

Genomics Relative to ER+ Breast Cancer

In August 2009, with no family history of breast cancer, I was diagnosed with an invasive lobular tumor which was ER+ and Her2 negative and I had a mastectomy. In September 2009 while researching various treatment options I decided to enter a study conducted by Dr. Joe Veltmann. First, I had my DNA tested by Genova Diagnostics. Genova tests approximately 50 genes that are the most prevalent in the majority of the population and the most modifiable. My test results revealed SNP's on CYP 450 1B1, CYP 450 2C9, COMT, and GSTM1(1p13.3) and GSTP1(1105v) four out of the five genes listed below. I then took a 24-hr urine test and found that I metabolized estrogen largely through carcinogenic pathways which are 4-Hydroxyestrone and 16a-Hydroxyestrone. If doctors had known this they would never have given me HRT. See charts in other attachments labeled UEM results.

Dr. Veltmann has seen a correlation between breast cancer and SNP's on genes CYP 450 1A1, CYP450 1B1, COMT, GSTM1 (1p13.3), and GSTP1 (1105v). The following is a discussion of each gene.

CYP 450 1A1 Detoxifies polycyclic aromatic hydrocarbons (PAHs) found in exhaust fumes charbroiled meats, cigarette smoke, and solvents; involved in the hydroxylation of estrone to 2-OH estrone; check for SNPs in phase 2 (COMT). If smoker, SNP associated with hyperinduction generating mutagenic metabolites and oxidative stress. SNP assoc with moderate risk for lupus, endometriosis (if also GSTM1) and low birth weight babies.

CYP 450 1B1 Upregulates hydroxylation of estrone to 4-OH estrone and may contribute to estrogen sensitive cancers. Environmental toxins PAHs (exhaust fumes, charbroiled meats, cigarette smoke, industrial solvents, PCBs, aflatoxin B1) up regulate enzyme leading to oxidative stress and quinone formation especially if taking HRT (conjugated equine estrogens), high BMI, or CYP1A1 polymorphism. HRT (CEE) are preferentially converted to 4-OH estrone.

COMT Tissue: Liver and gut. Associated with late-onset-alcoholism, anxiety, schizophrenia, bipolar disorder, increased sensitivity to pain, fibromyalgia, migraine, breast cancer due to impaired estrogen metabolism, decreased ability to catecholamines (L-Dopa, epinephrine, norepinephrine and estrogen metabolites)

In women, COMT associated with increased risk of breast cancer and lymph node metastasis. With two bad genes OR (odds ratio) is 4-5 fold or increased with SNPs in CYP1B1, GSTM1, GSTP1, GSTT1, exposure to estrogen (ERT>30months) or early menarche.

Upside: improved cognition and decreased risk of schizophrenia due to higher amounts of synaptic dopamine

GSTM1
1p13.3

Tissues: liver, gut, brain and skin. SNP impairs protection against stress associated with solvents, herbicides, fungicides and heavy metals resulting in cancers and fatigue syndromes. GST's are critical in removing cellular debris from free radical attacks

GSTP1
1105V

Tissues: liver, gut, brain and skin. SNP impairs protection against stress associated with solvents, herbicides, fungicides, and heavy metals resulting in breast cancer and fatigue syndromes. The more isozymes with SNPs within the GSTs, the greater the risk.

After 2 years of taking supplements and going on a diet consistent with my blood type which is A+, my estrogen metabolism has changed dramatically. The carcinogenic pathways, 4-Hydroxyestrone and 16 α -Hydroxyestrone have moved within the optimal balance of estrogen metabolites.