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Nutrigenomics

Reproductive Hormones

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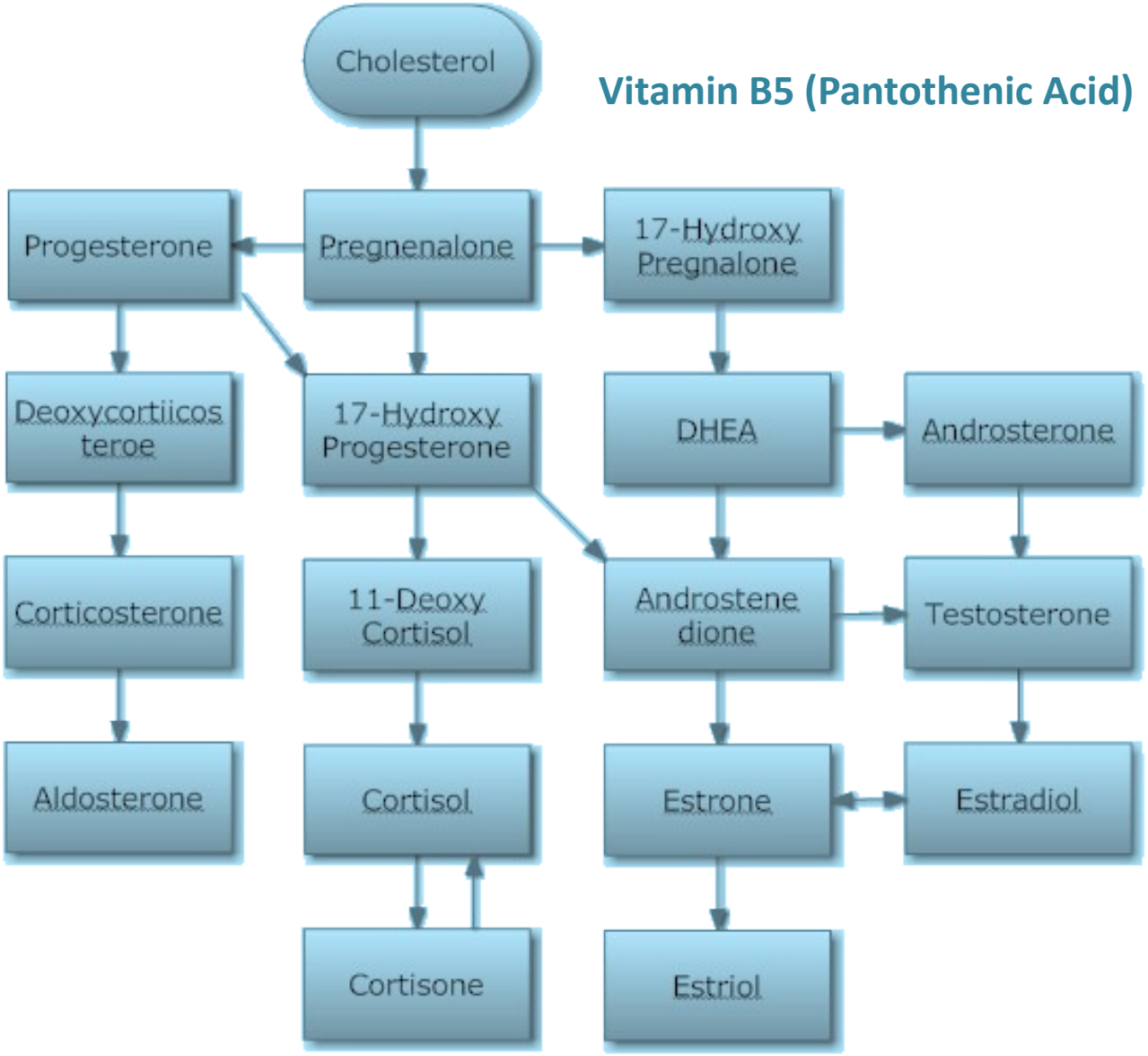
Steroid Hormones



Steroid Hormones To Measure in Blood

- Pregnenalone
- Progesterone
- Estrogen
  - Estrone
  - Estradiol
  - Estriol
- Testosterone
- DHEA-S
- Cortisol

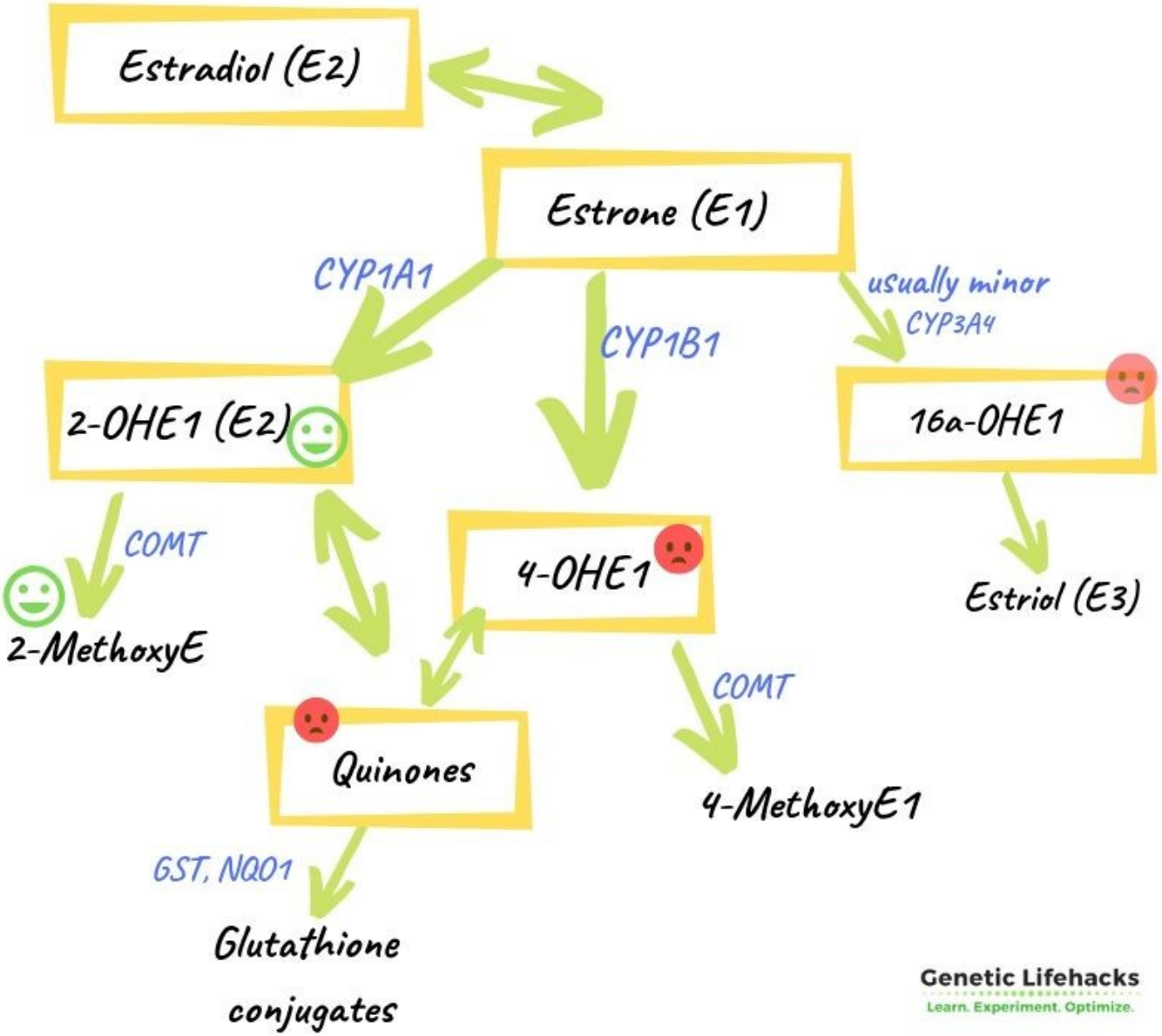
Signs Of Excess Estrogen In Women

- Weight gain
- Heavy periods
- Fibroids
- PMS
- Fibrocystic breasts
- Loss of sex drive
- Fatigue, depression, anxiety
- Hormone sensitive cancers

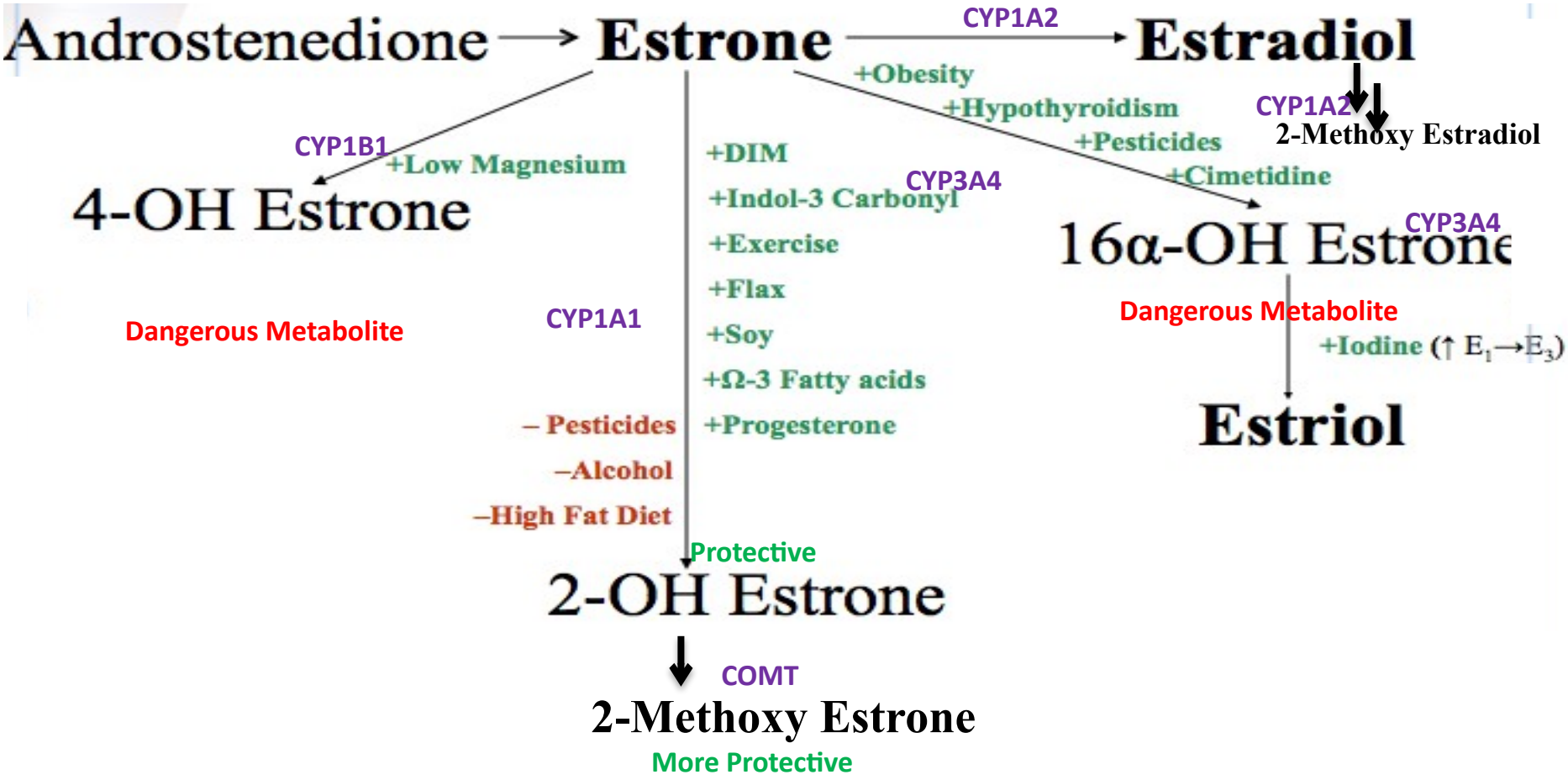
Signs Of Excess Estrogen In Men

- Gynecomastia (a.K.A. man boobs)
- Sexual dysfunction
- Loss of muscle mass
- Fatigue, depression, anxiety
- Hormone sensitive cancers

Estrogen elimination



Estrogen Genetics And Metabolism



How Caffeine Effects Estrogen Metabolism

- CYP1A2
- B vitamins and magnesium depletion → low progesterone ➔ estrogen dominance
- Increases cortisol ➔ less estrogen, progesterone and androgens
- Blocks adenosine A2A receptors in the brain ➔ decreased sleep
- Associated with miscarriage (https://www.ajog.org/article/S0002-9378(07)02025-X/fulltext)
- Increases inflammation - https://pubmed.ncbi.nlm.nih.gov/20178632/

CYP1A2 Research

Most active in catalyzing 2-hydroxylations

Between 40% and 50% of estrogens are hydroxylated at the C-2 position

Higher CYP1A2 activity was postulated to be associated with reduced risk for breast cancer

Caffeine has been used to evaluate CYP1A2 activity *in vivo*

CYP1A2 function was positively related to insulin and weakly, related to IGF-1 levels

Because both insulin and IGF-1 levels linked to increased risk for breast cancer and/or recurrence it suggests that CYP1A2 function is associated with increased rather than decreased breast cancer risk as hypothesized.

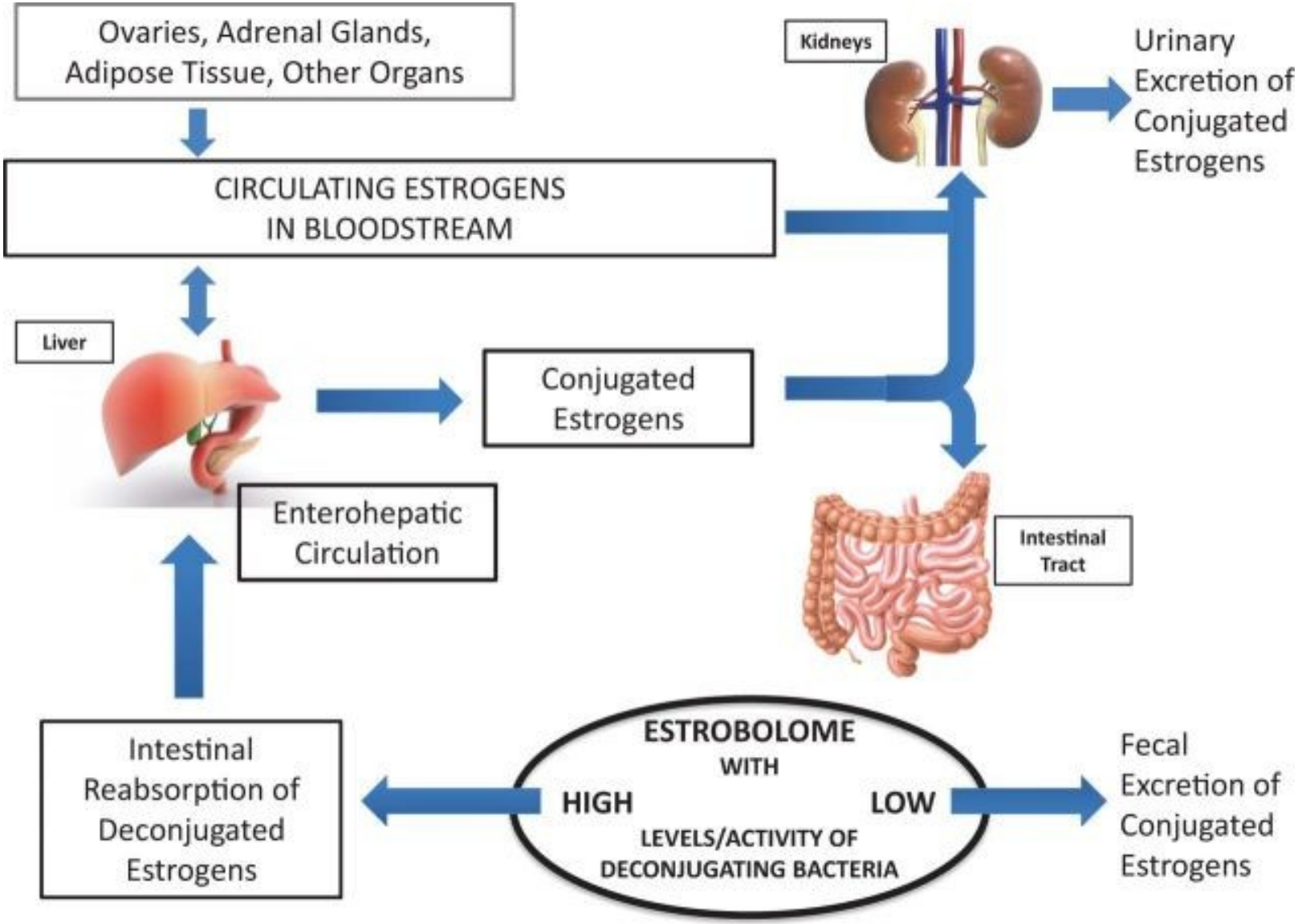
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC468638/#:~:text=CYP1A2%20is%20a%20major%20phase,%2D2%20position%20%5B4%5D

Caffeine and Breast Health

- Increased CYP1A2 function associated with increased risk for breast cancer
- Caffeine can induce CYP1A2 activity
- Dr. Anita Johnson says the most common culprit for breast pain is coffee

DETOX SNPs Related to Estrogen

- **CYP1A1:** Detoxifies polycyclic aromatic hydrocarbons - exhaust fumes, charbroiled meats, etc.
- **CYP1A2:** Caffeine and estrogen metabolism - 4-hydroxy estrogen
- **CYP1B1:** Helps detoxify estrogen - upregulation of the 4-OH estrogen
- **CYP3A4:** Metabolism of 60% of all known drugs – the most abundant detoxifying enzyme in the liver; metabolizes testosterone, cortisol, estrogen, and other steroids, plus organophosphates. Grapefruit juice inhibits; milk thistle inhibits in-vitro
- **GSTP1:** One of the glutathione S-transferase enzymes; detoxifies water-soluble environmental toxins, including many solvents, herbicides, fungicides, lipid peroxides, and heavy metals (e.g., mercury, cadmium, and lead).



https://pubmed.ncbi.nlm.nih.gov/27107051/

Estrogen Metabolism SNPs

Gene & Variation	rsID	Risk Allele	Function	Health Risks	Actions to Take to Protect: Avoid/Reduce These: Xeno-Estrogens *	Caffeine	Alcohol	Exposure to cigarette smoke	Exposure to gas fumes	Acid-blocking Rx	Tylenol & other Rx	Char-broiled meat	Processed meats	Sugar	Processed Foods	Cosmetics and cleaners	Pesticides	Heated & oxidized fats	Increase These: Exercise and Sweat	Hydration	Phase1 enhancing foods**	Omega 3 fats	Antioxidant intake	Foods that enhance Phase 1	Green Leafy Veggies	Sulfur-rich foods/MSM	Cruciferous vegetables	Mindfulness practices	Glutathione precursors	Glucoraphanin/Sulforaphane	Milk Thistle/Liver Support	Iron if deficient	Selenium	B vitamin intake	Folate (Vitamin B9)	Vitamin B12	Vitamin A	Vitamin C	Vitamin D	Vitamin E	Lab Testing: CBC	Vitamin D	Homocysteine	Hemoglobin A1c	Blood Spot Fatty Acid	DUTCH Test	Organic Acids	Stool Analysis	Advanced Lipid
CYP1A1 *2CA4889G C2453A	rs1048943 rs1799814	C T	• Detoxifies polycyclic aromatic hydrocarbons • Metabolizes excess estrogen • Responsible for 2-OH estrogen.	• uterine fibroids • fibrocystic breasts • cancer	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓			✓				✓		✓		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
CYP1A2 164A>C	rs762551	C	• Caffeine metabolism • Estrogen metabolism – upregulation of 4-OH, • Detoxifies acetaminophen • Detoxifies aflatoxin	• uterine fibroids • fibrocystic breasts • breast cancer • ovarian cancer • prostate cancer	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓			✓				✓		✓		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
CYP1B1 L432V N453S R48G	rs1056836 rs1800440 rs10012	C C C	• Helps detoxify estrogen • upregulation of the 4-OH estrogen	• uterine fibroids • fibrocystic breasts • breast cancer	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓			✓				✓		✓		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
CYP3A4 *1B	Rs2740579	C	• Breakdown of over 60% of drugs, including steroids • breakdown of organophosphate insecticides (e.g. parathion). • 16-OH estrogen.	• Prostate cancer • uterine fibroids • fibrocystic • breast cancer	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓			✓				✓		✓		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
HSD3	rs3765945	C	• Aids with the production of all classes of steroid hormones	• Essential hypertension • aldosterone level	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓			✓				✓		✓		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

Major Progesterone SNPs

- ✓ **PGR** – Progesterone Receptor
- ✓ **CYP3A4** – Progesterone Metabolism
- ✓ **CYP2C19** - rs4244285, CYP2C19*2, risk = A for non-functioning enzyme leading to decreased progesterone metabolism
- ✓ **APOE E4** – linked to highe luteal progesterone levels in women

PGR - The Progesterone Receptor

- ✓ **rs1042838 V660L**, risk = A for increased progesterone receptor, increased relative risk of ovarian cancer, uterine fibroids, breast cancer, endometrial cancer
- ✓ **rs71767**, risk = G for increased risk of preterm birth
- ✓ **rs10895068**, risk = A for increased relative risk of breast cancer, endometrial cancer
- ✓ **rs1042839**, risk = G for decreased risk of ovarian cancer

CYP3A4 - Progesterone Metabolism

Codes for a liver enzyme that is important in breaking down progesterone

- ✓ **rs4987161** risk=G for decreased function of enzyme
- ✓ **rs4986909** CYP3A4*13 risk = A for decreased function of the enzyme.
- ✓ **rs2740574** CYP3A4*1B, risk = C for altered function of the enzyme
- ✓ **rs4986910** CYP3A4*3 risk = G for decreased function
- ✓ **rs4986907**, Risk = T: CYP3A4*15A for decreased function

Major Testosterone SNPs

- ✓ **SHBG** – Sex Hormone Binding Globulin
- ✓ **FAM9B** – protein in the testes that is thought to be related to the formation of sperm. rs5934505, risk = T for lower average serum and free testosterone levels
- ✓ **FSHB** - regulates the function of either the ovaries or the testes. rs10835638, risk = T for risk of low follicle-stimulating hormone levels, reduced free testosterone and resulting in increased risk of male infertility
- ✓ **LIN28B** – codes for a cold-shock protein that is expressed in the testes and placenta. rs7759938 risk = C for lower testosterone levels

SHBG – Sex Hormone Binding Globulin

These variants associated with lower testosterone levels – the more minor alleles the men carried, the likelier they were to have low testosterone levels (<300ng/dl).

- ✓ **Rs12150660,** Risk = G for lower average free testosterone
- ✓ **rs6258**, risk = T for lower free testosterone, decreased SHBG binding affinity for testosterone (rare genotype)
- ✓ **rs6259**, risk = A for increased SHBG levels
- ✓ **rs1799941**, risk = A for higher SHBG levels, higher total testosterone levels

Major DHEA SNPs

Studies on twins and siblings show that DHEAS levels are about 60% heritable. Thus, while genetics plays a big role in DHEA and DHEAS levels, lifestyle and diet also are important here.

- ✓ **Intergenic region**, rs2185570, risk = C for lower DHEAS levels
- ✓ **TRIM4 gene**, rs17277546, risk = A for lower DHEAS levels
- ✓ **SULT2A1 gene**
  - ➢ **rs182420**, risk = C for somewhat lower levels of DHEAS
  - ➢ **rs2637125,** risk = A for decreased DHEAS
  - ➢ **rs2910397**, risk = T for higher DHEAS to DHEA ratio

Genetic Lifehacks

Learn. Experiment. Optimize.

http://drritamarie.s3.amazonaws.com/materials/BioFit/GeneticLifeHacks-Hormones.pdf

Hormones Topic Summary

Your genetic variants can impact your body's hormone production.
Please see the linked articles for details and complete references.

Article: Uterine Fibroids

Gene	RS ID	Effect Allele	Your Genotype	Notes About Effect Allele
ACE	rs4343	G	AG	Increased risk of fibroids
XPC	rs2228000	A	GG	Decreased risk of fibroids
XPC	rs873601	A	AG	AA: Increased risk of fibroids

SelfDecode™

http://drritamarie.s3.amazonaws.com/materials/BioFit/SelfDecode-FemaleReproductive.pdf

Female Sexual & Reproductive Health

Summary Report

SelfDecode

Reproductive Hormones

Reproductive hormones maintain your sexual and reproductive health. They affect everything from sex drive to sperm production, ovulation, and menstruation. A decline in these hormones is natural with age, but when they get out of balance, they can create problems for people of any age.

Your genetics of hormones like testosterone, estradiol, and DHEAS can tell you a lot about your reproductive health but also about many other aspects, including mental health and metabolism. This may help you make smarter choices about your health regimen.

TYPICAL LEVELS
Estradiol
Likely typical estradiol levels

HIGHER LEVELS
Bioavailable Testosterone (F)
Likely higher bioavailable testosterone levels

HIGHER LEVELS
SHBG
Likely higher SHBG levels

TYPICAL LEVELS
Testosterone (F)
Likely typical testosterone levels

TYPICAL LEVELS
DHEAS
Likely typical DHEAS levels

TYPICAL LEVELS
Prolactin
Likely typical prolactin levels

TYPICAL LEVELS
FSH
Likely typical FSH levels

http://drritamarie.s3.amazonaws.com/materials/BioFit/SelfDecode-HormoneHealth.pdf

