

Estrogen Gene Testing

A Woman's Guide



FERTILITY

BIRTH CONTROL MEDICATION



PREGNANCY

IN VITRO FERTILIZATION



BREAST CANCER

RECURRENCE & RISK REDUCTION



MENOPAUSE

HORMONAL REPLACEMENT THERAPY

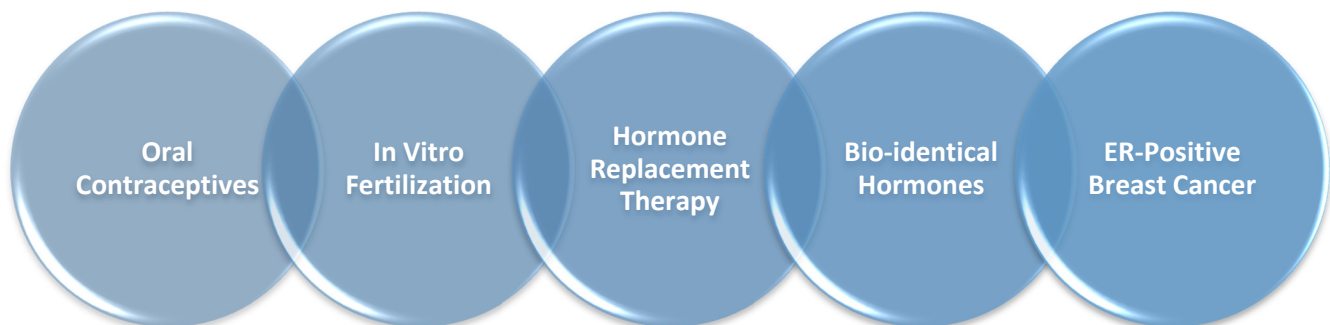
ESTROGEN: THE GOOD AND THE BAD

Estrogen is a hormone that is critically important in many biological processes. It is important for normal growth and development, and it controls sexual maturation and reproduction in women. There are two sources of estrogen; internal and external. Internal estrogen is made in the ovaries. The ovaries produce lots of estrogen during a woman's reproductive years, from the time a woman starts having menstrual periods to the time she enters menopause. External sources of estrogen are medication such as oral contraceptives, hormone replacement therapy (HRT), bio-identical hormones, and fertility treatments.

There are many types of estrogen in women's bodies. Some estrogens are good and some are bad. Even internal sources of estrogen can be bad for some women. Volumes of research have shown that the more estrogen that circulates within a woman's body throughout her life, the greater her chances of developing breast cancer.¹ The longer your ovaries produce estrogen (start having periods at a young age, late to start menopause), the greater your breast cancer risk.

External sources have well documented risks. Oral contraceptives often contain one or more types of estrogen, which provides a signal to the ovaries not to release an egg. Unfortunately, this oral estrogen exposure also increases breast cancer risk in the women who take the pill.² A woman's risk of breast cancer also goes up considerably when she takes hormone replacement therapy or HRT.^{3,4} Bio-identical HRT, or so-called "natural" HRT formulations, also contain estrogens and *also* increase breast cancer risk.⁵ Fertility treatments can increase the levels of estrogens in the blood by several times the normal levels, which can increase breast cancer risk, especially in women who have a family history of breast cancer.

Estrogen and Health: When Estrogen May Be Too High

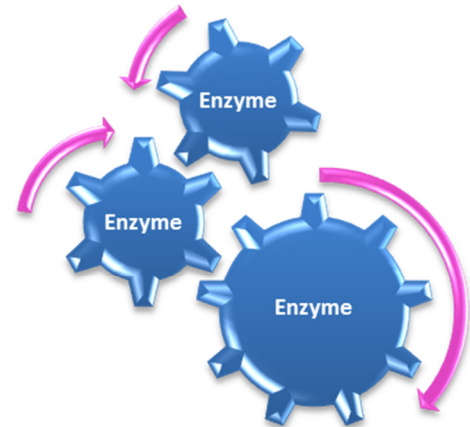


How can something made in my ovaries or prescribed by my doctor cause cancer?^{6,7,10} All women have ovaries and only 12% of women develop breast cancer. Hundreds of millions of women have taken estrogen based medications and only a small group of them develop breast cancer. We know estrogen exposure raises risk but how can we tell who is at risk. ***Estrogen Gene testing can help pinpoint which women in this vast group are more at risk. It is the way that women process estrogen*** that matters. Women who naturally make more of the bad estrogens have higher risk of breast cancer. The difference is in the genes.

IT'S IN YOUR GENES

It takes many different enzymes to process estrogen. Your specific assortment of enzymes determines whether you make more good estrogens than bad, or more bad than good. But what determines the sort of enzymes you will have? Your genes do. Your genes lay out the code or blueprint for these enzymes.

DNA is the blueprint
for the enzymes...



...and the enzymes
process estrogen

Over the past several decades, researchers have been studying the genes that are responsible for how a woman processes estrogen and free radicals. They have found that certain combinations of

mutations in these estrogen metabolism genes may increase the risk of breast cancer. These gene mutations are called SNPs (pronounced “snips”). SNPs on 1 or 2 estrogen metabolism genes are not enough to increase the risk of cancer by an appreciable amount, but SNPs on 3 or more of these genes can increase breast cancer risk by up to 13 times.⁸

ESTROGEN METABOLISM GENES ARE NOT BREAST CANCER GENES

It is important to note that ***estrogen metabolism genes are not breast cancer genes***. There has been a lot of publicity surrounding breast cancer genes like BRCA or another group of genes called ‘polygenetic susceptibility’. A woman who has the BRCA mutation, for example, has a 90% risk of inheriting breast cancer. While the risk of cancer is high in that woman, only 20% of all breast cancers are inherited this way. That means that 80% of all breast cancers are diagnosed in women who have no family history of breast cancer. It also means that breast cancer genes are not the whole story. If a woman wants to know her true risk, she needs to know about her estrogen metabolism genes.

KNOW YOUR PERSONAL RISK AND LOWER IT

The Estrogen Gene Test checks your DNA for six genes. All that is required is a simple swab of your saliva. Once processed, the Estrogen Gene Test identifies which SNPs are present in your DNA. It gives you a SNP profile. This information is important for two main reasons:

1. You will know your personal risk. This could range from no increased risk up to a 13-fold increased risk of breast cancer.
2. Your clinician will be able to formulate a plan. ***Even if you have SNPs in your DNA, it does not mean you are destined to develop breast cancer.*** If you have SNPs, you can minimize that risk through changes in lifestyle and the targeted use of supplements and nutritional interventions.
3. Your clinician will be able to monitor your estrogen and adjust your individualized plan. Your clinician can then test your 'point in time' estrogens or the levels of good and bad estrogens in your body. Your plan can be adjusted accordingly. ***You will have peace of mind.***

WHAT CAN I DO ONCE I KNOW MY SNP PROFILE?

Once you know your individual assortment of SNPs, your clinician can develop an individualized plan that can reduce that risk. If you have a SNP that reduces the activity of the COMT enzyme (also known as the stress gene), you may be given S-adenosyl methionine (SAM-E), cautioned to avoid excess alcohol, and trained in stress reduction techniques. On the other hand, if you have a SNP in the CYP3A4 gene, you may be encouraged to start taking the supplement, Dim-Pro.⁹

Your individual risk depends on your SNP profile.

Your individualized treatment is based on your SNP profile.

The Estrogen Gene Test measures your SNP Profile.

The Estrogen Gene Test: SNPs and Treatment

| Gene | Nutritional Intervention | Lifestyle Intervention |
|---------------|-------------------------------|--|
| CYP1A1 | DIM-Pro | Avoid cigarette smoke Avoid charbroiled meats Avoid Polycyclic aromatic hydrocarbons |
| CYP1B1 | DIM-Pro, Fish Oils | None yet known |
| CYP3A4 | DIM-Pro | None yet known |
| COMT | S-adenosyl methionine (SAM-E) | Stress reduction Avoid excess alcohol intake |
| GSTP1 | L-Glutathione | Avoid herbicides |
| GSTM1 | N-acetylcysteine | Avoid fungicides |
| GSTT1 | Vitamin A | Avoid insect sprays |
| | Vitamin C | Avoid industrial solvents |
| | Vitamin E | Avoid smoke |
| | Selenium, | Avoid mercury |
| | Milk thistle | Avoid cadmium |
| | Colorful fruits | Avoid lead |
| | Cruciferous vegetables | |
| MnSOD | Antioxidants | None yet known |

Your SNP Profile is Not Your Destiny!

Even if the Estrogen Gene Test determines that you have a troubling SNP profile, this does not mean that you will get breast cancer. This genetic pathway can be modified through nutrition, medication, and lifestyle changes.

The Hormonal Cancer Foundation and The Estrogen Gene Test Co. are continuing the extensive body of research on these genes by studying the long term results of modification of these genes. Currently there are 175 women enrolled in an observational study. 47 of the women have estrogen positive breast cancer and the remainder at high risk due to their genetic variations and prior estrogen exposure. To date, none of the participants have developed breast cancer or had a recurrence.

The sooner you find out your risk profile, the sooner you can shift your balance from bad estrogens to good estrogens.

There is hope. There is a solution.

REFERENCES

1. Yager JDD, N.E. Estrogen carcinogenesis in breast cancer. *N Eng J Med*. Jan 2006;354(3):270-282.
2. Breast cancer and hormonal contraceptives: collaborative reanalysis of individual data on 53 297 women with breast cancer and 100 239 women without breast cancer from 54 epidemiological studies. Collaborative Group on Hormonal Factors in Breast Cancer. *Lancet*. Jun 22 1996;347(9017):1713-1727.
3. Breast cancer and hormone replacement therapy: collaborative reanalysis of data from 51 epidemiological studies of 52,705 women with breast cancer and 108,411 women without breast cancer. Collaborative Group on Hormonal Factors in Breast Cancer. *Lancet*. Oct 11 1997;350(9084):1047-1059.
4. Fournier A, Berrino F, Riboli E, Avenel V, Clavel-Chapelon F. Breast cancer risk in relation to different types of hormone replacement therapy in the E3N-EPIC cohort. *Int J Cancer*. Apr 10 2005;114(3):448-454.
5. Sood R, Shuster L, Smith R, Vincent A, Jatoi A. Counseling postmenopausal women about bioidentical hormones: ten discussion points for practicing physicians. *J Am Board Fam Med*. Mar-Apr 2011;24(2):202-210.
6. Andrieu N, Duffy SW, Rohan TE, et al. Familial risk, abortion and their interactive effect on the risk of breast cancer--a combined analysis of six case-control studies. *Br J Cancer*. Sep 1995;72(3):744-751.
7. Gauthier E, Paoletti X, Clavel-Chapelon F. Breast cancer risk associated with being treated for infertility: results from the French E3N cohort study. *Hum Reprod*. Oct 2004;19(10):2216-2221.
8. Cerne JZP-P, M.; Novakovic, S.; Frkovic-Grazio, S.; Stegel, V.; Gersak, K. Combined effect of CYP1B1, COMT, GSTP1, and MnSOD genotypes and risk of postmenopausal breast cancer. *J Gynecol Oncol*. Jun 2011;22(2):110-119.
9. Bradlow HL. Review. Indole-3-carbinol as a chemoprotective agent in breast and prostate cancer. *In Vivo*. Jul-Aug 2008;22(4):441-445.