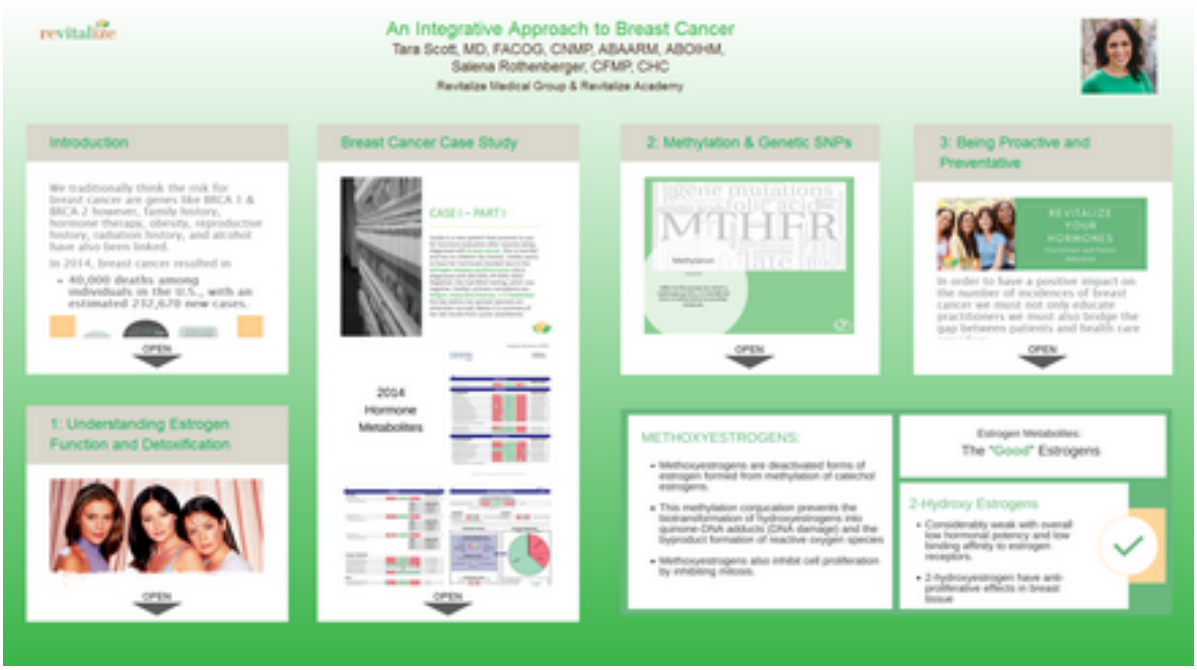
An Integrative Approach to Breast Cancer



Tara Scott, MD, FACOG, CNMP, ABAARM, ABOIHM,
Salena Rothenberger, CFMP, CHC

Revitalize Medical Group & Revitalize Academy

PRESENTED AT:

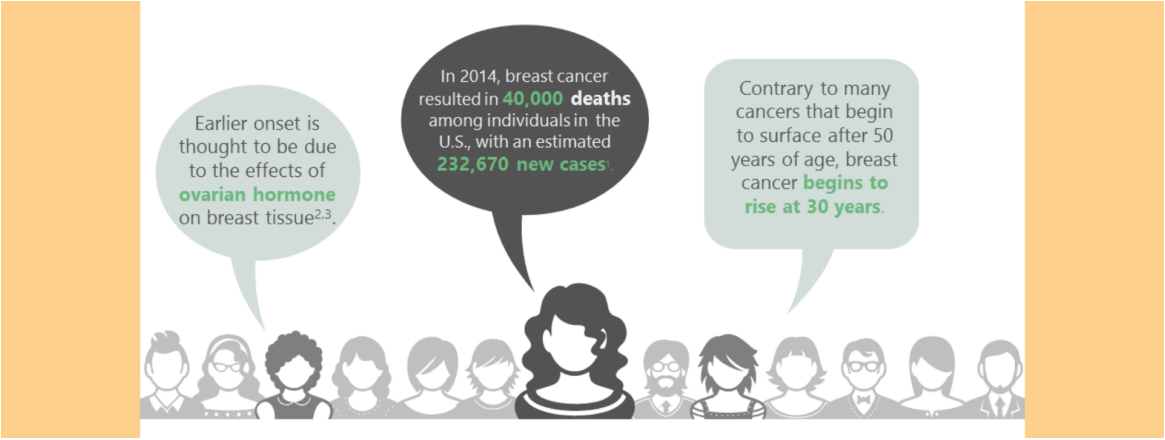
INTRODUCTION

[VIDEO] https://www.youtube.com/embed/NrTf4f6v4SM?feature=oembed&fs=1&modestbranding=1&rel=0&showinfo=0

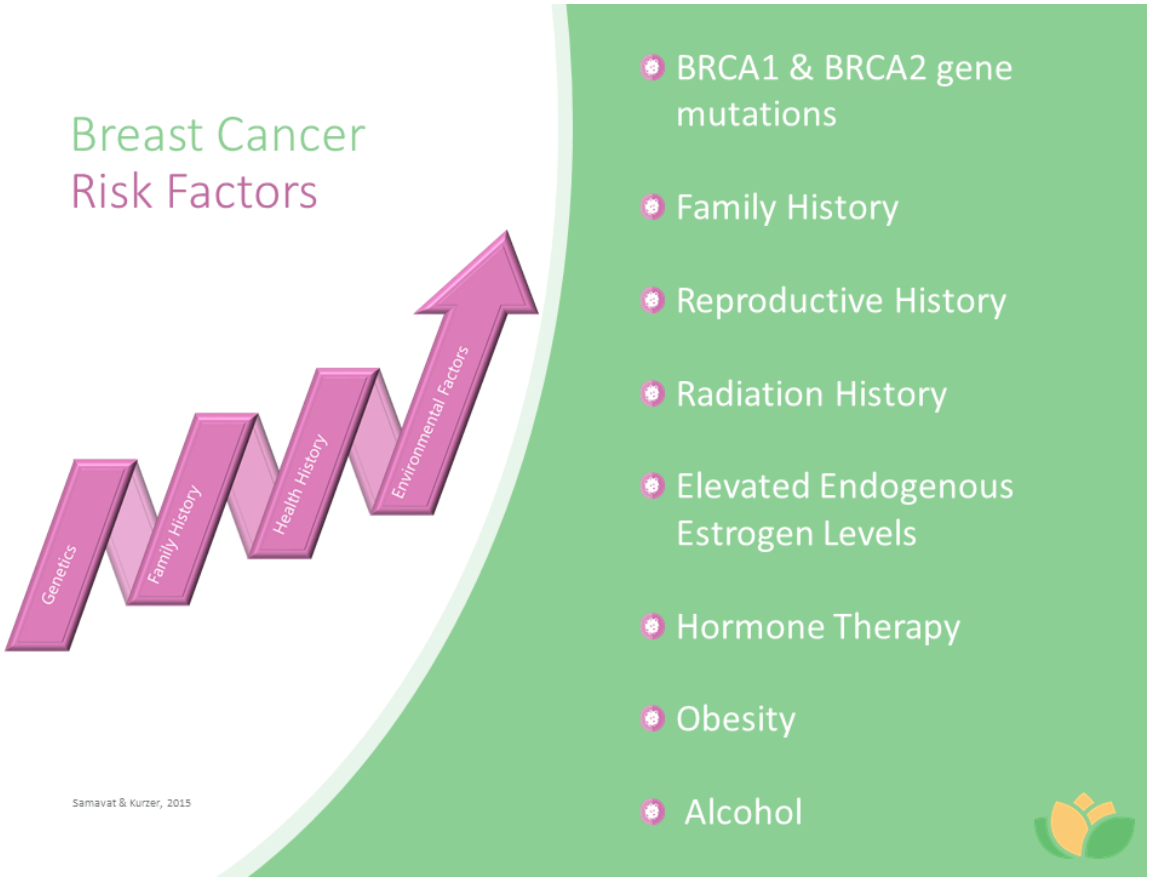
We traditionally think the risk for breast cancer are genes like BRCA 1 & BRCA 2 however, family history, hormone therapy, obesity, reproductive history, radiation history, and alcohol have also been linked.

In 2014, breast cancer resulted in

- 40,000 deaths among individuals in the U.S., with an estimated 232,670 new cases.



Contrary to many cancers that begin to surface after 50 years of age, breast cancer begins to rise at 30 years. Earlier onset is thought to be due to the effects of ovarian hormone on breast tissue.



We will explore the role of estrogen metabolism and key genes in methylation with my theory of excess estrogen as a link to breast cancer through reviewing:

- Functions of hormones and estrogen detoxification
- Review of methylation and basic genetic snps
- Discuss how MTHFR and COMT increase the risk of breast and uterine cancer
- Describe how to be more proactive and preventative

Note: Each section has a video to delve deeper into the slides and you are welcome to reach out to Dr. Scott with any questions.

1: UNDERSTANDING ESTROGEN FUNCTION AND DETOXIFICATION

We know that a balance of estrogen and progesterone are needed for an optimal menstrual cycle. We are going explore the function and detoxification of estrogen and show that an imbalance can put one at a higher risk for breast cancer.

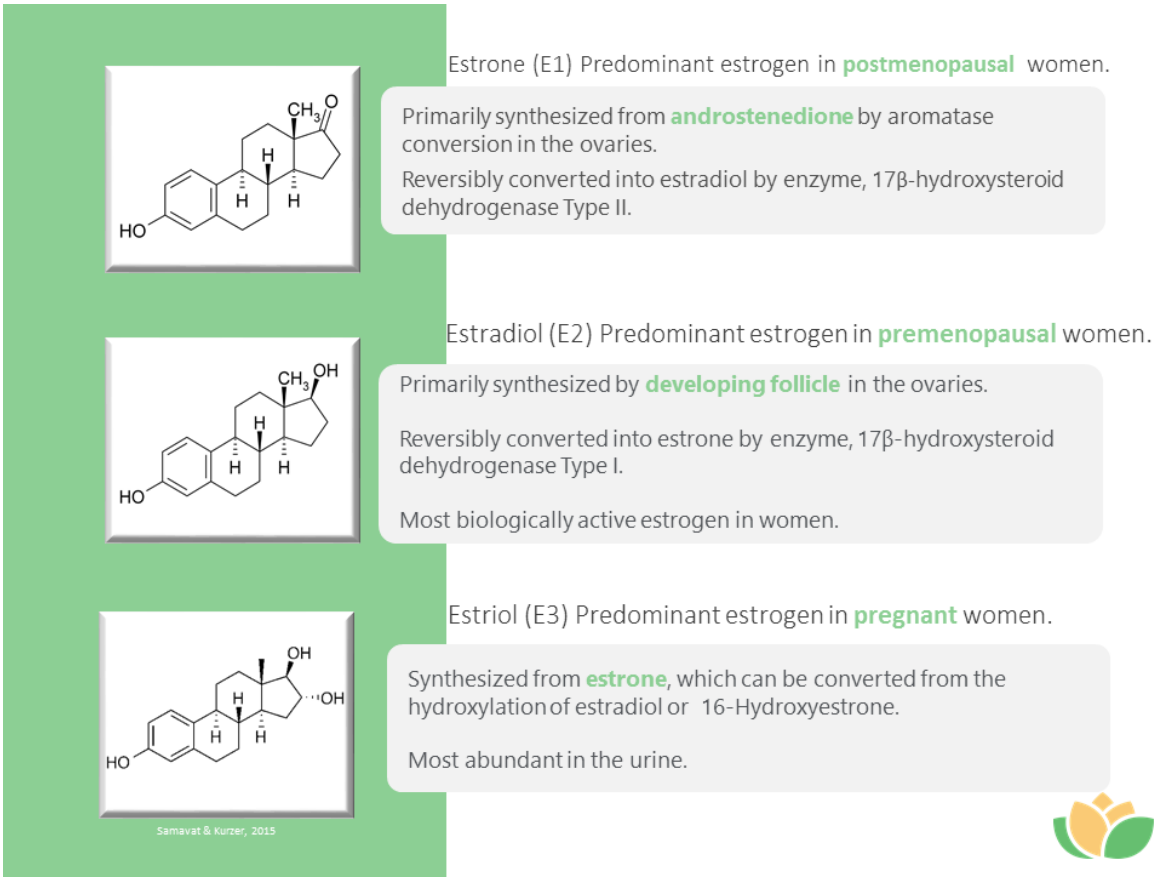
Key Hormone Functions

- Estrogen causes proliferation
- Progesterone inhibits proliferation, a decline in DNA synthesis, and interferes with estrogen receptors
- Estrogen stimulates many oncogene that mediate estrogen-induced growth
- Progesterone antagonizes transcription of oncogene mRNA

[VIDEO] https://www.youtube.com/embed/kRzEcwu9doE?feature=oembed&fs=1&modestbranding=1&rel=0&showinfo=0

Three Types of Estrogen

Estrogen promotes growth and body development along with slows bone loss.

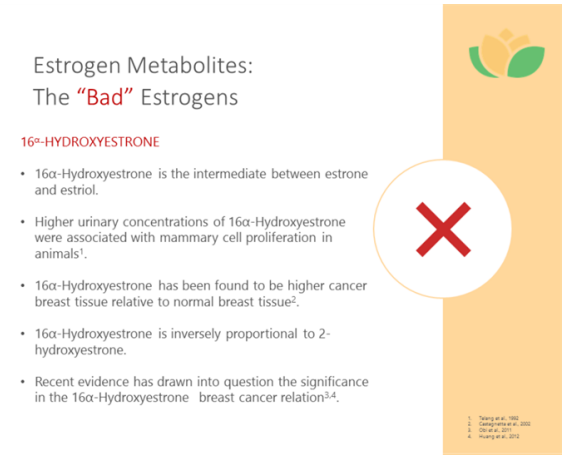


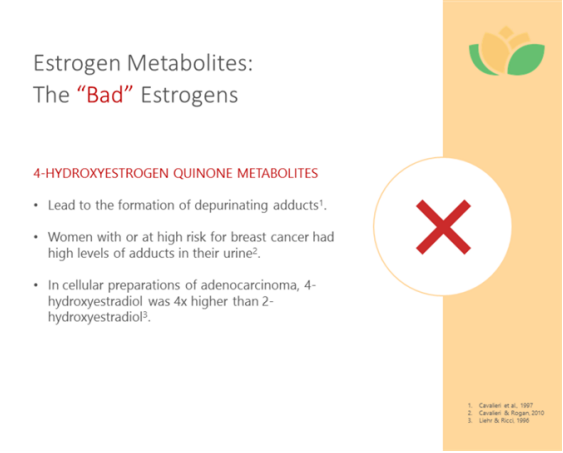
'The Three Sisters'

Estradiol is like the gal who is great at sports, academics, beautiful, good at everything

Estriol is like the meek, shy girl hiding behind the others

Estrone is like the girl who is good as well, however, she has a tendency to be goth and do things she shouldn't especially when she hangs with the wrong crowd





Reasons for Elevated Estrogen

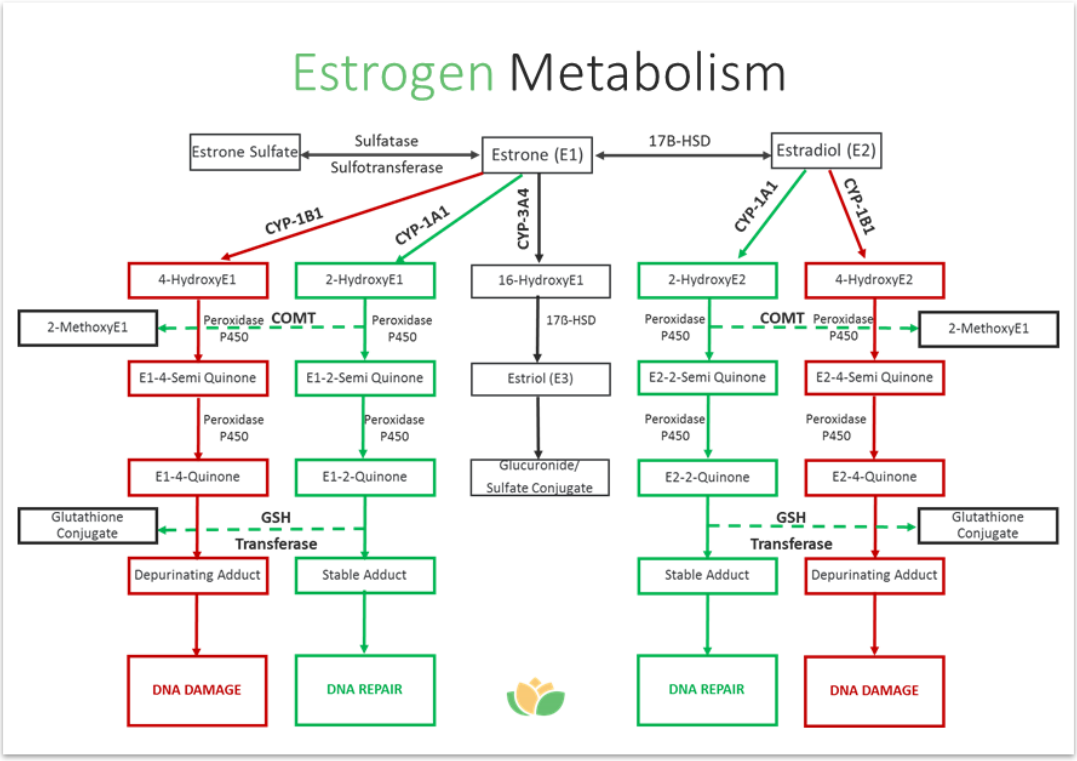
- Environmental Sources
- Obesity
- Genetics – You Can't Detox It
- Your Body Makes Too Much
- You Have Had A Hysterectomy And Are Not Taking Both Estrogen and Progesterone

Estrogen Detoxification

Step 1: Cytochrome P450

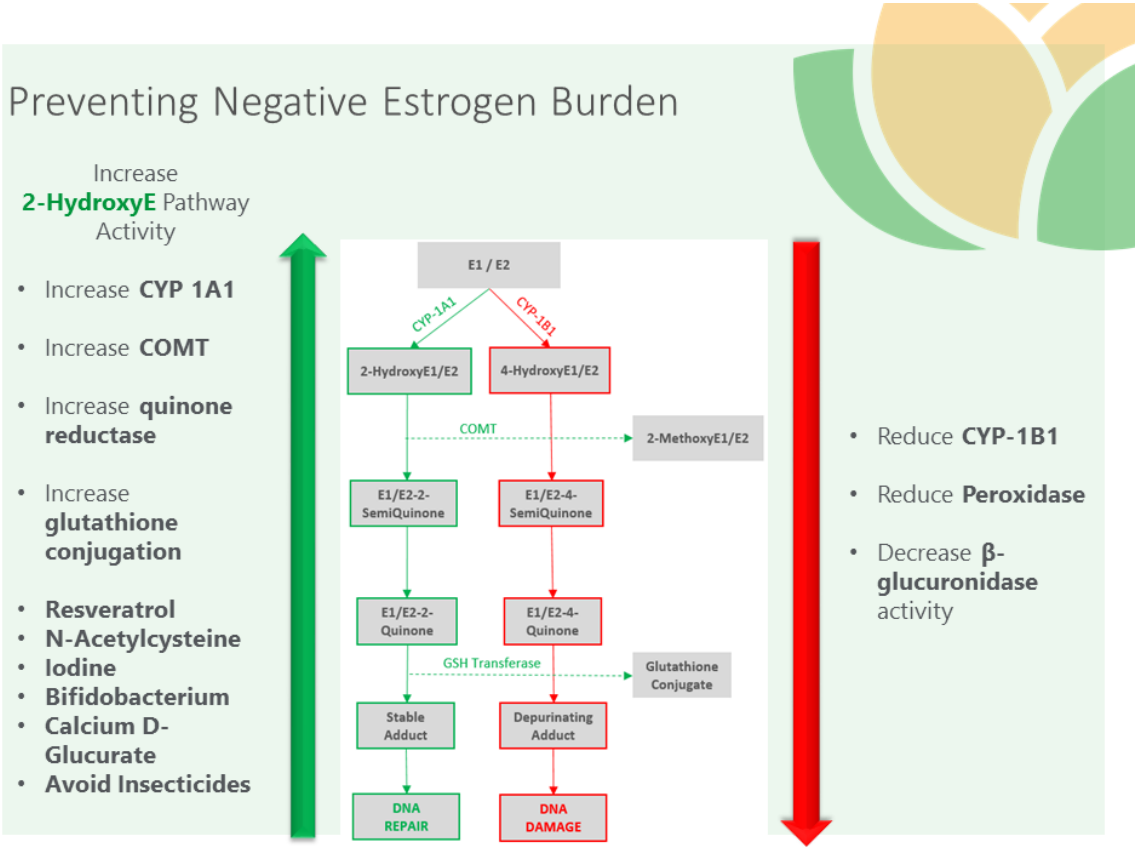
Step 2: COMT or Methylation

Step 3: Beta-glucuronidase



Preventing Negative Estrogen Burden

It is easier to Increase CYP 1A1 than to decrease CYP 1B1



BREAST CANCER CASE STUDY

CASE I – PART I

Cecilia is a new patient that presents to you for hormone evaluation after recently being diagnosed with **breast cancer**. She is married and has no children (by choice). Cecilia wants to have her hormones checked due to the **estrogen receptor positive tumor** she is diagnosed with (ER 95%; PR 95%; HER2 Negative). She had BRAC testing, which was negative. Cecilia's primary complaints are **fatigue, sleep disturbances**, and **headaches** the day before her periods (periods are otherwise normal). Below is a summary of her lab results from a prior practitioner.

[VIDEO] https://www.youtube.com/embed/G7G04D3whfI?feature=oembed&fs=1&modestbranding=1&rel=0&showinfo=0

2014 Hormone Metabolites

Complete Hormones (FMV)

GENOVA DIAGNOSTICS

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Asheville, NC 28801
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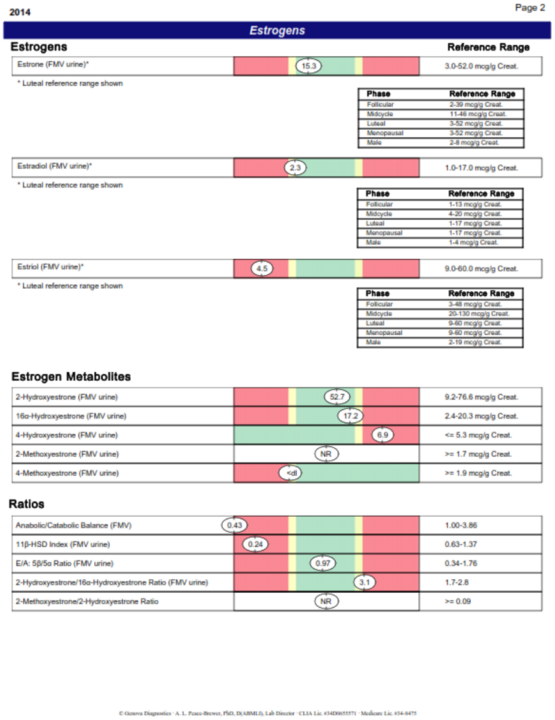
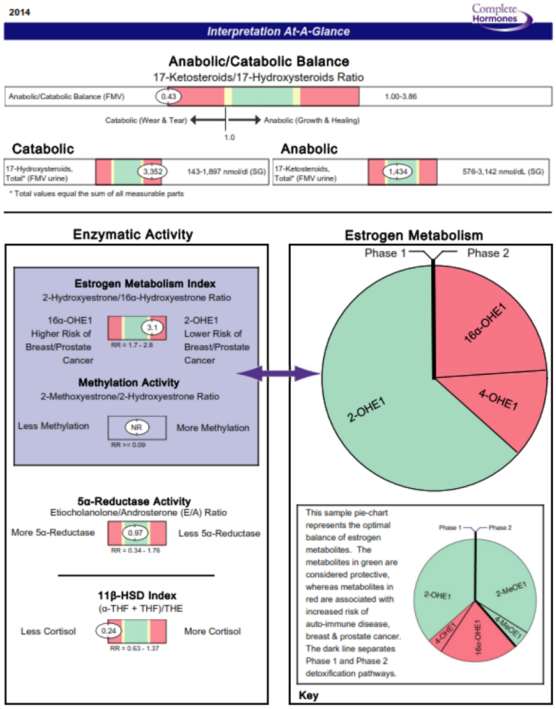
2014

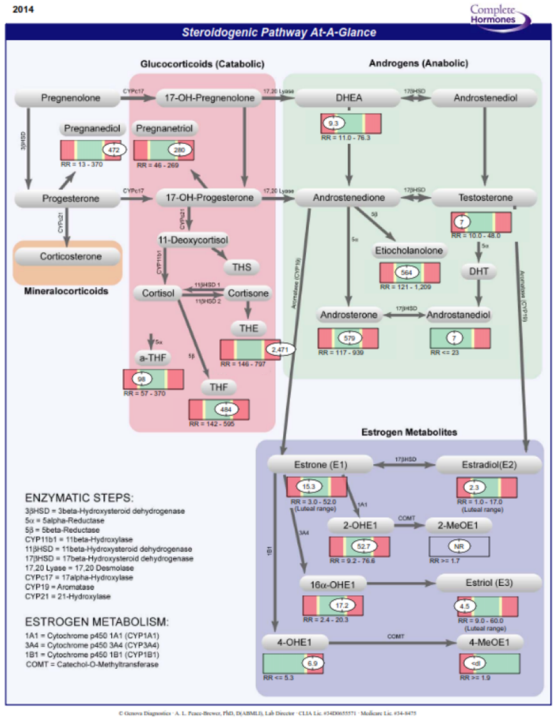
Progesterone		Reference Range
Pregnanediol (FMV urine)	472	13-370 nmol/dL (SG)

Androgens		
17-Ketosteroids		**Reference Range**
DHEA (FMV urine)	9.3	11.0-76.3 nmol/dL (SG)
Androsterone (FMV urine)	579	117-939 nmol/dL (SG)
Etiocholanolone (FMV urine)	964	121-1,209 nmol/dL (SG)
11-Keto-androsterone (FMV urine)	13	37-236 nmol/dL (SG)
11-Keto-etiocholanolone (FMV urine)	78	57-315 nmol/dL (SG)
11-Hydroxy-androsterone (FMV urine)	137	71-496 nmol/dL (SG)
11-Hydroxy-etiocholanolone (FMV urine)	54	64-363 nmol/dL (SG)
17-Ketosteroids, Total* (FMV urine)	1,434	576-3,142 nmol/dL (SG)
* Total values equal the sum of all measurable parts		
Testosterone (FMV urine)	7	10-48 nmol/dL (SG)
Androstanediol (FMV urine)	7	<= 23 nmol/dL (SG)

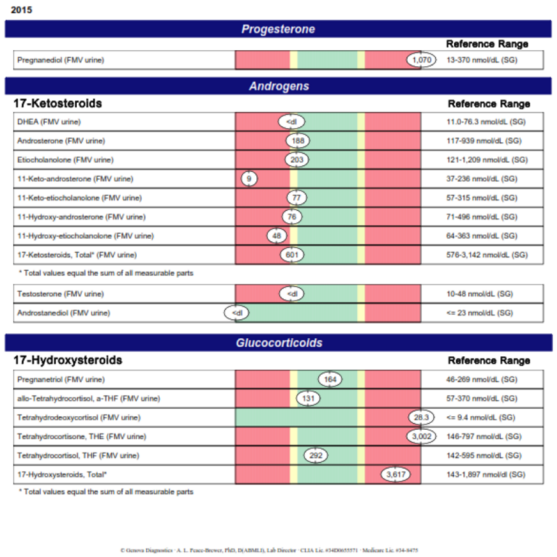
Glucocorticoids		
17-Hydroxysteroids		**Reference Range**
Pregnanetriol (FMV urine)	280	46-269 nmol/dL (SG)
allo-Tetrahydrocortisol, a-THF (FMV urine)	98	57-370 nmol/dL (SG)
Tetrahydrodeoxycortisol (FMV urine)	19.1	<= 9.4 nmol/dL (SG)
Tetrahydrocortisone, THE (FMV urine)	2,471	146-797 nmol/dL (SG)
Tetrahydrocortisol, THF (FMV urine)	484	142-595 nmol/dL (SG)
17-Hydroxysteroids, Total*	3,352	143-1,897 nmol/dl (SG)
* Total values equal the sum of all measurable parts		


2014
Page 2
Estrogens
Estrogens
Reference Range
Estrone (FMV urine)*
15.3
3.0-52.0 mcg/g Creat.
* Luteal reference range shown
Phase
Reference Range
Follicular
2-39 mcg/g Creat.
Midcycle
11-46 mcg/g Creat.
Luteal
3-52 mcg/g Creat.
Menopausal
3-52 mcg/g Creat.
Male
2-8 mcg/g Creat.
Estradiol (FMV urine)*
2.3
1.0-17.0 mcg/g Creat.
* Luteal reference range shown
Phase
Reference Range
Follicular
1-13 mcg/g Creat.
Midcycle
4-20 mcg/g Creat.
Luteal
1-17 mcg/g Creat.
Menopausal
1-17 mcg/g Creat.
Male
1-4 mcg/g Creat.
Estriol (FMV urine)*
4.5
9.0-60.0 mcg/g Creat.
* Luteal reference range shown
Phase
Reference Range
Follicular
3-48 mcg/g Creat.
Midcycle
20-130 mcg/g Creat.
Luteal
9-60 mcg/g Creat.
Menopausal
9-60 mcg/g Creat.
Male
2-19 mcg/g Creat.
Estrogen Metabolites
2-Hydroxyestrone (FMV urine)
52.7
9.2-76.6 mcg/g Creat.
16α-Hydroxyestrone (FMV urine)
17.2
2.4-20.3 mcg/g Creat.
4-Hydroxyestrone (FMV urine)
6.9
<= 5.3 mcg/g Creat.
2-Methoxyestrone (FMV urine)
NR
>= 1.7 mcg/g Creat.
4-Methoxyestrone (FMV urine)
<dl
>= 1.9 mcg/g Creat.
Ratios
Anabolic/Catabolic Balance (FMV)
0.43
1.00-3.86
11β-HSD Index (FMV urine)
0.24
0.63-1.37
E/A: 5β/5α Ratio (FMV urine)
0.97
0.34-1.76
2-Hydroxyestrone/16α-Hydroxyestrone Ratio (FMV urine)
3.1
1.7-2.8
2-Methoxyestrone/2-Hydroxyestrone Ratio
NR
>= 0.09


2014
Complete Hormones
Interpretation At-A-Glance
Anabolic/Catabolic Balance
17-Ketosteroids/17-Hydroxysteroids Ratio
Anabolic/Catabolic Balance (FMV)
0.43
1.00-3.86
Catabolic (Wear & Tear)
Anabolic (Growth & Healing)
1.0
Catabolic
17-Hydroxysteroids, Total* (FMV urine)
3,352
143-1,897 nmol/dl (SG)
Anabolic
17-Ketosteroids, Total* (FMV urine)
1,434
576-3,142 nmol/dL (SG)
* Total values equal the sum of all measurable parts
Enzymatic Activity
Estrogen Metabolism Index
2-Hydroxyestrone/16α-Hydroxyestrone Ratio
16α-OHE1 Higher Risk of Breast/Prostate Cancer
3.1
RR = 1.7 - 2.8
2-OHE1 Lower Risk of Breast/Prostate Cancer
Methylation Activity
2-Methoxyestrone/2-Hydroxyestrone Ratio
Less Methylation
NR
RR >= 0.09
More Methylation
5α-Reductase Activity
Etiocholanolone/Androsterone (E/A) Ratio
More 5α-Reductase
0.97
RR = 0.34 - 1.76
Less 5α-Reductase
11β-HSD Index
(α-THF + THF)/THE
Less Cortisol
0.24
RR = 0.63 - 1.37
More Cortisol
Estrogen Metabolism
Phase 1
Phase 2
16α-OHE1
2-OHE1
4-OHE1
This sample pie-chart represents the optimal balance of estrogen metabolites. The metabolites in green are considered protective, whereas metabolites in red are associated with increased risk of auto-immune disease, breast & prostate cancer. The dark line separates Phase 1 and Phase 2 detoxification pathways.
Key


2014
Complete Hormones
Steroidogenic Pathway At-A-Glance
Glucocorticoids (Catabolic)
Androgens (Anabolic)
Pregnenolone
17-OH-Pregnenolone
DHEA
Androstenediol
Pregnanediol
472
RR = 13 - 370
Pregnanetriol
280
RR = 46 - 269
9.3
RR = 11.0 - 76.3
Progesterone
17-OH-Progesterone
Androstenedione
Testosterone
7
RR = 10.0 - 48.0
11-Dexycortisol
Etiocholanolone
344
RR = 121 - 1,209
DHT
THS
Corticosterone
Mineralocorticoids
Cortisol
Cortisone
Androsterone
Androstanediol
579
RR = 117 - 939
7
RR <= 23
THE
2,471
RR = 146 - 797
α-THF
98
RR = 57 - 370
THF
484
RR = 142 - 595
Estrogen Metabolites
Estrone (E1)
Estradiol(E2)
15.3
RR = 3.0 - 52.0 (Luteal range)
2.3
RR = 1.0 - 17.0 (Luteal range)
2-OHE1
52.7
RR = 9.2 - 76.6
2-MeOE1
NR
RR >= 1.7
16α-OHE1
17.2
RR = 2.4 - 20.3
Estriol (E3)
4.5
RR = 9.0 - 60.0 (Luteal range)
4-OHE1
6.9
RR <= 5.3
4-MeOE1
<dl
RR >= 1.9
ENZYMATIC STEPS:
3βHSD = 3beta-Hydroxysteroid dehydrogenase
5α = 5alpha-Reductase
5β = 5beta-Reductase
CYP11b1 = 11beta-Hydroxylase
11βHSD = 11beta-Hydroxysteroid dehydrogenase
17βHSD = 17beta-Hydroxysteroid dehydrogenase
17,20 Lyase = 17,20 Desmolase
CYP17 = 17alpha-Hydroxylase
CYP19 = Aromatase
CYP21 = 21-Hydroxylase
ESTROGEN METABOLISM:
1A1 = Cytochrome p450 1A1 (CYP1A1)
3A4 = Cytochrome p450 3A4 (CYP3A4)
1B1 = Cytochrome p450 1B1 (CYP1B1)
COMT = Catechol-O-Methyltransferase

2015 Hormone Metabolites



Complete Hormones (FMV)

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2015

Progesterone

		Reference Range
Pregnanediol (FMV urine)	1,070	13-370 nmol/dL (SG)

Androgens

17-Ketosteroids

		Reference Range
DHEA (FMV urine)	<dl	11.0-76.3 nmol/dL (SG)
Androsterone (FMV urine)	188	117-939 nmol/dL (SG)
Etiocholanolone (FMV urine)	203	121-1,209 nmol/dL (SG)
11-Keto-androsterone (FMV urine)	9	37-236 nmol/dL (SG)
11-Keto-etiocholanolone (FMV urine)	77	57-315 nmol/dL (SG)
11-Hydroxy-androsterone (FMV urine)	76	71-496 nmol/dL (SG)
11-Hydroxy-etiocholanolone (FMV urine)	48	64-363 nmol/dL (SG)
17-Ketosteroids, Total* (FMV urine)	601	576-3,142 nmol/dL (SG)

* Total values equal the sum of all measurable parts

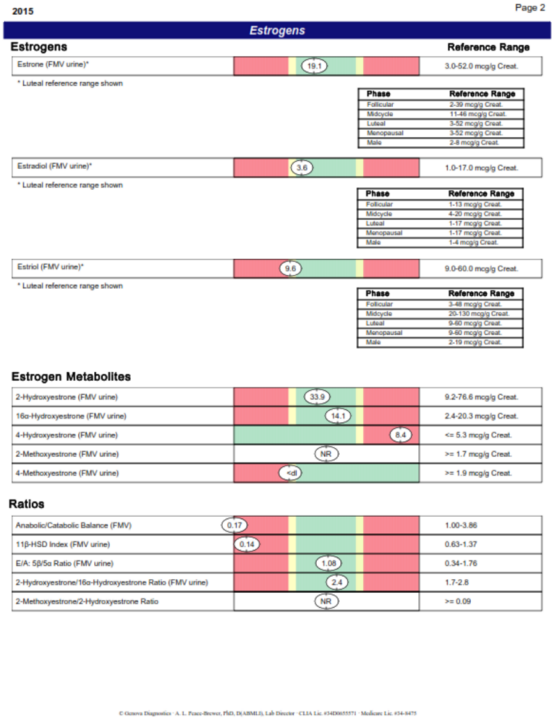
Testosterone (FMV urine)	<dl	10-48 nmol/dL (SG)
Androstanediol (FMV urine)	<dl	<= 23 nmol/dL (SG)

Glucocorticoids

17-Hydroxysteroids

		Reference Range
Pregnanetriol (FMV urine)	164	46-269 nmol/dL (SG)
allo-Tetrahydrocortisol, a-THF (FMV urine)	131	57-370 nmol/dL (SG)
Tetrahydrodeoxycortisol (FMV urine)	26.3	<= 9.4 nmol/dL (SG)
Tetrahydrocortisone, THE (FMV urine)	3,002	146-797 nmol/dL (SG)
Tetrahydrocortisol, THF (FMV urine)	292	142-595 nmol/dL (SG)
17-Hydroxysteroids, Total*	3,617	143-1,897 nmol/dl (SG)

* Total values equal the sum of all measurable parts



2015 Page 2

Estrogens

Estrogens

		Reference Range
Estrone (FMV urine)*	19.1	3.0-52.0 mcg/g Creat.

* Luteal reference range shown

Phase	Reference Range
Follicular	2-39 mcg/g Creat.
Midcycle	11-46 mcg/g Creat.
Luteal	3-52 mcg/g Creat.
Menopausal	3-52 mcg/g Creat.
Male	2-8 mcg/g Creat.

Estradiol (FMV urine)*	3.6	1.0-17.0 mcg/g Creat.

* Luteal reference range shown

Phase	Reference Range
Follicular	1-13 mcg/g Creat.
Midcycle	4-20 mcg/g Creat.
Luteal	1-17 mcg/g Creat.
Menopausal	1-17 mcg/g Creat.
Male	1-4 mcg/g Creat.

Estriol (FMV urine)*	9.6	9.0-60.0 mcg/g Creat.

* Luteal reference range shown

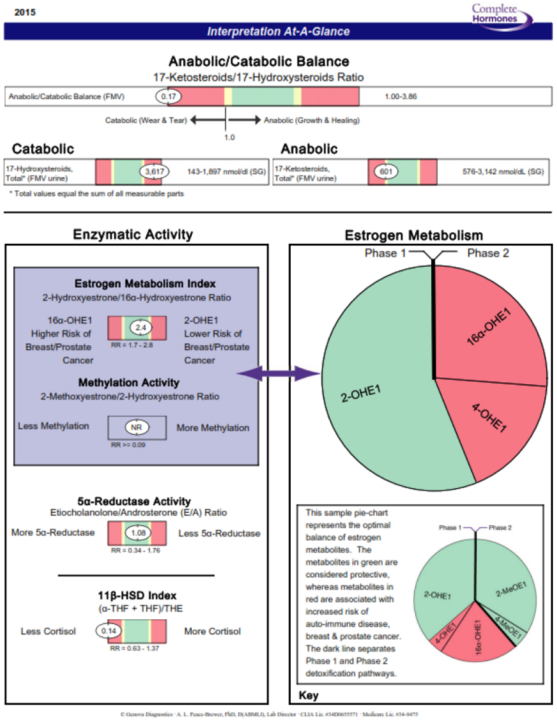
Phase	Reference Range
Follicular	3-48 mcg/g Creat.
Midcycle	20-130 mcg/g Creat.
Luteal	9-60 mcg/g Creat.
Menopausal	9-60 mcg/g Creat.
Male	2-19 mcg/g Creat.

Estrogen Metabolites

2-Hydroxyestrone (FMV urine)	33.9	9.2-76.6 mcg/g Creat.
16α-Hydroxyestrone (FMV urine)	14.1	2.4-20.3 mcg/g Creat.
4-Hydroxyestrone (FMV urine)	8.4	<= 5.3 mcg/g Creat.
2-Methoxestrone (FMV urine)	NR	>= 1.7 mcg/g Creat.
4-Methoxyestrone (FMV urine)	<dl	>= 1.9 mcg/g Creat.

Ratios

Anabolic/Catabolic Balance (FMV)	0.17	1.00-3.86
11β-HSD Index (FMV urine)	0.14	0.63-1.37
E/A: 5β/5α Ratio (FMV urine)	1.08	0.34-1.76
2-Hydroxyestrone/16α-Hydroxyestrone Ratio (FMV urine)	2.4	1.7-2.8
2-Methoxyestrone/2-Hydroxyestrone Ratio	NR	>= 0.09



2015

Complete Hormones

Interpretation At-A-Glance

Anabolic/Catabolic Balance

17-Ketosteroids/17-Hydroxysteroids Ratio

Anabolic/Catabolic Balance (FMV)	0.17	1.00-3.86

Catabolic (Wear & Tear) ← → Anabolic (Growth & Healing)

1.0

Catabolic			Anabolic		
17-Hydroxysteroids, Total* (FMV urine)	3,617	143-1,897 nmol/dl (SG)	17-Ketosteroids, Total* (FMV urine)	601	576-3,142 nmol/dL (SG)

* Total values equal the sum of all measurable parts

Enzymatic Activity

Estrogen Metabolism Index
2-Hydroxyestrone/16α-Hydroxyestrone Ratio

16α-OHE1 Higher Risk of Breast/Prostate Cancer — 2.4 (RR = 1.7 - 2.8) — 2-OHE1 Lower Risk of Breast/Prostate Cancer

Methylation Activity
2-Methoxyestrone/2-Hydroxyestrone Ratio

Less Methylation — NR (RR >= 0.09) — More Methylation

5α-Reductase Activity
Etiocholanolone/Androsterone (E/A) Ratio

More 5α-Reductase — 1.08 (RR = 0.34 - 1.76) — Less 5α-Reductase

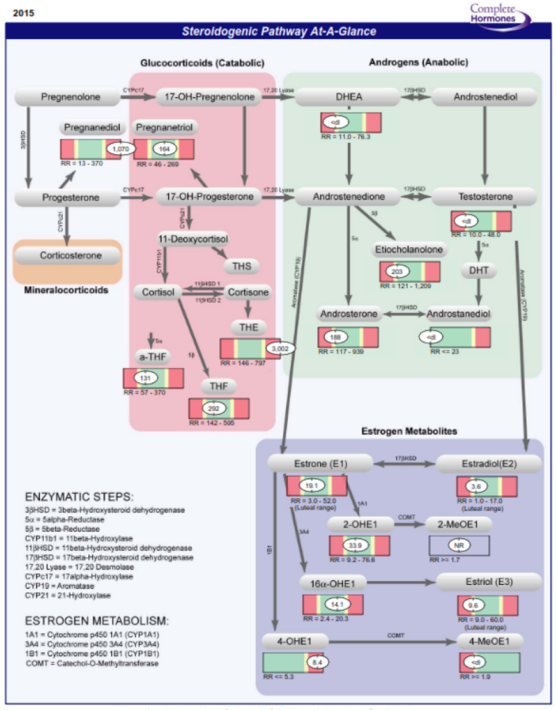
11β-HSD Index
(α-THF + THF)/THE

Less Cortisol — 0.14 (RR = 0.63 - 1.37) — More Cortisol

Estrogen Metabolism

This sample pie-chart represents the optimal balance of estrogen metabolites. The metabolites in green are considered protective, whereas metabolites in red are associated with increased risk of auto-immune disease, breast & prostate cancer. The dark line separates Phase 1 and Phase 2 detoxification pathways.

Key

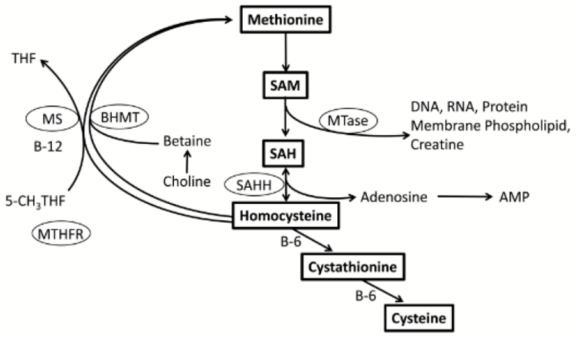


2016 Methylation Panel

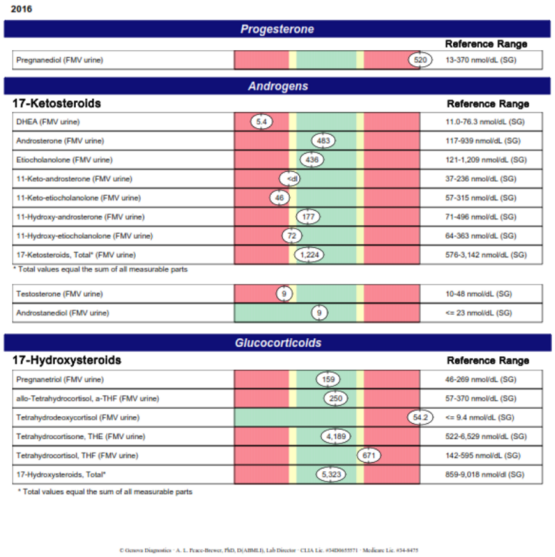
Methylation Profile; plasma

PRIMARY & INTERMEDIATE METABOLITES	RESULT/UNIT		REFERENCE INTERVAL
Methionine	3.0	µmol/dL	1.6 – 3.6
Cysteine	29	µmol/dL	20 – 38
S-adenosylmethionine (SAM)	111	nmol/L	86 – 145
S-adenosylhomocysteine (SAH)	12.6	nmol/L	10 – 22
Homocysteine	5.9	µmol/L	< 11
Cystathionine	0.01	µmol/dL	< 0.05

METHYLATION INDEX	RESULT	REFERENCE INTERVAL
SAM : SAH	8.8	> 4



2016 Hormone Metabolites



Complete Hormones (FMV)

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17-Ketosteroids

	Reference Range
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Androsterone (FMV urine) 483	117-939 nmol/dL (SG)
Etiocholanolone (FMV urine) 436	121-1,209 nmol/dL (SG)
11-Keto-androsterone (FMV urine) <dl	37-236 nmol/dL (SG)
11-Keto-etiocholanolone (FMV urine) 46	57-315 nmol/dL (SG)
11-Hydroxy-androsterone (FMV urine) 177	71-496 nmol/dL (SG)
11-Hydroxy-etiocholanolone (FMV urine) 72	64-363 nmol/dL (SG)
17-Ketosteroids, Total* (FMV urine) 1,224	576-3,142 nmol/dL (SG)

* Total values equal the sum of all measurable parts

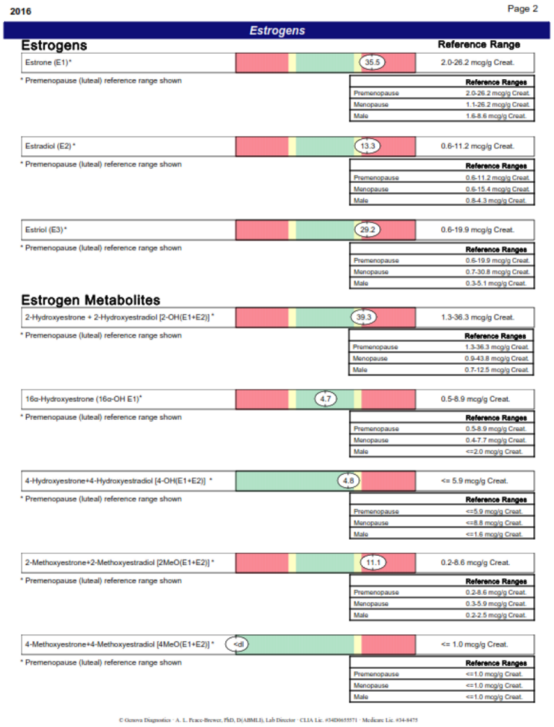
Testosterone (FMV urine) 9	10-48 nmol/dL (SG)
Androstanediol (FMV urine) 9	<= 23 nmol/dL (SG)

Glucocorticoids

17-Hydroxysteroids

	Reference Range
Pregnanetriol (FMV urine) 159	46-269 nmol/dL (SG)
allo-Tetrahydrocortisol, a-THF (FMV urine) 250	57-370 nmol/dL (SG)
Tetrahydrodeoxycortisol (FMV urine) 54.2	<= 9.4 nmol/dL (SG)
Tetrahydrocortisone, THE (FMV urine) 4,189	522-6,529 nmol/dL (SG)
Tetrahydrocortisol, THF (FMV urine) 671	142-595 nmol/dL (SG)
17-Hydroxysteroids, Total* 5,323	859-9,018 nmol/dl (SG)

* Total values equal the sum of all measurable parts



2016 Page 2

Estrogens

Estrogens

	Reference Range
Estrone (E1)* 35.5	2.0-26.2 mcg/g Creat.

* Premenopause (luteal) reference range shown

Reference Ranges	
Premenopause	2.0-26.2 mcg/g Creat.
Menopause	1.1-26.2 mcg/g Creat.
Male	1.6-8.6 mcg/g Creat.

Estradiol (E2)* 13.3	0.6-11.2 mcg/g Creat.

* Premenopause (luteal) reference range shown

Reference Ranges	
Premenopause	0.6-11.2 mcg/g Creat.
Menopause	0.6-15.4 mcg/g Creat.
Male	0.8-4.3 mcg/g Creat.

Estriol (E3)* 29.2	0.6-19.9 mcg/g Creat.

* Premenopause (luteal) reference range shown

Reference Ranges	
Premenopause	0.6-19.9 mcg/g Creat.
Menopause	0.7-30.8 mcg/g Creat.
Male	0.3-5.1 mcg/g Creat.

Estrogen Metabolites

2-Hydroxyestrone + 2-Hydroxyestradiol [2-OH(E1+E2)]* 39.3	1.3-36.3 mcg/g Creat.

* Premenopause (luteal) reference range shown

Reference Ranges	
Premenopause	1.3-36.3 mcg/g Creat.
Menopause	0.9-43.8 mcg/g Creat.
Male	0.7-12.5 mcg/g Creat.

16α-Hydroxyestrone (16α-OH E1)* 4.7	0.5-8.9 mcg/g Creat.

* Premenopause (luteal) reference range shown

Reference Ranges	
Premenopause	0.5-8.9 mcg/g Creat.
Menopause	0.4-7.7 mcg/g Creat.
Male	<=2.0 mcg/g Creat.

4-Hydroxyestrone+4-Hydroxyestradiol [4-OH(E1+E2)] * 4.8	<= 5.9 mcg/g Creat.

* Premenopause (luteal) reference range shown

Reference Ranges	
Premenopause	<=5.9 mcg/g Creat.
Menopause	<=8.8 mcg/g Creat.
Male	<=1.6 mcg/g Creat.

2-Methoxyestrone+2-Methoxyestradiol [2MeO(E1+E2)] * 11.1	0.2-8.6 mcg/g Creat.

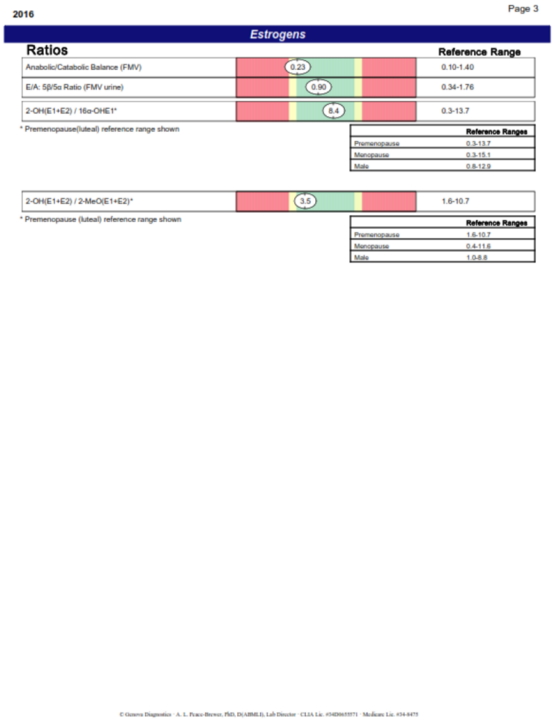
* Premenopause (luteal) reference range shown

Reference Ranges	
Premenopause	0.2-8.6 mcg/g Creat.
Menopause	0.3-5.9 mcg/g Creat.
Male	0.2-2.5 mcg/g Creat.

4-Methoxyestrone+4-Methoxyestradiol [4MeO(E1+E2)] * <dl	<= 1.0 mcg/g Creat.

* Premenopause (luteal) reference range shown

Reference Ranges	
Premenopause	<=1.0 mcg/g Creat.
Menopause	<=1.0 mcg/g Creat.
Male	<=1.0 mcg/g Creat.



2016 Page 3

Estrogens

Ratios

	Reference Range
Anabolic/Catabolic Balance (FMV) 0.23	0.10-1.40
E/A: 5β/5α Ratio (FMV urine) 0.90	0.34-1.76
2-OH(E1+E2) / 16α-OHE1* 8.4	0.3-13.7

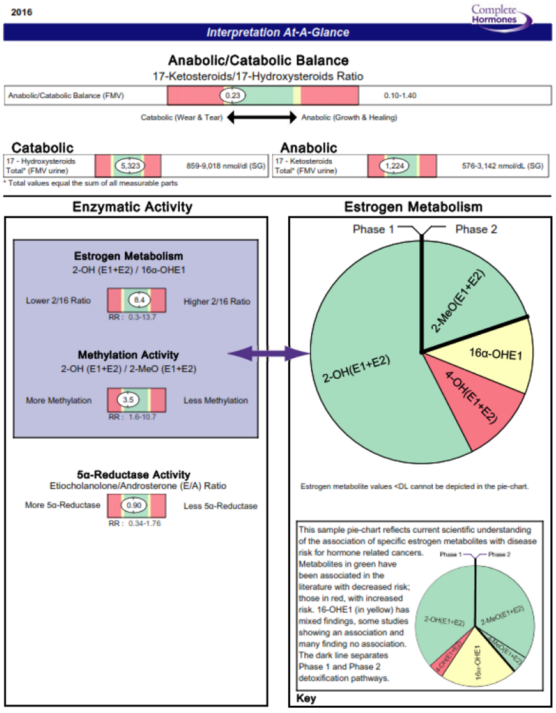
* Premenopause(luteal) reference range shown

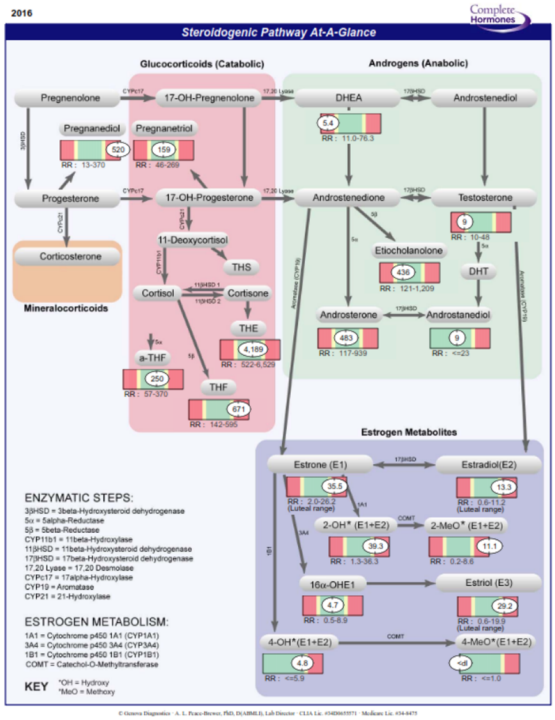
Reference Ranges	
Premenopause	0.3-13.7
Menopause	0.3-15.1
Male	0.8-12.9

2-OH(E1+E2) / 2-MeO(E1+E2)* 3.5	1.6-10.7

* Premenopause (luteal) reference range shown

Reference Ranges	
Premenopause	1.6-10.7
Menopause	0.4-11.6
Male	1.0-8.8



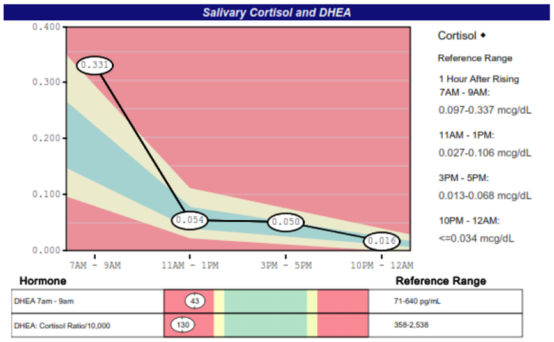


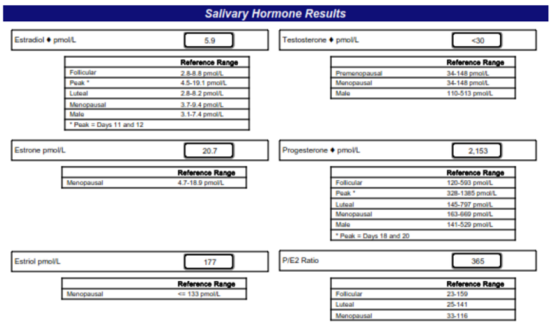
2016 Saliva

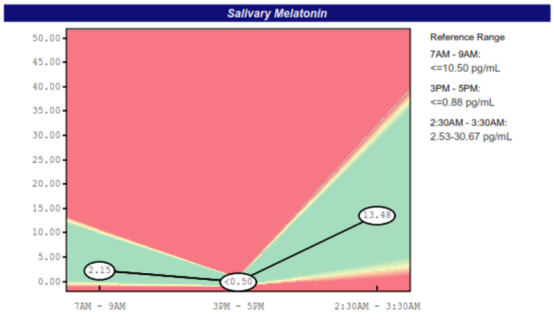
One Day Hormone Check - Salivary Profile

Therapeutic Cohort Results

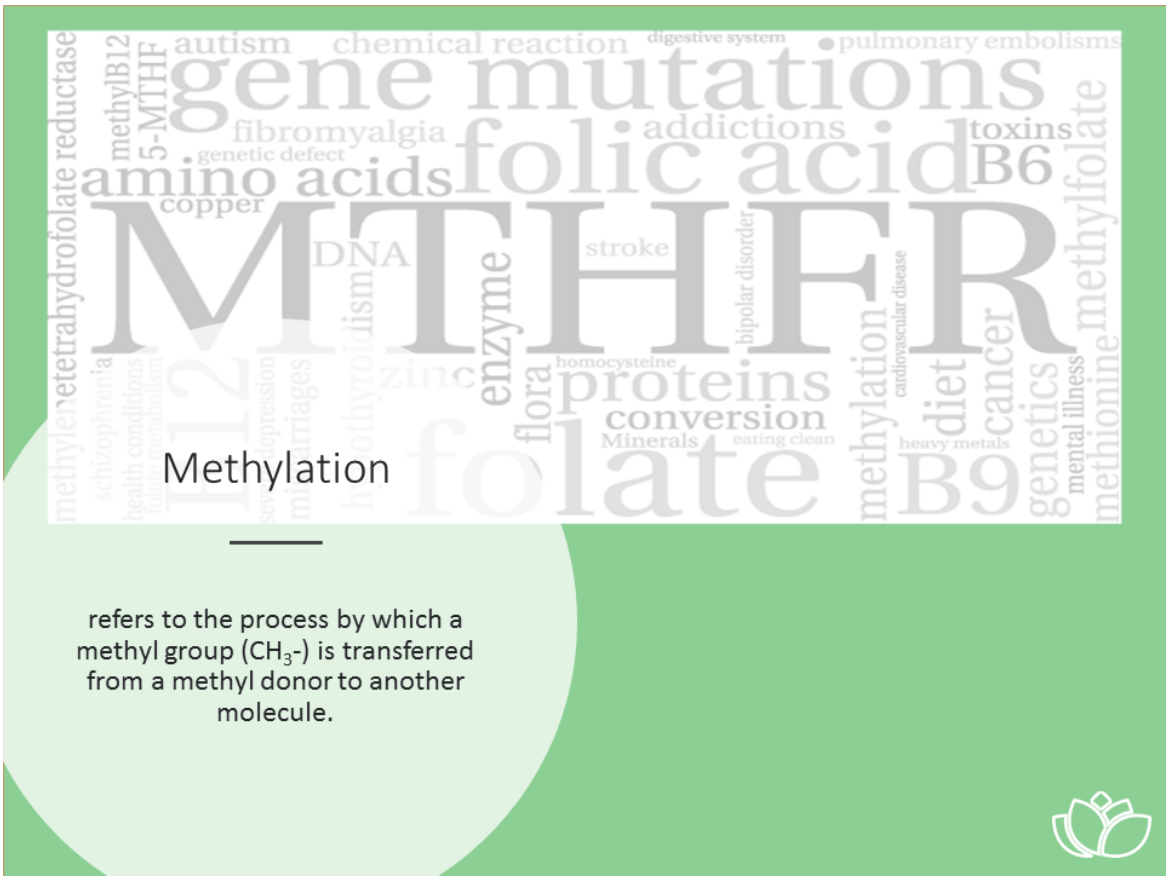
Hormone	Result †	QUINTILE DISTRIBUTION 1st 2nd 3rd 4th 5th	Therapeutic Range*
Estradiol (E2)	5.9		2.9-13.7 pmol/L
Estrone (E1)	20.7		5.5-26.1 pmol/L
Estriol (E3)	177		<=135 pmol/L
Testosterone	<30		34-183 pmol/L
Progesterone	2,153		174-1,417 pmol/L
P/E2 Ratio	365		29-192







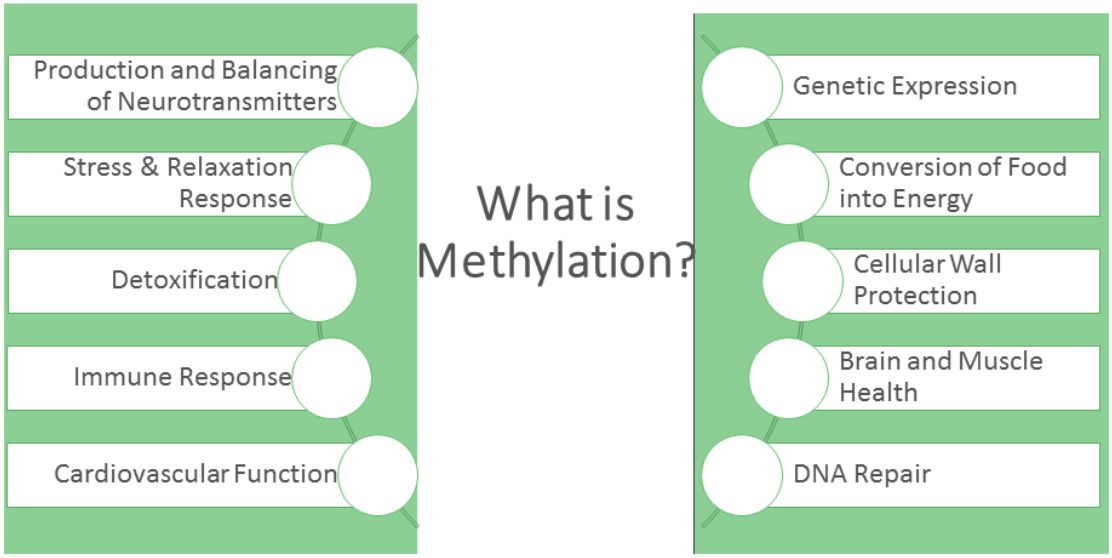
2: METHYLATION & GENETIC SNPS



Genetics 101

Methylation is a chemical reaction adding a methyl group to something such as a gene, enzyme, hormone, neurotransmitter, or vitamin in your body.

MTHFR is one of the more 'famous' genes however there are many more genes involved.



A Chemical reaction adding a “methyl group” to something such as a gene, enzyme, hormone, neurotransmitter or vitamin in your body

[VIDEO] https://www.youtube.com/embed/0sqW8IW6uXI?feature=oembed&fs=1&modestbranding=1&rel=0&showinfo=0

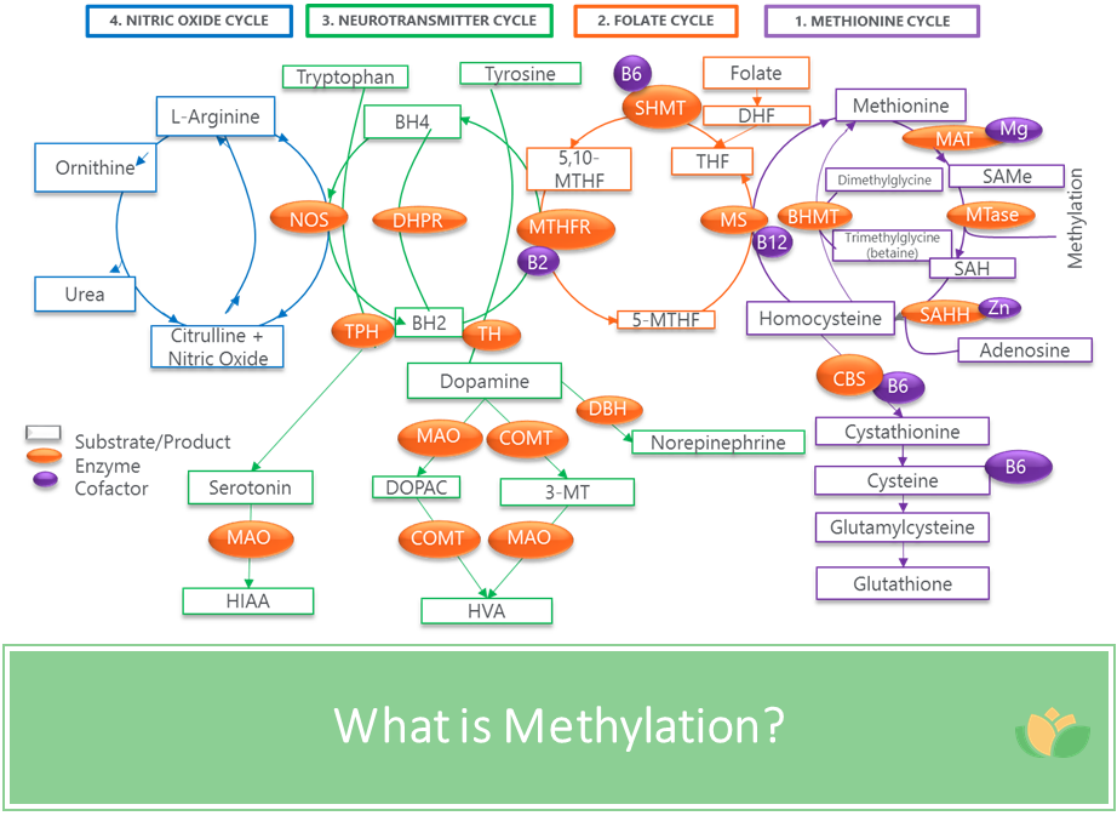
Not All SNPS Are The Same

- Homozygous = 2 variants
- Heterozygous = 1 variant
- Wild Type = No variant

Pathway Overview

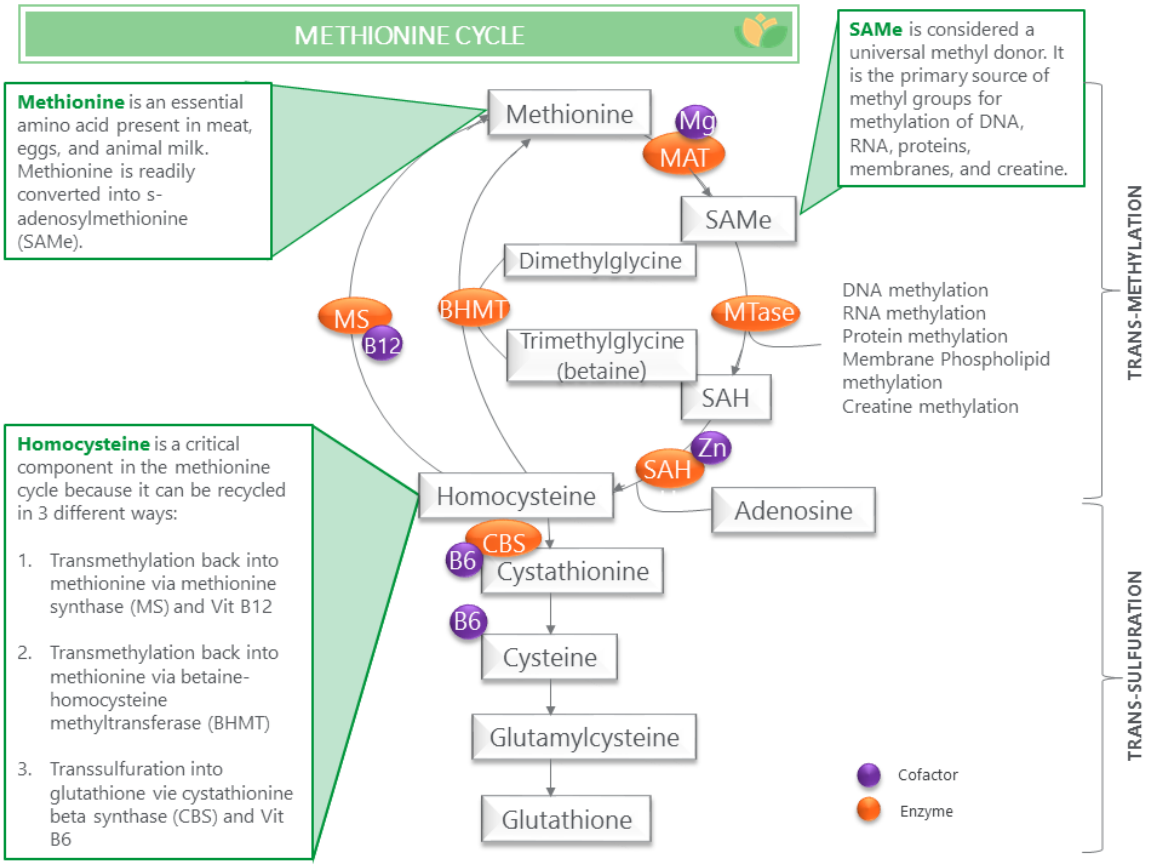
Some of the key processes methylation is involved in are:

- Detoxification
- Epigenetic Modification
- Neurotransmitter Synthesis
- Pyrimidine and Purine Synthesis

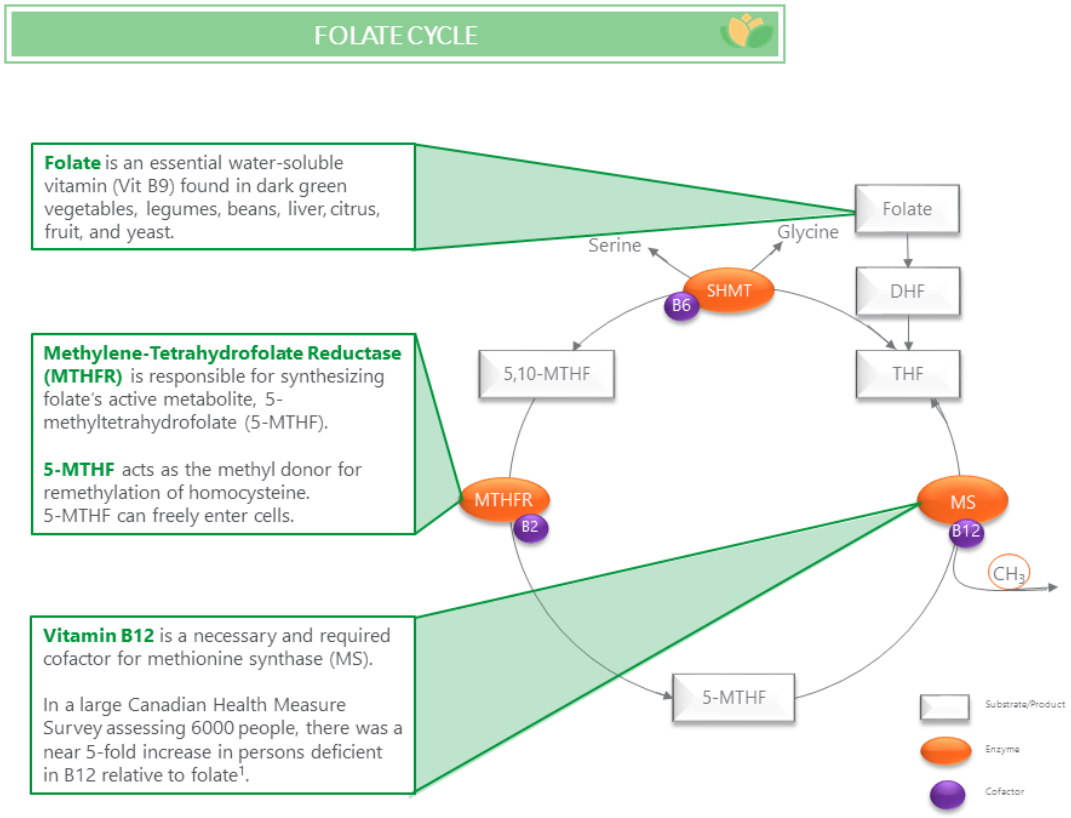


What is Methylation?

The Methionine Cycle



The Folate Cycle



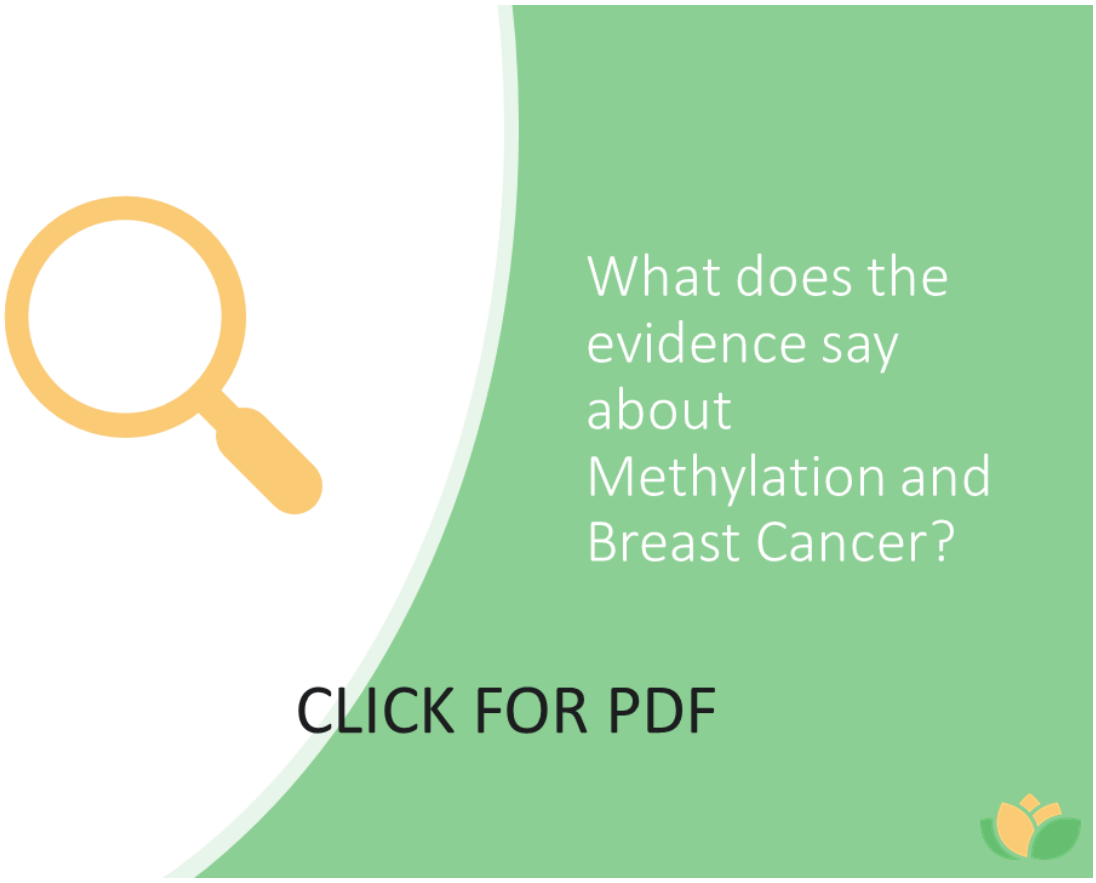
Estrogen Related SNPs

- MTHFR

- MTHFD1
- COMT
- CYP 1A1
- CYP 1B1
- GSH
- ESR1
- PGR
- SULT1
- STS

Key Breast Cancer Related SNPs

- MTHFR
- COMT
- CYP 19A1
- CYP 1B1
- CYP 2D6



(https://revitalizemed.com/wp-content/uploads/2020/05/Methylation-and-Breast-Cancer.pdf)

GENETIC POLYMORPHISMS

MTHFR C677T Treatment

MTHFR C677T can be enhanced by treatment with folate and/or vitamin B12.

- E.g., In a study that assessed individuals with high dietary folate intake (>225 mcg/day), serum folate levels were significantly lower in individuals with 677TT that those with 677CC[1].
- Authors recommended that individuals homozygous for 677TT consume approximately 1.4 times more folate to reach levels seen in individuals with 677CC of 677TC genotypes[1].

1. Nishio et al., 2008

Catechol-O-Methyl Transferase (COMT)

COMT is a responsible for the metabolism of monoamines and catechol estrogens.

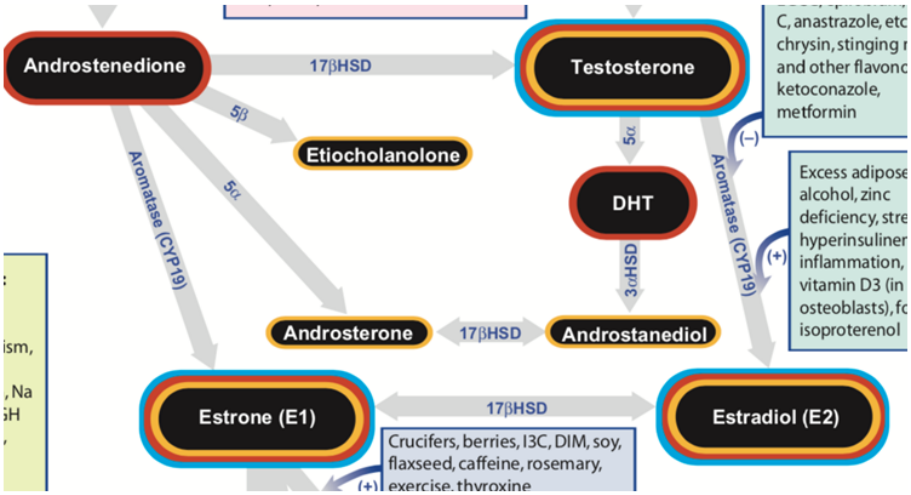
COMT V158M involves a base change from valine to methionine at base pair 158.

COMT V158M results in reduced COMT activity.

Reduced COMT activity is associated with higher dopamine and norepinephrine levels1, lower pain tolerance[2], and catechol estrogen accumulation (DNA damage)[3]

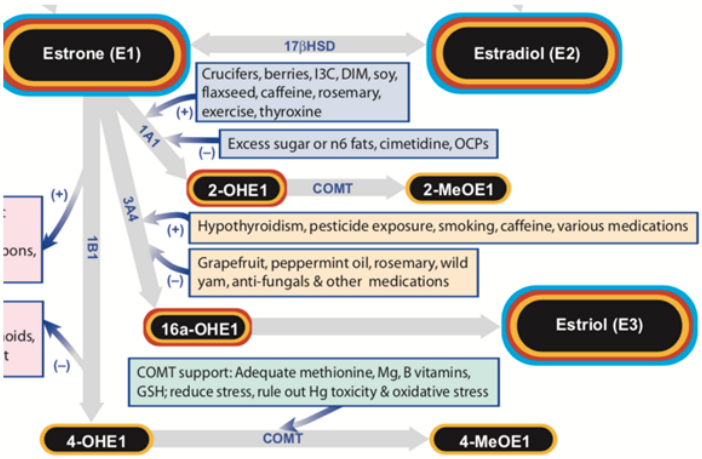
E.g., Individuals with homozygous 158MM genotype administered significantly more morphine post-surgery[2].

1. Kötyuk et al., 2015
2. Tan et al., 2016
3. Ashton et al., 2006



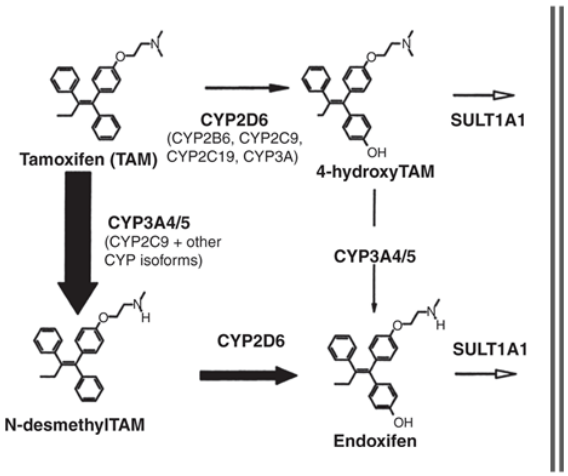
CYP 19A1

- Converts Androgens (androstenedione and testosterone) into estrogens (estradiol and estrone)
- If this is a fast version, it will make estrogen dominance worse



CYP 1B1

- Metabolizes estrogen in 4 OH estrogens
- If this is FAST, will increase the risk of estrogen dominance , especially if coupled with a slow COMT



Genetics of CYP2D6

Genetic Type	CYP2D6 Activity	Ethnic Differences (Approximate)
Poor metabolizers	None	Caucasians 6%-10% Mexican Americans 3%-6% African Americans 2%-5% Asians ~1%
Intermediate metabolizers	Low	Not established
Extensive metabolizers	Normal	Most people are extensive metabolizers
Ultrarapid metabolizers	High	Finns and Danes 1% North Americans (white) 4% Greeks 10% Portuguese 10% Saudis 20% Ethiopians 30%

CYP 2D6

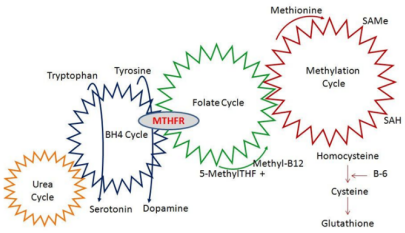
Converts Tamoxifen into endoxifen which is the active metabolite

Symptoms of Methylation Imbalance

- Breast Cancer

- Elevated Homocysteine
- Endometrial Cancer
- Estrogen Imbalances
- Fatigue
- Fibroids, Endometriosis, Heavy Periods
- Intolerance to Oral Contraceptives
- Migraines
- Miscarriages
- Sensitivities to Sulfite Containing Foods

Which Patients Should Be
Evaluated for Methylation Issues?



Those with:

- Breast Cancer
- Elevated Homocysteine
- Endometrial Cancer
- Estrogen Imbalances
- Fatigue
- Fibroids, Endometriosis, Heavy Periods
- Intolerance to Oral Contraceptives
- Migraines
- Miscarriages
- Sensitivities to Sulfite Containing Foods

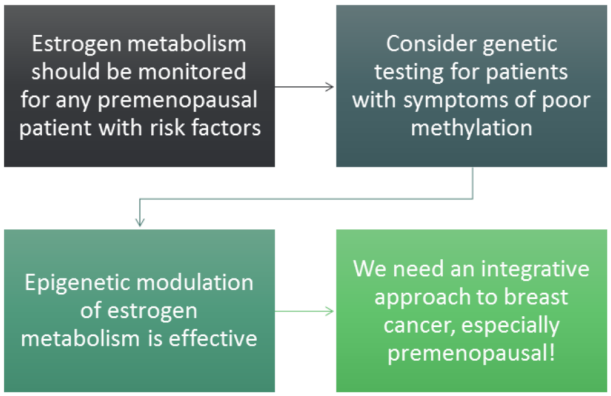
We DON'T Treat the SNP

It is important to evaluate the entire picture and not treat the SNP. We need to look at the entire methylation and adjoining pathways, co-factors, environmental, and lifestyle factors when assessing methylation.

3: BEING PROACTIVE AND PREVENTATIVE

[VIDEO] https://www.youtube.com/embed/mhH5ujgWtWs?feature=oembed&fs=1&modestbranding=1&rel=0&showinfo=0

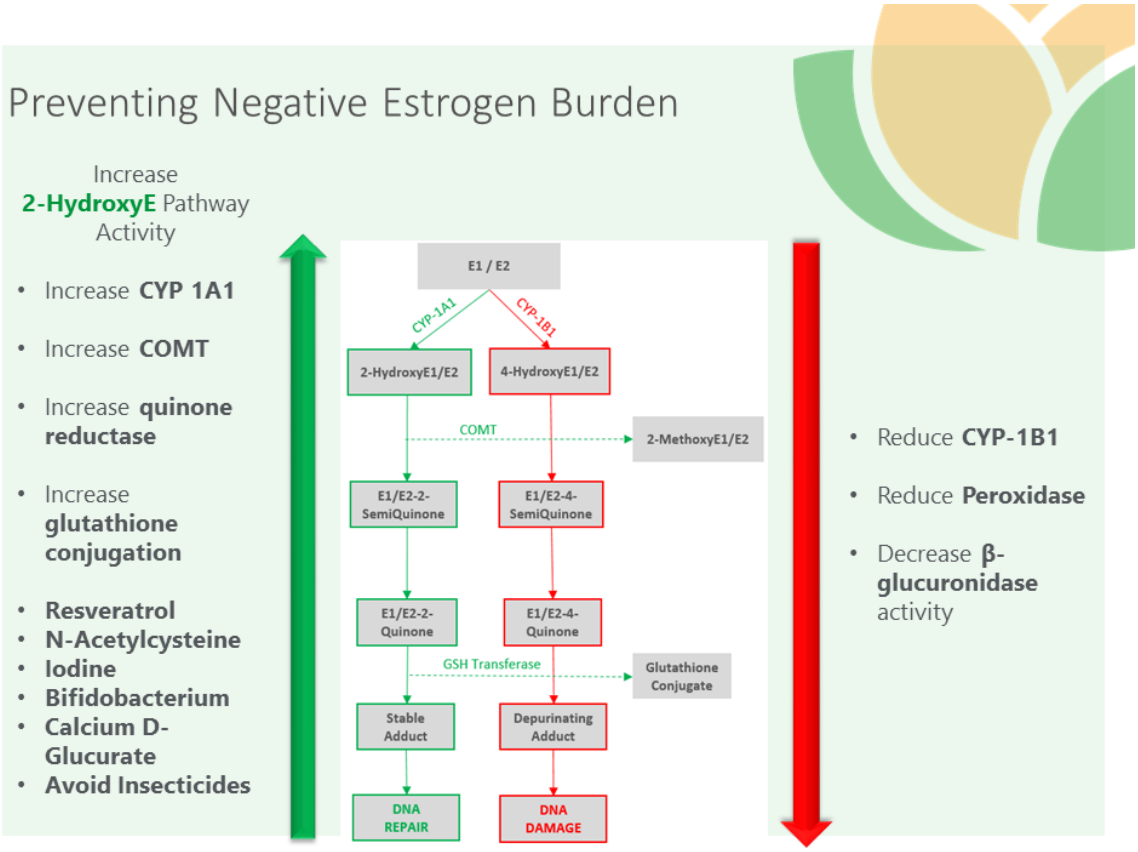
In order to have a positive impact on the number of incidences of breast cancer we must not only educate practitioners we must also bridge the gap between patients and health care providers.



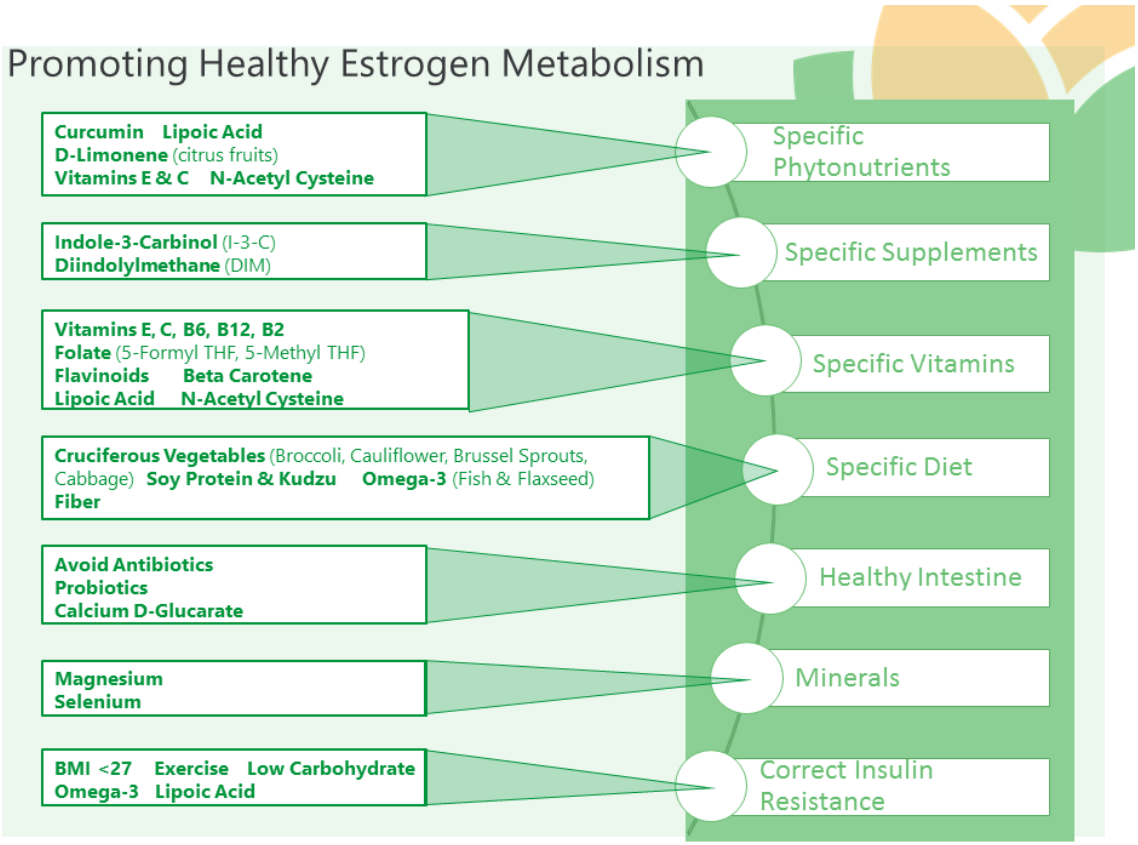
Preventing Estrogen Burden

Remember it is easier to increase CYP 1A1 than it is to decrease CYP 1B1

- Support COMT
- Increase Glutathione Conjugation
- Supplements such as
  - Resveratrol
  - NAC
  - Bifidobacterium
  - Calcium D-Glucurate
  - Potentially, Iodine
- Avoid Pesticides
- Reduce Peroxidase



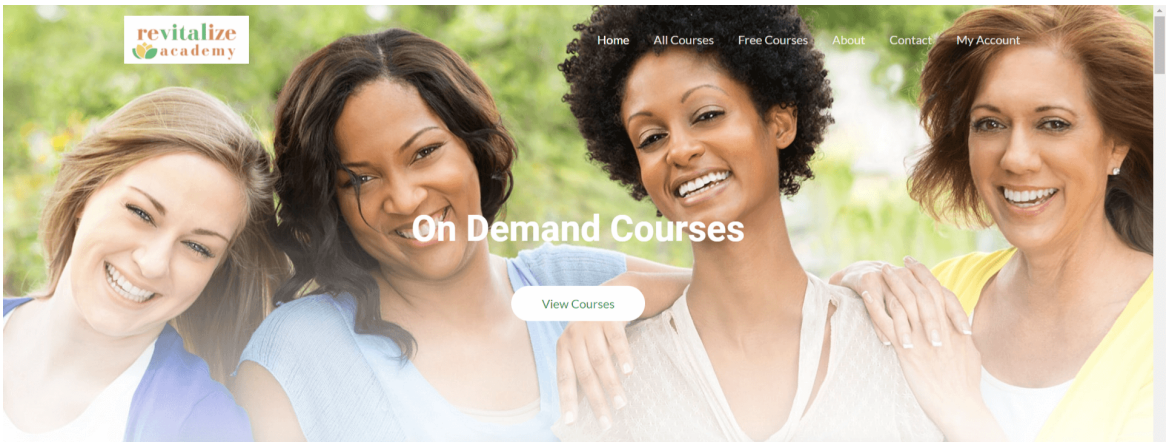
Other Ways to Optimize Estrogen Metabolism



Patient & Provider Education

Perhaps the most important part of reducing the number of deaths from breast cancer lies in paying it forward. Revitalize Academy was born out of a passion and mission to that very thing by educating and empowering others to take a **proactive** and **preventative** approach to their health and wellness.

(https://academy.revitalizemed.com)



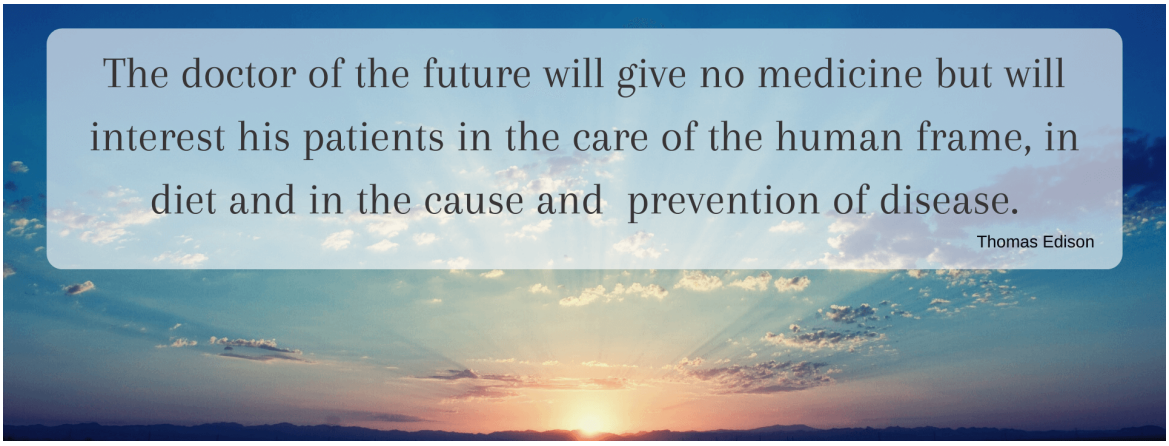
(https://academy.revitalizemed.com)

The academy has in-depth series on women's hormones, men's hormones, and advanced modules in a variety of topics such as, Breast Cancer. All of the modules present complex material in a way that allows individuals to understand the "what, how, and why" behind hormones and their health.

- Actionable Training
- Easy to Understand
- Premium Content

(https://academy.revitalizemed.com/courses/breast-cancer/)

What Next?



CV

TARA SCOTT, MD

CMO and Founder,
Revitalize Medical Group

PROFILE

Dr. Scott has been in front of an audience since she was the president of speech team in high school. This evolved in educating on hormone therapy, having taught doctors in five continents about an integrative approach. With over 20 years' experience practicing OB/GYN, and additional training in Integrative and Functional medicine, Dr. Scott shares a wealth of information by lecturing.

Recently, she put her knowledge to an online, on demand learning academy for both patients and providers.

CONTACT

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tscott@revitalizemed.com

EDUCATION

University of Akron June 1986- August 1988
B.S in Natural Science, Summa Cum Laude

Northeastern Ohio Medical University- 1988-1992
Medical Doctor

Internship- Akron General Medical Center- Transitional Year 1992-1993

Residency- OB/GYN- Summa Health. 1993-1997

Advanced Fellowship, Functional Medicine- A4M, 2010-2012

WORK EXPERIENCE

Summa Health. Medical Director, Integrative Medicine
June 2017– Present
Hired to design and run an Integrative Medicine Department

Revitalize Medical Group. Chief Medical Officer and Founder
June 2013- Present
Founded the areas first Functional and Integrative Medicine Practice- training and supervising NPs, PAs, and NDs

LP3 Network- Speaker- 2010 to present
Created a CME course on an Integrative Approach to Hormone Balancing
Presented in the US, Canada, Australia, Philippines

Paragon Health Associates Feb 2006 until June 2016
Ob/GYN Group Practice

Clinical Assoc. Professor, NEOMED- Lectures OB/GYN residents

Lifespan Women's Health Care
May 2004–February 2006
Started an OB/GYN practice from the ground up

Valley OB/GYN – Staff Physician
1997-2004

CERTIFICATIONS/MEMBERSHIP

-Board Certified, American Board of OB/GYN- December 1999
-Menopause Practitioner- North American Menopause Society- 2006
-Advanced Fellow in Anti-Aging and Regenerative and Functional - Medicine- 2012
-American Board of Integrative Medicine May 2016 (APBS)
-Institute of Functional Medicine- 2017- AFMCP, Hormone, Immune, GI

RESEARCH PRESENTATIONS AND SPEAKING ENGAGEMENTS

"Elective Repeat Cesarean Delivery Versus Trial of Labor: Morbidities in a Community Hospital Setting" - Presented at ACOG 46th Annual Clinical Meeting- May 1998

"Menopause Matters" Nurses CME day at Summa Hospital, October 2007
Also presented to the public May 2009

"Menopause for Residents" Grand Rounds Presentation at Summa Health Systems, May 2008, June 2009, May 2010

"Polycystic Ovarian Syndrome" Grand Rounds Presentation at Summa Health Systems, June 2010; Feb 2013

Women's Health Day- Keynote speaker- July 2011, July 2012- Jewish Community Center
"Hormone Balance and Health"

Go Red for Women- Medical Message, May 2012- Akron Quaker Hilton-
American Heart Association

"Menopause Update" Grand Rounds Summa Health Systems February 2013

"Women's Wellness" Naples, Florida March 2013- Summa Circle of Women Philanthropists

"Update on Hormonal Contraception" Grand Rounds, Summa, May 2013

"Menopause Update" First Annual Geriatric update- AGMC, Feb 2014

"Go Red for Women: The Heat is on! Hormones and your Heart" Feb 2015

"An Integrative approach to Thyroid Disease" Pharmacology Conference for Advanced Practice Nurses, Summa Health System, February 2018

"An Integrative Approach to Breast Cancer" Spring Meeting, A4M, May 2019

INTERNATIONAL SPEAKING ENGAGEMENTS

"Introduction to Hormone Balancing" – Sao Paolo, Brazil, July 6, 2013-
Consulfarma National Conference of Compounding Pharmacies

"DHEA and Testosterone: The Forgotten Hormones of Menopause"- Singapore
August 24, 2013. Singapore International Congress of Ob/Gyn
May 2016, International OB/GYN meeting in
Barcelona, Spain

Functional Hormone Restoration Therapy- 2-day course for LP3 Network. Presented since 2 2010 around the US, Canada, Australia, New Zealand, Malaysia, Philippines

ABSTRACT

There seems to be an increase incidence of premenopausal breast cancer in the United States. Traditionally, HRT has been blamed as a causative factor and also genetics with BRAC 1 and 2. However, these premenopausal patients are not on hormone therapy and many are negative for BRAC genes. My hypothesis is that there are other single nucleotide pleomorphisms (SNPs) that put a patient and increased risk of breast cancer, namely MTHFR 677, MTHFR 1298, and COMT.

MTHFR and COMT genes are involved in methylation processes in the body. This process is a large component of Phase 2 detoxification, especially for estrogen. My theory is that patients with SNPs in MTHFR and COMT have an impaired ability to get rid of estrogens and thus have an accumulation or back up of Estrone or the toxic metabolite 4-OH Estrone which can increase the risk of breast cancer. As a result, there is an imbalance in the hormones that cause hyperplasia (estrogens) and regulation an apoptosis (progesterone) in the breast.

Goals and Objectives:

- Review Estrogen detoxification and discuss epigenetic modulation of the enzymes involved
- Discuss genomics and methylation
- Demonstrate which SNPs may possibly be involved with breast cancer risk
- Provide a literature search on articles already published about methylation and breast cancer risk
- Demonstrate a case study where identifying methylation defects and epigenetic modulation was effective at decreasing harmful 4 OH estrone metabolites.
- Detail a plan to make prevention the target rather than early detection through
  - Raising awareness of practitioners regarding methylation and breast cancer, and an integrative approach
  - Educate patients about hormone risks factors that are tied to increased breast cancer risk- through the Revitalize Academy

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