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| Table S1 Tunicate orthologs of vertebrate proteins |  |
| Tunicate gene Unique ID\* | HGNC symbol | Uniprot | Expect value\*\* | Description taken from GeneCards database (see Methods) | SelectedReferences |
| Phmamm.g00013747 | ADGRL3 | Q9HAR2 | 0 as Latrophilin 3 of *Phallusia mammilata* | Plays a role in cell-cell adhesion and neuron guidance . | 56 |
| Cirobu.g00013347 | AES aka TLES | Q08117 | 4.00E-59 | similar in sequence to theDrosophila enhancer of split groucho, a protein involved in neurogenesis during embryonic development.  |  |
| Cirobu.g00012489 | AKAP2 | Q9Y2D5 | 4.00E-25 |  May be involved in establishing polarity in signaling systems  |  |
| Phmamm.g00004896 | ASXL3 | Q9C0F0 | 2E-43 - as *Phallusia mammillata* SXL3 precursor | act by forming multiprotein complexes, which are required to maintain the transcriptionally repressive state of homeotic genes throughout development. |  |
| Phmamm.g00004987 | CALD1 | Q05682 | 5E-38 as non-muscle caldesmon of *Phallusia mamillata* | plays an essential role in the regulation of smooth muscle and nonmuscle contraction. | 57 |
| Cirobu.g00003956 | CBLN1 | P23435 | 9.00E-39 | connecting synapses  |  |
| Cirobu.g00002666 | CDH1 | P12830 | 1E-115 as Ciona cadherin isoform X1 | Involved in mechanisms regulating cell-cell adhesions, mobility and proliferation of epithelial cells  | 58 |
| Cirobu.g00010294 | CDH2 | P19022 | 5.00E-12 | may be involved in neuronal recognition mechanism, may regulate dendritic spine density and control neural tube closure (GeneCards ) | 59 |
| Cirobu.g00002666 | CDH7 | Q9ULB5 | 2.00E-147 | cadherin 7 |  |
| Coinfl.g00007259 | CDH8 | P55286 | 7E-152 as Ciona Type II cadherin | expressed in brain and is putatively involved in synaptic adhesion, axon outgrowth and guidance . | 58 |
| Cisavi.g00011235 | CDH11 | P55287 | 2E-109 as *Ciona intestinali*s cadherin precursor | its upregulation during differentiation, suggests a specific function in bone development and maintenance . | 60 |
| Cirobu.g00001398 | CDH16 | O75309 | 3E-40 as *Ciona savigny* Type II cadherin | may play a role in the morphological organization of liver and intestine . |  |
| Cirobu.g00002666 | CDH18 | Q13634 | 2E-146 as Ciona Type II cadherin | This particular cadherin is expressed specifically in the central nervous system and is putatively involved in synaptic adhesion, axon outgrowth and guidance .  | 58 |
| Cirobu.g00009056 | CLDN1 | O95832 | 8.00E-42 | Tight junctions  | 28 |
| Cirobu.g00002206 | CLDN18 | P56856 | 1.00E-29 | Claudin18.Claudins are integral membrane proteins and components of tight junction strands, serving as a physical barrier between epithelial or endothelial cell sheets .  |  |
| Cirobu.g00002476 | CLDN19 | Q8N6F1 | 2.00E-40 | Tight junctions  | 28 |
| Cirobu.g00012793 | CLDND1 | Q9NY35 | 4.00E-21 | Located in cell surface.  | 61 |
| Cirobu.g00014646 | COL22A1 | Q8NFW1 | 0 | Acts as a cell adhesion ligand for skin epithelial cells and fibroblasts |  |
| Boleac.g00009169 | COL23A1 | Q86Y22 | 5.00E-113 | contains a single pass hydrophobic transmembrane domain . | 62 |
|  Cirobu.g00014791 | CRYGN | Q8WXF5 | 6E-17 vs gamma crystallin S (aka Cirobu.g00014791) of Ciona intestinalis | Crystallins are the dominant structural components of the vertebrate eye lens . | 46 |
|  Cirobu.g00014791 | CRYGS | P22914 | E-16 vs gamma crystallin S (aka Cirobu.g00014791) of Ciona intestinalis | Crystallins are the dominant structural components of the vertebrate eye lens . | 46 |
| Cirobu.g00008072 | DLX2 | Q07687 | 3E-29 as DLX-b of Oikopleura dioica |  DLX gene family contain a homeobox that is related to that of Distal-less (Dll), a gene expressed in the head and limbs of the developing | 63 |
| Cirobu.g00005203 | DLX3 | O60479 | 2 E-35 as DLX-c of Oikopleura dioica | Mutations in this gene have been associated with the autosomal dominant conditions trichodentoosseous syndrome a  | 63 |
| Cirobu.g00005364 | EFNA1 | P20827 | 4E-15 - as Phallus mammillata A-a precursor | crucial for migration, repulsion and adhesion during neuronal, vascular and epithelial development. | 64 |
| Cirobu.g00015386 | EFNA2 | O43921 | 1E-19 - as Phallus mammillata A-b precursor | crucial for migration, repulsion and adhesion during neuronal, vascular and epithelial development. | 30 |
| Cirobu.g00005966 | EFNA3 | P52797 | 4E-17 - as Phallus mammillata A-c precursor | Among its related pathways are Nervous system development and EPH-Ephrin signaling. | 64 |
| Cirobu.g00005966 | EFNA4 | P52798 | 1E-20 - as Phallus mammillata A-d precursor | implicated in mediating developmental events, especially in the nervous system and in erythropoiesis.  | 30 |
| Cirobu.g00005364 | EFNA5 | P52803 | 3E-21 - as *Ciona intestinalis* precursor | crucial for migration, repulsion and adhesion during neuronal, vascular and epithelial development. |  |
| Cirobu.g00013004 | FAM3D | Q96BQ1 | 2.00E-58 | regulation of glucose metabolism  | 65 |
| Cirobu.g00013155 | FBXO24 | O75426 | 2.00E-76 | involved in ubiquitinylation.  | 66 |
| Cirobu.g00012273 | FGF12 | P61328 | 5E-63 as *Botryllus schlosseri* fibroblast growth factor 11/12/13/14 | FGF family members possess broad mitogenic and cell survival activities, and are involved in a variety of biological processes, including embryonic development, cell growth, morphogenesis, tissue repair, tumor growth and invasion . | 67 |
| Cirobu.g00014816 | FGF5 | P12034 | 1E-31 as Ciona intestinalis fibroblast growth factor 4/5/6 | FGF family members possess broad mitogenic and cell survival activities, and are involved in a variety of biological processes, including embryonic development, cell growth, morphogenesis, tissue repair, tumor growth and invasion . | 67 |
| Cisavi.g00003564 | FLRT2 | O43155 | 3.00E-62 | regulates early embryonic vascular and neural development . | 68 |
| Cirobu.g00007675 | FLRT3 | Q9NZU0 | 2E-54 as *Ciona intestinalis* FLRT | Functions in cell-cell adhesion, cell migration and axon guidance . | 68 |
| Cirobu.g00013271 | FZD3 | Q9NPG1 | 2.00E-147 | May be involved in transduction and intercellular transmission of polarity information during tissue morphogenesis (CeneCards) |  |
| Cirobu.g00013271 | FZD6 | O60353 | 3E-134 vs PhallusiaFZ3/6 | May be involved in transduction and intercellular transmission of polarity information during tissue morphogenesis (CeneCards) |  |
| Cirobu.g00015669 | GJA4 | P35212 | 4.00E-41 | Gap Junction Protein Alpha 4 |  |
| Cirobu.g00002251 | GJA5 | P36382 | 1.00E-32 | Gap Junction Protein Alpha 5 |  |
| Cirobu.g00004266 | GJA8 | P48165 | 3.00E-57 | Gap Junction Protein Alpha 8 |  |
| Cirobu.g00007788 | GJB1 | P08034 | 6.00E-34 | Gap Junction Protein Beta 1 |  |
| Cirobu.g00007721 | GJB2 | P29033 | 7.00E-35 | Gap Junction Protein Beta 2 |  |
| Cirobu.g00014910 | GJB6 | O95452 | 3.00E-47 | Gap Junction Protein Beta 6 |  |
| Cirobu.g00006387 | GJC1 | P36383 | 3.00E-67 | Gap Junction Protein Gamma 1 |  |
| Harore.g00000543 | GNRH1 | P01148 | 6E-8 as Halocynthia roretzi hormone | Acts on the brain, retina, sympathetic nervous system, gonads and placenta in certain species. (From Aniseed) | 69 |
| Cirobu.g00014915 | H1FOO | Q8IZA3 | 9.00E-27 | pseudogene no summaries |  |
| Cirobu.g00014541 | HSPB1 | P04792 | 1.00E-46 | When overexpressed in C.elegans HSBP1 has severe effects on survival of the animals after thermal and chemical stress  |  |
| Cirobu.g00005867 | IRX5 | P78411 | 4E-28 as IRX-e of *Oikpleuro dioica* | Involved in craniofacial and gonadal development .  | 70 |
| Cirobu.g00007177 | MAGED1 | Q9Y5V3 | 7.00E-42 | May enhance ubiquitin ligase activity of RING-type zinc finger-containing E3 ubiquitin-protein ligases .  | 37 |
| Cirobu.g00007177 | MAGED2 | Q9UNF1 | 1.00E-47 | thought to play a role in cell cycle regulation and response to stress  | 37 |
| Cirobu.g00007177 | MAGED3 | Q12816 | 2.00E-41 | aka TRO trophinin - mediates cell adhesion between trophoblastic cells and the epithelial cells of the endometrium .  | 37 |
| Cirobu.g00007177 | MAGED4 | Q96JG8 | 4.00E-41 | May enhance ubiquitin ligase activity of RING-type zinc finger-containing E3 ubiquitin-protein ligases .  | 37 |
| Boschl.g00017367 | MIA | Q16674 | 1.00E-14 | involved in extracellular matrix organization . |  |
| Cirobu.g00006549 | MYADML2 | A6NDP7 | 3.00E-12 | elements of the machinery that controls specialized pathways of membrane traffic and cell signaling | 71 |
| Cirobu.g00000146 | MYBPC1 | Q00872 | 0 | plays an important role in muscle contraction by recruiting muscle-type creatine kinase to myosin filaments. |  |
| Cirobu.g00000146 | MYBPC2 | Q14324 | 0 |  The protein encoded by this locus is referred to as the fast-type isoform .  |  |
| Cirobu.g00000146 | MYBPC3 | Q14896 | 0 | heart muscle actin-binding  | 72 |
| Boschl.g00071919 | MYH1 | P12882 | 0 as myosin heavy chain, cardiac muscle isoform *Ciona intestinalis* | Myosin is a major contractile protein which converts chemical energy into mechanical energy through the hydrolysis of ATP.  | 73 |
| Harore.g00014293 | MYH13 | Q9UKX3 | 0 as embryonic muscle myosin heavy chain *Halocynthia roretzi* | Predicted to enable microfilament motor activity | 73 |
| Harore.g00003537 | MYH15 | Q9Y2K3 | 0 as embryonic muscle myosin heavy chain *Halocynthia roretzi* |  Predicted to be involved in extraocular skeletal muscle development . | 73 |
| Cirobu.g00005587 | MYH4 | Q9Y623 | 0 as myosin heavy chain, cardiac muscle isoform *Ciona intestinalis* | Located in myofibril. | 73 |
| Harore.g00010698 | MYH8 | P13535 | 0 as embryonic muscle myosin heavy chain *Halocynthia roretzi* | This gene is predominantly expressed in fetal skeletal muscle .  | 73 |
| Cirobu.g00008856 | MYL4 | P12829 | 2E-74 as smooth muscle isoform X3 of Ciona intestinalis | encodes a myosin alkali light chain that is found in embryonic muscle and adult atria . | 74 |
| Cirobu.g00008931 | MYL5 | Q02045 | 2.00E-82 | mitotic spindle  | 75 |
| Cirobu.g00009534 | MYL7 | Q01449 | 3E-73 as smooth muscle isoform X1 of Ciona intestinalis | predicted to enable calcium ion binding activity . | 76 |
| Phmamm.g00001992 | MYOM1 | P52179 | 7.00E-93 | Binds myosin, titin, and light meromyosin . | 77 |
| Cirobu.g00001822 | NECTIN1 | Q15223 | 6.00E-24 | an adhesion protein that plays a role in the organization of adherens junctions and tight junctions in epithelial and endothelial cells . |  |
| Cirobu.g00001822 | NECTIN3 | Q9NQS3 | 6.00E-31 | precursor of adaptive immunity system  | 78 |
| Cirobu.g00008036 | PALLD | Q8WX93 | 1.00E-109 | Cytoskeletal protein required for organization of normal actin cytoskeleton. Roles in establishing cell morphology, motility, cell adhesion and cell-extracellular matrix interactions  | 79 |
| Cirobu.g00011526 | PITX3 | O75364 | 2E-63 as pituitary homeobox pitx isoform a/b [Ciona intestinalis] | involved in lens formation during eye development . | 80 |
| Cisavi.g00003397 | PCDH12 | Q9NPG4 | 7E-83 as protocadherin *Ciona savignyi* | Acts as a regulator of cell migration, probably via increasing cell-cell adhesion . | 22 |
| Cisavi.g00009430 | PCDHGB7 | Q9Y5F8 | 5E-89 as protocadherin *Ciona savignyi* | neural cadherin-like cell adhesion protein most likely playing a critical role in the establishment and function of specific cell-cell connections in the brain.  |  |
| Cisavi.g00002522 | RGS18 | Q9NS28 | 4.00E-27 | Inhibits signal transduction by increasing the GTPase activity of G protein alpha subunits thereby driving them into their inactive GDP-bound form. |  |
| Boleac.g00006277 | SERPINA4 | P29622 | 3.00E-41 | Predicted to enable serine-type endopeptidase inhibitor activity  |  |
| Cirobu.g00003628 | STXBP6 | Q8NFX7 | 3.00E-38 | As amisyn\_Role in the SNARE conplex . in synapse vesicle fusion | 81 |
| Boleac.g00003200 | SYNPO2 | Q9UMS6 | 2.00E-13 |  Involved in positive regulation of actin filament bundle assembly; positive regulation of cell migration . |  |
| Cirobu.g00008275 | TFAP2B | Q92481 | 1E-124 vs generic TFAP2 |  involved in a large spectrum of important biological functions including proper eye, face, body wall, limb and neural tube development |  |
| Cirobu.g00000301 | TFAP2E | Q6VUC0 | 6E-109 vs generic TFAP2 |  involved in a large spectrum of important biological functions including proper eye, face, body wall, limb and neural tube development |  |
| Cirobu.g00003009 | TMEM150B | A6NC51 | 8.00E-19 | May have some role in extracellular matrix engulfment or growth factor receptor recycling, both of which can modulate cell survival . |  |
| Cirobu.g00007201 | TMPRSS11A | Q6ZMR5 | 2.00E-44 | may play a role in cellular senescence. Overexpression inhibits cell growth and induce G1 cell cycle arrest . |  |
| Phfumi.g00001551 | TMPRSS12 | Q86WS5 | 2.00E-58 | Required for normal sperm motility and binding to the zona pellucida . |  |
| Cirobu.g00006671 | TNNT1 | P13805 | 8E-85 as TroponinT, slow skletal muscle of *Ciona intestinalis* | This protein is the slow skeletal troponin T subunit.  | 82 |
| Cirobu.g00012836 | ZIC3 | O60481 | 5.00E-63 | functions as a transcription factor in early stages of left-right body axis formation in higher animals  | 83 |
| Cirobu.g00014064+A45 | ZMAT1 | Q5H9K5 | 2.00E-17 | This gene encodes a protein containing(C2H2)-type zinc fingers, which are similar to those found in the nuclear matrix protein matrin 3 . |  |