**SUPPLEMENTARY INFORMATION**

A close-up of a frog

Description automatically generated

**Fig. S1. CryoViz Imaging of murine hind limbs.** IA-delivery of QDot labelled wild-type murine MSCs showed a positive signal cluster at the injection point at 1 hour post injection (A) and localized minor signals at 72 hours post injection (B) showing a rapid decline in cell survival (C).

A group of graphs showing different cells

Description automatically generated

**Fig. S2. Cell sorting of IA-administered GFP+ MSCs**. Cell debris was gated out from the scatter plot. Doublets were excluded and live cells selected as DRAQ7 positive. GFP+ MSCs were identified using a negative control and the gate was used for cell sorting (A). Sorted cells were analysed for purity using the same gating strategy (B).

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Receptor | Isotype | Clone | Fluoro-chrome | Supplier |
| CD105 | Rat IgG2a, κ | MJ7/18 | APC | BioLegend (120413) |
| CD106 | Rat IgG2a, κ | 429 (MVCAM.A) | PE | BioLegend (105713) |
| CD140b | Rat IgG2a, κ | APB5 | APC | eBioscience (17-1402-80) |
| CD146 | Rat IgG2a | ME-9F1 | PE | BioLegend (134703) |
| CD29 | Armenian hamster IgG | eBioHMb1-1 (HMb1-1) | APC | eBioscience (17-0291-80) |
| CD44 | Rat IgG2b, κ | IM7 | PE | BioLegend (103007) |
| CD90.2 | Rat IgG2a, κ | 53-2.1 | PE | BD Pharmingen (553005) |
| Ly-6A/E (Sca-1) | Rat IgG2a, κ | E13-161.7 | APC | BioLegend (122511) |
| CD11b | Rat IgG2b, κ | M1/70 | PE | BD Pharmingen (557397) |
| CD45 | Rat IgG2b, κ | 30-F11 | PE | BD Pharmingen (553081) |

**Table S1. Antibodies for cell surface marker characterization**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Experimental replicate | Joint condition | Yield | % Injected | % Purity |
| Retrieval 1 | SHAM | 952 | 0.040 | / |
| CIOA | 7964 | 0.332 | / |
| Retrieval 2 | SHAM | 331 | 0.014 | 77.8% |
| CIOA | 634 | 0.026 | 88.9% |
| Retrieval 3 | SHAM | 251 | 0.010 | 69.2% |
| CIOA | 1067 | 0.044 | 90 % |

**Table S2: Cell sorting of retrieved MSCs from SHAM and CIOA murine joints**. MSCs were consistently retrieved in higher number from CIOA vs SHAM joints. Purity of the retrieved cell populations was analyzed for retrieval experiments 2 and 3 showing elevated values in SHAM (69-77.8%) and CIOA (88.9-90%) joints.

Diagram

Description automatically generated

**Fig. S3. Characterisation of retrieved MSCs.** A: Proliferation rates of MSCs before (pre-IA) and after (post-IA) *in vivo* administration and FACS sorting (right) n=1. B: Clonogenicity of MSCs before (pre-IA) and after (post-IA) *in vivo* administration and FACS sorting (Mean±SEM, n=1, 3 technical replicates) C: Osteogenic differentiation of retrieved MSCs. Alizarin Red Staining (A) and calcium quantification (B) of MSC monolayers in osteogenic differentiation medium before (pre-IA) and after (post-IA) in vivo administration and FACS-sorting. Mean±SEM (n=1, 3 technical replicates). D: Adipogenic differentiation of retrieved MSCs. Oil red-O staining (A) and semi-quantification (B) of MSC monolayers in adipogenic differentiation medium, before (pre-IA) and after (post-IA) in vivo administration and FACS-sorting. Mean±SEM (n=1, 3 technical replicates) E: Representative inverted microscopy images of cultured MSCs before (pre-IA) and after (post-IA) *in vivo* administration and FACS-sorting. Scale bar = 100µm. F: Chondrogenic differentiation of retrieved MSCs. Safranin-O (red) and Fast Green (green) staining of chondrogenically-differentiated pellets (A). Incomplete Chondrogenic Medum (ICM), Complete Chondrogenic Medium (CCM). Quantification of glycosaminoglycans (GAG) (B), DNA (C) and GAG/DNA ratio (D) for chondrogenic-differentiated pellets of MSCs, before (pre-IA) and after (post-IA) *in vivo* administration and FACS sorting.

|  |  |  |  |
| --- | --- | --- | --- |
| Receptor | Fluorochrome | Clone | Supplier |
| **CD4** | PerCP/Cy5.5 | RM4-5 | BioLegend (100540) |
| **CD8** | APC | 53-6.7 | BioLegend (100712) |
| **CD25** | PE | PC61 | BioLegend (102008) |

**Table S3. Antibodies used in T cell co-culture analysis**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Receptor | Isotype | Fluoro-chrome | Clone | Supplier |
| **CD11b** | Rat IgG2b, κ | PE | M1/70 | BD Pharmingen (557397) |
| **Isotype Ctrl** | Rat IgG2b, κ | PE | A95-1 | BD Pharmingen (553989) |
| **CD45.2** | Mouse IgG2a, κ | APC | 104 | BioLegend (109813) |
| **Isotype Ctrl** | Mouse IgG2a, κ | APC | MOPC-173 | BioLegend (400221) |
| **F4/80** | Rat IgG2a, κ | PE/Cy7 | BM8 | BioLegend (123113) |
| **Isotype Ctrl** | Rat IgG2a, κ | PE/Cy7 | RTK2758 | BioLegend (400521) |
| **CD206** | Rat IgG2a, κ | Brilliant Violet 421 | C068C2 | BioLegend (141717) |
| **CD86** | Rat IgG2a, κ | Brilliant Violet 510 | GL-1 | BioLegend (105039) |
| **F4/80** | Rat IgG2a, κ | APC | BM8 | BioLegend (123115) |
| **I-A/I-E (MHC-II)** | Rat IgG2b, κ | PE | M5/114.15.2 | BioLegend (107607) |

**Table S4. Antibodies used for macrophage characterization**

**Diagram, engineering drawing

Description automatically generated**

**Fig. S4. Identification of the *in vivo* immunological profile in a collagenase induced OA.** (A) Macrophage populations identified in the inguinal lymph nodes (i) and Spleen (ii) of Sham and CIOA groups over 56 days following CIOA. The % of MHC-II+/CD11b+ cells increased early (D14) in ILN and later (D28) in Spleen in CIOA versus Sham, while % of MHC-I+/CD11b+ cells increased in late OA (D49) in the Spleen. An increase in the % of CD86+/CD11b+ cells was also observed late (D56) in ILN and early (D21) in Spleen. (B) T cell populations found within the inguinal lymph nodes and Spleen of Sham and CIOA groups over 56 days following CIOA: CD3+ (i), CD3+/CD4+ (ii), CD3+/CD8+ (iii). Activation of T cells was analysed via measurement of CD69+ (iv) and CD25+ (v) populations.

|  |  |
| --- | --- |
| Cytokines | |
| G-CSF | IL-17A |
| GM-CSF | IL-23p19 |
| GRO-α/CXCL1/KC | IL-27 |
| HGF | IP-10/CXCL10/CRG-2 |
| IFN-γ | MCP-1/CCL2/JE |
| IL-1 α | M-CSF |
| IL-1 β | MMP-3 |
| IL-3 | MMP-9 |
| IL-6 | RAGE |
| IL-10 | RANTES/CCL5 |
| IL-12 (p70) | S100A8 |
| IL-13 | VEGF |
| IL-16 | Thrombospondin-4 |
| TNF- α |  |

**Table S5. Cytokines selected for Bioplex analysis**

**A picture containing text

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**Fig. S5. Analysis of cytokine levels of a panel of OA associated cytokines over 56 days following CIOA in Sham versus CIOA.** The concentration of each cytokine is shown relative to the CIOA group, with the average concentration in the CIOA group divided by the average concentration of the Sham group.

Chart, scatter chart

Description automatically generated

**Fig. S6. Number of GFP+MSCs retrieved from CIOA and SHAM joints for RNA sequencing.** For each time point cells were pooled and retrieved from n=8 mice (16 knee joints).

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**Fig. S7. Heatmap of activated canonical pathways.** Retrieved MSCs at early 12-hour (A, B) and late 3-day time-points (C, D), showing activation of the majority of pathways at the early retrieval time point of 12 hours.

**Diagram, venn diagram

Description automatically generated**

**Fig. S8 Overlay of Predicted secreted elements in retrieved MSCs at D14 and D56** Venn diagram representing time-point specific and common proteins secreted by retrieved MSCs, indicating a higher number of elements at 56D.

Chart

Description automatically generated

**Fig. S9.** **Common expressed genes in licensed and retrieved MSCs.** (**A**)Heatmap representing a hierarchal comparison of the predicted secreted elements from three-day retrieved cells at 14D and 56D CIOA and in vitro licensed cells with IL-6 and the triple combination (IL-6, MCP-1 and IFN-γ) licensing. (**B**) Venn diagram comparison of the predicted secretome of retrieved cells and licensed MSCs indicate eight common elements (**C**) Up-regulation and down-regulation of common genes expressed in the predicted secretome of retrieved and licensed MSCs (**D**) RNA Sequencing expression of BRINP3 in (**D**) *in vitro* licensed GFP+MSCs with IL-6 and triple combination vs naïve GFP+MSCs and in (**E)** three-day retrieved GFP+MSCs at 14D and 56D CIOA vs SHAM

|  |  |  |
| --- | --- | --- |
| #GeneSymbol | GeneName | Log2FC |
| Prokr1 | prokineticin receptor 1 | 4,46194 |
| F13a1 | coagulation factor XIII, A1 subunit | 4,07296 |
| Grem1 | gremlin 1, DAN family BMP antagonist | 3,64384 |
| Megf6 | multiple EGF-like-domains 6 | 3,43041 |
| Atp6v0d2 | ATPase, H+ transporting, lysosomal V0 subunit D2 | 3,41636 |
| Ngp | neutrophilic granule protein | 3,35971 |
| Fam198a | family with sequence similarity 198, member A | 3,27547 |
| Pcdhga1 | protocadherin gamma subfamily A, 1 | 3,13658 |
| Ccser1 | coiled-coil serine rich 1 | 3,11062 |
| Xpnpep2 | X-prolyl aminopeptidase (aminopeptidase P) 2, membrane-bound | 3,02054 |
| Trp53inp1 | transformation related protein 53 inducible nuclear protein 1 | 2,8636 |
| Oas2 | 2'-5' oligoadenylate synthetase 2 | 2,83016 |
| Rnd1 | Rho family GTPase 1 | 2,7993 |
| Fgl2 | fibrinogen-like protein 2 | 2,77837 |
| F8 | coagulation factor VIII | 2,72218 |
| Gm14308 | predicted gene 14308 | 2,68641 |
| Mmp12 | matrix metallopeptidase 12 | 2,62773 |
| Mmp13 | matrix metallopeptidase 13 | 2,61103 |
| Prg4 | proteoglycan 4 (megakaryocyte stimulating factor, articular superficial zone protein) | 2,60831 |
| Gdpd2 | glycerophosphodiester phosphodiesterase domain containing 2 | 2,59065 |
| Neurl1b | neuralized E3 ubiquitin protein ligase 1B | 2,56539 |
| Cmpk2 | cytidine monophosphate (UMP-CMP) kinase 2, mitochondrial | 2,56079 |
| Ccl20 | chemokine (C-C motif) ligand 20 | 2,55258 |
| Angptl1 | angiopoietin-like 1 | 2,54484 |
| Dnajc27 | DnaJ heat shock protein family (Hsp40) member C27 | 2,52886 |
| 1500015O10Rik | RIKEN cDNA 1500015O10 gene | 2,52443 |
| Acp6 | acid phosphatase 6, lysophosphatidic | 2,50574 |
| Zfp420 | zinc finger protein 420 | 2,48501 |
| Egfl6 | EGF-like-domain, multiple 6 | 2,478 |
| Bnip3l-ps | BCL2/adenovirus E1B interacting protein 3-like, pseudogene | 2,45969 |
| Cdkn1c | cyclin-dependent kinase inhibitor 1C (P57) | 2,45235 |
| Nos2 | nitric oxide synthase 2, inducible | 2,4331 |
| Ifit3 | interferon-induced protein with tetratricopeptide repeats 3 | 2,42527 |
| Gpnmb | glycoprotein (transmembrane) nmb | 2,42514 |
| Fbln7 | fibulin 7 | 2,40116 |
| Apod | apolipoprotein D | 2,37814 |
| Chodl | chondrolectin | 2,36039 |
| Elmo1 | engulfment and cell motility 1 | 2,35538 |
| Zfp59 | zinc finger protein 59 | 2,34563 |
| Fam71f2 | family with sequence similarity 71, member F2 | 2,33429 |
| Fndc1 | fibronectin type III domain containing 1 | 2,33131 |
| Camsap3 | calmodulin regulated spectrin-associated protein family, member 3 | 2,33072 |
| Ifi207 | interferon activated gene 207 | 2,31823 |
| Slc16a2 | solute carrier family 16 (monocarboxylic acid transporters), member 2 | 2,3028 |
| Akr1c18 | aldo-keto reductase family 1, member C18 | 2,30042 |
| Oas1b | 2'-5' oligoadenylate synthetase 1B | 2,2966 |
| Zfp781 | zinc finger protein 781 | 2,28503 |
| Gbp5 | guanylate binding protein 5 | 2,27757 |
| Mmp2 | matrix metallopeptidase 2 | 2,21567 |

|  |  |  |
| --- | --- | --- |
| Gm4951 | predicted gene 4951 | 2,21413 |
| Naalad2 | N-acetylated alpha-linked acidic dipeptidase 2 | 2,20552 |
| Mmp3 | matrix metallopeptidase 3 | 2,19535 |
| Rassf2 | Ras association (RalGDS/AF-6) domain family member 2 | 2,19313 |
| Ggt5 | gamma-glutamyltransferase 5 | 2,18908 |
| Igfbp5 | insulin-like growth factor binding protein 5 | 2,18433 |
| Ddit4 | DNA-damage-inducible transcript 4 | 2,17282 |
| Pcdhb9 | protocadherin beta 9 | 2,17245 |
| Ppargc1a | peroxisome proliferative activated receptor, gamma, coactivator 1 alpha | 2,15562 |
| Igf1 | insulin-like growth factor 1 | 2,12985 |
| Cdc42bpg | CDC42 binding protein kinase gamma (DMPK-like) | 2,12138 |
| Htra4 | HtrA serine peptidase 4 | 2,12138 |
| Ptx4 | pentraxin 4 | 2,12138 |
| Ctla2a | cytotoxic T lymphocyte-associated protein 2 alpha | 2,11018 |
| Il6 | interleukin 6 | 2,06588 |
| Zfp27 | zinc finger protein 27 | 2,05549 |
| Il27ra | interleukin 27 receptor, alpha | 2,05035 |
| Usp18 | ubiquitin specific peptidase 18 | 2,0461 |
| Zfp239 | zinc finger protein 239 | 2,01545 |
| Pla2g4b | phospholipase A2, group IVB (cytosolic) | 2,01347 |
| Fam102a | family with sequence similarity 102, member A | 2,01199 |
| Pcdhb14 | protocadherin beta 14 | 2,00804 |
| Zfp185 | zinc finger protein 185 | 1,99468 |
| Vtn | vitronectin | 1,97564 |
| F830016B08Rik | RIKEN cDNA F830016B08 gene | 1,96627 |
| Myo7a | myosin VIIA | 1,96214 |
| Iigp1 | interferon inducible GTPase 1 | 1,95898 |
| Klhl10 | kelch-like 10 | 1,95635 |
| Map3k8 | mitogen-activated protein kinase kinase kinase 8 | 1,95389 |
| Mfsd6 | major facilitator superfamily domain containing 6 | 1,93677 |
| Bmper | BMP-binding endothelial regulator | 1,92203 |
| Ctsw | cathepsin W | 1,91696 |
| Sfrp2 | secreted frizzled-related protein 2 | 1,91013 |
| Mx1 | MX dynamin-like GTPase 1 | 1,87973 |
| Usp27x | ubiquitin specific peptidase 27, X chromosome | 1,87646 |
| Nr1h4 | nuclear receptor subfamily 1, group H, member 4 | 1,87646 |
| Il33 | interleukin 33 | 1,87473 |
| Rad51d | RAD51 paralog D | 1,87002 |
| Col8a2 | collagen, type VIII, alpha 2 | 1,8636 |
| Sfrp4 | secreted frizzled-related protein 4 | 1,86068 |
| Plcl2 | phospholipase C-like 2 | 1,85907 |
| Rcan2 | regulator of calcineurin 2 | 1,85064 |
| Zfp867 | zinc finger protein 867 | 1,85024 |
| Hs6st2 | heparan sulfate 6-O-sulfotransferase 2 | 1,84515 |
| Aoc3 | amine oxidase, copper containing 3 | 1,84514 |
| Hilpda | hypoxia inducible lipid droplet associated | 1,8411 |
| Itgb2 | integrin beta 2 | 1,8348 |
| Fam131b | family with sequence similarity 131, member B | 1,83402 |
| Hk2 | hexokinase 2 | 1,82919 |
| Tnfsf9 | tumor necrosis factor (ligand) superfamily, member 9 | 1,81989 |
| Fyb2 | FYN binding protein 2 | 1,81352 |

**Table S6. Top 100 up-regulated DEGs in retrieved MSCs (14D CIOA vs 14D SHAM).**

|  |  |  |
| --- | --- | --- |
| #GeneSymbol | GeneName | Log2FC |
| Uba52 | ubiquitin A-52 residue ribosomal protein fusion product 1 | -7,32197 |
| Acan | aggrecan | -3,69007 |
| Olr1 | oxidized low density lipoprotein (lectin-like) receptor 1 | -3,60373 |
| Dpm3 | dolichyl-phosphate mannosyltransferase polypeptide 3 | -2,9975 |
| Ndufb7 | NADH:ubiquinone oxidoreductase subunit B7 | -2,88509 |
| Gtpbp6 | GTP binding protein 6 (putative) | -2,78429 |
| Wdr62 | WD repeat domain 62 | -2,74532 |
| Fam19a5 | family with sequence similarity 19, member A5 | -2,74356 |
| Elob | elongin B | -2,7287 |
| Lrrc29 | leucine rich repeat containing 29 | -2,72311 |
| Ccdc124 | coiled-coil domain containing 124 | -2,70284 |
| Dohh | deoxyhypusine hydroxylase/monooxygenase | -2,64849 |
| Timm13 | translocase of inner mitochondrial membrane 13 | -2,63643 |
| Ltbp4 | latent transforming growth factor beta binding protein 4 | -2,63024 |
| Bola2 | bolA-like 2 (E. coli) | -2,60279 |
| Pbp2 | phosphatidylethanolamine binding protein 2 | -2,59269 |
| Pcdhgb6 | protocadherin gamma subfamily B, 6 | -2,57926 |
| Znhit2 | zinc finger, HIT domain containing 2 | -2,56475 |
| P2ry2 | purinergic receptor P2Y, G-protein coupled 2 | -2,54545 |
| Lgr6 | leucine-rich repeat-containing G protein-coupled receptor 6 | -2,50834 |
| Angptl7 | angiopoietin-like 7 | -2,48176 |
| Edf1 | endothelial differentiation-related factor 1 | -2,47101 |
| Olfm2 | olfactomedin 2 | -2,43324 |
| Lrfn4 | leucine rich repeat and fibronectin type III domain containing 4 | -2,4302 |
| Mt2 | metallothionein 2 | -2,41012 |
| Hspb1 | heat shock protein 1 | -2,40978 |
| Unc13c | unc-13 homolog C | -2,4045 |
| Chpf | chondroitin polymerizing factor | -2,39721 |
| Slurp1 | secreted Ly6/Plaur domain containing 1 | -2,38753 |
| Zfp763 | zinc finger protein 763 | -2,38073 |
| Junb | jun B proto-oncogene | -2,37058 |
| Tppp3 | tubulin polymerization-promoting protein family member 3 | -2,31318 |
| C1qtnf2 | C1q and tumor necrosis factor related protein 2 | -2,31208 |
| Chtf18 | CTF18, chromosome transmission fidelity factor 18 | -2,30891 |
| L1cam | L1 cell adhesion molecule | -2,29031 |
| Crip2 | cysteine rich protein 2 | -2,27929 |
| Pold1 | polymerase (DNA directed), delta 1, catalytic subunit | -2,25264 |
| Fam213a | family with sequence similarity 213, member A | -2,25135 |
| Acsbg1 | acyl-CoA synthetase bubblegum family member 1 | -2,24772 |
| Cep131 | centrosomal protein 131 | -2,23732 |
| Kcnk5 | potassium channel, subfamily K, member 5 | -2,21841 |
| Tpgs1 | tubulin polyglutamylase complex subunit 1 | -2,21367 |
| Zfp82 | zinc finger protein 82 | -2,20889 |
| Smad9 | SMAD family member 9 | -2,20806 |
| Ccnd1 | cyclin D1 | -2,18187 |
| Mfsd3 | major facilitator superfamily domain containing 3 | -2,16819 |
| Aldh1a3 | aldehyde dehydrogenase family 1, subfamily A3 | -2,15602 |
| Lamb2 | laminin, beta 2 | -2,14246 |
| Acad10 | acyl-Coenzyme A dehydrogenase family, member 10 | -2,12345 |
| Tmem26 | transmembrane protein 26 | -2,12345 |
| Fam19a2 | family with sequence similarity 19, member A2 | -2,11672 |
| Trib3 | tribbles pseudokinase 3 | -2,11016 |
| Fgfr3 | fibroblast growth factor receptor 3 | -2,09753 |
| Acpp | acid phosphatase, prostate | -2,09207 |
| Fancd2 | Fanconi anemia, complementation group D2 | -2,09152 |
| Icam5 | intercellular adhesion molecule 5, telencephalin | -2,08095 |
| Hspa1a | heat shock protein 1A | -2,0742 |
| Thap7 | THAP domain containing 7 | -2,06643 |
| Slc12a9 | solute carrier family 12 (potassium/chloride transporters), member 9 | -2,06569 |
| Stra6 | stimulated by retinoic acid gene 6 | -2,06248 |
| Rnaseh2c | ribonuclease H2, subunit C | -2,0614 |
| Cspg4 | chondroitin sulfate proteoglycan 4 | -2,05874 |
| Gchfr | GTP cyclohydrolase I feedback regulator | -2,05575 |
| Psmb10 | proteasome (prosome, macropain) subunit, beta type 10 | -2,0538 |
| Igfbp6 | insulin-like growth factor binding protein 6 | -2,04166 |
| Ccdc141 | coiled-coil domain containing 141 | -2,01787 |
| Card10 | caspase recruitment domain family, member 10 | -2,0167 |
| Erdr1 | erythroid differentiation regulator 1 | -2,00335 |
| Zfp189 | zinc finger protein 189 | -2,00018 |
| Hspbp1 | HSPA (heat shock 70kDa) binding protein, cytoplasmic cochaperone 1 | -2,00016 |
| Lgals7 | lectin, galactose binding, soluble 7 | -1,99739 |
| Klrg2 | killer cell lectin-like receptor subfamily G, member 2 | -1,98652 |
| Polr2f | polymerase (RNA) II (DNA directed) polypeptide F | -1,95696 |
| Zfp414 | zinc finger protein 414 | -1,92811 |
| Jmjd4 | jumonji domain containing 4 | -1,92514 |
| Pcolce2 | procollagen C-endopeptidase enhancer 2 | -1,91977 |
| Cenpm | centromere protein M | -1,9166 |
| Ptpn22 | protein tyrosine phosphatase, non-receptor type 22 (lymphoid) | -1,89205 |
| Glis1 | GLIS family zinc finger 1 | -1,88842 |
| Zswim3 | zinc finger SWIM-type containing 3 | -1,88834 |
| Slc6a17 | solute carrier family 6 (neurotransmitter transporter), member 17 | -1,88775 |
| Lmna | lamin A | -1,88056 |
| Csnk1g2 | casein kinase 1, gamma 2 | -1,8566 |
| Odaph | odontogenesis associated phosphoprotein | -1,85124 |
| Ubtd1 | ubiquitin domain containing 1 | -1,84807 |
| Kcnn4 | potassium intermediate/small conductance calcium-activated channel, subfamily N, member 4 | -1,84666 |
| Fzr1 | fizzy and cell division cycle 20 related 1 | -1,84279 |
| Scrn2 | secernin 2 | -1,83715 |
| Tspo | translocator protein | -1,82875 |
| Ndufs7 | NADH:ubiquinone oxidoreductase core subunit S7 | -1,82691 |
| Aldh16a1 | aldehyde dehydrogenase 16 family, member A1 | -1,81978 |
| Mif | macrophage migration inhibitory factor (glycosylation-inhibiting factor) | -1,81817 |
| Ndufa11 | NADH:ubiquinone oxidoreductase subunit A11 | -1,81742 |
| Emilin1 | elastin microfibril interfacer 1 | -1,81466 |
| Ppbp | pro-platelet basic protein | -1,81348 |
| Plekhh3 | pleckstrin homology domain containing, family H (with MyTH4 domain) member 3 | -1,80605 |
| Orai1 | ORAI calcium release-activated calcium modulator 1 | -1,80563 |
| Trp53i13 | transformation related protein 53 inducible protein 13 | -1,79746 |
| Esco2 | establishment of sister chromatid cohesion N-acetyltransferase 2 | -1,79543 |
| Plppr4 | phospholipid phosphatase related 4 | -1,79478 |

**Table S7. Top 100 down-regulated DEGs in retrieved MSCs (14D CIOA vs 14D SHAM)**

|  |  |  |
| --- | --- | --- |
| #GeneSymbol | GeneName | Log2FC |
| Ctss | cathepsin S | 6,14732 |
| Lcn2 | lipocalin 2 | 6,05642 |
| C1qb | complement component 1, q subcomponent, beta polypeptide | 6,02481 |
| Pgf | placental growth factor | 5,1662 |
| C1qc | complement component 1, q subcomponent, C chain | 5,14797 |
| Arg1 | arginase, liver | 5,10158 |
| Cxcl3 | chemokine (C-X-C motif) ligand 3 | 5,02552 |
| Scn7a | sodium channel, voltage-gated, type VII, alpha | 4,99685 |
| Gm4724 | predicted gene 4724 | 4,96816 |
| Serpina3n | serine (or cysteine) peptidase inhibitor, clade A, member 3N | 4,95951 |
| Susd2 | sushi domain containing 2 | 4,87606 |
| Cpne4 | copine IV | 4,78674 |
| Odaph | odontogenesis associated phosphoprotein | 4,77609 |
| Pcdhgb2 | protocadherin gamma subfamily B, 2 | 4,71834 |
| Zfp420 | zinc finger protein 420 | 4,71811 |
| Penk | preproenkephalin | 4,67959 |
| Apcdd1 | adenomatosis polyposis coli down-regulated 1 | 4,6746 |
| Tyrobp | TYRO protein tyrosine kinase binding protein | 4,60864 |
| Zfp955b | zinc finger protein 955B | 4,60864 |
| Moxd1 | monooxygenase, DBH-like 1 | 4,57232 |
| Snx11 | sorting nexin 11 | 4,5135 |
| Mgat4a | mannoside acetylglucosaminyltransferase 4, isoenzyme A | 4,50043 |
| Alox5ap | arachidonate 5-lipoxygenase activating protein | 4,47985 |
| Gbp9 | guanylate-binding protein 9 | 4,4382 |
| Ms4a6d | membrane-spanning 4-domains, subfamily A, member 6D | 4,4378 |
| Hexim2 | hexamethylene bis-acetamide inducible 2 | 4,4271 |
| Csf3 | colony stimulating factor 3 (granulocyte) | 4,41153 |
| Gtpbp8 | GTP-binding protein 8 (putative) | 4,37722 |
| Cd177 | CD177 antigen | 4,36111 |
| Serping1 | serine (or cysteine) peptidase inhibitor, clade G, member 1 | 4,36012 |
| Gm28042 | predicted gene, 28042 | 4,29198 |
| Tarsl2 | threonyl-tRNA synthetase-like 2 | 4,24399 |
| Fcnb | ficolin B | 4,2069 |
| Lyz2 | lysozyme 2 | 4,18611 |
| Gm12258 | predicted gene 12258 | 4,18164 |
| B3galt4 | UDP-Gal:betaGlcNAc beta 1,3-galactosyltransferase, polypeptide 4 | 4,12975 |
| C1qa | complement component 1, q subcomponent, alpha polypeptide | 4,11649 |
| Cd300c2 | CD300C molecule 2 | 4,11649 |
| Zfp748 | zinc finger protein 748 | 4,11363 |
| Laptm5 | lysosomal-associated protein transmembrane 5 | 4,10309 |
| Enox1 | ecto-NOX disulfide-thiol exchanger 1 | 4,08959 |
| D3Ertd751e | DNA segment, Chr 3, ERATO Doi 751, expressed | 4,08959 |
| Eif5a2 | eukaryotic translation initiation factor 5A2 | 4,02287 |
| Cxcr6 | chemokine (C-X-C motif) receptor 6 | 4,02003 |
| Zfp790 | zinc finger protein 790 | 3,98951 |
| C5ar1 | complement component 5a receptor 1 | 3,97664 |
| A430033K04Rik | RIKEN cDNA A430033K04 gene | 3,97657 |
| Cxcl9 | chemokine (C-X-C motif) ligand 9 | 3,97136 |
| Sfrp1 | secreted frizzled-related protein 1 | 3,96821 |
| Rnf113a2 | ring finger protein 113A2 | 3,96188 |
| Tctn3 | tectonic family member 3 | 3,93965 |
| Slc25a26 | solute carrier family 25 (mitochondrial carrier, phosphate carrier), member 26 | 3,92865 |
| Kif26b | kinesin family member 26B | 3,91005 |
| Bbs12 | Bardet-Biedl syndrome 12 (human) | 3,90273 |
| Thnsl2 | threonine synthase-like 2 (bacterial) | 3,85067 |
| Fkrp | fukutin related protein | 3,85036 |
| Prdm9 | PR domain containing 9 | 3,8462 |
| Thsd1 | thrombospondin, type I, domain 1 | 3,83803 |
| Cdh23 | cadherin 23 (otocadherin) | 3,82177 |
| Spry3 | sprouty RTK signaling antagonist 3 | 3,82177 |
| Zfp781 | zinc finger protein 781 | 3,82177 |
| 1700066M21Rik | RIKEN cDNA 1700066M21 gene | 3,81831 |
| Fmod | fibromodulin | 3,79743 |
| Coro1a | coronin, actin binding protein 1A | 3,7887 |
| Steap4 | STEAP family member 4 | 3,77971 |
| Cdhr1 | cadherin-related family member 1 | 3,77188 |
| Lilrb4a | leukocyte immunoglobulin-like receptor, subfamily B, member 4A | 3,77188 |
| Ccdc39 | coiled-coil domain containing 39 | 3,73763 |
| Pf4 | platelet factor 4 | 3,73763 |
| Apln | apelin | 3,71607 |
| Chrd | chordin | 3,70245 |
| Cyb561d1 | cytochrome b-561 domain containing 1 | 3,68485 |
| Sema4f | sema domain, immunoglobulin domain (Ig), TM domain, and short cytoplasmic domain | 3,68469 |
| Hck | hemopoietic cell kinase | 3,68469 |
| Havcr2 | hepatitis A virus cellular receptor 2 | 3,64828 |
| Tcfl5 | transcription factor-like 5 (basic helix-loop-helix) | 3,64828 |
| Iba57 | IBA57 homolog, iron-sulfur cluster assembly | 3,64828 |
| Pcdhb16 | protocadherin beta 16 | 3,64517 |
| Duoxa1 | dual oxidase maturation factor 1 | 3,63518 |
| Pcsk9 | proprotein convertase subtilisin/kexin type 9 | 3,62973 |
| Trmt12 | tRNA methyltranferase 12 | 3,62547 |
| Zfp280b | zinc finger protein 280B | 3,61137 |
| Ddias | DNA damage-induced apoptosis suppressor | 3,61094 |
| Mylpf | myosin light chain, phosphorylatable, fast skeletal muscle | 3,59189 |
| Thbs4 | thrombospondin 4 | 3,58663 |
| Pcsk6 | proprotein convertase subtilisin/kexin type 6 | 3,5726 |
| Arhgef6 | Rac/Cdc42 guanine nucleotide exchange factor (GEF) 6 | 3,56318 |
| Mamdc2 | MAM domain containing 2 | 3,55957 |
| Wnt7b | wingless-type MMTV integration site family, member 7B | 3,55718 |
| B3gat2 | beta-1,3-glucuronyltransferase 2 (glucuronosyltransferase S) | 3,55302 |
| Il1b | interleukin 1 beta | 3,53321 |
| Ubd | ubiquitin D | 3,53321 |
| Chrdl1 | chordin-like 1 | 3,52242 |
| Zfp995 | zinc finger protein 995 | 3,51423 |
| Cd48 | CD48 antigen | 3,51309 |
| Plac1 | placental specific protein 1 | 3,51309 |
| Comp | cartilage oligomeric matrix protein | 3,50445 |
| Fabp4 | fatty acid binding protein 4, adipocyte | 3,49271 |
| Cotl1 | coactosin-like 1 (Dictyostelium) | 3,48679 |
| Cd83 | CD83 antigen | 3,47204 |

**Table S8.** **Top 100 up-regulated DEGs in retrieved MSCs (56D CIOA vs 56D SHAM*)***

|  |  |  |
| --- | --- | --- |
| #GeneSymbol | GeneName | Log2FC |
| 1700030J22Rik | RIKEN cDNA 1700030J22 gene | -5,10552 |
| Acot11 | acyl-CoA thioesterase 11 | -5,05112 |
| Zbtb14 | zinc finger and BTB domain containing 14 | -4,67226 |
| Zbtb3 | zinc finger and BTB domain containing 3 | -4,62415 |
| Snx32 | sorting nexin 32 | -4,56498 |
| Efcc1 | EF hand and coiled-coil domain containing 1 | -4,51226 |
| Ube2cbp | ubiquitin-conjugating enzyme E2C binding protein | -4,46883 |
| Pcdhb4 | protocadherin beta 4 | -4,37138 |
| Kctd19 | potassium channel tetramerisation domain containing 19 | -4,06474 |
| Tspan32 | tetraspanin 32 | -4,01509 |
| Tppp | tubulin polymerization promoting protein | -3,96367 |
| Cacng1 | calcium channel, voltage-dependent, gamma subunit 1 | -3,85497 |
| Exd2 | exonuclease 3'-5' domain containing 2 | -3,8233 |
| Iyd | iodotyrosine deiodinase | -3,78264 |
| Cd72 | CD72 antigen | -3,76773 |
| Igflr1 | IGF-like family receptor 1 | -3,76773 |
| Samd12 | sterile alpha motif domain containing 12 | -3,76773 |
| Depdc7 | DEP domain containing 7 | -3,75266 |
| Ppl | periplakin | -3,75041 |
| Avil | advillin | -3,74685 |
| Dnajc22 | DnaJ heat shock protein family (Hsp40) member C22 | -3,72204 |
| Zfp493 | zinc finger protein 493 | -3,70445 |
| Ahrr | aryl-hydrocarbon receptor repressor | -3,69726 |
| Napsa | napsin A aspartic peptidase | -3,67485 |
| Cct6b | chaperonin containing Tcp1, subunit 6b (zeta) | -3,67485 |
| Dynap | dynactin associated protein | -3,64253 |
| Hspa1l | heat shock protein 1-like | -3,62609 |
| Lrrc71 | leucine rich repeat containing 71 | -3,59263 |
| Apba1 | amyloid beta (A4) precursor protein binding, family A, member 1 | -3,58183 |
| Cntnap4 | contactin associated protein-like 4 | -3,55746 |
| Pth1r | parathyroid hormone 1 receptor | -3,52331 |
| Lrba | LPS-responsive beige-like anchor | -3,51222 |
| Ism1 | isthmin 1, angiogenesis inhibitor | -3,50545 |
| Bcan | brevican | -3,48735 |
| Kcnt2 | potassium channel, subfamily T, member 2 | -3,48201 |
| U90926 | cDNA sequence U90926 | -3,46904 |
| Trim43a | tripartite motif-containing 43A | -3,46904 |
| 1700012B09Rik | RIKEN cDNA 1700012B09 gene | -3,45048 |
| Tmc4 | transmembrane channel-like gene family 4 | -3,43226 |
| Prnd | prion like protein doppel | -3,43169 |
| Fam163a | family with sequence similarity 163, member A | -3,41265 |
| Rragd | Ras-related GTP binding D | -3,39627 |
| Olfr99 | olfactory receptor 99 | -3,39336 |
| Fbxl2 | F-box and leucine-rich repeat protein 2 | -3,38342 |
| Cxcl13 | chemokine (C-X-C motif) ligand 13 | -3,37378 |
| Nek11 | NIMA (never in mitosis gene a)-related expressed kinase 11 | -3,37378 |
| Fgf2 | fibroblast growth factor 2 | -3,35497 |
| Zfp296 | zinc finger protein 296 | -3,35397 |
| Ptgdr2 | prostaglandin D2 receptor 2 | -3,35397 |
| AI481877 | expressed sequence AI481877 | -3,35397 |
| Coch | cochlin | -3,31346 |
| Cela3b | chymotrypsin-like elastase family, member 3B | -3,31346 |
| Slc25a29 | solute carrier family 25 (mitochondrial carrier, palmitoylcarnitine transporter), member 29 | -3,2928 |
| Dpysl5 | dihydropyrimidinase-like 5 | -3,28016 |
| Acad11 | acyl-Coenzyme A dehydrogenase family, member 11 | -3,26172 |
| Ptx4 | pentraxin 4 | -3,24616 |
| Bglap3 | bone gamma-carboxyglutamate protein 3 | -3,22892 |
| Dnase2b | deoxyribonuclease II beta | -3,18471 |
| Nfe2l3 | nuclear factor, erythroid derived 2, like 3 | -3,18471 |
| Ifna4 | interferon alpha 4 | -3,18471 |
| Eri2 | exoribonuclease 2 | -3,17447 |
| Ttll11 | tubulin tyrosine ligase-like family, member 11 | -3,16208 |
| Iqck | IQ motif containing K | -3,1527 |
| Zfp941 | zinc finger protein 941 | -3,15052 |
| Pla2g4b | phospholipase A2, group IVB (cytosolic) | -3,1406 |
| Prkcb | protein kinase C, beta | -3,13594 |
| Vmn2r1 | vomeronasal 2, receptor 1 | -3,11575 |
| Sv2a | synaptic vesicle glycoprotein 2 a | -3,11495 |
| Mmab | methylmalonic aciduria (cobalamin deficiency) cblB type homolog (human) | -3,10925 |
| Lipc | lipase, hepatic | -3,06789 |
| Sec1 | secretory blood group 1 | -3,06789 |
| Coro2a | coronin, actin binding protein 2A | -3,04335 |
| Rbm12b1 | RNA binding motif protein 12 B1 | -3,04335 |
| Capn12 | calpain 12 | -3,04335 |
| Slc14a2 | solute carrier family 14 (urea transporter), member 2 | -3,01837 |
| Tle4 | transducin-like enhancer of split 4 | -3,01609 |
| Zfp599 | zinc finger protein 599 | -3,01096 |
| Omd | osteomodulin | -2,99825 |
| Mob3b | MOB kinase activator 3B | -2,96687 |
| Xkr8 | X-linked Kx blood group related 8 | -2,94963 |
| Fbxo44 | F-box protein 44 | -2,945 |
| Lrrc46 | leucine rich repeat containing 46 | -2,94078 |
| Slc2a13 | solute carrier family 2 (facilitated glucose transporter), member 13 | -2,92384 |
| Evi2b | ecotropic viral integration site 2b | -2,91396 |
| Kcna4 | potassium voltage-gated channel, shaker-related subfamily, member 4 | -2,90568 |
| Xrcc2 | X-ray repair complementing defective repair in Chinese hamster cells 2 | -2,89839 |
| Spats1 | spermatogenesis associated, serine-rich 1 | -2,88664 |
| Adtrp | androgen dependent TFPI regulating protein | -2,88664 |
| Tnfsf13 | tumor necrosis factor (ligand) superfamily, member 13 | -2,88664 |
| Kdm8 | lysine (K)-specific demethylase 8 | -2,86564 |
| Vwc2l | von Willebrand factor C domain-containing protein 2-like | -2,85878 |
| Glt28d2 | glycosyltransferase 28 domain containing 2 | -2,84294 |
| Il1rap | interleukin 1 receptor accessory protein | -2,83394 |
| Ssc4d | scavenger receptor cysteine rich family, 4 domains | -2,83037 |
| Arhgap15 | Rho GTPase activating protein 15 | -2,83037 |
| Pcdhga2 | protocadherin gamma subfamily A, 2 | -2,82696 |
| Slc8a1 | solute carrier family 8 (sodium/calcium exchanger), member 1 | -2,81667 |
| Nudt6 | nudix (nucleoside diphosphate linked moiety X)-type motif 6 | -2,80635 |
| Rab11fip4 | RAB11 family interacting protein 4 (class II) | -2,80139 |
| Gm527 | predicted gene 527 | -2,80139 |

**Table S9. Top 100 down-regulated DEGs in retrieved MSCs (56D CIOA vs 56D SHAM)**

|  |  |  |  |
| --- | --- | --- | --- |
| **14D Retrieved MSCs** | | | |
| **Upstream Regulator** | **p-value** | **Activation Z-Score** | **Expressed LogRatio** |
| IL1B | 2.21E-20 | 2.455 |  |
| TNF | 1.60E-18 | 0.983 |  |
| IFNG | 5.45-18 | 4.137 |  |
| TP53 | 3.50E-16 | 0.127 | -0.058 |
| APP | 2.86E-14 | 1.363 | -0.197 |
| STAT3 | 5.73E-14 | 0.048 | 0.098 |
| SIRT1 | 1.30E-13 | -1.450 | -0.002 |
| TGFB1 | 6.13E-13 | -2.264 | 0.125 |
| NFKBIA | 9.20E-13 | 2.345 | -0.142 |
| HIF1A | 1.40-12 | 2.156 | 0.293 |
| **56D Retrieved MSCs** | | | |
| **Upstream Regulator** | **p-value** | **Activation Z-score** | **Expressed LogRatio** |
| IFNG | 7.73E-14 | 1.900 |  |
| TCL1A | 6.77E-13 | 2.813 |  |
| STAT3 | 2.01E-12 | 2.398 | 0.383 |
| IFNAR1 | 7.18E-11 | -0.637 | 0.000 |
| TMEM173 | 3.37E-10 | 1.540 | -0.635 |
| STAT1 | 8.01E-09 | 0.448 | -1.083 |
| IL1B | 8.23E-09 | 4.193 | 3.533 |
| OSM | 4.46E-08 | 3.098 |  |
| IFN alpha/beta | 9.52E-08 | -0.524 |  |
| IRF3 | 9.52E-08 | -1.292 | -0.229 |
| CCR2 | 1.03-07 | 2.276 | 1.569 |
| PTGER4 | 3.37E-07 | 1.038 | 0.000 |

**Table S10. Predicted upstream regulators for early and late OA retrieved MSCs with the corresponding p-value, activation z-score and the expressed log ratio when identified as DEGs.**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Gene Ontology Enrichment of 14D Differentially Expressed Genes | | | | | | | | |
| GO Biological Process | **P-value** | | | **Adjusted p-value** | | **Odds ratio** | | **Combined score** |
| Regulation Of Smooth Muscle Cell Migration (GO:0014910) | 0.000006146 | | | 0.01045 | | 8.91 | | 106.91 |
| Extracellular Matrix Organization (GO:0030198) | 9,75E-08 | | | 4,97E-04 | | 3.50 | | 80.71 |
| Extracellular Matrix Disassembly (GO:0022617) | 2,05E-04 | | | 0.0005237 | | 4.70 | | 72.37 |
| Positive Regulation Of Smooth Muscle Cell Migration (GO:0014911) | 0.0006129 | | | 0.1840 | | 9.16 | | 67.79 |
| Establishment Of Apical/Basal Cell Polarity (GO:0035089) | 0.001347 | | | 0.2370 | | 7.64 | | 50.48 |
| GO Molecular Function | **P-value** | | | **Adjusted p-value** | | **Odds ratio** | | **Combined score** |
| Insulin-Like Growth Factor II Binding (GO:0031995) | 0.002542 | | | 0.4876 | | 9.82 | | 58.66 |
| Collagen Binding (GO:0005518) | 0.00001203 | | | 0.006924 | | 4.85 | | 54.9 |
| Integrin Binding (GO:0005178) | 0.000002850 | | | 0.003280 | | 3.90 | | 49.79 |
| Adenyl Nucleotide Binding (GO:0030554) | 0.01051 | | | 1.000 | | 6.25 | | 28.46 |
| Adenyl-Nucleotide Exchange Factor Activity (GO:0000774) | 0.01051 | | | 1.000 | | 6.25 | | 28.46 |
| GO Cellular Component | **P-value** | | | **Adjusted p-value** | | **Odds ratio** | | **Combined score** |
| Platelet Dense Granule Lumen (GO:0031089) | 0.0002255 | | | 0.1006 | | 8.18 | | 68.70 |
| Filopodium Membrane (GO:0031527) | 0.001347 | | | 0.2003 | | 7.64 | | 50.48 |
| Pseudopodium (GO:0031143) | 0.005713 | | | 0.4246 | | 7.64 | | 39.44 |
| Platelet Dense Granule (GO:0042827) | 0.001777 | | | 0.1982 | | 5.45 | | 34.54 |
| Mitotic Spindle Midzone (GO:1990023) | 0.007898 | | | 0.4403 | | 6.87 | | 33.27 |
| Gene Ontology Enrichment of 56D Differentially Expressed Genes | | | | | | | | |
| GO Biological Process | | **P-Value** | **Adjusted P-Value** | | **Odds Ratio** | | **Combined Score** | |
| Leukocyte Aggregation (GO:0070486) | | 0.00006036 | 0.1540 | | 8.91 | | 86.53 | |
| Amino Acid Import Across Plasma Membrane (GO:0089718) | | 0.001184 | 0.5035 | | 7.13 | | 48.02 | |
| Regulation Of Macrophage Differentiation (GO:0045649) | | 0.0002761 | 0.2348 | | 5.75 | | 47.16 | |
| Positive Regulation Of Macrophage Differentiation (GO:0045651) | | 0.002218 | 0.4715 | | 6.23 | | 38.10 | |
| T-Helper Cell Lineage Commitment (GO:0002295) | | 0.002218 | 0.4526 | | 6.23 | | 38.10 | |
| GO Molecular Function | | **P-Value** | **Adjusted P-Value** | | **Odds Ratio** | | **Combined Score** | |
| Cxcr Chemokine Receptor Binding (GO:0045236) | | 0.00002116 | 0.02436 | | 5.87 | | 63.16 | |
| Basic Amino Acid Transmembrane Transporter Activity (GO:0015174) | | 0.0001595 | 0.09179 | | 6.23 | | 54.51 | |
| Nadph Binding (GO:0070402) | | 0.0005897 | 0.2263 | | 6.23 | | 46.36 | |
| Azole Transmembrane Transporter Activity (GO:1901474) | | 0.008560 | 0.6568 | | 6.23 | | 29.68 | |
| Phospholipase Activator Activity (GO:0016004) | | 0.008560 | 0.6158 | | 6.23 | | 29.68 | |
| GO Cellular Component | | **P-Value** | **Adjusted P-Value** | | **Odds Ratio** | | **Combined Score** | |
| Rad51b-Rad51c-Rad51d-Xrcc2 Complex (GO:0033063) | | 0.01409 | 1.000 | | 5.34 | | 22.78 | |
| Atp-Binding Cassette (Abc) Transporter Complex (GO:0043190) | | 0.02122 | 1.000 | | 4.68 | | 18.02 | |
| Replication Fork (GO:0005657) | | 0.01503 | 1.000 | | 2.88 | | 12.08 | |
| Primary Lysosome (GO:0005766) | | 0.04029 | 1.000 | | 3.74 | | 12.01 | |
| Scf Ubiquitin Ligase Complex (GO:0019005) | | 0.009876 | 1.000 | | 2.31 | | 10.66 | |

**Table S11. Top 5 Gene ontology enrichment terms for differentially expressed genes in early and late OA retrieved MSCs.** For each data set of DEGs we identified the enriched biological processes, molecular functions and cellular components with the corresponding p-value, adjusted p-value, odds ratio and combined score.

Chart

Description automatically generated

**Fig. S10. BRINP3 as licensing factor for MSCs.** (A):Morphology of control (i) and licensed hBM-MSCs (ii-v) with BRINP3 at corresponding concentrations of 10, 25, 50 and 100 ng/ml. All images were taken after 96 h of cultures. (B): IDO assay. The evaluation of the IDO production was assessed on the supernatants of cells licensed with IFNγ as positive control and BRINP3, after 96 h of cultures (72 h of exposure to the licensing factors). (C): qRT-PCR expression of anti-inflammatory genes after licensing with BRINP3 at 50 ng/ml. In each graph different expression results of five anti-inflammatory genes results are showed (IDO1, TSG-6, PTGS-2, IL-6, IL-10). Sample defined as “Ctrl” refers to unlicensed cell cultures used as controls. Results are represented as mean values ± SD of 3 independent experiments (3 donors). Ct values have been normalized to an unlicensed control and to a housekeeping gene (ACTB) prior the calculations of the ΔΔCt values. Results were considered significant when p-value was below 0.05.

|  |  |
| --- | --- |
| Missing Gene | Matching Synonym |
| Ecrg4 | 1500015O10Rik |
| wisp2 | Ccn5 |
| Siglec10 | Siglecg |
| Ero1b | Ero1lb |
| Nov | Ccn3 |
| Ctgf | Ccn2 |
| Chi3l1 | Chil1 |
| Txn | Txn1 |
| Cyr61 | Ccn1 |
| Plac9 | Plac9b |
| C4bpa | C4bp |
| Dnase2b | Dnase2a |
| Lilrb3 | Pirb |
| Mtnd4 | mt-nd4 |
| Mtnd6 | mt-nd4 |
| Il4r | Il4ra |
| Gsdmdc1 | Gsdmd |
| Pigy | Pyurf |
| Mic13 | 2410015M20Rik |
| 2610524H06Rik | 1500011B03Rik |
| Tmem167a | Tmem167 |
| Gpi | Gpi1 |
| Ca12 | Car12 |
| Ugt1a6 | Ugt1a6a |
| Kitlg | Kitl |
| Ca11 | Car11 |

**Table S12: Mismatched gene names between Ensemble annotation and symbols from expression data**

A collage of multiple images of blue and green

Description automatically generated

**Fig. S11.** Expression of BRINP3 in human teratomas at low magnification (A) and high magnification (B) images for antibody validation