**Supplementary Table 5.** All statistically significant GO Molecular functions revealed by MetaCore software analysis using 371 genes, for which the 1,034 probes showing different DNA methylation levels between 34 samples of early-onset endometrioid endometrial cancer tissue (EE) (patient age <40 yr) and 40 samples of late-onset endometrioid endometrial cancer tissue (LE) were designed (listed in Supplementary Table 4).

| Molecular functions   | P value                |
|---|------------------------|
| sequence-specific DNA binding   | 2.05×10 <sup>-19</sup> |
| transcription factor activity, sequence-specific DNA binding  | 2.39×10 <sup>-19</sup> |
| nucleic acid binding transcription factor activity  | 2.48×10 <sup>-19</sup> |
| RNA polymerase II transcription factor activity, sequence-specific DNA binding                                  | 3.14×10 <sup>-16</sup> |
| DNA binding   | 2.05×10 <sup>-10</sup> |
| transcription regulatory region sequence-specific DNA binding   | 2.15×10 <sup>-10</sup> |
| transcription factor activity, RNA polymerase II core promoter proximal region sequence-specific binding        | 2.81×10 <sup>-10</sup> |
| neurokinin receptor binding   | 5.08×10 <sup>-10</sup> |
| substance P receptor binding  | 5.08×10 <sup>-10</sup> |
| sequence-specific double-stranded DNA binding   | 7.65×10 <sup>-10</sup> |
| transcription regulatory region DNA binding   | 9.47×10 <sup>-10</sup> |
| regulatory region DNA binding   | 1.01×10 <sup>-9</sup>  |
| regulatory region nucleic acid binding  | 1.13×10 <sup>-9</sup>  |
| neuropeptide receptor activity  | 3.30×10 <sup>-9</sup>  |
| gated channel activity  | 6.48×10 <sup>-9</sup>  |
| double-stranded DNA binding   | 7.49×10 <sup>-9</sup>  |
| RNA polymerase II regulatory region sequence-specific DNA binding   | 9.49×10 <sup>-9</sup>  |
| voltage-gated potassium channel activity  | 1.06×10 <sup>-8</sup>  |
| RNA polymerase II regulatory region DNA binding   | 1.19×10 <sup>-8</sup>  |
| transcriptional activator activity, RNA polymerase II transcription regulatory region sequence-specific binding | $1.24 \times 10^{-8}$  |
| voltage-gated cation channel activity   | 2.12×10 <sup>-8</sup>  |
| channel activity  | 2.71×10 <sup>-8</sup>  |
| passive transmembrane transporter activity  | 2.82×10 <sup>-8</sup>  |
| core promoter proximal region sequence-specific DNA binding   | 2.93×10 <sup>-8</sup>  |
| core promoter proximal region DNA binding   | 3.18×10 <sup>-8</sup>  |
| ion channel activity  | 6.07×10 <sup>-8</sup>  |
| transcriptional activator activity. RNA polymerase II core promoter proximal region sequence-specific binding   | 6.58×10 <sup>-8</sup>  |
| RNA polymerase II core promoter proximal region sequence-specific DNA binding                                   | $7.36 \times 10^{-8}$  |
| substrate-specific channel activity   | $1.00 \times 10^{-7}$  |
| transcription factor activity. RNA polymerase II distal enhancer sequence-specific binding                      | $1.09 \times 10^{-7}$  |
| hinding   | $2.83 \times 10^{-7}$  |
| voltage-gated channel activity  | $3.99 \times 10^{-7}$  |
| voltage-gated ion channel activity  | $3.99 \times 10^{-7}$  |
| notassium channel activity  | $4.31 \times 10^{-7}$  |
| notassium ion transmembrane transporter activity  | $9.24 \times 10^{-7}$  |
| cation channel activity   | $1.58 \times 10^{-6}$  |
| neuronentide recentor hinding   | $1.76 \times 10^{-6}$  |
| metal ion transmembrane transporter activity  | $2.29 \times 10^{-6}$  |
| neuroligin family protein hinding   | $2.23 \times 10^{-6}$  |
| calcium channel regulator activity  | $2.17 \times 10^{-6}$  |
| inorganic cation transmembrane transporter activity   | $2.74 \times 10^{-6}$  |
| transmitter-gated ion channel activity  | 6 50×10 <sup>-6</sup>  |
| transmitter-gated channel activity  | 6.50×10 <sup>-6</sup>  |
| transcriptional repressor activity. RNA polymerase II transcription regulatory region sequence-specific hinding | $8.00 \times 10^{-6}$  |
| G protein coupled paptide recentor activity   | $8.00 \times 10^{-6}$  |
| ligand-gated channel activity   | $8.02 \times 10^{-6}$  |
| ligand gated ion channel activity   | 8.55×10 <sup>-6</sup>  |
| nentide recentor activity   | $9.35 \times 10^{-6}$  |
| peptide receptor activity   | $1.10 \times 10^{-5}$  |
| HMG box domain hinding  | $1.12 \times 10^{-5}$  |
| channel regulator activity  | $1.37 \times 10^{-5}$  |
| enamer regulator activity   | 1.47^10                |

| neuropeptide Y receptor activity  | 2.39×10 <sup>-5</sup> |
|---|-----------------------|
| ion channel regulator activity  | 3.16×10 <sup>-5</sup> |
| ligand-gated anion channel activity   | 3.31×10 <sup>-5</sup> |
| ion transmembrane transporter activity  | 3.46×10 <sup>-5</sup> |
| nucleic acid binding  | 4.18×10 <sup>-5</sup> |
| GABA-gated chloride ion channel activity  | 5.19×10 <sup>-5</sup> |
| cation transmembrane transporter activity   | 5.42×10 <sup>-5</sup> |
| monovalent inorganic cation transmembrane transporter activity  | 7.30×10 <sup>-5</sup> |
| extracellular ligand-gated ion channel activity   | 9.13×10 <sup>-5</sup> |
| transcriptional repressor activity, RNA polymerase II core promoter proximal region sequence-specific binding | 1.00×10 <sup>-4</sup> |
| transmembrane transporter activity  | 1.35×10 <sup>-4</sup> |
| substrate-specific transmembrane transporter activity   | 1.38×10 <sup>-4</sup> |
| substrate-specific transporter activity   | 3.40×10 <sup>-4</sup> |
| cation binding  | 7.63×10 <sup>-4</sup> |
| transporter activity  | 8.28×10 <sup>-4</sup> |
| organic cyclic compound binding   | 9.76×10 <sup>-4</sup> |
| ammonium ion binding  | $1.14 \times 10^{-3}$ |
| receptor binding  | 1.29×10 <sup>-3</sup> |
| ligand-gated cation channel activity  | 1.72×10 <sup>-3</sup> |
| heterocyclic compound binding   | 1.76×10 <sup>-3</sup> |
| somatostatin receptor activity  | 1.88×10 <sup>-3</sup> |
| peptide YY receptor activity  | 1.88×10 <sup>-3</sup> |
| protein dimerization activity   | 1.94×10 <sup>-3</sup> |
| E-box binding   | 2.07×10 <sup>-3</sup> |
| GABA-A receptor activity  | 2.20×10 <sup>-3</sup> |
| protein heterodimerization activity   | 2.41×10 <sup>-3</sup> |
| delayed rectifier potassium channel activity  | 2.56×10 <sup>-3</sup> |
| chromatin binding   | 2.61×10 <sup>-3</sup> |
| cyclic nucleotide binding   | 2.73×10 <sup>-3</sup> |
| pancreatic polypeptide receptor activity  | 2.80×10 <sup>-3</sup> |
| polypeptide N-acetylgalactosaminyltransferase activity  | 2.96×10 <sup>-3</sup> |
| GABA receptor activity  | 3.39×10 <sup>-3</sup> |
| activating transcription factor binding   | 3.52×10 <sup>-3</sup> |
| transmembrane receptor activity   | 3.85×10 <sup>-3</sup> |
| neuropeptide binding  | 3.86×10 <sup>-3</sup> |
| benzodiazepine receptor activity  | 3.88×10 <sup>-3</sup> |
| amino acid binding  | 3.96×10 <sup>-3</sup> |
| enhancer sequence-specific DNA binding  | 4.25×10 <sup>-3</sup> |
| metal ion binding   | 4.51×10 <sup>-3</sup> |
| [heparan sulfate]-glucosamine 3-sulfotransferase 1 activity   | 5.13×10 <sup>-3</sup> |
| drug binding  | 5.15×10 <sup>-3</sup> |
| G-protein coupled receptor binding  | 5.86×10 <sup>-3</sup> |
| glutamate receptor activity   | 6.12×10 <sup>-3</sup> |
| neurotransmitter binding  | 6.12×10 <sup>-3</sup> |
| cAMP binding  | 6.78×10 <sup>-3</sup> |
| ferrous iron binding  | 6.78×10 <sup>-3</sup> |
| chloride channel activity   | 7.06×10 <sup>-3</sup> |
| transcription factor activity, transcription factor binding   | 7.07×10 <sup>-3</sup> |
| excitatory extracellular ligand-gated ion channel activity  | 7.21×10 <sup>-3</sup> |
| enhancer binding  | 7.60×10 <sup>-3</sup> |
| AT DNA binding  | 8.09×10 <sup>-3</sup> |
| iron ion transmembrane transporter activity   | 8.09×10 <sup>-3</sup> |
| co-receptor binding   | 8.09×10 <sup>-3</sup> |
| transcription factor activity, protein binding  | 8.39×10 <sup>-3</sup> |
| protein binding   | 8.42×10 <sup>-3</sup> |
| protein domain specific binding   | 9.66×10 <sup>-3</sup> |
|   |                       |

| inhibitory extracellular ligand-gated ion channel activity                         | 9.79×10 <sup>-2</sup> |
|--|-----------------------|
| transcription corepressor activity   | 0.010                 |
| transmembrane signaling receptor activity  | 0.012                 |
| co-SMAD binding  | 0.017                 |
| transcription cofactor activity  | 0.017                 |
| transcription factor binding   | 0.013                 |
| chloride transmembrane transporter activity  | 0.013                 |
| signal transducer activity   | 0.014                 |
| growth hormone secretagogue receptor activity                                      | 0.014                 |
| thyroxine 5-deiodinase activity  | 0.014                 |
| 3-hydroxyanthranilate 3,4-dioxygenase activity                                     | 0.014                 |
| pituitary adenylate cyclase activating polypeptide activity                        | 0.014                 |
| suramin binding  | 0.014                 |
| pituitary adenylate cyclase-activating polypeptide receptor binding                | 0.014                 |
| intracellular sodium activated potassium channel activity                          | 0.014                 |
| neuropeptide Y receptor binding  | 0.014                 |
| thyrotropin-releasing hormone activity   | 0.014                 |
| choline:sodium symporter activity  | 0.014                 |
| cysteine dioxygenase activity  | 0.014                 |
| [heparan sulfate]-glucosamine 3-sulfotransferase 2 activity                        | 0.014                 |
| glutamine N-acyltransferase activity   | 0.014                 |
| acetylgalactosaminyltransferase activity   | 0.015                 |
| chromatin DNA binding  | 0.015                 |
| chemoattractant activity   | 0.016                 |
| receptor activity  | 0.017                 |
| molecular transducer activity  | 0.017                 |
| protein phosphatase 2A binding   | 0.017                 |
| anion channel activity   | 0.017                 |
| growth factor activity   | 0.018                 |
| protein kinase A catalytic subunit binding   | 0.018                 |
| signaling receptor activity  | 0.019                 |
| glycine binding  | 0.020                 |
| guanylate kinase activity  | 0.020                 |
| dopamine binding   | 0.020                 |
| 3',5'-cyclic-AMP phosphodiesterase activity  | 0.020                 |
| calcium-dependent protein binding  | 0.023                 |
| heparan sulfate sulfotransferase activity  | 0.023                 |
| gamma-catenin binding  | 0.023                 |
| transcriptional repressor activity, RNA polymerase II transcription factor binding | 0.024                 |
| BRE binding  | 0.028                 |
| prostaglandin J receptor activity  | 0.028                 |
| glycine-gated chloride ion channel activity  | 0.028                 |
| trivalent inorganic cation transmembrane transporter activity                      | 0.028                 |
| volume-sensitive chloride channel activity   | 0.028                 |
| neurotrophin TRKB receptor binding   | 0.028                 |
| ferric iron transmembrane transporter activity                                     | 0.028                 |
| toxin activity   | 0.028                 |
| hydroxymethylglutaryl-CoA lyase activity   | 0.028                 |
| oxysterol 7-alpha-hydroxylase activity   | 0.028                 |
| prostaglandin D receptor activity  | 0.028                 |
| ionotropic glutamate receptor activity   | 0.028                 |
| extracellular-glutamate-gated ion channel activity                                 | 0.028                 |
| protein kinase A regulatory subunit binding  | 0.031                 |
| catecholamine binding  | 0.031                 |
| protein phosphatase binding  | 0.032                 |
| metallopeptidase activity  | 0.032                 |

| protein kinase A binding   | 0.034 |
|--|-------|
| protein homodimerization activity  | 0.036 |
| neurotransmitter:sodium symporter activity   | 0.037 |
| transforming growth factor beta receptor binding   | 0.039 |
| transcription factor activity, RNA polymerase II transcription factor binding                    | 0.040 |
| protein phosphatase 1 binding  | 0.040 |
| integrin binding   | 0.041 |
| thyroxine 5'-deiodinase activity   | 0.041 |
| cannabinoid receptor activity  | 0.041 |
| dopamine:sodium symporter activity   | 0.041 |
| phenylalanine 4-monooxygenase activity   | 0.041 |
| calcium- and calmodulin-regulated 3',5'-cyclic-GMP phosphodiesterase activity                    | 0.041 |
| calmodulin-dependent cyclic-nucleotide phosphodiesterase activity                                | 0.041 |
| glial cell-derived neurotrophic factor receptor activity   | 0.041 |
| vasoactive intestinal polypeptide receptor activity  | 0.041 |
| glutamate decarboxylase activity   | 0.041 |
| inward rectifier potassium channel activity  | 0.044 |
| 3',5'-cyclic-nucleotide phosphodiesterase activity   | 0.044 |
| acetylcholine receptor binding   | 0.044 |
| metalloaminopeptidase activity   | 0.044 |
| ion channel binding  | 0.044 |
| phosphatidylinositol bisphosphate binding  | 0.047 |
| cyclic-nucleotide phosphodiesterase activity   | 0.047 |
| phospholipid-translocating ATPase activity   | 0.047 |
| transmitter-gated ion channel activity involved in regulation of postsynaptic membrane potential | 0.047 |
| carbon-carbon lyase activity   | 0.049 |