medical sciences forum

*Supplementary Materials*

# Potential Candidate Gene and Underlying Molecular Mechanism Involving in Tumorigenesis of Endometriosis-Associated Ovarian Cancer (EAOC) in Asian Populations †

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**Table S1.** Selected Whole Exome Sequencing (WES) data from published articles.

| Reference | Study Location | Study Design | Subjects | Diagnosis | Samples | Tissue Sampling |
|---|---|---|---|---|---|---|
| [8] | Japan | WES in discovery cohort | 13 | Endometriosis | 13 | endometriotic epithelium (ectopic endometriotic) |
| | | | | | 5 | uterine endometrial epithelium |
| | | | 6 | Non-endometriosis* | 6 | uterine endometrial epithelium |
| [9] | China | WES for mutational landscape in cohort | 16 | Endometriosis | 16 | Eutopic |
| | | | | | 16 | Ectopic |
| [10] | Taiwan | 410 cancer-related gene sequencing in cohort patients | 22 | Epithelial ovarian cancer | 22 | Endometrioid |
| | | | 23 | | 23 | Clear Cell |
| [11] | China | WES in cohort | 42 | ovarian clear cell carcinoma | 84 | ovarian tissues (both clear cell and adjacent normal tissues) |
| [12] | Korea | WES use cohort patient for genomic landscape | 15 | ovarian clear cell carcinoma | 5 | tissue associated with endometriosis |
| | | | | | 10 | tissue non-associated endometriosis |

* Non-endometriosis = Ovarian cystadenoma, Ovarian fibroma, Myoma uteri.

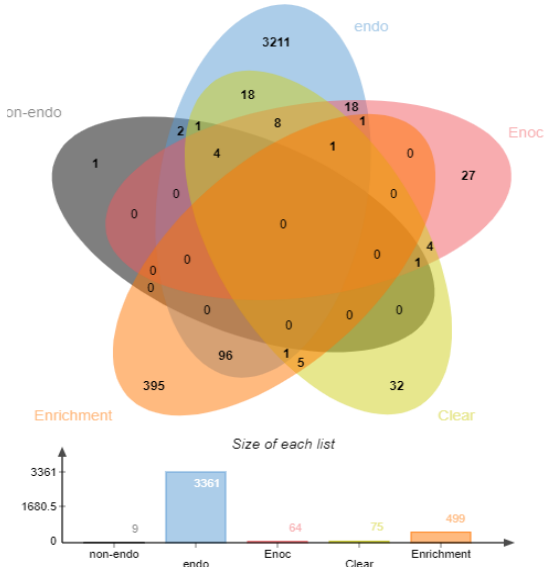
**Table S2.** Microarray Data Collection Information.

| GEO Series | Tissue Samples | Samples | Sample Characteristic | Platform |
|---|---|---|---|---|
| GSE7846 | HEECs (Human Endometrium Endothelial Cells) | 5 | Eutopic endothelium from a patient with endometriosis | GPL570 [HG-U133_Plus_2] Affymetrix Human Genome U133 Plus 2.0 Array |
| | | 5 | endothelium from normal control | |
| GSE65986 | ovarian cancer tissue | 25 | Clear cell | GPL570 [HG-U133_Plus_2] Affymetrix Human Genome U133 Plus 2.0 Array |
| | | 14 | Endometrioid | |

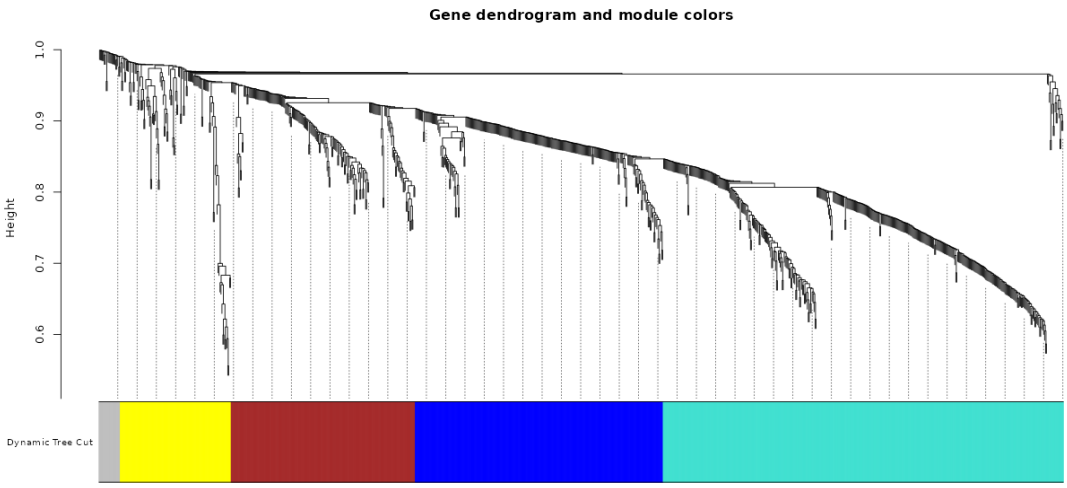
**Table S3.** Filtered exonic variants in genes of interest based on functional impact in WES data.

| Gene | Histotype | cDNA change | Protein Change | Variant ID |
|---|---|---|---|---|
| *MYH11* | *Eu- Endometriosis | **c.323G>A** | p.R108Q | - |
| | *Ec-Endometriosis | c.808C>T | p.R270W | COSV55541820 |
| | Endometrioid | **c.323G>A** | p.R108Q | - |
| | Clear Cell | c.4260G>C | p.K1420N | - |
| | Clear Cell | c.4822G>A | p.E1608K | rs777768672 |
| *KRT5* | *Ec-Endometriosis | c.1127G>A | p.G376D | - |
| | Clear Cell | c.992G>A | p.R331H | rs56729325 |
| | Clear Cell | c.1343G>A | p.R448Q | rs148276250 |
| *PDGFRA* | *Eu-Endometriosis | c.2942G>A | p.R981H | rs368266633 |
| | *Eu-Endometriosis | c.2671C>T | p.L891F | rs759510574 |
| | Endometrioid | c.2450G>A | p.R817H | rs79948560 |
| | Endometrioid | c.2566T>G | p.F856V | - |

* Eu-Endometriosis (Eutopic endometriosis), Ec-Endometriosis (Ectopic endometriosis).




(**a**)




(**b**)

**Figure S1.** Co-expression network analysis using WGCNA package in iDEP. (**a**) Diagram Venn of overlapping gene interest between functional variant of WES data and co-expression network of mRNA expression; (**b**) Gene dendogram and recognition module. Each module was given an individual color as an identifier, including ten different modules.

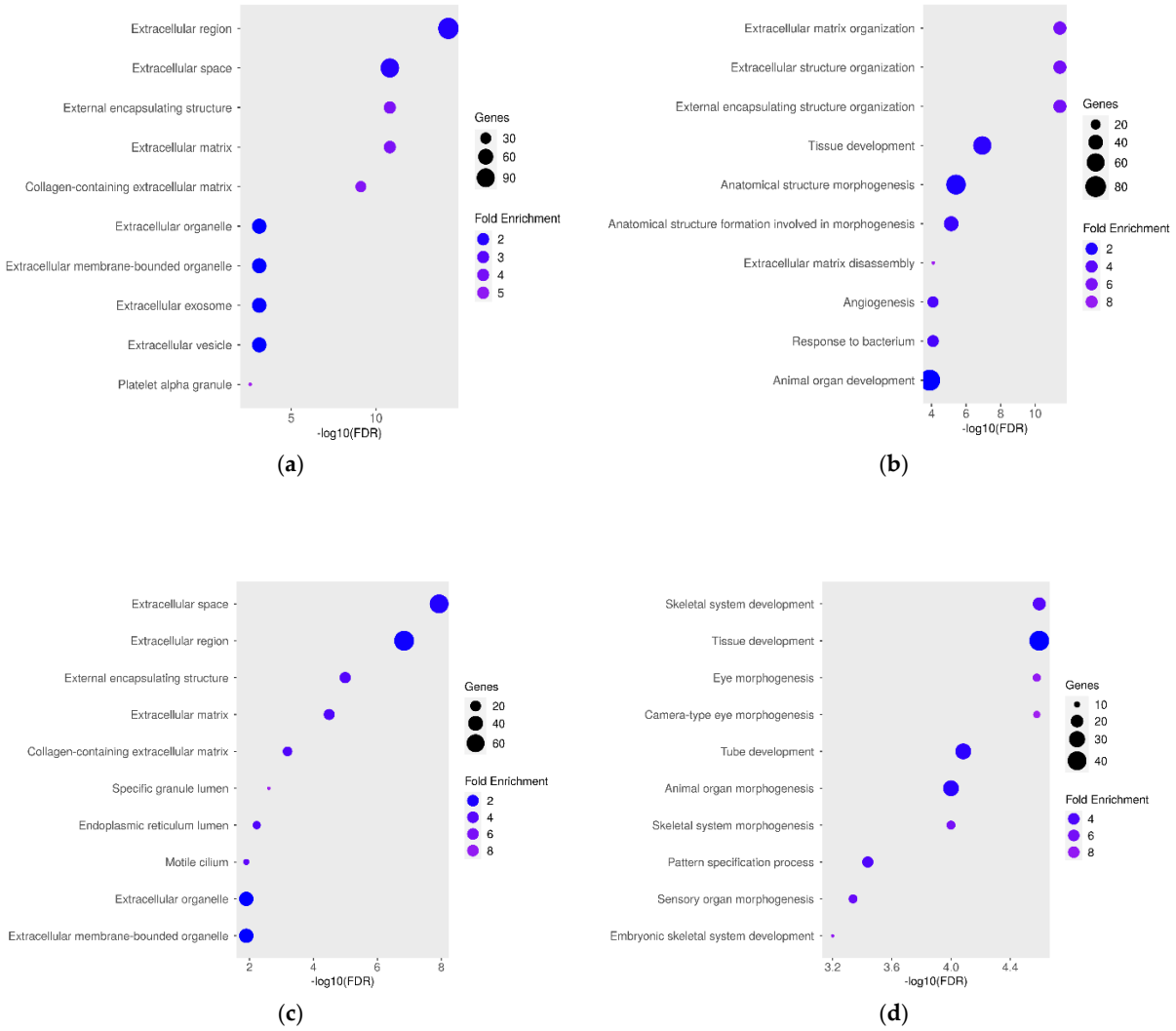
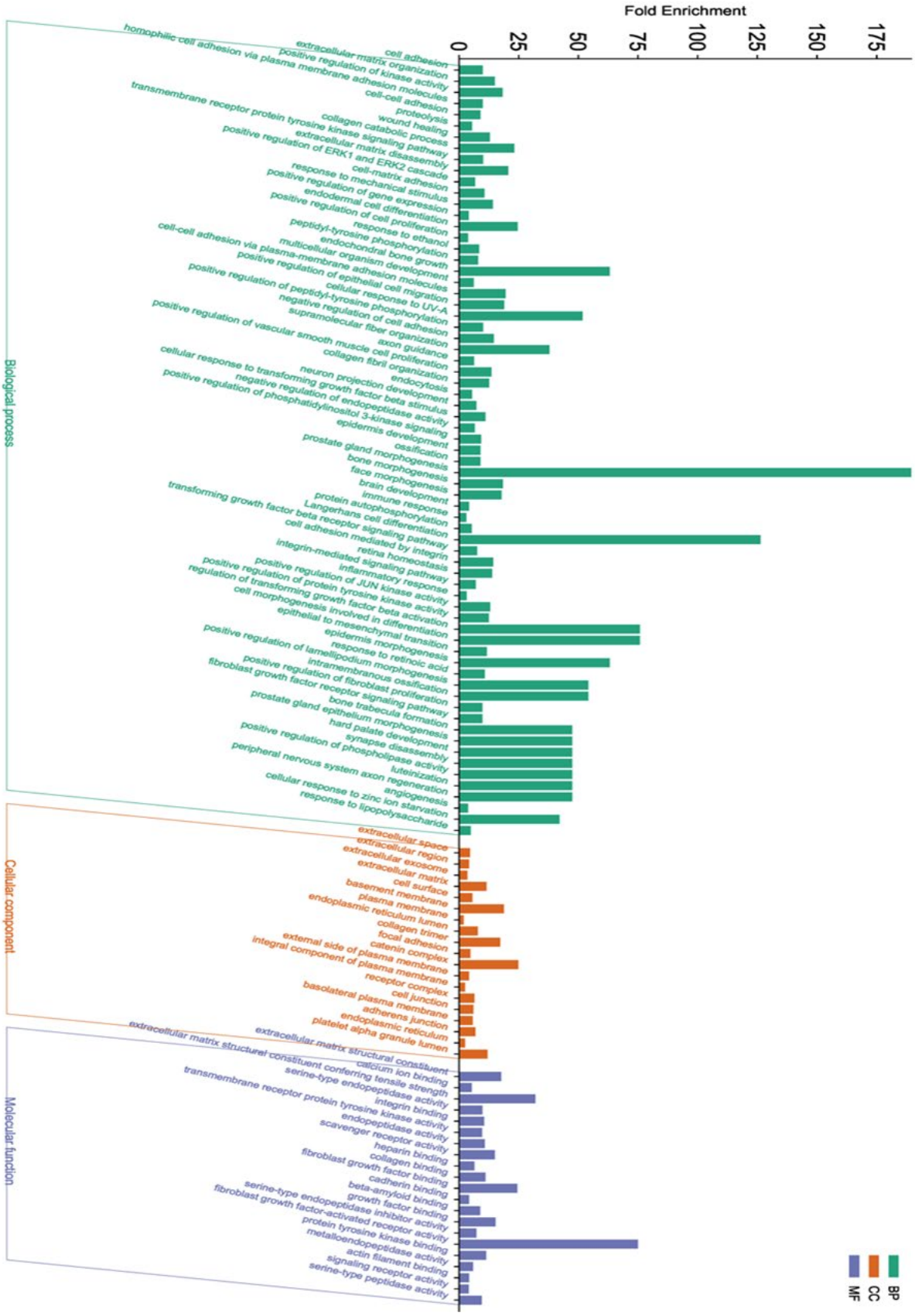
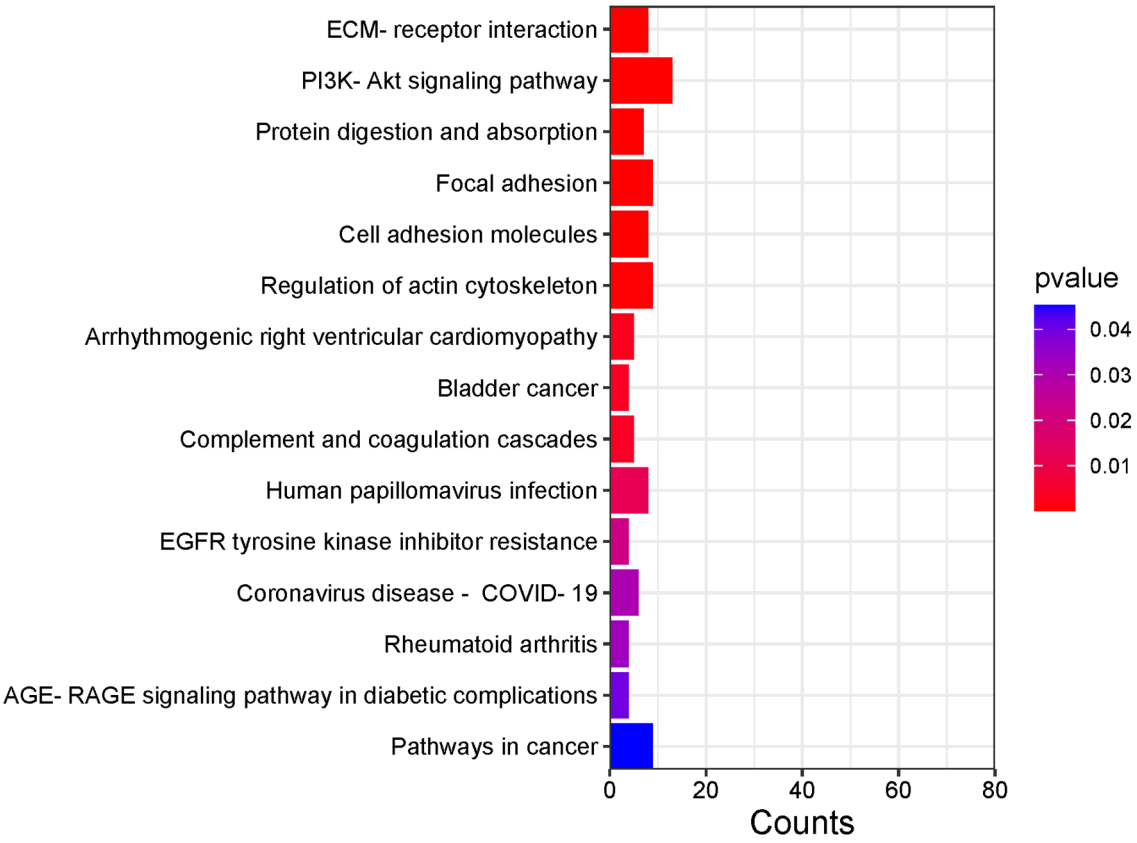



**Figure S2.** Bar plot of GO enrichment analysis for 2 modules (Brown and blue) in iDEP result. (**a**) Cellular Component bar plot of the hub genes identified in the blue module *PDGFRA*; (**b**) Molecular function bar plot of the hub genes identified in the blue module *PDGFRA*; (**c**) Cellular component of the hub genes identified in the brown module *KRT5* and *MYH11*; (**d**) Molecular function bar plot of the hub genes identified in brown module *KRT5* and *MYH11*.

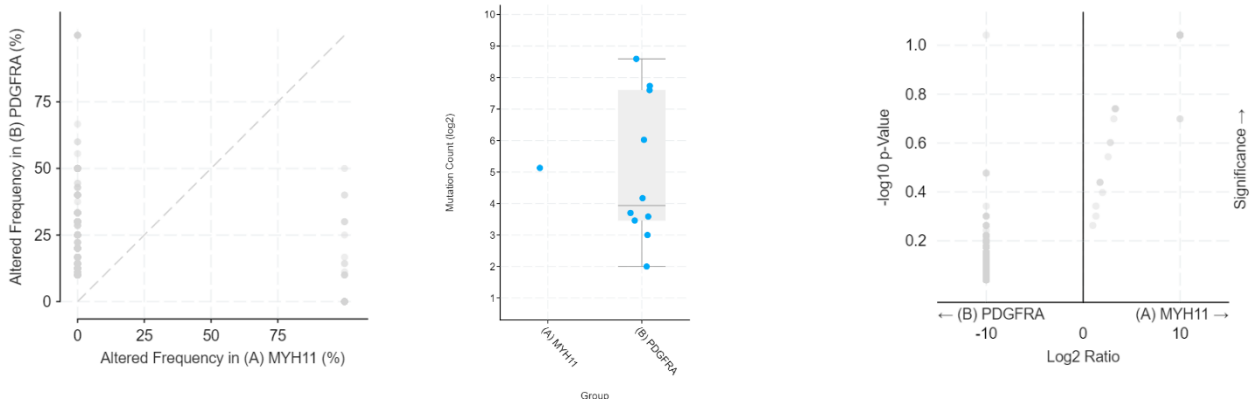

Fold Enrichment
0
25
50
75
100
125
150
175
Biological process
homophilic cell adhesion via plasma membrane adhesion molecules
cell adhesion
extracellular matrix organization
positive regulation of kinase activity
cell-cell adhesion
transmembrane receptor protein tyrosine kinase signaling pathway
proteolysis
wound healing
collagen catabolic process
extracellular matrix disassembly
positive regulation of ERK1 and ERK2 cascade
cell-matrix adhesion
response to mechanical stimulus
positive regulation of gene expression
endodermal cell differentiation
positive regulation of cell proliferation
response to ethanol
peptidyl-tyrosine phosphorylation
endochondral bone growth
cell-cell adhesion via plasma-membrane adhesion molecules
multicellular organism development
positive regulation of epithelial cell migration
cellular response to UV-A
positive regulation of peptidyl-tyrosine phosphorylation
negative regulation of cell adhesion
supramolecular fiber organization
positive regulation of vascular smooth muscle cell proliferation
axon guidance
collagen fibril organization
endocytosis
cellular response to transforming growth factor beta stimulus
neuron projection development
negative regulation of endopeptidase activity
positive regulation of phosphatidylinositol 3-kinase signaling
epidermis development
ossification
prostate gland morphogenesis
bone morphogenesis
face morphogenesis
brain development
immune response
protein autophosphorylation
Langerhans cell differentiation
transforming growth factor beta receptor signaling pathway
cell adhesion mediated by integrin
retina homeostasis
integrin-mediated signaling pathway
inflammatory response
positive regulation of JUN kinase activity
regulation of transforming growth factor beta activation
cell morphogenesis involved in differentiation
epithelial to mesenchymal transition
epidermis morphogenesis
positive regulation of lamellipodium morphogenesis
response to retinoic acid
intramembranous ossification
positive regulation of fibroblast proliferation
fibroblast growth factor receptor signaling pathway
bone trabecula formation
prostate gland epithelium morphogenesis
hard palate development
synapse disassembly
positive regulation of phospholipase activity
luteinization
peripheral nervous system axon regeneration
angiogenesis
cellular response to zinc ion starvation
response to lipopolysaccharide
Cellular component
extracellular space
extracellular region
extracellular exosome
extracellular matrix
cell surface
basement membrane
plasma membrane
endoplasmic reticulum lumen
collagen trimer
focal adhesion
catenin complex
external side of plasma membrane
integral component of plasma membrane
receptor complex
cell junction
basolateral plasma membrane
adherens junction
endoplasmic reticulum
platelet alpha granule lumen
extracellular matrix structural constituent
Molecular function
extracellular matrix structural constituent conferring tensile strength
calcium ion binding
serine-type endopeptidase activity
transmembrane receptor protein tyrosine kinase activity
integrin binding
endopeptidase activity
scavenger receptor activity
heparin binding
fibroblast growth factor binding
collagen binding
cadherin binding
beta-amyloid binding
serine-type endopeptidase inhibitor activity
fibroblast growth factor-activated receptor activity
growth factor binding
protein tyrosine kinase binding
metalloendopeptidase activity
actin filament binding
signaling receptor activity
serine-type peptidase activity
BP
CC
MF

(**a**)




(**b**)

**Figure S3.** GO analysis and Hallmark pathway enrichment of 104 genes from overlapping WES and mRNA data in EAOC. (**a**) GO analysis of overlapping genes in EAOC visualized on a bar chart clustered by molecular functions, cellular component and biological process; (**b**) KEGG Hallmark pathway enrichment of overlapping gene in EAOC visualized on a bar chart, showing number of shared genes (count) and *p* value.




(**a**) (**b**) (**c**)

**Figure S4.** Summarize of cBioportal in GENIE cohort of Clear Cell Ovarian Carcinoma and Endometrioid Ovarian Carcinoma. (**a**) Altered frequency plot between *MYH11* and *PDGFRA*; (**b**) Mutation count plot between *MYH11* and *PDGFRA*; (**c**) Enrichment mutation between *MYH11* and *PDGFRA*.

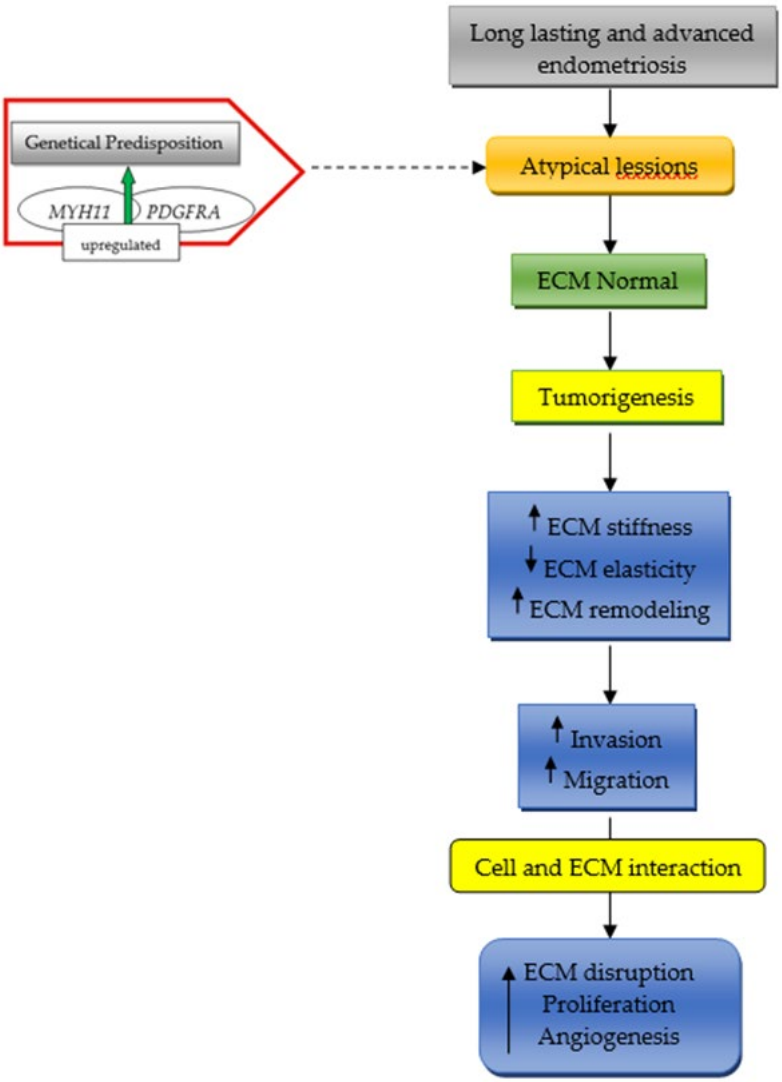



**Figure S5.** An overview of tumorigenesis involving genetic predisposition and PDGFRA in extracellular matrix (Adapted from Ref. [21]).