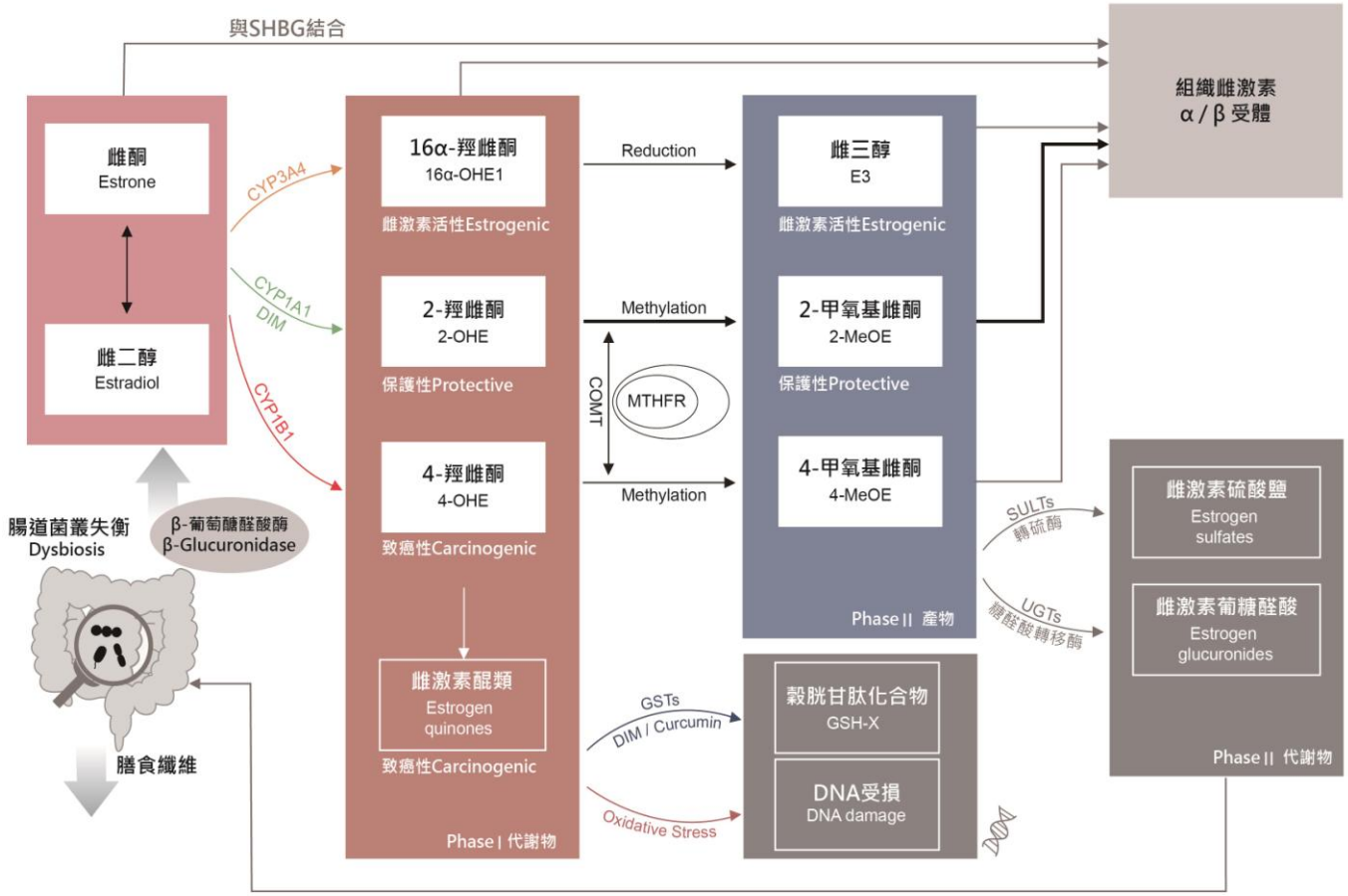
Gnosis Laboratories (M) Sdn. Bhd. (577284-A)
HQ: 1-1 & 1-2, Jalan USJ 21/11, 47630 Subang Jaya, Selangor
Tel: 603-58858501/ 8502/ 8503, 603-58858510

Patient Name : Jane Doe
IC No : 010203-04-5678
Refer From : CLINIC XYZ
Profile: : FNEMH: Estrogen Metabolism Profile

Lab No : 02401123456
Reported Date : 18/11/2024

Estrogen-META® Analysis



Phase I Liver Detoxification:
Cytochrome P450 Activity

	Result	2.5th 16th 50th 84th 97.5th	Reference range (Expected value)
2-OHE1 / 16α-OHE1 ratio	1.9		0.37-2.81 (0.77-2.81)

Phase II Liver Detoxification:
Methylation

	Result	2.5th 16th 50th 84th 97.5th	
2-MeOE1 / 2-OHE1 ratio	0.22 ⬇		≥ 0.26 (≥0.40)

Carcinogenic Estrogen Metabolite

		2.5th 16th 50th 84th 97.5th	
4-Hydroxyestrone (4-OHE1)	0.917		≤ 1.24 (≤0.31)

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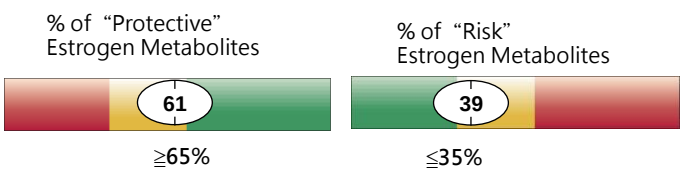
Estrogen Metabolism	Result ng/mg-Cr	Pre-menopause (Expected value)	Postmenopause Without HRT (Expected value)	Male (Expected value)
Phase I Estrogen Metabolites				
2-OHE1	3.83	0.43-8.37	0.25-4.82	0.32-1.36
4-OHE1	0.917	≤ 1.24 (≤0.31)	≤ 0.58 (≤0.1)	≤ 0.19 (≤0.09)
16α-OHE1	2.04	0.45-8.88	0.25-2.97	0.29-1.70
Phase I Estrogen Metabolism Balance				
2-OHE1/16α-OHE1	1.9	0.37-2.81 (0.77-2.81)	0.43-2.98 (0.82-2.98)	0.43-2.30 (0.81-2.30)
Phase II Estrogen Metabolites				
2-MeOE1	0.833	0.17-3.74	0.07-1.13	0.11-0.41
Phase II Estrogen Methylation Balance				
2-MeOE1 / 2-OHE1	0.22 ⬇	≥ 0.26 (≥0.40)	≥ 0.18 (≥0.30)	≥ 0.23 (≥0.32)

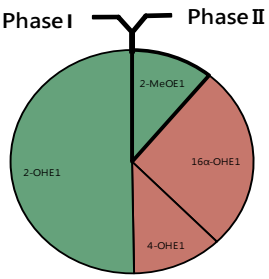
Adjusted by Creatinine: Creatinine : 24.0 mg/dl

※ The test result is based on the premenopausal reference value as the interpretation standard. The result will be higher when creatinine <50, and the result will be lower when creatinine >150. It is recommended that you make interpretation corrections based on the actual status and gender of the customer.

This sample pie-chart represents the optimal balance of estrogen metabolites. The dark line separates Phase 1 and Phase 2 detoxification pathways.

1.**Green Region**: The metabolites in green are considered protective.
2.**Red Region**: The metabolites in red are associated with increased risk





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Estrogen-META® Analysis

Estrogen Metabolism

Liver is the main site for estrogen metabolism, which produces the estrogen metabolites through phase I hydroxylation, phase II methylation, and glucuronidation as well as sulfation. These metabolic byproducts will then release into urine and stool for removal. Some of the estrogen metabolites have estrogenic properties, and are related to various endocrine disorders. Both liver detox function and gut microbial flora influence the degradation of estrogen.

Phase I Liver Detoxification: Cytochrome P450 Activity

Estrogen is metabolized by three kinds of cytochrome P450 enzymes in the liver. Both estrone (E1) and estriol (E2) are hydroxylated to 2-OHE1, 16α-OHE1 and 4-OHE1 respectively through three different detox pathways in the liver. Among those, 4-OH pathway is considered the most genotoxic, as the byproducts 4-OHE1 can be converted into estrogen quinones by oxidative stress, which can damage DNA according to medical researches. 16α-OHE1 and 4-OHE1 generate stronger estrogenic and proliferation property, therefore both are considered as inflammatory estrogen metabolites. Many researches pointed out that if the amount of 4-OHE1 and 16α-OHE1 is far more than 2-OHE1, there is elevated risk for breast cancer.

1. 2-hydroxyestrone, 2-OHE1

2-OHE1 is the estrogen metabolite that has protective effect, that it indicates reduced risk of breast cancer, cervical intraepithelial neoplasm and osteoporosis. For the females using oral contraceptive or hormone replacement therapy, tracking 2-OHE level is especially important for the safety. Among all the food, DIM (diindolylmethane) in the cruciferous vegetables can support the efficiency of 2-OH pathway.

2-OHE1 Level is normal.

2. 4-Hydroxyestrone, 4-OHE1

Most of the 4-OHE1 can be transferred into 4-MeOE1 by COMT in phase II liver detoxification, the rest part will convert to quinones/semiquinones catalyzed through oxidation, which induce free radical damage. When COMT SNPs or COMT enzyme activity is low, the efficiency of methylation cycle and 4-MeOE1 pathway will slow down, producing more quinine metabolites. In this process, free radicals will damage fat, protein and DNA. High level of 4-OHE1 is considered as carcinogenic estrogen metabolite, because 4-OHE1 is higher infinity to estrogen receptors than estrogen. 4-OHE1 can be found in breast tissue, ovary, adrenal gland, uterus etc., and also in breast cancer tissue, indicate that it is related to cancer development.

4-OHE1 level is normal.

3. 16α-hydroxyestrone, 16α-OHE1

16α-OHE1 generates the strongest estrogenic among all the estrogen metabolites. High level of 16α-OHE1 is related to lupus erythematosus, breast cancer and obesity. Keep 16α-OHE1 in normal range can prevent disease risk. When overall estrogen level is high, or estrogen dominance presents, together with high level of 16α-OHE1, this might worsen the symptoms of estrogen dominance. Conversely, if estrogen level is low, high 16α-OHE1 can rebalance the symptoms

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Estrogen-META® Analysis

of low estrogen.
16α-OHE1 is normal.

4. 2-OHE1/16α-OHE1

In the phase I stage, the ideal situation is that the most estrogen degrade through the most protective 2-OH pathway, producing metabolite 2-OHE1. If the ratio of 2-OHE1 / 16α-OHE1 is low, represent that there is higher ratio of estrogen metabolized by 16-OH pathway, creating more 16α-OHE1, which might increase the risk of estrogen-related diseases, e.g. breast cancer, lupus and prostate cancer.
2-OHE1 / 16α-OHE1 is normal.

Phase II Liver Detoxification: Methylation

2-OHE1 and 4-OHE1 are metabolized through methylation pathway in the liver, degraded into 2-MeOE and 4-MeOE separately. Whether this phase II detoxification works well or not, it depends on the nutrients involved in the methylation cycle, e.g. magnesium, folate, vitamin B6 and B12 etc., which are the cofactors for sufficient methyl donors. In addition, methylation cycle genes SNPs, i.e. COMT and MTHFR are also very important. If 4-OHE1 is not totally metabolized by methylation, the rest will convert into quinones through oxidation, which can damage the DNA in the body. If the anti-oxidative capacity in the body is not sufficient, quinones will cause carcinogenic effect with ROS (reactive oxygen species).

5. 2-MeOE1

2-OHE1 converts into 2-MeOE1 by COMT enzyme in the phase II liver detoxification, in order to degrade 2-OHE1 into weaker estrogenic metabolite. Low level of 2-MeOE1 indicates insufficient methylation activity.
2-MeOE1 is normal.

6. 2-MeOE1/2-OHE1

The ratio of 2-MeOE1/2-OHE1 is considered as the marker for evaluation of phase II liver methylation. Low ratio indicates insufficient methylation activity, which is associated to COMT SNPs, insufficient methylation nutrients, and high production of catecholamine during high stress.
2-MeOE1/2-OHE1 is low. Mixed-form vitamin B12 (methylcobalamin, adenosylcobalamin and hydroxylcobalamin) 400-800mcg, Quatrefolic® 5-MTHF 200-800mcg, B2 (riboflavin 5'-phosphate) 10-20mg, vitamin B6 (pyridoxal 5'-phosphate and pyridoxine HCl) 100-200mg, TMG 250-500mg are recommended.

Phase II Liver Detoxification: Glucuronidation

Glucuronidation is one of the main reactions for estrogen metabolism and other environmental toxins excretion. Estrogen metabolites are binding with glucuronic acid by glucuronidation reaction, in order to excrete through kidney. Unfortunately, if gut dysbiosis presents, gut flora produces large amount of β-glucuronidase, which degrades the conjugation of estrogen-glucuronide and releases the estrogen back to circulation through enterohepatic circulation reabsorption. Therefore, high activity of β-glucuronidase increases the risk of breast cancer. A high-fat and low-fiber diet will increase the activity of β-glucuronidase, probiotics can rebalance gut flora. Other nutrients like

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Calcium-D-Glucarate can inhibit the activity of intestinal harmful bacteria, support liver glucuronidation reaction.

Lifestyle Suggestion

- Eat sufficient amount of cruciferous vegetables, sulfur-containing vegetables such as garlic onions, and fresh fruits to support antioxidant capacity.
- Eat more green leafy vegetables, seafood, and fish to support the metabolic pathway of methylation.
- Eat more fruits and whole grains which contain rich water-soluble fiber, in order to improve the intestinal flora.

Functional Medicine Test Suggestion

- 1067 Male Hormone Profile
- 1068 Premenopause Hormone Profile
- 1069 Postmenopause Hormone Profile
- 1134 Estro Genomics®

*** The above report suggestions for physicians' reference only ***