**Prioritization of genes**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Genes prev. assoc. with soft tissue injury (published)** | **Genes interacting with prev. assoc. genes (Genemania)** | **Filtered genes for Family A and B** | **Filtered genes for Family A** | **Filtered genes for Family B** |
|  |  |  |  |  |
| COL1A1 | COL5A2 | ABCA13 | ABCA13 | ABCC1 |
| COL3A1 | COL1A2 | ABCD4 | AK2 | PMS2 |
| COL5A1 | COL2A1 | ACAD9 | AK3 | ATP10A |
| COL11A1 | COL14A1 | AK2 | CAPN2 | ABCD4 |
| COL11A2 | COL5A3 | AK3 | CATSPER2 | ACAD9 |
| COL12A1 | MMP2 | ATP10A | COL11A1 | DHODH |
| COL27A1 | MMP7 | CAPN2 | COL12A1 | SLC26A7 |
| TNC | MMP9 | CATSPER2 | EYS | PKHD1L1 |
| THBS2 | MMP11 | COL11A1 | F13A1 | COL12A1 |
| FBN2 | MMP13 | COL12A1 | F5 | HNF4G |
| MMP1 | MMP14 | DHODH | GDF9 | INHA |
| MMP3 | MMP15 | EYS | GUCY2C | GMPR2 |
| MMP10 | MMP16 | F13A1 | KCNJ12 | GKN2 |
| MMP12 | MMP20 | F5 | KIF23 | RTEL1 |
| MMP8 | TIMP1 | GDF9 | KMT2C | GMPR |
| TIMP2 | TIMP3 | GKN2 | MASP1 | DPYD |
| ACAN | TIMP4 | GMPR2 | MLH1 | MLH3 |
| BGN | FGF1 | GUCY2C | MPZL3 | SLC26A4 |
| DCN | SPARC | HNF4G | MYO18A | RTEL1-TNFRSF6B |
| LUM | DDR1 | INHA | NLRP14 | IYD |
| IL1B |  | IPP | NPHP4 | FOXE1 |
| 1IL1RN |  | KCNJ12 | OVCH2 | ZBED2 |
| IL6 |  | KIF23 | PEX6 | TPO |
| IL6R |  | KMT2C | PMM1 | TSHR |
| VEGFA |  | MASP1 | PNKD | INPP5J |
| KDR |  | MLH1 | SI | MLH1 |
| CASP8 |  | MPZL3 | SLC7A2 | FNDC1 |
| GDF5 |  | MYO18A | SPG11 | IMPDH2 |
| MIR608 |  | NLRP14 | TTC38 | PLA2R1 |
| ADIPOQ |  | NPHP4 |  | TG |
| ANKH |  | OR4B1 |  | DDX11 |
| TNAP |  | OVCH2 |  | ERCC2 |
| ADAMTS17 |  | PEX6 |  | C16orf89 |
| ADAMTS10 |  | PKHD1L1 |  | IMPDH1 |
| EFEMP1 |  | PMM1 |  |  |
| DEFB1 |  | PMS2 |  |  |
| ESRRB |  | PNKD |  |  |
| FGF3 |  | RTEL1 |  |  |
| FGF10 |  | SEC24D |  |  |
| FGFR1 |  | SI |  |  |
| ITGB3 |  | SLC26A7 |  |  |
|  |  | SLC7A2 |  |  |
|  |  | SPG11 |  |  |
|  |  | TTC38 |  |  |
|  |  |  |  |  |

**Enrichment Analysis**

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| --- | --- | --- | --- |
| **Enrichment** | **P-value** | **Adjusted P-value** | **Database** |
| **Pathway** | | | |
| **Genes Previously Associated with Soft tissue Injury** |  |  |  |
| PI3K-Akt signaling pathway | 8.99E-11 | 2.77E-08 | KEGG-Human 2019 |
| Protein digestion and absorption | 5.85E-10 | 9.01E-08 |
| Rheumatoid arthritis | 1.1E-06 | 0.000118 |
| Extracellular matrix organization\_Homo sapiens\_R-HSA-1474244 | 1.91E-32 | 2.92E-29 | Reactome 2016 |
| Degradation of the extracellular matrix\_Homo sapiens\_R-HSA-1474228 | 7.10E-13 | 5.43E-10 |
| Collagen formation\_Homo sapiens\_R-HSA-1474290 | 6.47E-12 | 3.30E-09 |
| Assembly of collagen fibrils and other multimeric structures\_Homo sapiens\_R-HSA-2022090 | 1.46E-11 | 5.60E-09 |
| Integrin signalling pathway\_Homo sapiens\_P00034 | 2.76E-08 | 3.09E-06 | Panther 2016 |
| Plasminogen activating cascade\_Homo sapiens\_P00050 | 4.23E-04 | 2.37E-02 |
| FGF signaling pathway\_Homo sapiens\_P00021 | 1.09E-03 | 4.09E-02 |
| **Family A and B** |  |  |  |
| Complement and coagulation cascades | 3.0e-7 | 1.0e-4 | KEGG-Human 2019 |
| Purine metabolism | 6.0e-7 | 9.2e-4 |
| Mismatch repair | 6.9e-5 | 7.1e-3 |
| Lectin Induced Complement Pathway\_Homo sapiens\_h\_lectinPathway | 1.2e-5 | 2.7e-3 | Biocarta 2016 |
| Metabolism of nucleotides\_Homo sapiens\_R-HSA-15869 | 1.0e-5 | 9.1e-4 | Reactome 2016 |
| Lectin pathway of complement activation\_Homo sapiens\_R-HSA-166662 | 1.0e-5 | 6.2e-4 |
| Common Pathway of Fibrin Clot Formation\_Homo sapiens\_R-HSA-140875 | 6.0e-5 | 3.1e-2 |
| Mannose metabolism\_Homo sapiens\_P02752 | 1.8e-4 | 2.0e-2 | Panther 2016 |
| **Family A** |  |  |  |
| Complement and coagulation cascades | 3.0e-9 | 9.0e-7 | KEGG-Human 2019 |
| Thiamine metabolism | 1.0e-5 | 1.6e-3 |
| Purine metabolism | 3.6e-5 | 3.7e-3 |
| Mismatch repair | 3.9e-5 | 3.0e-3 |
| Lectin Induced Complement Pathway\_Homo sapiens\_h\_lectinPathway | 6.5e-6 | 1.5e-3 | Biocarta 2016 |
| Common Pathway of Fibrin Clot Formation\_Homo sapiens\_R-HSA-140875 | 4.5e-7 | 6.9e-4 | Reactome 2016 |
| Hemostasis\_Homo sapiens\_R-HSA-109582 | 2.8e-5 | 1.6e-2 |
| Mannose metabolism\_Homo sapiens\_P02752 | 1.2e-4 | 6.9e-3 | Panther 2016 |
| De novo purine biosynthesis\_Homo sapiens\_P02738 | 5.7e-5 | 6.4e-3 |
| **Family B** |  |  |  |
| ABC transporters | 8.0e-10 | 2.5e-7 | KEGG-Human 2019 |
| Mismatch repair | 2.1e-7 | 3.2e-5 |
| Protein processing in endoplasmic reticulum | 3.7e-5 | 3.9e-3 |
| Multi-Drug Resistance Factors\_Homo sapiens\_h\_mrpPathway | 2.3e-7 | 5.3e-5 | Biocarta 2016 |
| Metabolism\_Homo sapiens\_R-HSA-1430728 | 2.8e-12 | 4.3e-9 | Reactome 2016 |
| Metabolism of nucleotides\_Homo sapiens\_R-HSA-15869 | 4.6e-8 | 3.5e-5 |
| ABC-family proteins mediated transport\_Homo sapiens\_R-HSA-382556 | 5.9e-8 | 2.9e-5 |

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| **Enrichment** | **P-value** | **Adjusted P-value** | **Database** |
| **Go Biological Processes** | | | |
| **Previously associated Genes** |  |  |  |
| extracellular matrix organization (GO:0030198) | 1.54E-28 | 7.83E-25 | GO Biological Process 2018 |
| extracellular matrix disassembly (GO:0022617) | 4.63E-14 | 1.18E-10 |  |
| collagen fibril organization (GO:0030199) | 1.74E-13 | 2.96E-10 |  |
| **Family A and B** |  |  |  |
| establishment of protein localization to peroxisome (GO:0072663) | 1.4e-6 | 7.3e-3 | GO Biological Process 2018 |
| peroxisomal transport (GO:0043574) | 3.0e-6 | 5.7e-3 |  |
| complement activation, lectin pathway (GO:0001867) | 8.0e-6 | 8.2e-3 |  |
| mismatch repair (GO:0006298) | 2.0e-6 | 6.7e-3 |  |
| **Family A** |  |  |  |
| establishment of protein localization to peroxisome (GO:0072663) | 8.0e-7 | 4.1e-3 | GO Biological Process 2018 |
| peroxisomal transport (GO:0043574) | 1.3e-6 | 3.3e-3 |  |
| nucleobase-containing small molecule interconversion (GO:0015949) | 2.2e-6 | 3.7e-3 |  |
| **Family B** |  |  |  |
| cargo loading into COPII-coated vesicle (GO:0090110) | 1.2e-8 | 6.1e-5 | GO Biological Process 2018 |
| antigen processing and presentation of peptide antigen via MHC class I (GO:0002474) | 5.6e-7 | 9.4e-4 |  |
| mismatch repair (GO:0006298) | 9.5e-7 | 1.2e-3 |  |

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| **Enrichment** | **P-value** | **Adjusted P-value** | **Database** |
| **Molecular Function** | | | |
| **Previously associated Genes** |  |  |  |
| growth factor receptor binding (GO:0070851) | 7.38E-10 | 8.50E-07 | GO Molecular Function 2018 |
| metalloendopeptidase activity (GO:0004222) | 2.29E-07 | 0.0001319 |  |
| platelet-derived growth factor binding (GO:0048407) | 1.30E-06 | 5.00E-04 |  |
| integrin binding (GO:0005178) | 1.42E-06 | 4.10E-04 |  |
| growth factor receptor binding (GO:0070851) | 7.38E-10 | 8.50E-07 |  |
| **Family A and B** |  |  |  |
| adenylate kinase activity (GO:0004017) | 1.4e-6 | 1.6e-3 | GO Molecular Function 2018 |
| **Family A** |  |  |  |
| adenylate kinase activity (GO:0004017) | 2.0e-9 | 2.5e-6 | GO Molecular Function 2018 |
| nucleotide kinase activity (GO:0019201) | 5.0e-7 | 3.1e-4 |  |
| satellite DNA binding (GO:0003696) | 1.7e-4 | 2.5e-2 |  |
| histone methyltransferase activity (H3-K4 specific) (GO:0042800) | 1.3e-5 | 2.9e-3 |  |
| **Family B** |  |  |  |
| ATPase-coupled anion transmembrane transporter activity (GO:0043225) | 1.2e-8 | 2.7e-6 | GO Molecular Function 2018 |
| hydrolase activity, acting on acid anhydrides, catalyzing transmembrane movement of substances (GO:0016820) | 6.0e-10 | 3.5e-7 |  |

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| **Enrichment** | **P-value** | **Adjusted P-value** | **Database** |
| **Human Phenotype** | | | |
| **Previously associated Genes** |  |  |  |
| Osteoarthritis (HP:0002758) | 2.27E-12 | 4.04E-09 | Human Phenotype Ontology |
| **Family A and B** |  |  |  |
| Autosomal recessive inheritance (HP:0000007) | 5.0e-10 | 8.1e-8 | Human Phenotype Ontology |
| **Family A** |  |  |  |
| Abnormality of the common coagulation pathway (HP:0010990) | 1.5e-6 | 8.7e-5 | Human Phenotype Ontology |
| Autosomal recessive inheritance (HP:0000007) | 1.9e-7 | 8.4e-5 |  |
| **Family B** |  |  |  |
| Autosomal recessive inheritance (HP:0000007) | 6.9e-7 | 1.2e-4 | Human Phenotype Ontology |