	Starting Dosage Range	Comments
Magnesium L-Threonate	2000mg of Magnesium L- Threonate providing 144mg elemental magnesium /day	<ul> <li>Magnesium L-Threonate supports healthy memory and cognition by optimizing magnesium levels in the brain.<sup>21-26</sup></li> <li>Magnesium L-threonate is a unique form of magnesium that is delivered into the brain where it maintains the quantity of synaptic connections between brain cells<sup>27,28</sup> and inhibits the dysregulation of important brain cell signaling pathways.</li> </ul>
Huperzine	600mcg-800mcg/day	• Huperzine, extracted from the Chinese club moss is an herbal supplement that has been shown to maintain healthy levels of acetylcholine. <sup>29-34</sup> Acetylcholine is needed for learning and memory and declines in Alzheimer's disease.

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KCL-SamRepAPOE-20190822