### Table S1: Gene ontology (GO) of up and down regulated genes for paired analysis of E2 vs Con-Ve; EPA vs Con-Ve and EPA vs E2

| Term                          | GO E2 vs Con-Ve increased expression | Term                          | GO E2 vs Con-Ve decreased expression | Term                          | GO EPA vs Con-Ve increased expression | Term                          | GO EPA vs Con-Ve decreased expression | Term                          | GO EPA vs E2 increased expression | Term                          | GO EPA vs E2 decreased expression |
|-------------------------------|--------------------------------------|-------------------------------|--------------------------------------|-------------------------------|--------------------------------------|-------------------------------|--------------------------------------|-------------------------------|---------------------------------|-------------------------------|---------------------------------|
| myosin filament               | FC (Log): 9                         | myosin complex                | FC (Log): 2                         |   | CHOP-C/EBP complex             | FC (Log): 3                    | troponin complex                | FC (Log): 8                     | TAP complex                    | FC (Log): 3                    | troponin complex                | FC (Log): 8                     |
| muscle myosin complex         | FC (Log): 4                         | extrinsic component of external side of plasma membrane | FC (Log): 4                    |   | junctional sarcoplasmic reticulum membrane | FC (Log): 3                    | MHC class I protein complex      | FC (Log): 9                    | junctional sarcoplasmic reticulum membrane | FC (Log): 3                    |
| sarcomeric reticulum lumen    | FC (Log): 3                         | high-density lipoprotein particle | FC (Log): 4                    |   | MHC class I protein complex     | FC (Log): 10                   | muscle myosin complex           | FC (Log): 3                    | IPAF inflammasome complex       | FC (Log): 3                    | myosin filament                 | FC (Log): 19                   |
| cardiac myofibril             | FC (Log): 2                         | very-low-density lipoprotein particle | FC (Log): 3                    |   | myosin filament                | FC (Log): 10                   | extrinsic component of external side of plasma membrane | FC (Log): 4                    | myosin filament                | FC (Log): 13                   |
| myofibril                     | FC (Log): 12                        | MHC class I protein complex    | FC (Log): 5                    |   | laminin-5 complex              | FC (Log): 3                    | IPAF inflammasome complex       | FC (Log): 3                    | muscle myosin complex           | FC (Log): 6                    |
| interstitial matrix           | FC (Log): 5                         | blood microparticle            | FC (Log): 11                   |   | very-low-density lipoprotein particle | FC (Log): 10                   | striated muscle thin filament    | FC (Log): 3                    | Golgi medial cisterna           | FC (Log): 7                    |
| I band                        | FC (Log): 7                         | apical part of cell            | FC (Log): 6                    |   | Golgi lumen                    | FC (Log): 5                    | junctional membrane complex     | FC (Log): 3                    | endoplasmic reticulum exit site | FC (Log): 7                    |
| striated muscle thin filament | FC (Log): 4                         | extracellular space            | FC (Log): 67                   |   | high-density lipoprotein particle | FC (Log): 5                    | muscle tendon junction          | FC (Log): 3                    | integral component of luminal side of endoplasmic reticulum membrane | FC (Log): 5                    |
| sarcomere                     | FC (Log): 8                         | extracellular region           | FC (Log): 77                   |   | interstitial matrix             | FC (Log): 4                    | terminal web                    | FC (Log): 3                    | phagocytic vesicle membrane     | FC (Log): 13                   |
| myosin complex                | FC (Log): 10                        | proteinaceous extracellular matrix | FC (Log): 13                   |   | Golgi medial cisterna           | FC (Log): 4                    | sarcoplasmic reticulum lumen    | FC (Log): 3                    | integral component of nuclear inner | FC (Log): 4                    | unconventional myosin complex | FC (Log): 3                    |
| Protein/Complex/Region | Density | Value | Protein/Complex/Region | Density | Value |
|------------------------|---------|-------|------------------------|---------|-------|
| contractile fiber      | 3       | 3.85  | extracellular matrix   | 11      | 1.26  |
| endoplasmic reticulum  | 4       | 2.26  | myosin II complex      | 4       | 3.18  |
| exit site              | 5       | 2.27  | muscle tendon junction | 3       | 3.39  |
| M band                 | 3       | 3.64  | cell surface           | 22      | 1.16  |
| vacuole                | 8       | 1.95  | I band                 | 12      | 3.18  |
| phagocytic vesicle     | 8       | 1.89  | high-density lipoprotein particle | 5 | 2.13 |
| membrane               | 11      | 1.15  | extracellular matrix   | 43      | 1.42  |
| M band                 | 3       | 3.46  | endoplasmic reticulum  | 23      | 1.05  |
| vacuole                | 8       | 1.89  | myofibril              | 19      | 3.11  |
| exocytotic vesicle     | 11      | 1.41  | collagen network       | 3       | 3.13  |
| sarcolemma             | 6       | 2.77  | melanosome             | 11      | 1.31  |
| stress fiber           | 5       | 2.77  | Z disc                 | 48      | 2.82  |
| basement membrane      | 6       | 2.50  | collagen trimer        | 9       | 1.30  |
| collagen trimer        | 5       | 2.81  | caveola                | 11      | 1.23  |
| actin filament         | 4       | 2.43  | extracellular region   | 19      | 1.25  |
| basement membrane      | 10      | 1.28  | costamere              | 7       | 2.74  |
| dystrophin-associated glycoprotein complex | 5 | 2.81 |
| dystrophin-associated glycoprotein complex | 7 | 2.85 |
| dystrophin-associated glycoprotein complex | 7 | 2.85 |
| dystrophin-associated glycoprotein complex | 2 | 2.87 | extracellular space | 5 | 1.25 | contractile ring | 3 | 3.13 |
| actin cytoskeleton | 8   | 1.86 | cytoplasmic, membrane-bounded vesicle | 15  | 1.18 | actomyosin | 4   | 2.73 | cell surface | 75  | 1.13 | myofibril | 86   | 2.78 |
|--------------------|-----|------|-------------------------------------|-----|------|-----------|-----|------|-------------|-----|------|-----------|-----|------|
| apical plasma membrane | 10  | 1.48 | secretory granule | 11  | 1.16 | voltage-gated sodium channel complex | 5   | 2.70 | melanosome | 12  | 1.13 | I band | 54   | 2.78 |
| cell surface | 16  | 1.22 | lysosome | 31  | 1.09 | interstitial matrix | 6   | 2.68 | organelle membrane | 11  | 1.10 | contractile fiber part | 81   | 2.77 |
| extracellular region | 41  | 1.10 | cell surface | 57  | 1.04 | myosin complex | 18  | 2.65 | perikaryon | 16  | 0.97 | contractile fiber | 89   | 2.77 |
| extracellular space | 28  | 0.77 | blood microparticle | 12  | 1.04 | stress fiber | 23  | 2.64 | cytoplasmic, membrane-bounded vesicle | 16  | 0.96 | Z disc | 48   | 2.76 |
| extracellular exosome | 42  | 0.52 | perikaryon | 13  | 0.98 | intercalated disc | 17  | 2.60 | blood microparticle | 14  | 0.95 | sarcosome | 76   | 2.75 |
| cytoplasm | 92  | 0.34 | neuronal cell body | 41  | 0.81 | sarcoplasmic reticulum membrane | 11  | 2.60 | membrane raft | 24  | 0.75 | myosin complex | 25   | 2.75 |
| membrane | 92  | 0.27 | neuron projection | 32  | 0.79 | plasma membrane raft | 4   | 2.60 | lysosomal membrane | 21  | 0.72 | sarcoplasmic reticulum | 24   | 2.71 |
| axon | 27  | 0.73 | sarcoplasmic reticulum | 19  | 2.57 | intercalated disc | 23  | 2.64 | extracellular exosome | 19  | 4   | costamere | 7   | 2.69 |
| extracellular exosome | 194 | 0.72 | neuronal muscular junction | 20  | 2.51 | neuronal cell body | 45  | 0.63 | complex of collagen trimers | 7   | 2.69 |
| intracellular membrane-bounded organelle | 48  | 0.54 | (T-tubule | 16  | 2.35 | intracellular membrane-bounded organelle | 63  | 0.62 | flotillin complex | 4   | 2.67 |
| cytosol | 104 | 0.41 | A band | 7   | 2.35 | axon | 31  | 0.62 | neuronal muscular junction | 23  | 2.65 |
| endoplasmic reticulum | 77  | 0.41 | integrin complex | 7   | 2.35 | endoplasmic reticulum | 10  | 0.57 | voltage-gated sodium channel complex | 5   | 2.64 |
| integral component of plasma membrane | 65  | 0.39 | lamellipodium membrane | 5   | 2.26 | cytoplasmic vesicle | 51  | 0.54 | interstitial matrix | 6   | 2.63 |
| mitochondrion | 93  | 0.30 | sarcosome | 30  | 2.21 | cytosol | 13  | 0.48 | sarcoplasm | 26   | 2.62 |
| membrane | 343 | 0.16 | axonal growth cone | 6   | 1.96 | integral component of plasma membrane | 84  | 0.45 | A band | 15   | 2.54 |
| basement membrane | 20  | 1.91 | endoplasmic reticulum membrane | 52  | 0.43 | integrin complex | 10  | 2.54 |
| Term                              | Code | Unit | Term                                      | Code | Unit | Term                                      | Code | Unit |
|----------------------------------|------|------|-------------------------------------------|------|------|-------------------------------------------|------|------|
| presynaptic active zone          | 6    |      | Golgi apparatus                           | 86   | 0.41 | banded collagen fibril                    | 4    | 2.54 |
| basal plasma membrane            | 8    | 1.79 | perinuclear region of cytoplasm           | 49   | 0.38 | fibrillar collagen trimer                 | 4    | 2.54 |
| cortical actin cytoskeleton       | 8    | 1.76 | membrane                                  | 43   | 0.18 | protein complex involved in cell adhesion | 10   | 2.41 |
| actin cytoskeleton               | 36   | 1.70 | cytoplasm                                 | 40   | 0.17 | actomyosin                                | 23   | 2.40 |
| cytoplasmic side of plasma       | 8    | 1.63 | membrane                                  |      |      | stress fiber                              | 20   | 2.38 |
| filopodium                       | 13   | 1.62 |                                          |      |      | contractile actin filament bundle         | 20   | 2.38 |
| lateral plasma membrane          | 9    | 1.60 |                                          |      |      | sodium channel complex                    | 5    | 2.36 |
| Glainellipodium                  | 25   | 1.47 |                                          |      |      | intercalated disc                         | 16   | 2.32 |
| presynapse                       | 9    | 1.38 |                                          |      |      | T-tubule                                  | 17   | 2.31 |
| proteinaceous extracellular matrix | 43   | 1.31 |                                          |      |      | filopodium membrane                       | 5    | 2.28 |
| actin filament                   | 9    | 1.27 |                                          |      |      | actin filament bundle                     | 20   | 2.24 |
| receptor complex                 | 17   | 1.21 |                                          |      |      | basement membrane                         | 25   | 2.09 |
| growth cone                      | 20   | 1.19 |                                          |      |      | sarcolemma                                | 36   | 2.04 |
| postsynaptic density             | 30   | 1.19 |                                          |      |      | cell-cell contact zone                    | 17   | 2.03 |
| endomembrane system              | 14   | 1.16 |                                          |      |      | extracellular matrix component            | 31   | 2.02 |
| bicellular tight junction         | 16   | 1.15 |                                          |      |      | cortical actin cytoskeleton               | 15   | 2.01 |
| basolateral plasma membrane      | 24   | 1.10 |                                          |      |      | actin cytoskeleton                        | 101  | 1.95 |
| cytoplasmic vesicle membrane     | 14   | 1.09 |                                          |      |      | filopodium                                | 20   | 1.79 |
| cell junction                    | 83   | 1.07 |                                          |      |      | cortical actin cytoskeleton               | 18   | 1.74 |
| focal adhesion                   | 45   | 1.07 |                                          |      |      | lamellipodium                             | 32   | 1.68 |
| cytoskeleton                     | 11   | 0.96 |                                          |      |      | presynaptic active zone                   | 6    | 1.63 |
| axon                             | 39   | 0.94 |                                          |      |      | proteinaceous extracellular matrix        | 63   | 1.61 |
| Text                         | TF  | TF  |
|------------------------------|-----|-----|
| cell cortex                  | 15  | 0.92|
| cell surface                 | 62  | 0.84|
| cell-cell junction           | 19  | 0.78|
| apical plasma membrane       | 31  | 0.78|
| cell-cell adherens junction  | 29  | 0.74|
| microtubule                  | 30  | 0.74|
| postsynaptic membrane        | 20  | 0.71|
| synapse                      | 45  | 0.70|
| perinuclear region of cytoplasm | 60 | 0.66|
| dendrite                     | 42  | 0.64|
| neuronal cell body           | 45  | 0.62|
| integral component of plasma membrane | 91 | 0.56|
| Golgi membrane               | 32  | 0.53|
| endoplasmic reticulum        | 10  | 3   | 0.50|
| endoplasmic reticulum membrane | 54 | 0.47|
| cell projection              | 54  | 0.46|
| cytoplasmic vesicle          | 48  | 0.43|
| cytoplasm                    | 49  | 0.43|
| membrane                     | 50  | 0.40|
| cytosol                      | 12  | 2   | 0.31|
| plasma membrane              | 33  | 2   | 0.31|
| extracellular exosome        | 17  | 2   | 0.23|
| cell division site part      | 10  | 1.59|
| cell division site           | 10  | 1.59|
| collagen trimer              | 15  | 1.56|
| lateral plasma membrane      | 9   | 1.54|
| basal plasma membrane        | 7   | 1.54|
| cell cortex part             | 22  | 1.53|
| kinesin complex              | 9   | 1.52|
| cell surface furrow          | 8   | 1.51|
| cleavage furrow              | 8   | 1.51|
| plasma membrane raft         | 17  | 1.49|
| actin filament               | 16  | 1.43|
| cell cortex                  | 38  | 1.35|
| caveola                      | 14  | 1.35|
| basal part of cell           | 9   | 1.32|
| postsynaptic specialization   | 34  | 1.32|
| postsynaptic density         | 34  | 1.32|
| transcriptional repressor complex | 11 | 1.28|
| cell leading edge            | 52  | 1.27|
| actin-based cell projection  | 29  | 1.27|
| apical junction complex      | 20  | 1.24|
| excitatory synapse           | 35  | 1.24|
| extracellular matrix         | 69  | 1.21|
| cytoplasmic region           | 41  | 1.19|
| Term                          | Value 1 | Value 2 |
|-------------------------------|---------|---------|
| ruffle                        | 21      | 1.18    |
| cell-substrate adherens junction | 50   | 1.14    |
| receptor complex               | 41      | 1.14    |
| site of polarized growth       | 24      | 1.14    |
| cell-substrate junction        | 50      | 1.13    |
| growth cone                    | 23      | 1.11    |
| dendritic spine                | 19      | 1.11    |
| neuron spine                   | 19      | 1.09    |
| focal adhesion                 | 47      | 1.07    |
| synapse                       | 104     | 1.05    |
| postsynapse                    | 53      | 1.05    |
| basolateral plasma membrane    | 27      | 1.01    |
| bicellular tight junction       | 15      | 1.00    |
| synapse part                   | 79      | 0.99    |
| terminal bouton                | 13      | 0.98    |
| occluding junction             | 15      | 0.97    |
| apical plasma membrane         | 37      | 0.97    |
| postsynaptic membrane          | 25      | 0.97    |
| adherens junction              | 77      | 0.97    |
| anchoring junction             | 79      | 0.96    |
| cytoskeleton                   | 225     | 0.95    |
| cell-cell adherens junction    | 36      | 0.94    |
| plasma membrane receptor complex | 18  | 0.94    |
| cell junction                  | 154     | 0.94    |
| synaptic membrane              | 33      | 0.93    |
| Term                                         | Score |
|----------------------------------------------|-------|
| leading edge membrane                        | 16    |
| cation channel complex                       | 17    |
| integral component of endoplasmic reticulum membrane | 14 |
| cell-cell junction                           | 73    |
| apical part of cell                          | 45    |
| plasma membrane region                       | 106   |
| neuron projection terminus                   | 21    |
| plasma membrane protein complex              | 50    |
| intrinsic component of endoplasmic reticulum membrane | 14 |
| cytoskeletal part                            | 160   |
| transmembrane transporter complex            | 30    |
| ion channel complex                          | 27    |
| axon terminus                                | 19    |
| transporter complex                          | 30    |
| perinuclear region of cytoplasm              | 71    |
| transport vesicle                            | 31    |
| membrane microdomain                         | 33    |
| membrane raft                                | 33    |
| supramolecular fiber                         | 67    |
| polymeric cytoskeletal fiber                 | 67    |
| Term                              | Score | Confidence |
|----------------------------------|-------|------------|
| axon                             | 54    | 0.73       |
| axon part                        | 29    | 0.72       |
| presynapse                       | 31    | 0.72       |
| microtubule                      | 38    | 0.71       |
| dendrite                         | 59    | 0.70       |
| neuron projection                | 115   | 0.68       |
| cell surface                     | 81    | 0.67       |
| neuronal cell body               | 58    | 0.67       |
| cell body                        | 65    | 0.65       |
| neuron part                      | 144   | 0.64       |
| membrane region                  | 36    | 0.61       |
| plasma membrane part             | 222   | 0.61       |
| cell projection                  | 182   | 0.59       |
| somatodendritic compartment     | 79    | 0.59       |
| integral component of plasma membrane | 115 | 0.58     |
| cell projection part             | 91    | 0.55       |
| nuclear envelope                 | 36    | 0.54       |
| intrinsic component of plasma membrane | 117 | 0.53     |
| endoplasmic reticulum membrane   | 73    | 0.52       |
| endoplasmic reticulum            | 128   | 0.51       |
| nuclear outer membrane-endoplasmic reticulum membrane network | 73 | 0.49 |
| non-membrane-bounded organelle   | 328   | 0.49       |
| Intracellular non-membrane-bounded organelle | 328 0.49 |
|-------------------------------------------|---------|
| Golgi apparatus part                      | 58 0.48 |
| Golgi membrane                            | 41 0.46 |
| Endoplasmic reticulum part                | 79 0.45 |
| Golgi apparatus                            | 101 0.41 |
| Endomembrane system                        | 277 0.40 |
| Microtubule cytoskeleton                   | 83 0.39 |
| Protein complex                            | 303 0.34 |
| Cytoplasmic part                           | 517 0.33 |
| Cytoplasm                                  | 743 0.32 |
| Cytoplasmic, membrane-bounded vesicle      | 77 0.31 |
| Cytoplasmic vesicle                        | 85 0.30 |
| Extracellular region part                  | 276 0.30 |
| Intracellular vesicle                      | 85 0.30 |
| Cell periphery                             | 406 0.27 |
| Vesicle                                    | 250 0.27 |
| Membrane-bounded vesicle                   | 238 0.27 |
| Plasma membrane                            | 391 0.25 |
| Extracellular region                        | 303 0.24 |
| Organelle part                             | 504 0.20 |
| Extracellular vesicle                      | 176 0.20 |
| Extracellular exosome                      | 175 0.20 |
| Extracellular organelle                    | 176 0.19 |
| Intracellular part                          | 869 0.17 |
| Macromolecular complex                     | 326 0.16 |
| Term               | Count | Avg Frequency |
|--------------------|-------|---------------|
| intracellular      | 896   | 0.16          |
| intracellular organelle | 748   | 0.16          |
| intracellular organelle part | 473   | 0.14          |
| organelle part     | 801   | 0.13          |
| cell               | 1018  | 0.05          |
| cell part          | 1015  | 0.05          |
Table S2: Gene functional category (GFC) of up and down regulated genes for paired analysis of E2 vs Con-Ve; EPA vs Con-Ve and EPA vs E2

| E2 vs Con-Ve upregulated genes | E2 vs Con-Ve downregulated genes | EPA vs Con-Ve upregulated genes | EPA vs Con-Ve downregulated genes | EPA vs E2 upregulated genes | EPA vs E2 downregulated genes |
|--------------------------------|---------------------------------|---------------------------------|---------------------------------|-----------------------------|-------------------------------|
| GFC                            | FC (Log)                        | GFC                             | FC (Log)                        | GFC                         | No.                           | FC (Log)                        |
| Thick filament* 9 6.22 Collagen degradation 5 4.33 VLDL 5 3.46 Thick filament* 10 4.05 Protein kinase inhibitor 4 2.48 Thick filament* 10 4.01 |
| Muscle protein* 19 5.18 VLDL 3 4.22 Collagen degradation 6 3.09 Cholesterol biosynthesis 15 3.90 Iron transport 9 2.26 Cholesterol biosynthesis 15 3.85 |
| Myosin* 11 4.51 Acute phase 5 3.78 MHC I 4 2.90 Muscle protein* 35 3.75 Collagen degradation 7 2.06 Muscle protein* 36 3.74 |
| Sarcoplasmic reticulum* 5 3.71 Antiviral defense 18 3.62 Sushi 13 2.74 Sterol biosynthesis 16 3.62 MHC I 8 2.04 Sterol biosynthesis 16 3.57 |
| Motor protein* 13 3.34 Complement pathway 4 3.34 Antioxidant 4 2.69 Sodium/potassium transport 4 3.32 Sushi 12 1.97 Steroid biosynthesis 18 3.19 |
| Chloride channel 4 3.11 Innate immunity 34 3.27 Iron transport 6 2.66 Steroid biosynthesis 18 3.24 Complement pathway 8 1.85 Sarcoplasmic reticulum* 17 3.11 |
| Basement membrane 3 3.09 Iron transport 3 3.16 Complement pathway 7 2.65 Cholesterol metabolism 24 3.12 Chemotaxis 18 1.74 Cholesterol metabolism 23 3.01 |
| Extracellular matrix 20 3.08 Chemotaxis 12 3.13 Acute phase 6 2.54 Sterol metabolism 25 3.01 Serine esterase 6 1.74 Myosin* 19 2.93 |
| Chloride 5 2.89 Heparin-binding 9 3.12 Peroxidase 5 2.46 Myosin* 19 2.98 Antioxidant 5 1.70 Sterol metabolism 24 2.90 |
| Actin-binding 17 2.75 Immunity 44 2.91 Heparin-binding 16 2.45 Sarcoplasmic reticulum* 14 2.88 Neurotransmitter transport 6 1.66 Protein kinase inhibitor 5 2.78 |
| Carbohydrate metabolism 5 2.43 Sushi 5 2.87 Gamma-carboxyglutamic acid 4 2.43 Steroid metabolism 25 2.75 Amino-acid transport 6 1.66 Steroid metabolism 24 2.64 |
| Calmodulin-binding 7 2.32 Inflammatory response 15 2.67 HDL 4 2.43 Protein kinase inhibitor 4 2.51 Antiviral defense 23 1.58 Myogenesis* 10 2.46 |
| Voltage-gated channel 6 2.13 Pyrrolidone carboxylic acid 5 2.54 Pyrrolidone carboxylic acid 12 2.30 CBS domain 5 2.39 Heparin-binding 16 1.46 CBS domain 5 2.34 |
| Immunoglobulin domain 16 1.73 Serine protease inhibitor 7 2.51 Proteoglycan 9 2.28 Actin-binding 60 2.25 Copper 8 1.43 Basement membrane 9 2.31 |
| Cell adhesion 14 1.60 Cytokine 15 2.36 Signal transduction inhibitor 7 2.08 Lipid biosynthesis 37 2.20 Inflammatory response 28 1.40 Actin-binding 64 2.29 |
| Calcium 23 1.47 Nucleotide/transferase 5 2.17 Biomembranization 5 2.06 Myogenesis* 8 2.19 Proteoglycan 8 1.38 Heparan sulfate 4 2.27 |
| Secreted 41 1.28 Lipid 5 2.01 Serine 6 2.05 LIM domain 16 2.11 FAD 18 1.34 Notch signaling 11 2.17 |
| Disulfide bond | Transport | Protease inhibitor | 7 | 1.18 | Proteolysis | 16 | 2.04 | Sodium channel | 6 | 2.09 | Pyrollidone | 12 | 1.30 | Motor protein* | 29 | 2.13 |
|---------------|----------|-------------------|---|------|------------|---|------|----------------|---|------|------------|---|------|----------------|---|------|
| Developmental protein | Hydroxylation | 5 | 1.96 | Sulfation | 6 | 2.01 | Motor protein* | 27 | 2.07 | Innate immunity | 54 | 1.28 | Laminin EGF-like domain | 7 | 2.12 |
| Glycoprotein | Zymogen | 11 | 1.82 | Growth factor | 21 | 2.00 | Integrin | 11 | 2.05 | Serine protease inhibitor | 10 | 1.22 | Calmodulin-binding | 29 | 2.01 |
| Ion transport | Extracellular matrix | 11 | 1.68 | Extracellular matrix | 36 | 1.89 | Calmodulin-binding | 28 | 2.01 | Lipid transport | 10 | 1.20 | Integrin | 11 | 2.00 |
| Methylation | Microsome | 6 | 1.64 | Inflammatory response | 24 | 1.85 | Basement membrane | 7 | 1.99 | Immunity | 77 | 1.19 | Lipid biosynthesis | 33 | 1.99 |
| Signal | Secreted | 73 | 1.57 | GPI-anchor | 20 | 1.79 | Lammin EGF-like domain | 6 | 1.95 | Glycosidase | 12 | 1.17 | LIM domain | 15 | 1.97 |
| Nucleotide-binding | GTP-binding | 14 | 1.53 | Innate immunity | 31 | 1.64 | Cell shape | 5 | 1.94 | Hydroxylation | 10 | 1.15 | Mitogen | 7 | 1.91 |
| Coiled coil | Polymorphism | 8 | 1.39 | Zymogen | 26 | 1.56 | Notch signaling pathway | 9 | 1.93 | Flavoprotein | 19 | 1.12 | Cell shape | 5 | 1.89 |
| Cytoplasm | Lipoprotein | 26 | 1.19 | Lipid degradation | 12 | 1.54 | Fatty acid biosynthesis | 10 | 1.88 | Metalloproteinase | 18 | 1.11 | SH3-binding | 11 | 1.82 |
| Phosphoprotein | Disulfide bond | 100 | 1.13 | Carbohydrate metabolism | 11 | 1.53 | SH3-binding | 11 | 1.87 | Lipid degradation | 11 | 1.10 | Extracellular matrix | 42 | 1.79 |
| | Glycoprotein | 109 | 0.97 | Lipid transport | 10 | 1.51 | Exocytosis | 12 | 1.86 | Acute phase | 6 | 1.09 | Collagen | 15 | 1.77 |
| | Hydrolyase | 46 | 0.94 | Immunity | 47 | 1.50 | cAMP | 6 | 1.81 | Proto-oncogene | 11 | 1.06 | Exocytosis | 11 | 1.68 |
| | Protease | 15 | 0.92 | Flavoprotein | 15 | 1.48 | Phospholipid biosynthesis | 8 | 1.79 | Lysosome | 35 | 1.05 | Fatty acid biosynthesis | 9 | 1.68 |
| | Endoplasmic reticulum | 27 | 0.89 | Angiogenesis | 14 | 1.47 | Tight junction | 14 | 1.75 | Signal transduction inhibitor | 8 | 1.05 | Neurogenesis | 40 | 1.64 |
| | RNA-binding | 16 | 0.87 | Hydroxylation | 10 | 1.46 | Endocytosis | 19 | 1.68 | Cytokine | 26 | 1.01 | Endocytosis | 19 | 1.63 |
| | Signal | 117 | 0.82 | Metalloproteinase | 16 | 1.44 | Phospholipid metabolism | 8 | 1.67 | Peroxisome | 11 | 1.01 | Alternative promoter usage | 9 | 1.58 |
| | Nucleotide-binding | 39 | 0.61 | Secreted | 18 | 8 | 1.43 | Alternative promoter usage | 9 | 1.63 | Extracellular matrix | 32 | 1.00 | Voltage-gated channel | 21 | 1.57 |
| | Zinc | 43 | 0.49 | FAD | 13 | 1.42 | Signal transduction inhibitor | 6 | 1.58 | Growth factor | 18 | 0.99 | Tight junction | 12 | 1.48 |
| | Metal-binding | 66 | 0.41 | Cytokine | 22 | 1.41 | Voltage-gated channel | 19 | 1.48 | Sodium | 12 | 0.97 | Cell adhesion | 65 | 1.45 |
| | Cytoplasm | 79 | 0.30 | Collagen | 9 | 1.36 | Extracellular matrix | 32 | 1.44 | Lyase | 14 | 0.91 | Intermediate filament | 10 | 1.36 |
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| Residues       | Value | Cell function/Process                                                                 | Value | Other function/Process    |
|---------------|-------|--------------------------------------------------------------------------------------|-------|---------------------------|
| Monoxygenase  | 12    | Cell adhesion                                                                        | 1.13  | Peroxidase                | 5     | Developmental protein     | 116   | 1.20                      |
| EGF-like      | 20    | Cell junction                                                                        | 1.11  | GPI-anchor                | 18    | Calcium                   | 96    | 1.16                      |
| Lysosome      | 22    | Fatty acid metabolism                                                                | 1.10  | Protease inhibitor        | 14    | EGF-like domain           | 26    | 1.16                      |
| Heme          | 15    | GTPase activation                                                                    | 1.09  | Hemostasis                | 7     | Hydroxylation             | 10    | 1.13                      |
| Oxidoreductase| 56    | Sodium transport                                                                     | 1.08  | NAD                        | 20    | Differentiation           | 73    | 1.12                      |
| Serine        | 15    | Angiogenesis                                                                         | 1.07  | Polymorphism               | 24    | Cleavage on pair of basic residues | 28  | 1.12                      |
| Neurogenesis  | 21    | Cleavage on pair of basic residues                                                  | 1.04  | Microsome                 | 15    | GTPase activation         | 18    | 1.09                      |
| Iron          | 31    | Potassium transport                                                                  | 1.00  | Disulfide bond            | 12    | 1.16                      |
| Disulfide bond| 25    | Myristate                                                                            | 0.98  | Angiogenesis              | 16    | 0.63                      |
| Glycoprotein  | 30    | Sodium                                                                                | 0.97  | NAD                       | 13    | Hydrolyase                | 150   | 0.62                      |
| Cell adhesion | 35    | Proto-oncogene                                                                        | 0.88  | Glycoprotein              | 11    | 1.09                      |
| Protease      | 41    | Guanine-nucleotide-releasing factor                                                  | 0.87  | Nucleotidyltransferase    | 88    | 1.08                      |
| Signal        | 32    | Calcium                                                                               | 0.81  | GTP-binding               | 14    | 1.07                      |
| Lipid         | 30    | Developmental protein                                                                | 0.80  | EGF-like domain           | 102   | 1.06                      |
| Metabolism    | 56    | Lipid-binding                                                                         | 0.80  | Cleavage on pair           | 24    | 1.04                      |
| Lipoprotein   | 56    | NADP                                                                                 | 0.80  | Ion channel               | 18    | 1.04                      |
| Hydrolase     | 11    | Microtubule                                                                           | 0.77  | Lipid metabolism          | 27    | 1.03                      |
| Developmental protein | 67    | Potassium                                                                            | 0.73  | NADP                      | 12    | 0.99                      |
| Differentiation| 44    | Cytoskeleton                                                                          | 0.72  | Oxidoreductase            | 106   | 0.98                      |
| Calcium       | 56    | EGF-like domain                                                                       | 0.71  | Carbohydrate metabolism  | 22    | 0.97                      |
| Apoptosis     | 30    | Ion channel                                                                           | 0.57  | Cell adhesion             | 31    | 0.88                      |
| Immunoglobulin domain | 29    | Lipid-binding                                                                         | 0.55  | Lipoprotein               | 18    | 0.86                      |
| Metal-binding | 16    | Differentiation                                                                       | 0.23  | Heme                      | 58    | 0.84                      |
| Synapse       | 32    | NADP                                                                                 | 0.84  | Signal                    | 371   | 0.49                      |
| Methyltransferase | 22    | Lipoprotein                                                                           | 0.84  | Ion transport             | 66    | 0.52                      |
| Postsynaptic cell membrane | 16    | Lipid-binding                                                                         | 16    | Postsynaptic cell membrane | 16    | 0.81                      |
| Synapse       | 32    | NADP                                                                                 | 0.84  | Signal                    | 371   | 0.49                      |
| Protein Function                  | % Coefficient | Protein Function                  | % Coefficient |
|----------------------------------|---------------|-----------------------------------|---------------|
| Glycosyltransferase              | 0.82          | Iron                              | 0.48          |
| Signal-anchor                    | 0.82          | Magnesium                         | 0.47          |
| Iron                             | 0.77          | Apoptosis                         | 0.46          |
| Kinase                           | 0.73          | Protease                          | 0.43          |
| Apoptosis                        | 0.70          | Serine/threonine/threonine kinase | 0.70          |
| Differentiation                  | 0.69          | Endoplasmic reticulum             | 0.39          |
| Lipoprotein                      | 0.66          | Calcium                           | 0.38          |
| Methylation                      | 0.66          | Nucleotide-binding                | 0.27          |
| Palmitate                        | 0.65          | Developmental protein             | 0.26          |
| Magnesium                        | 0.61          | Ion transport                     | 0.26          |
| Magnesium                        | 0.61          | Transport                         | 0.25          |
| ATP-binding                      | 0.61          | Metal-binding                     | 0.15          |
| Transferase                      | 0.58          | Cytoplasm                         | 0.13          |
| Nucleotide-binding               | 0.56          | ATP-binding                       | 0.55          |
| Disulfide bond                   | 0.56          | Cytoplasm                         | 0.55          |
| Serine/threonine/threonine kinase| 0.56          | Alternative splicing              | 0.52          |
| Cytoplasmic vesicle              | 0.55          | Endoplasmic reticulum             | 0.50          |
| Alternative splicing             | 0.54          | Ubl conjugation                   | 0.50          |
| Endoplasmic reticulum            | 0.53          | Cell cycle                        | 0.47          |
| Phosphoprotein                   | 0.52          | Transferase                       | 0.46          |
| Disulfide bond                   | 0.52          | Activator                         | 0.44          |
| Transferase                      | 0.48          | Secreted                          | 0.38          |
| Repressor                        | 0.47          | Metal-binding                     | 0.30          |
| Golgi apparatus                  | 0.40          | Transcription regulation          | 0.29          |
| Secreted                         | 0.38          | Transport                         | 0.28          |
| Ubl conjugation                  | 0.30          | Signal                            | 0.28          |
| Metal-binding                    | 0.29          | Transcription                     | 0.25          |
| Transport                        | 0.27          | Cell membrane                     | 0.24          |
|                      |        |        |                      |        |        |
|----------------------|--------|--------|----------------------|--------|--------|
| Cell membrane        | 226    | 0.26   | Membrane             | 496    | 0.14   |
| Signal               | 273    | 0.26   |                      |        |        |
| Membrane             | 493    | 0.18   |                      |        |        |

*Genes associated with muscle structure and function*
| Gene symbol | Genes expressed in EPA and not in E2 treated cells |
|-------------|--------------------------------------------------|
| Cxcl9       | Gpc4                                             |
| Prss35      | Plb1                                             |
| Serpinb6c   | Ager                                             |
| Gipc2       | Sectm1a                                          |
| Ang2        | Snord95                                          |
| Apol8       | Fam178b                                          |
| Gm10615     | Erv3                                             |
| Tubb4a      | Vsnl1                                           |
| 9530053A07Rik | Ido2                                        |
| Creb314     | Gm6297                                           |
| Gm14379     | BC061194                                         |
| Gm4787      | Atp13a4                                          |
| Ugt1a6b     | Otop1                                            |
| Isml        | Mx1                                             |
| 2310014F06Rik | Prl2c5                               |
| Cesld       | AA467197                                         |
| AW549542    | Zfp33b                                           |
| 2810454H06Rik | Oas1c                                      |
| Pacrg       | Gm1661                                           |
| Gm11517     | Cd46                                             |
| P2rx3       | Dennd2d                                          |
| Fbxw10      | Gm20045                                          |
| C430002N11Rik | Hmha1                                         |
| Stard6      | Hlf                                              |
| Serpinsn    | Srgn                                             |
| Geps        | Rnase1                                           |
| Klra2       | Slc16a9                                          |
| Plek        | Gm13483                                          |
| Kcnmb2      | Snord72                                          |
| Pde1a       | Gm13483                                          |
| Nos2        | Serpin1                                          |
| Notum       | 9430018G01Rik                                    |
| Birc3       | E230016K23Rik                                    |
| Mmp8        | Ttl13                                            |
| Epsap1      | Apo1                                             |
| Serpins3h   | Phactr1                                          |
| Il6         | Gsta2                                            |
| Ncf4        | Ces1f                                            |
| Steap4      | Akr1c12                                          |
| Gm2022      | Tnip3                                            |
| Mmp3        | Gm16685                                          |
| Mrgp3       | Orm3                                             |
| Pem2        | Gm11428                                          |
| Tnfrsf9     | Cdx3                                             |
| Mpeg1       | Cdx3                                             |
| Lypd6b      | Ces1g                                            |
| Atp8b4      | Serpins3i                                        |
| Ncf4        | Serpins3i                                        |
| Len2        | Tnfra1                                           |
### Table S4: Genes expressed in E2 but not in EPA treated cells.

| Gene  | Gene  | Gene  | Gene  |
|-------|-------|-------|-------|
| Gzmd  | Nudt15| Palmd | Gm5532|
| Dscam | Myoz1 | Aim11 | Arx   |
| Wnt7b | Kcnh7 | Gm10421| Kkrb1a|
| Gm19383| Ramp1 | Ankmy1| Gm17638|
| Fes    | Gm7889| Adams16| LOC100862154|
| Csn3   | Padi3 | Pthlh | Rippyl1|
| Klk10  | Syt7  | 9430070013Rik| Chst13|
| Rasgrp3| Pcsin1| Nrarp | Art5   |
| Tceal5 | Dok3  | Fam78a| Nup210 |
| Tdrd9  | S100a14| Cd163 | Ysk4   |
| Mpp3   | Temis | Upk1b | Atp6v1c2|
| Hoxc12 | Odf3l1| B3galt2| I830127107Rik|
| Gpr37  | Cpa4  | Krt31  | Gm10494|
| Lmnc3  | Slco5a1| Emid2 | St8sia2|
| Pof1b  | Gm19976| Chi3l1| Pard6b |
| F2rl2  | Grb10 | Ampd1 | Crabp1 |
| Pp7n7  | Neu2  | Gzmm  | Tmn3   |
| Gm14230| Otoa | Clrn1  | Tcf23  |
| Efcab5 | Flrt1 | Traf1  | Ctsw   |
| Lrcc4  | Nfe2  | Gpr113 | Prox1  |
| Fut1   | Ptgsd | 1500015010Rik| Grhl3|
| Nwd1   | Adams17| Cplx3 | Gbp11  |
| Plac1  | Best3 | Cacng6| Agmat  |
| Jakmip1| Asb16 | Tex16  | Isx    |
| Cyp11a1| Cdh17 | Mafa   | Clnd2  |