UBERON:0000992 female gonad

(Unique DEGs among top-100 found by the distance-based method, 43 genes)
6 genes are specifically directly related to female gonad
2 additional genes are relevant to female gonad

ankrd12: ankyrin repeat domain 12:

This gene encodes a member of the ankyrin repeats-containing cofactor family. These proteins may **inhibit the transcriptional activity of nuclear receptors** through the recruitment of histone deacetylases. The encoded protein interacts with p160 coactivators and also represses transcription mediated by the coactivator alteration/deficiency in activation 3 (ADA3).
May recruit HDACs to the p160 coactivators/nuclear receptor complex to inhibit ligand-dependent transactivation.

ar: androgen receptor:

The androgen receptor gene is more than 90 kb long and codes for a protein that has 3 major functional domains: the N-terminal domain, DNA-binding domain, and androgen-binding domain. **The protein functions as a steroid-hormone activated transcription factor.** Upon binding the hormone ligand, the receptor dissociates from accessory proteins, translocates into the nucleus, dimerizes, and then **stimulates transcription of androgen responsive genes**. This gene contains 2 polymorphic trinucleotide repeat segments that encode polyglutamine and polyglycine tracts in the N-terminal transactivation domain of its protein. Expansion of the polyglutamine tract from the normal 9-34 repeats to the pathogenic 38-62 repeats causes spinal bulbar muscular atrophy (SBMA, also known as Kennedy's disease). Mutations in this gene are also associated with complete androgen insensitivity (CAIS).
Steroid hormone receptors are ligand-activated transcription factors that regulate eukaryotic gene expression and affect cellular proliferation and differentiation in target tissues. Transcription factor activity is modulated by bound coactivator and corepressor proteins. Transcription activation is down-regulated by NR0B2. Activated, but not phosphorylated, by HIPK3 and ZIPK/DAPK3.

arf4: ADP ribosylation factor 4:

This gene is a member of the human ARF gene family whose members encode small guanine nucleotide-binding proteins that stimulate the ADP-ribosyltransferase activity of cholera toxin and play a role in vesicular trafficking and as activators of phospholipase D. The gene products include 5 ARF proteins and 11 ARF-like proteins and constitute one family of the RAS superfamily. The ARF proteins are categorized as class I, class II and class III; this gene is a class II member. The members of each class share a common gene organization. The ARF4 gene spans approximately 12kb and contains six exons and five introns. This gene is the most divergent member of the human ARFs. Conflicting map positions at 3p14 or 3p21 have been reported for this gene.
GTP-binding protein that **functions as an allosteric activator of the cholera toxin catalytic subunit**, an ADP- ribosyltransferase. **Involved in protein trafficking**; may **modulate vesicle budding and uncoating within the Golgi apparatus**.

camk2b: calcium/calmodulin dependent protein kinase II beta:

The product of this gene belongs to the serine/threonine protein kinase family and to the Ca(2+)/calmodulin-dependent protein kinase subfamily. Calcium signaling is crucial for several aspects of plasticity at glutamatergic synapses. In mammalian cells, the enzyme is composed of four different chains: alpha, beta, gamma, and delta. The product of this gene is a beta chain. It is possible that distinct isoforms of this chain have different cellular localizations and interact differently with calmodulin.
Calcium/calmodulin-dependent protein kinase that functions autonomously after Ca(2+)/calmodulin-binding and autophosphorylation, and is **involved in dendritic spine and synapse formation, neuronal plasticity and regulation of sarcoplasmic reticulum Ca(2+) transport in skeletal muscle**. In neurons, plays an essential structural role in the reorganization of the actin cytoskeleton during plasticity by binding and bundling actin filaments in a kinase-independent manner. This structural function is required for correct targeting of CaMK2A.

chl1: cell adhesion molecule L1 like:

The protein encoded by this gene is a member of the L1 gene family of **neural cell adhesion molecules**. It is **a neural recognition molecule that may be involved in signal transduction pathways**. The deletion of one copy of this gene may be responsible for mental defects in patients with 3p- syndrome. This protein may also play a role in the growth of certain cancers.
Extracellular matrix and cell adhesion protein that **plays a role in nervous system development and in synaptic plasticity**. Both soluble and membranous forms promote neurite outgrowth of cerebellar and hippocampal neurons and suppress neuronal cell death. Plays a role in neuronal positioning of pyramidal neurons and in regulation of both the number of interneurons and the efficacy of GABAergic synapses. May play a role in **regulating cell migration in nerve regeneration and cortical development**.

col6a2: collagen type VI alpha 2 chain:

This gene encodes one of the three alpha chains of type VI collagen, a beaded **filament collagen found in most connective tissues**. The product of this gene contains several domains similar to von Willebrand Factor type A domains. These domains have been shown to bind extracellular matrix proteins, an interaction that explains the importance of this collagen in organizing matrix components. Mutations in this gene are associated with Bethlem myopathy and Ullrich scleroatonic muscular dystrophy. Three transcript variants have been identified for this gene.
Collagen VI acts as a cell-binding protein.

fbn2: fibrillin 2:

Fibrillins are structural components of 10-12 nm extracellular calcium-binding microfibrils, which occur either in association with elastin or in elastin-free bundles. Fibrillin-2-containing microfibrils **regulate the early process of elastic fiber assembly**. **Regulates osteoblast maturation** by controlling TGF-beta bioavailability and calibrating TGF-beta and BMP levels, respectively.

gja1: gap junction protein alpha 1 :

This gene is a member of the connexin gene family. The encoded protein is a component of gap junctions, which are composed of arrays of intercellular channels that provide a route for the diffusion of low molecular weight materials from cell to cell. The encoded protein is the major protein of gap junctions in the heart that are thought to **have a crucial role in the synchronized contraction of the heart and in embryonic development**. A related intronless pseudogene has been mapped to chromosome 5. Mutations in this gene have been associated with oculodentodigital dysplasia, autosomal recessive craniometaphyseal dysplasia and heart malformations.
Gap junction protein that **acts as a regulator of bladder capacity**. A gap junction consists of a cluster of closely packed pairs of transmembrane channels, the connexons, through which materials of low MW diffuse from one cell to a neighboring cell. May **play a critical role in the physiology of hearing** by participating in the recycling of potassium to the cochlear endolymph. Negative regulator of bladder functional capacity- acts by enhancing intercellular electrical and chemical transmission, thus sensitizing bladder muscles.

gls: glutaminase:

This gene encodes the K-type mitochondrial glutaminase. The encoded protein is an phosphate-activated amidohydrolase that catalyzes the hydrolysis of glutamine to glutamate and ammonia. This protein is **primarily expressed in the brain and kidney plays an essential role in generating energy for metabolism**, **synthesizing the brain neurotransmitter glutamate and maintaining acid-base balance in the kidney**. Catalyzes the first reaction **in the primary pathway for the renal catabolism of glutamine**. Plays a role in maintaining acid-base homeostasis. **Regulates the levels of the neurotransmitter glutamate in the brain**. Isoform 2 lacks catalytic activity.

iapp: islet amyloid polypeptide:

This gene encodes a member of the **calcitonin family of peptide hormones**. This **hormone is released from pancreatic beta cells** following food intake to **regulate blood glucose levels and act as a satiation signal**. Human patients with type 1 and advanced type 2 diabetes exhibit reduced levels of the encoded hormone in blood and pancreas. This protein also exhibits a bactericidal, antimicrobial activity.
Selectively inhibits insulin-stimulated glucose utilization and glycogen deposition in muscle, while not affecting adipocyte glucose metabolism.

ins1: insulin I:

This gene **encodes insulin**, a peptide hormone that plays a vital role in the regulation of carbohydrate and lipid metabolism. The encoded precursor protein undergoes proteolytic cleavage to produce a disulfide-linked heterodimeric functional protein that is stored in secretory granules. An increase in blood glucose levels, among others, induces the release of insulin from the secretory granules. Mice deficient in the functional hormone encoded by this gene develop diabetes mellitus.
Insulin decreases blood glucose concentration. It increases cell permeability to monosaccharides, amino acids and fatty acids. It accelerates glycolysis, the pentose phosphate cycle, and glycogen synthesis in liver.

ins2: insulin II;

This gene **encodes insulin**, a peptide hormone that plays a vital role in the regulation of carbohydrate and lipid metabolism. The encoded precursor protein undergoes proteolytic cleavage to produce a disulfide-linked heterodimeric functional protein that is stored in secretory granules. An increase in blood glucose levels, among others, induces the release of insulin from the secretory granules. Mice deficient in the functional hormone encoded by this gene develop diabetes mellitus.

Insulin decreases blood glucose concentration. It increases cell permeability to monosaccharides, amino acids and fatty acids. It accelerates glycolysis, the pentose phosphate cycle, and glycogen synthesis in liver.

nfia: nuclear factor I/A:

Recognizes and binds the palindromic sequence 5'- TTGGCNNNNNGCCAA-3' **present in viral and cellular promoters** and in the origin of replication of adenovirus type 2. These proteins are **individually capable of activating transcription and replication**.

nid1: nidogen 1:

Sulfated glycoprotein widely distributed in basement membranes and tightly **associated with laminin**. **Also binds to collagen IV and perlecan**. It probably has a role in cell-extracellular matrix interactions.

pcsk2: proprotein convertase subtilisin/kexin type 2 :

Involved in the processing of hormone and other protein precursors at sites comprised of pairs of basic amino acid residues. Responsible for the release of glucagon from proglucagon in pancreatic A cells.

rbp1: retinol binding protein 1, cellular:

Intracellular transport of retinol.

sat1: spermidine/spermine N1-acetyl transferase 1:

Enzyme which **catalyzes the acetylation of polyamines**. Substrate specificity-norspermidine = spermidine >> spermine > N(1)-acetylspermine > putrescine. This **highly regulated enzyme allows a fine attenuation of the intracellular concentration of polyamines**. Also **involved in the regulation of polyamine transport out of cells**. Acts on 1,3-diaminopropane, 1,5-diaminopentane, putrescine, spermidine (forming N(1)- and N(8)-acetylspermidine), spermine, N(1)-acetylspermidine and N(8)-acetylspermidine.

scg5: secretogranin V:

Acts as a molecular chaperone for PCSK2/PC2, preventing its premature activation in the regulated secretory pathway. Binds to inactive PCSK2 in the endoplasmic reticulum and facilitates its transport from there to later compartments of the secretory pathway where it is proteolytically matured and activated. Also required for cleavage of PCSK2 but does not appear to be involved in its folding. **Plays a role in regulating pituitary hormone secretion**. The C-terminal peptide inhibits PCSK2 in vitro.

sst: somatostatin:

Somatostatin inhibits the release of somatotropin.

snrpn: small nuclear ribonucleoprotein N:

This locus represents a paternally-expressed imprinted gene that encodes a component of the small nuclear ribonucleoprotein complex, which functions in pre-mRNA processing. Genomic and genetic changes in this region result in growth defects and lethality; the corresponding region in human is the critical region for Prader-Willi Syndrome. Alternative promoter use and alternative splicing result in a multitude of transcript variants encoding the same protein. Transcript variants may be bicistronic and also encode the SNRPN upstream reading frame protein (Snurf) from an upstream open reading frame. In addition, long spliced transcripts for small nucleolar RNA host gene 14 (Snhg14) may originate from the promoters at this locus and incorporate exons shared with this gene. May be **involved in tissue-specific alternative RNA processing events**.

soat1: sterol O-acyltransferase 1:

Catalyzes the formation of fatty acid-cholesterol esters, which are less soluble in membranes than cholesterol. **Plays a role in lipoprotein assembly and dietary cholesterol absorption**.

pyy: peptide YY:

This gut peptide **inhibits exocrine pancreatic secretion**, has a vasoconstrictory action and **inhibitis jejunal and colonic mobility**.

fermt2: fermitin family member 2:

Scaffolding protein that **enhances integrin activation** mediated by TLN1 and/or TLN2, but activates integrins only weakly by itself. Binds to membranes enriched in phosphoinositides. Enhances integrin-mediated cell adhesion onto the extracellular matrix and cell spreading; this requires both its ability to interact with integrins and with phospholipid membranes. **Required for the assembly of focal adhesions**. **Participates in the connection between extracellular matrix adhesion sites and the actin cytoskeleton**.

ttr: transthyretin:

This gene encodes a carrier protein **responsible for the transport of thyroid hormones and retinol**. The protein consists of a tetramer of identical subunits. Due to increased stability of the tetramer form of this encoded protein in mouse, compared to the human protein, this gene product has a reduced tendency to form amyloid fibrils. In humans, this protein binds beta-amyloid preventing its aggregation and providing a neuroprotective role in Alzheimer's disease.

Thyroid hormone-binding protein. Probably **transports thyroxine from the bloodstream to the brain**.

tuba4a: tubulin, alpha 4A:

Tubulin is the **major constituent of microtubules**. It binds two moles of GTP, one at an exchangeable site on the beta chain and one at a non-exchangeable site on the alpha chain.

tubb4a: tubulin, beta 4A class IVA:

Tubulin is the **major constituent of microtubules**. It binds two moles of GTP, one at an exchangeable site on the beta chain and one at a non-exchangeable site on the alpha chain.

vcl: vinculin:

Actin filament (F-actin)-binding protein involved in cell-matrix adhesion and cell-cell adhesion. Regulates cell- surface E-cadherin expression and potentiates mechanosensing by the E-cadherin complex. May also **play important roles in cell morphology and locomotion**.

nrsn1: neurensin 1:

May play an **important role in neural organelle transport, and in transduction of nerve signals or in nerve gro**wth. May play a role in **neurite extension**.

wt1: Wilms tumor 1 homolog:

This gene encodes a transcription factor that contains four zinc-finger motifs at the C-terminus and a proline/glutamine-rich DNA-binding domain at the N-terminus. It **plays an essential role in the normal development of the urogenital system**, and the orthologous human gene is mutated in a small subset of patients with Wilm's tumors. The mRNA for this gene has been shown to initiate translation from non-AUG (CUG) and AUG translation start sites, resulting in different isoforms.

Transcription factor that plays an important role in cellular development and cell survival. Regulates the expression of numerous target genes, including EPO. **Plays an essential role for development of the urogenital system.** Recognizes and binds to the DNA sequence 5'-CGCCCCCGC-3'. It has a tumor suppressor as well as an oncogenic role in tumor formation. Function may be isoform-specific- isoforms lacking the KTS motif may act as transcription factors. Isoforms containing the KTS motif may bind mRNA and play a role in mRNA metabolism or splicing.

zfpm2: zinc finger protein, multitype 2

Transcription regulator that **plays a central role in heart morphogenesis and development of coronary vessels from epicardium**, by regulating genes that are essential during cardiogenesis. Essential cofactor that acts via the formation of a heterodimer with transcription factors of the GATA family GATA4, GATA5 and GATA6. Such heterodimer can both activate or repress transcriptional activity, depending on the cell and promoter context. **Also required in gonadal differentiation**, possibly be regulating expression of SRY. Probably acts a corepressor of NR2F2.

slc6a1: solute carrier family 6 (neurotransmitter transporter, GABA), member 1:

Terminates the action of GABA by its high affinity sodium-dependent reuptake into presynaptic terminals.

kctd14: potassium channel tetramerisation domain containing 14.

gpm6a: glycoprotein m6a:

Involved in neuronal differentiation, including differentiation and migration of neuronal stem cells. **Plays a role in neuronal plasticity and is involved in neurite and filopodia**

outgrowth, filopodia motility and probably **synapse formation**. Gpm6a-induced filopodia formation involves mitogen-activated protein kinase (MAPK) and Src signaling pathways. Conflictingly, PubMed-22162747 reports that induced cellular protrusions are simple membrane-wrapped tubules without actin or tubulin-based cytoskeletons.

ndrg4: N-myc downstream regulated gene 4:

Contributes to the **maintenance of intracerebral BDNF levels within the normal range**, which is necessary for the preservation of spatial learning and the **resistance to neuronal cell death caused by ischemic stress**. May enhance growth factor- induced ERK1 and ERK2 phosphorylation. May attenuate NGF-promoted ELK1 phosphorylation in a microtubule-dependent manner.

dlg2: discs large MAGUK scaffold protein 2:

Required for **perception of chronic pain** through NMDA receptor signaling. **Regulates surface expression of NMDA receptors in dorsal horn neurons of the spinal cord**. Interacts with the cytoplasmic tail of NMDA receptor subunits as well as inward rectifying potassium channels. **Involved in regulation of synaptic stability** at cholinergic synapses. Part of the postsynaptic protein scaffold of excitatory synapses.

tenm2: teneurin transmembrane protein 2:

Involved in neural development, regulating the **establishment of proper connectivity within the nervous system**. Acts as a ligand of the ADGRL1 receptor. Promotes the formation of filopodia and enlarged growth cone in neuronal cells. Mediates axon guidance and homophilic and heterophilic cell-cell adhesion. May function as a cellular signal transducer.

tenm4: teneurin transmembrane protein 4.

Involved in neural development, regulating the **establishment of proper connectivity within the nervous system**. Plays a role in the establishment of the anterior-posterior axis during gastrulation. Regulates the differentiation and cellular process formation of oligodendrocytes and myelination of small- diameter axons in the central nervous system (CNS). Promotes activation of focal adhesion kinase. May function as a cellular signal transducer.

adamts19: a disintegrin-like and metallopeptidase (reprolysin type) with thrombospondin type 1 motif, 19:

This gene encodes a member of "a disintegrin and metalloproteinase with thrombospondin motifs" (ADAMTS) family of multi-domain matrix-associated metalloendopeptidases that have diverse roles in tissue morphogenesis and pathophysiological remodeling, in inflammation and in vascular biology. **This gene is predominantly expressed in the ovary** with lower levels of expression observed in kidney, heart, skeletal muscle, lung and testis. The encoded preproprotein undergoes proteolytic processing to generate an active protease.

lrrc4c: leucine rich repeat containing 4C:

May **promote neurite outgrowth of developing thalamic neurons**.

bnc2: basonuclin 2:

Probable transcription factor specific for skin keratinocytes. May **play a role in the differentiation of spermatozoa and oocytes**.

lrrtm4: leucine rich repeat transmembrane neuronal 4:

May play a role in the **development and maintenance of the vertebrate nervous system**. Exhibits strong synaptogenic activity, restricted to excitatory presynaptic differentiation.

arhgap28: Rho GTPase activating protein 28:

GTPase activator for the Rho-type GTPases by converting them to an inactive GDP-bound state.

nfasc: neurofascin:

This gene encodes an L1 family immunoglobulin cell adhesion molecule with multiple IGcam and fibronectin domains. The protein **functions in neurite outgrowth, neurite fasciculation, and organization of the axon initial segment** (AIS) and **nodes of Ranvier on axons** during early development. Both the AIS and nodes of Ranvier contain high densities of voltage-gated Na+ (Nav) channels which are clustered by interactions with cytoskeletal and scaffolding proteins including this protein, gliomedin, ankyrin 3 (ankyrin-G), and betaIV spectrin. This protein links the AIS extracellular matrix to the intracellular cytoskeleton. This gene undergoes extensive alternative splicing, and the full-length nature of some variants has not been determined.

Cell adhesion, ankyrin-binding protein which **may be involved in neurite extension, axonal guidance, synaptogenesis, myelination and neuron-glial cell interactions**.