

In the name of GOD





University of Science and Culture

GM3-synthase (hST3Gal V) gene expression in endometriotic tissues of women with endometriosis

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Outline

❖ Background:

- Endometriosis
- GM3 ganglioside *and GM3 synthase* gene

❖ Objective

❖ Methods

❖ Results

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Background

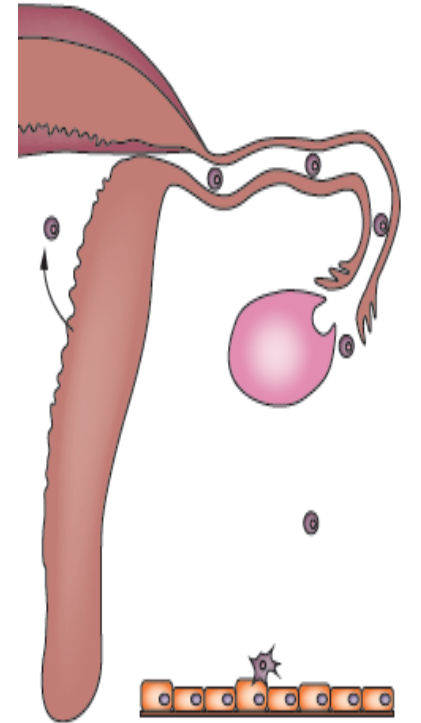
Endometriosis

Is an estrogen-dependent disease, and common in reproductive-age.

Often associated with chronic pelvic pain and infertility.

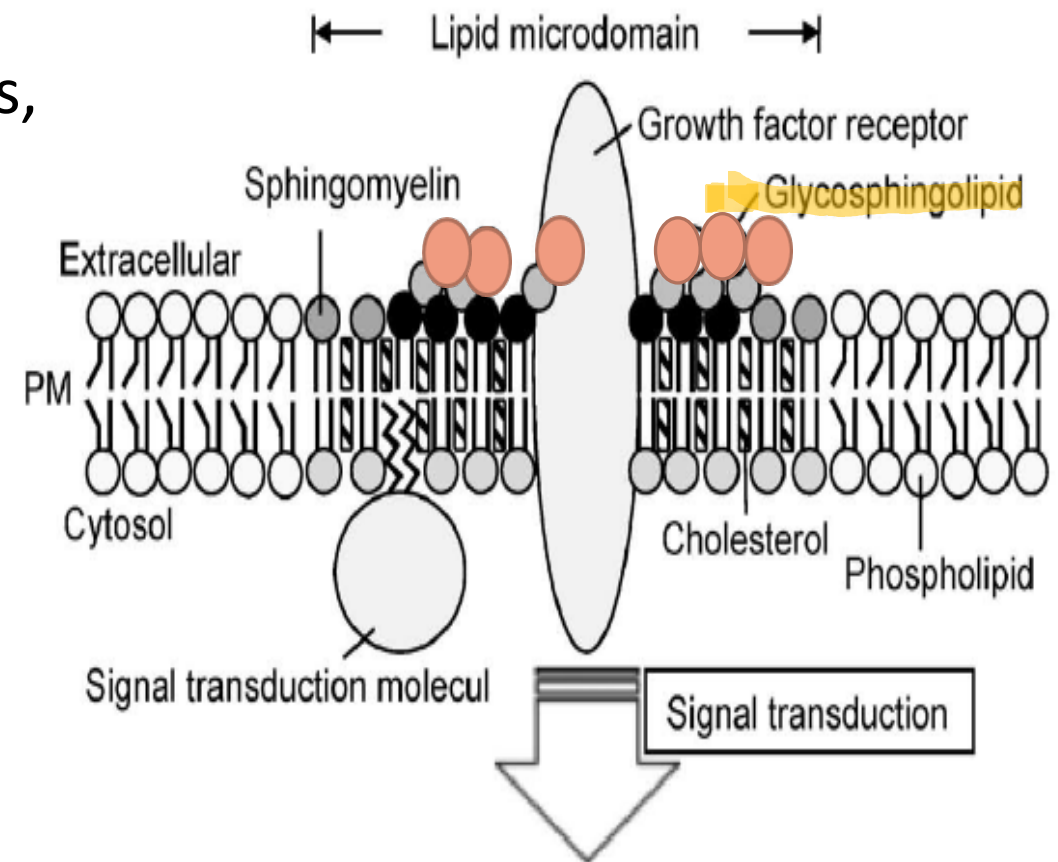
Considered as a multifactor disease affected by hormonal, immunological, genetical, epigenetical and environmental factors.

The retrograde menstruation hypothesis (Sampson's theory) is the most convincing theory about origin of endometriosis.

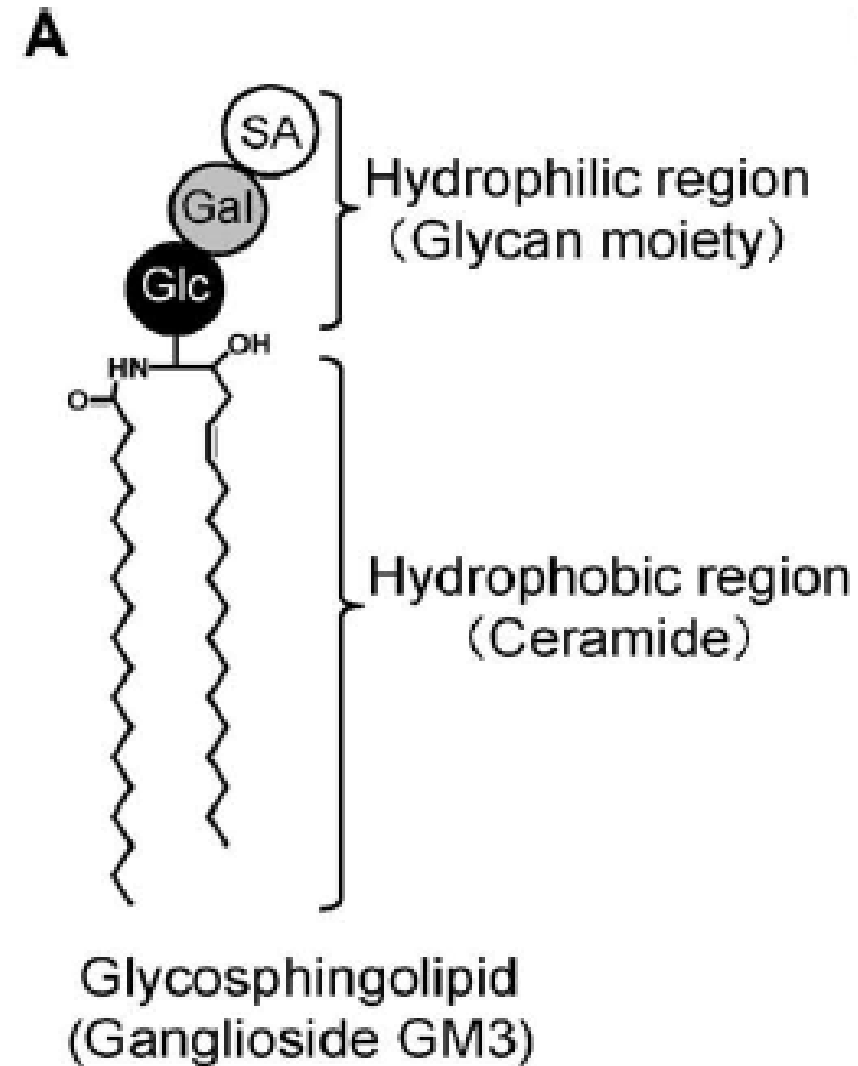


Gangliosides

- ✓ Changes in the cell surface glycosylation is a common phenotype observed during cell differentiation, tissue development cancers, and oncogenesis.
- ✓ Gangliosides:
 - Are ubiquitous in mammalian cells.
 - Consist of a negatively charged sialic acids.
 - Play a role in a variety of **biological processes**.



- ✓ The synthesis of cellular sialic acid is regulated by two enzymes: sialyltransferases (STs) and sialidases.
- ✓ Altered mRNA expressions of sialyltransferases was reported in some articles.
- ✓ The expression levels of GM3 is primarily regulated by its synthetic enzyme encoded by the **human *ST3Gal V*** gene (also named ***GM3 synthase***).



Tittle	Journal/ Date	Result
Silencing of <i>GM3- synthase</i> suppresses lung metastasis of murine breast cancer cells.	Breast Cancer Research 2008	<i>GM3- synthase</i> silencing in 4T1 cells significantly inhibited cell migration, invasion and anchorage-independent growth in vitro, and lung metastasis in vivo. In addition, overexpression of <i>GM3- synthase</i> in nonmetastatic 67NR cells significantly induced cell migration and anchorage-independent growth .
Elevated mRNA level of <i>hST6Gal I</i> and <i>hST3Gal V</i> positively correlates with the high risk of pediatric acute leukemia.	Leukemia research 2010	Differential expression of <i>ST6Gal I</i> , <i>GM3- synthase (ST3Gal V)</i> and <i>GD3- synthase (ST8Sial)</i> between the lymphoblasts and normal lymphocytes, which positively correlates with the high risk of pediatric ALL .
Ganglioside synthase knockout in oncogene-transformed fibroblasts depletes gangliosides and impairs tumor growth.	Oncogene 2010	Combined knockout of two key ganglioside synthesis enzymes, <i>GM3- synthase (GM3S)</i> and <i>GM2- synthase (GM2S)</i> in murine embryonic fibroblasts led to inhibit migration ability .
Human <i>GM3 synthase</i> attenuates taxol-triggered apoptosis associated with downregulation of Caspase-3 in ovarian cancer cells.	Journal of cancer therapy 2012	<i>GM3- synthase</i> overexpression inhibited Taxol-triggered caspase-3 activation, revealing that upregulation of <i>GM3- synthase</i> prevents apoptosis and hence reduces the efficacy of Taxol therapy .
Ganglioside GM3 and its role in cancer.	Current medicinal chemistry. 21018	GM3 is more exposed in strongly metastatic line than the weakly metastatic line. Furthermore, mutant clones that have lost the GM3 expression show lower metastatic potential.

Objective

- ✓ Since before now, the expression levels of *hST3Gal V (GM3- Synthase)* gene in endometriosis have not been measured, therefore in this study, we examined the changes of *hST3Gal V* gene expression in ectopic and eutopic endometrial tissues of women with endometriosis in compared with control group.

Criteria

This study conducted 10 ectopic samples, 10 eutopic samples and 10 control samples from women referred to the Royan Institute.

Including criteria

Patient groups:

- Confirmed endometriosis with laparoscopic surgery
- Age 20-45 years
- Having regular menstrual cycles
- Not taking hormone medication in the last 3 months

Control group:

- Absence of endometriosis
- Age 20-45 years
- Having regular menstrual cycles
- Not taking hormone medication in the last 3 months

Excluding criteria

Patient groups:

- Endometrial cell changes such as hyperplasia and endometrial carcinoma
- Benign uterine masses such as fibroids and polyps
- Autoimmune diseases, endocrine diseases and cancers

Control group:

- Endometriosis
- PCO
- Uterine anomalies
- Inflammatory diseases, autoimmunity and cancers
- Ovarian Dermoid Cysts
- Ectopic pregnancy history

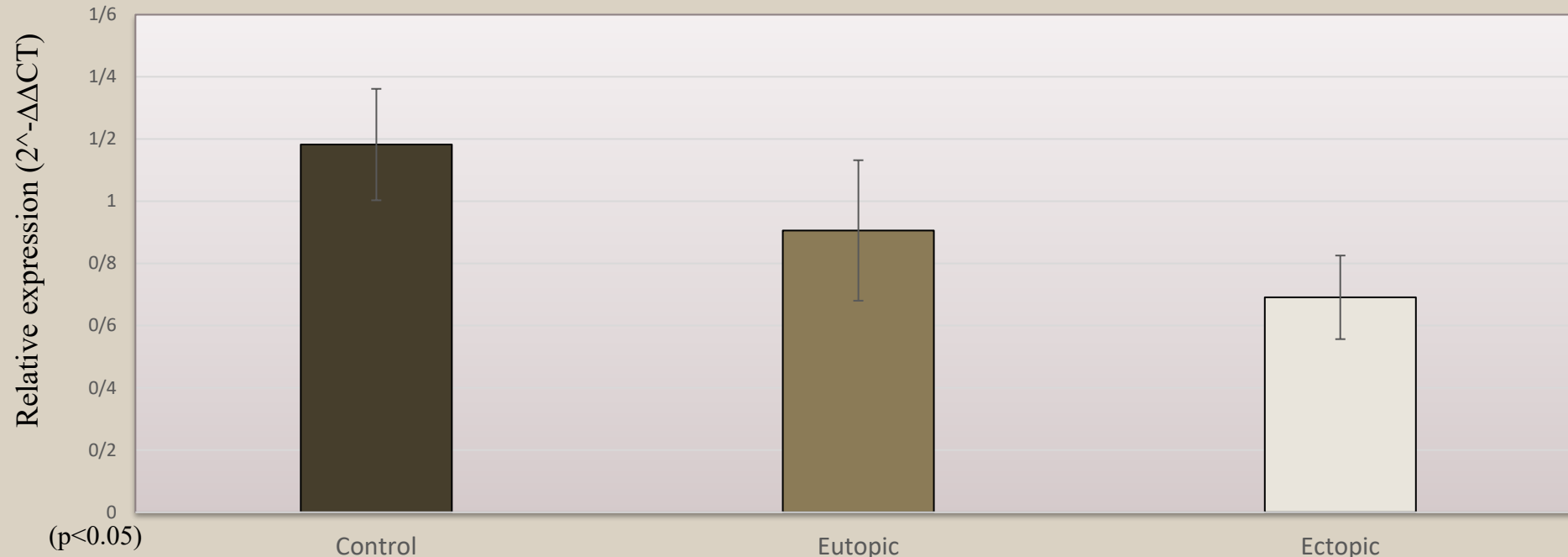
Methods

For evaluation of *hST3Gal V* gene expression in endometrial tissues of women with endometriosis, and comparison with control samples we performed:

1. RNA extraction and cDNA synthesis.
2. Primer design for *hST3Gal V* gene and *GAPDH* gene as housekeeping gene.
3. Measurement of gene expression by using Real- time PCR.
4. Data analysis by using One-way ANOVA as statical method. Values were expressed as mean \pm SEM and the results were considered significant at the level ($p < 0.05$).

Results

Results showed that the *hST3Gal V* gene expression was reduced in eutopic samples than control group ($p= 0.538$) and *hST3Gal V* gene expression in ectopic samples was reduced than both eutopic and control groups ($p= 0.696$ and $p= 0.153$, respectively).



The expression levels of *hST3Gal V* gene in endometriotic groups and control group.

Conclusion

It seems that the lower expression of *hST3Gal V* gene in endometriosis is involved in the etiology of the disease.

Thanks for your attentions!

