**Table S1: Gene Ontology enrichment of the top 200 genes correlated with *Esr1* and *Gr* in 12 brain regions.**

| | *Esr1* | | *Gr* | |
|---|---|---|---|---|
| | Term | P-value | Term | P-value |
| Cerebellum (CB) | synaptic transmission (GO:0007268) | 5.08E-05 | regulation of receptor internalization (GO:0002090) | 4.39E-03 |
| | regulation of membrane potential (GO:0042391) | 1.20E-04 | glucose catabolic process (GO:0006007) | 1.48E-02 |
| | calcium ion import (GO:0070509) | 4.63E-04 | sympathetic nervous system development (GO:0048485) | 1.48E-02 |
| | regulation of type 2 immune response (GO:0002828) | 2.23E-03 | regulation of early endosome to late endosome transport (GO:2000641) | 7.78E-03 |
| | single-organism behavior (GO:0044708) | 1.46E-03 | intracellular protein transmembrane transport (GO:0065002) | 5.67E-03 |
| | neuropeptide hormone activity (GO:0005184) | 2.25E-03 | RNA polymerase II transcription corepressor activity (GO:0001106) | 2.20E-03 |
| | neuropeptide receptor binding (GO:0071855) | 3.09E-03 | ATPase activator activity (GO:0001671) | 1.03E-02 |
| | peptidase activator activity (GO:0016504) | 7.71E-03 | heparan sulfate sulfotransferase activity (GO:0034483) | 1.03E-02 |
| | gated channel activity (GO:0022836) | 6.79E-03 | transcription corepressor activity (GO:0003714) | 4.96E-03 |
| | hormone activity (GO:0005179) | 1.94E-03 | insulin-like growth factor receptor binding (GO:0005159) | 1.16E-02 |
| Cortical subplate (CTXsp) | regulation of hormone levels (GO:0010817) | 1.15E-04 | alkali metal ion binding (GO:0031420) | 8.09E-03 |
| | pattern specification process (GO:0007389) | 7.26E-05 | potassium ion binding (GO:0030955) | 4.34E-03 |
| | regionalization (GO:0003002) | 1.99E-04 | death receptor activity (GO:0005035) | 6.09E-03 |
| | neurogenesis (GO:0022008) | 3.64E-04 | prenyltransferase activity (GO:0004659) | 1.04E-02 |
| | negative regulation of embryonic development (GO:0045992) | 1.24E-03 | MAP kinase activity (GO:0004707) | 9.20E-03 |
| | RNA polymerase II core promoter proximal region sequence-specific DNA binding transcription factor activity (GO:0000982) | 1.36E-03 | peroxisomal transport (GO:0043574) | 8.18E-04 |
| | receptor antagonist activity (GO:0048019) | 4.51E-03 | protein localization to peroxisome (GO:0072662) | 1.21E-02 |
| | receptor inhibitor activity (GO:0030547) | 5.23E-03 | protein targeting to peroxisome (GO:0006625) | 1.21E-02 |
| | neurotransmitter binding (GO:0042165) | 9.58E-03 | membrane hyperpolarization (GO:0060081) | 2.22E-03 |
| | excitatory extracellular ligand-gated ion channel activity (GO:0005231) | 7.46E-03 | aerobic respiration (GO:0009060) | 2.10E-02 |
| Hippocampal formation (HPF) | uterus development (GO:0060065) | 5.96E-06 | calcium channel regulator activity (GO:0005246) | 3.30E-04 |
| | maternal process involved in female pregnancy (GO:0060135) | 1.82E-04 | MAP kinase phosphatase activity (GO:0033549) | 7.37E-04 |
| | polyol catabolic process (GO:0046174) | 9.22E-03 | channel regulator activity (GO:0016247) | 5.82E-04 |
| | dopaminergic neuron differentiation (GO:0071542) | 5.94E-03 | receptor signaling protein activity (GO:0005057) | 2.56E-04 |
| | regulation of hair cycle (GO:0042634) | 1.01E-02 | substrate-specific channel activity (GO:0022838) | 2.15E-03 |
| | plus-end-directed microtubule motor | 7.04E-03 | single-organism behavior (GO:0044708) | 1.87E-06 |

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|---|---|---|---|---|
| | activity (GO:0008574) | | | |
| | neurotransmitter:sodium symporter activity (GO:0005328) | 8.57E-03 | gamma-aminobutyric acid signaling pathway (GO:0007214) | 1.07E-05 |
| | immunoglobulin binding (GO:0019865) | 1.11E-02 | regulation of synaptic transmission (GO:0050804) | 1.46E-05 |
| | neurotransmitter transporter activity (GO:0005326) | 1.30E-02 | behavior (GO:0007610) | 2.14E-05 |
| | hyaluronic acid binding (GO:0005540) | 1.11E-02 | cognition (GO:0050890) | 7.02E-06 |
| Hypothalamus (HY) | feeding behavior (GO:0007631) | 1.31E-04 | regulation of oligodendrocyte differentiation (GO:0048713) | 1.31E-03 |
| | pigment cell differentiation (GO:0050931) | 1.47E-03 | circadian behavior (GO:0048512) | 1.91E-03 |
| | melanocyte differentiation (GO:0030318) | 1.17E-03 | rhythmic behavior (GO:0007622) | 2.27E-03 |
| | insulin-like growth factor receptor signaling pathway (GO:0048009) | 7.80E-03 | positive regulation of glial cell differentiation (GO:0045687) | 1.31E-03 |
| | adult feeding behavior (GO:0008343) | 4.38E-03 | positive regulation of mesenchymal cell proliferation (GO:0002053) | 2.47E-04 |
| | peptide hormone binding (GO:0017046) | 3.63E-03 | cysteine-type endopeptidase inhibitor activity involved in apoptotic process (GO:0043027) | 4.82E-04 |
| | insulin receptor binding (GO:0005158) | 3.35E-03 | acid phosphatase activity (GO:0003993) | 3.92E-03 |
| | ligand-gated ion channel activity (GO:0015276) | 1.95E-03 | cysteine-type endopeptidase regulator activity involved in apoptotic process (GO:0043028) | 2.85E-03 |
| | ligand-gated channel activity (GO:0022834) | 1.95E-03 | glycoprotein binding (GO:0001948) | 2.62E-03 |
| | growth factor binding (GO:0019838) | 4.99E-03 | heparan sulfate proteoglycan binding (GO:0043395) | 7.20E-03 |
| Isocortex | monoamine transport (GO:0015844) | 8.19E-04 | negative regulation of phosphorylation (GO:0042326) | 3.32E-07 |
| | positive regulation of myeloid leukocyte cytokine production involved in immune response (GO:0061081) | 4.06E-03 | negative regulation of phosphorus metabolic process (GO:0010563) | 3.11E-07 |
| | oocyte development (GO:0048599) | 5.41E-03 | negative regulation of protein kinase activity (GO:0006469) | 8.72E-07 |
| | central nervous system neuron development (GO:0021954) | 1.86E-03 | negative regulation of kinase activity (GO:0033673) | 1.69E-06 |
| | type B pancreatic cell development (GO:0003323) | 4.06E-03 | negative regulation of protein phosphorylation (GO:0001933) | 3.80E-06 |
| | immunoglobulin binding (GO:0019865) | 8.76E-04 | phosphoric ester hydrolase activity (GO:0042578) | 4.04E-05 |
| | hydrolase activity, hydrolyzing N-glycosyl compounds (GO:0016799) | 1.42E-02 | phosphoprotein phosphatase activity (GO:0004721) | 2.25E-05 |
| | dicarboxylic acid transmembrane transporter activity (GO:0005310) | 1.66E-02 | MAP kinase phosphatase activity (GO:0033549) | 9.84E-04 |
| | MAP kinase activity (GO:0004707) | 6.44E-03 | Hsp70 protein binding (GO:0030544) | 2.23E-03 |
| | sodium channel regulator activity (GO:0017080) | 2.04E-02 | phosphatase activity (GO:0016791) | 6.84E-04 |
| Midbrain | H4 histone acetyltransferase activity (GO:0010485) | 6.86E-04 | regulation of postsynaptic membrane potential (GO:0060078) | 1.48E-07 |
| | neurotransmitter transporter activity (GO:0005326) | 2.30E-03 | regulation of dendritic spine morphogenesis (GO:0061001) | 3.39E-06 |
| | cofactor binding (GO:0048037) | 1.60E-03 | regulation of membrane potential | 1.70E-06 |

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|---|---|---|---|---|
| | | | (GO:0042391) | |
| | structural constituent of ribosome (GO:0003735) | 1.32E-03 | regulation of excitatory postsynaptic membrane potential (GO:0060079) | 1.07E-06 |
| | peptide hormone binding (GO:0017046) | 5.27E-03 | positive regulation of excitatory postsynaptic membrane potential (GO:2000463) | 4.35E-05 |
| | cholesterol biosynthetic process (GO:0006695) | 5.50E-09 | ephrin receptor binding (GO:0046875) | 9.17E-07 |
| | sterol biosynthetic process (GO:0016126) | 1.41E-08 | metal ion transmembrane transporter activity (GO:0046873) | 3.64E-04 |
| | organic hydroxy compound biosynthetic process (GO:1901617) | 1.13E-06 | kinase binding (GO:0019900) | 6.07E-04 |
| | organic hydroxy compound metabolic process (GO:1901615) | 2.13E-05 | potassium ion transmembrane transporter activity (GO:0015079) | 3.52E-04 |
| | isoprenoid biosynthetic process (GO:0008299) | 1.23E-04 | gated channel activity (GO:0022836) | 9.05E-04 |
| Medulla (MY) | learning or memory (GO:0007611) | 3.62E-08 | oxidoreductase activity, acting on a sulfur group of donors, NAD(P) as acceptor (GO:0016668) | 4.21E-03 |
| | cognition (GO:0050890) | 1.64E-07 | transforming growth factor beta receptor binding (GO:0005160) | 1.65E-02 |
| | regulation of synaptic transmission (GO:0050804) | 2.40E-06 | enzyme activator activity (GO:0008047) | 4.35E-03 |
| | memory (GO:0007613) | 2.12E-06 | protein homodimerization activity (GO:0042803) | 3.22E-03 |
| | single-organism behavior (GO:0044708) | 2.28E-05 | RNA polymerase II distal enhancer sequence-specific DNA binding transcription factor activity involved in positive regulation of transcription (GO:0001205) | 1.78E-02 |
| | protein kinase C activity (GO:0004697) | 6.70E-04 | serine family amino acid catabolic process (GO:0009071) | 3.45E-04 |
| | clathrin binding (GO:0030276) | 3.31E-02 | L-serine metabolic process (GO:0006563) | 8.68E-05 |
| | HMG box domain binding (GO:0071837) | 1.44E-02 | response to reactive oxygen species (GO:0000302) | 2.27E-04 |
| | neurotransmitter:sodium symporter activity (GO:0005328) | 1.59E-02 | excretion (GO:0007588) | 7.08E-04 |
| | semaphorin receptor binding (GO:0030215) | 5.26E-03 | placenta development (GO:0001890) | 4.06E-03 |
| Olfactory areas (OLF) | T cell mediated immunity (GO:0002456) | 1.12E-03 | phosphatidylinositol dephosphorylation (GO:0046856) | 1.21E-03 |
| | alpha-beta T cell differentiation involved in immune response (GO:0002293) | 7.33E-04 | inactivation of MAPK activity (GO:0000188) | 5.19E-04 |
| | T cell differentiation involved in immune response (GO:0002292) | 7.33E-04 | negative regulation of protein modification process (GO:0031400) | 6.09E-04 |
| | alpha-beta T cell activation involved in immune response (GO:0002287) | 7.33E-04 | negative regulation of protein phosphorylation (GO:0001933) | 6.80E-04 |
| | G-protein coupled receptor signaling pathway, coupled to cyclic nucleotide second messenger (GO:0007187) | 1.05E-04 | negative regulation of transferase activity (GO:0051348) | 1.30E-03 |
| | heparan sulfate proteoglycan binding (GO:0043395) | 5.76E-04 | MAP kinase phosphatase activity (GO:0033549) | 1.00E-03 |
| | proteoglycan binding (GO:0043394) | 1.93E-03 | phosphatase activity (GO:0016791) | 7.24E-04 |

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|---|---|---|---|---|
| | excitatory extracellular ligand-gated ion channel activity (GO:0005231) | 9.02E-04 | protein tyrosine phosphatase activity (GO:0004725) | 1.07E-03 |
| | neurotransmitter receptor activity (GO:0030594) | 5.02E-04 | calcium-dependent protein binding (GO:0048306) | 4.65E-04 |
| | protein phosphatase binding (GO:0019903) | 1.40E-03 | phosphoric ester hydrolase activity (GO:0042578) | 2.01E-03 |
| Pons (P) | cell-cell adhesion (GO:0098609) | 4.17E-07 | positive regulation of cardiac muscle hypertrophy (GO:0010613) | 4.86E-04 |
| | cell-cell adhesion via plasma-membrane adhesion molecules (GO:0098742) | 3.96E-07 | positive regulation of muscle hypertrophy (GO:0014742) | 4.86E-04 |
| | homophilic cell adhesion via plasma membrane adhesion molecules (GO:0007156) | 1.52E-06 | positive regulation of cellular component movement (GO:0051272) | 3.57E-04 |
| | heterophilic cell-cell adhesion via plasma membrane cell adhesion molecules (GO:0007157) | 3.35E-04 | positive regulation of locomotion (GO:0040017) | 4.38E-04 |
| | regulation of cell adhesion (GO:0030155) | 3.98E-04 | pigmentation (GO:0043473) | 4.42E-04 |
| | excitatory extracellular ligand-gated ion channel activity (GO:0005231) | 1.46E-03 | cGMP binding (GO:0030553) | 2.91E-05 |
| | extracellular ligand-gated ion channel activity (GO:0005230) | 9.06E-04 | RAGE receptor binding (GO:0050786) | 2.18E-04 |
| | extracellular-glutamate-gated ion channel activity (GO:0005234) | 1.51E-02 | cyclic nucleotide binding (GO:0030551) | 3.91E-04 |
| | ionotropic glutamate receptor activity (GO:0004970) | 1.66E-02 | sodium:dicarboxylate symporter activity (GO:0017153) | 4.68E-03 |
| | hexosaminidase activity (GO:0015929) | 1.10E-02 | calcium ion binding (GO:0005509) | 3.48E-03 |
| Palladium (PAL) | toxin metabolic process (GO:0009404) | 1.71E-04 | 2-oxoglutarate metabolic process (GO:0006103) | 5.47E-04 |
| | synaptic transmission (GO:0007268) | 2.72E-05 | regulation of steroid hormone biosynthetic process (GO:0090030) | 3.89E-04 |
| | response to steroid hormone (GO:0048545) | 1.22E-04 | multicellular organismal aging (GO:0010259) | 5.47E-04 |
| | positive regulation of secretion (GO:0051047) | 4.89E-05 | brown fat cell differentiation (GO:0050873) | 2.50E-04 |
| | behavior (GO:0007610) | 9.85E-05 | steroid metabolic process (GO:0008202) | 3.03E-04 |
| | neuropeptide hormone activity (GO:0005184) | 8.81E-08 | endodeoxyribonuclease activity, producing 5'-phosphomonoesters (GO:0016888) | 1.02E-02 |
| | GABA-A receptor activity (GO:0004890) | 1.07E-06 | GTPase activating protein binding (GO:0032794) | 7.96E-03 |
| | GABA receptor activity (GO:0016917) | 2.00E-06 | anion:anion antiporter activity (GO:0015301) | 2.31E-02 |
| | hormone activity (GO:0005179) | 8.71E-06 | receptor signaling complex scaffold activity (GO:0030159) | 1.54E-02 |
| | extracellular ligand-gated ion channel activity (GO:0005230) | 4.02E-05 | cysteine-type endopeptidase inhibitor activity involved in apoptotic process (GO:0043027) | 1.68E-02 |
| Striatum (STR) | CD4-positive, alpha-beta T cell differentiation (GO:0043367) | 1.13E-04 | synaptic transmission (GO:0007268) | 1.12E-07 |
| | epithelial cell maturation (GO:0002070) | 7.15E-04 | potassium ion transmembrane transport (GO:0071805) | 4.08E-06 |
| | T-helper cell differentiation (GO:0042093) | 6.06E-04 | cellular potassium ion transport (GO:0071804) | 4.08E-06 |
| | alpha-beta T cell differentiation involved in immune response (GO:0002293) | 8.35E-04 | potassium ion transport (GO:0006813) | 1.36E-05 |

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|---|---|---|---|---|
| | neuron projection guidance (GO:0097485) | 2.51E-04 | regulation of ion transmembrane transport (GO:0034765) | 1.63E-04 |
| | ligand-activated sequence-specific DNA binding RNA polymerase II transcription factor activity (GO:0004879) | 1.38E-04 | potassium ion transmembrane transporter activity (GO:0015079) | 6.99E-06 |
| | steroid hormone receptor activity (GO:0003707) | 2.44E-04 | potassium channel activity (GO:0005267) | 1.77E-05 |
| | 14-3-3 protein binding (GO:0071889) | 8.64E-04 | voltage-gated potassium channel activity (GO:0005249) | 2.01E-05 |
| | chloride channel activity (GO:0005254) | 6.68E-04 | inward rectifier potassium channel activity (GO:0005242) | 8.04E-05 |
| | anion channel activity (GO:0005253) | 1.05E-03 | monovalent inorganic cation transmembrane transporter activity (GO:0015077) | 3.48E-04 |
| Thalamus (TH) | synaptic transmission (GO:0007268) | 3.17E-06 | regulation of transmembrane transporter activity (GO:0022898) | 3.10E-06 |
| | chloride transmembrane transport (GO:1902476) | 8.57E-06 | regulation of ion transmembrane transporter activity (GO:0032412) | 2.43E-06 |
| | chloride transport (GO:0006821) | 1.50E-05 | regulation of transporter activity (GO:0032409) | 6.15E-06 |
| | nephron epithelium morphogenesis (GO:0072088) | 1.74E-04 | regulation of metal ion transport (GO:0010959) | 1.44E-05 |
| | nephron tubule morphogenesis (GO:0072078) | 1.74E-04 | regulation of ion transmembrane transport (GO:0034765) | 2.82E-05 |
| | extracellular ligand-gated ion channel activity (GO:0005230) | 3.15E-08 | quaternary ammonium group binding (GO:0050997) | 4.82E-04 |
| | ligand-gated ion channel activity (GO:0015276) | 7.41E-07 | steroid hormone receptor activity (GO:0003707) | 4.85E-04 |
| | ligand-gated channel activity (GO:0022834) | 7.41E-07 | SMAD binding (GO:0046332) | 1.03E-03 |
| | excitatory extracellular ligand-gated ion channel activity (GO:0005231) | 5.99E-06 | phospholipid binding (GO:0005543) | 1.50E-03 |
| | chloride transmembrane transporter activity (GO:0015108) | 1.35E-05 | ephrin receptor binding (GO:0046875) | 5.41E-03 |