



An Integrated Gene Approach to Estrog Metabolism

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Estrogen Genes

- ❑ CYP17A1 rs6162
- ❑ CYP1A1rs2606345
- ❑ CYP1B1rs1056836
- ❑ COMT rs4680
- ❑ NQ01rs1800566
- ❑ GSTP1 rs1695



CYP17A1 rs6162

- ❑ Normal Allele is A Variant Allele is G
- ❑ Cytochrome P450 enzyme that catalyzes 17 alpha hydroxylase and 17,20-lyase in adrenals and gonads.
- ❑ Affects conversions of pregnenolone into DHEA and androstenedione, but greatly favours DHEA affecting estrogen levels.



CYP17A1 G Allele

- Increased enzymatic production and activity.
- Increased estrogen levels.
- Early menarche.
- Increased infertility, PCOS, cysts and fibroids.
- Increased risk of estrogen receptored cancers, especially in those treated with HRT.

Cancer Res 59, 1999: 4870-4875

Int J Cancer, 2012, 130: 338-348

Acta Obstet Gynecol 2013 92:1188-1193



Support for CYP17A1 G Allele

- ❑ DIM
- ❑ Sulphoraphanes
- ❑ Broccoli sprouts.
- ❑ Reduction in stress.
- ❑ Organic fruits and vegetables.



CYP17A1 A Allele

- Decreased enzymatic production and activity.
- Decreased estrogen levels.
- Late onset menarche.

J Clin Endocrinol Metab. 2003, 88:799-803



CYP1A1rs2606345

- ❑ Normal Allele is A Variant Allele is C
- ❑ Cytochrome P450 enzyme that increases the metabolism of xenobiotics (BP-7,8-dihydrodiol-9,10-epoxide) found in cigarettes and charred meats.
- ❑ Major enzyme that converts estrogens into the 2-OH form.



CYP1A1 A Allele

- ❑ Decreased enzymatic activity.* Note this is the “normal allele”.
- ❑ Less conversion to 2-OH estrogen increasing PCOS, fibroids and estrogen receptored cancers.
- ❑ Low enzyme induction of xenobiotics reducing breast, prostate and colon cancers via inflammatory toxicity.
- ❑ *Environ Health Glob Access Sci* 2014 ;13:19
- ❑ *DNA Cell Biol.* 2011;30:585-595



Support for CYP1A1 A Allele

- ❑ DIM
- ❑ Sulphoraphanes
- ❑ Broccoli Sprouts
- ❑ Be very cautious with HRT, Bio-Identical hormones, herbal estrogens and DHEA.



CYP1A1 C Allele

- Increased enzymatic activity.
- Greater conversion to 2-OH estrogen decreasing PCOS, fibroids and estrogen receptored cancers.
- High enzyme induction of xenobiotics increasing breast, prostate and colon cancers via inflammatory toxicity.

Am J Med., 2006, 119;544-551

Environ Health Glob Access Sci 2014 ;13:19



Support for CYP1A1 C Allele

- Liposomal Glutathione
- NAC
- Ensure to check Phase 11 SNPS
- Avoid BBQ'd meats.



CYP1B1 rs1056836

Normal Allele is C Variant Allele is G

Cytochrome P450 enzyme that catalyzes several drugs, pro-carcinogens, cholesterol, fats and steroids.

Greatest activity in breast tissue.

Induces DNA single-stranded breaks increasing 8-hydroxy-2-deoxyguanosine levels increasing tissue damage and hormonal related disease.

Major enzyme that converts estrogens into the 4-OH form

Cancer Res., 2000, 60:3440-3444

Breast J 2014, 20:468-480

CYP1B1 C Allele

Decreased enzymatic activity.

Decreased 4-OH estrogen production.

Higher induction of xenobiotics.

Stimulated greatly by environmental toxins.

Basic Clin Pharmacol Toxicol. 2018 Sep; 123(3): 335-346.



Support for CYP1B1 C Allele

- ❑ Liposomal Glutathione
- ❑ NAC
- ❑ Ensure to check Phase 11 SNPS
- ❑ Organic cleaning agents and detergents.



CYP1B1 G Allele

- ❑ Higher Enzymatic activity.
- ❑ 3-fold increase in 4-OH production.
- ❑ Increase risk of PCOS, fibroids, and estrogen receptored cancers.
- ❑ Lower enzymatic induction of xenobiotics decreasing risk of breast, colon and prostate cancer via toxicity.
- ❑ *Cancer Epidemiol., 2009, 33;24-30*
- ❑ *BMC Cancer 2010, 10;638*



Support for CYP1B1 G Allele

- DIM
- Sulforaphanes
- Broccoli sprouts
- Extreme caution with HRT, Bio-Identical hormones, BCP and herbal estrogens.
- Avoid inorganic fruits and vegetables.

Cancer Epidemiol. Biomarkers Prev., 2008, 17;1751-1759.

Cancer Prev., 2010, 3;727-737



COMT rs4680

- ❑ Normal Allele is G Variant Allele is A
- ❑ Catechol-O-Methyltransferase metabolizes catecholamines, some pharmaceuticals and estrogen (both 2-OH and 4-OH).
- ❑ Adds a methyl group from SAM-e to convert an active metabolite into a less active one.
- ❑ Increased COMT activity reduces its metabolites by up to 50%



COMT G Allele

- ❑ Higher enzymatic activity with increased clearance of estrogens.
- ❑ Reduced risk of estrogenic receptored cancers.
- ❑ Increased clearance of adrenaline and noradrenaline, decreasing anxiety and stress response.
- ❑ Increased clearance of dopamine, increasing addictive behaviours, ADD, focus and concentration.



Support for COMT G Allele

- ❑ Tyrosine
- ❑ L-dopa
- ❑ Exercise
- ❑ Walnuts
- ❑ Aged cheese



COMT A Allele

- Lower enzymatic activity with decreased clearance of estrogens
- increased risk of breast and endometrial cancers.
- Decreased clearance of adrenaline and noradrenaline, increasing anxiety and the stress response.
- Decreased clearance of dopamine, improving focus and concentration, reducing addictive behaviours.

J Breast Cancer 2014, 17:149

BMC Cancer 2008 14;8(6)



Support for COMT A

- Stress Management
- Casein Tryptic Decapeptide
- DIM
- Broccoli Sprouts



Genetic Integration

- CYP17A1- G/A
- CYP1A1 – A/A
- CYP1B1 – G/G
- COMT – A/A
- GSTP1 – G/G
- NQ01 – G/A

- CYP17A1- G/A
- CYP1A1 – C/C
- CYP1B1 –C/C
- COMT – G/G
- GSTP1 – A/G
- NQ01 – G/A



Case Study 3

- 32 year old female with breast cancer.
- Had grown tumors 5 separate times in a 3 year period. The last one in skeletal muscle??
- Undergone max doses of chemo and radiation.
- Non-smoker, balanced organic diet, exercised regularly.
- Strong family history of breast cancer, but all members negative for BRCA1 and 2.



Case Study 3

- CYP17A1- G/A – higher starting estrogen.
- CYP1A1 – A/A – little conversion to 2-OH estrogen
- CYP1B1 – G/G – increased conversion to 4-OH
- COMT – A/A – slow clearance of estrogen
- GSTP1 – G/G – slow clearance of estrogen and zeno's
- NQ01 – G/A – slow clearance of estrogen and zeno's



Case Study 3

- Liposomal Glutathione – 1 cap BID empty stomach.
- NAC – 1 cap BID empty stomach.
- DIM, Sulphoraphane, Resveratrol combo – 2 caps BID empty stomach.
- Mushroom combo – 1 cap BID
- Live frozen cartilage – 1 bottle per day



Case Study 3

- 3 month follow up CA-15-3 reduced from 72 to 51 U/ml and CA 27.29 reduced from 69 to 39 U/ml.
- 6 month CT scan – 2 existing tumors had shrunk by 60% and no new tumor growth.
- 1 year follow up CA-15-3 was 22 U/ml and CT scan revealed 2 small “dots”. Biopsy – calcification only.
- 2 yr F/U all blood work normal, CT unchanged.
- 8 years – in good health.!



Case Study 4

- ❑ 51 year old menopausal woman with hot flashes and sweats during the day and night.
- ❑ She was soaking through shirts twice a day.
- ❑ Flashes were disrupting her sleep greatly, and the fatigue would make things worse the next day.
- ❑ No personal history of fibroids, cysts or cancers.



Case Study 4

- CYP17A1- G/A – increased estrogen
- CYP1A1 – C/C – good conversion to 2-OH
- CYP1B1 –C/C – little conversion to 4-OH
- COMT – G/G - good clearance of estrogen
- GSTP1 – A/G -less clearance of estrogen and zeno's
- NQ01 – G/A - -less clearance of estrogen and zeno's



Case Study 4

- ❑ She had tried herbal estrogen and progesterone therapies, but they only reduced the flashes and sweats by about 15-20%.
- ❑ She did not want to go on traditional HRT.
- ❑ Sent her to a colleague for bio-identicals to boost levels for 6 months.



Case Study 4

- At 6 months her flashes and sweats had been minimal for the past 3 months.
- We began to reduce the bio-identicals over time and added in a Dong Quai, Red Clover, Schisandra combo – 2 caps BID for 8 weeks.
- She then stopped all bio-identicals, and 4 weeks later dropped the herbal combo to 1 BID, increasing to 2 BID as needed.



Case Study 4

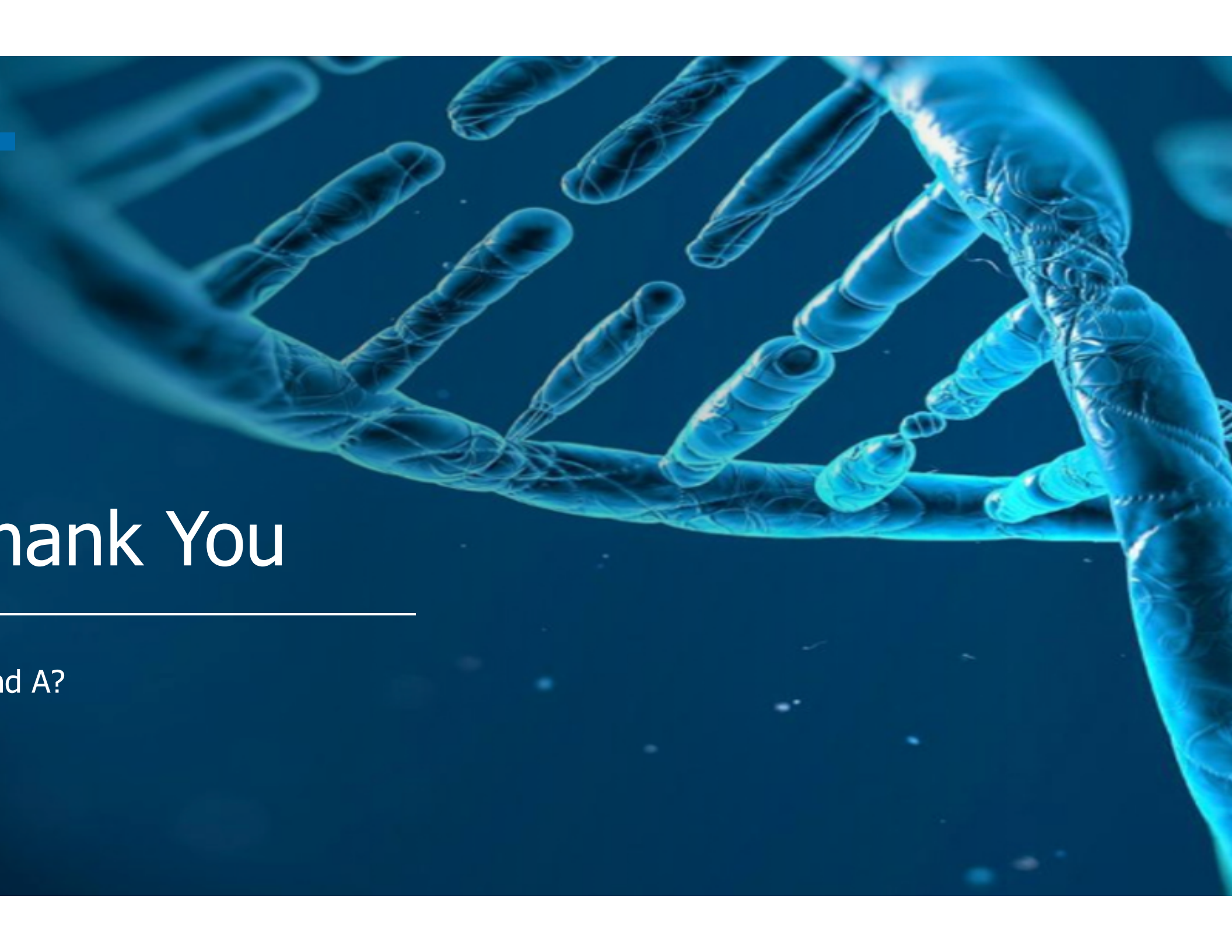
- As her hormones continued to drop over the next 2.5 years, she alternated the herbal combo 1 BID with 2 BID prn.
- All flashes and sweats were “95%” controlled.
- 3 years later she is off all hormonal support and symptom free.



Putting it all Together.

- Our body is a unit, when you change one area or pathway it will ultimately change another.
- Just because we have a gene, does not mean we are expressing it.
- Be sure not to turn on the adverse expression of a gene via turning on another gene.
- Know all the pieces of the puzzle and put them together.





Thank You

and A?