
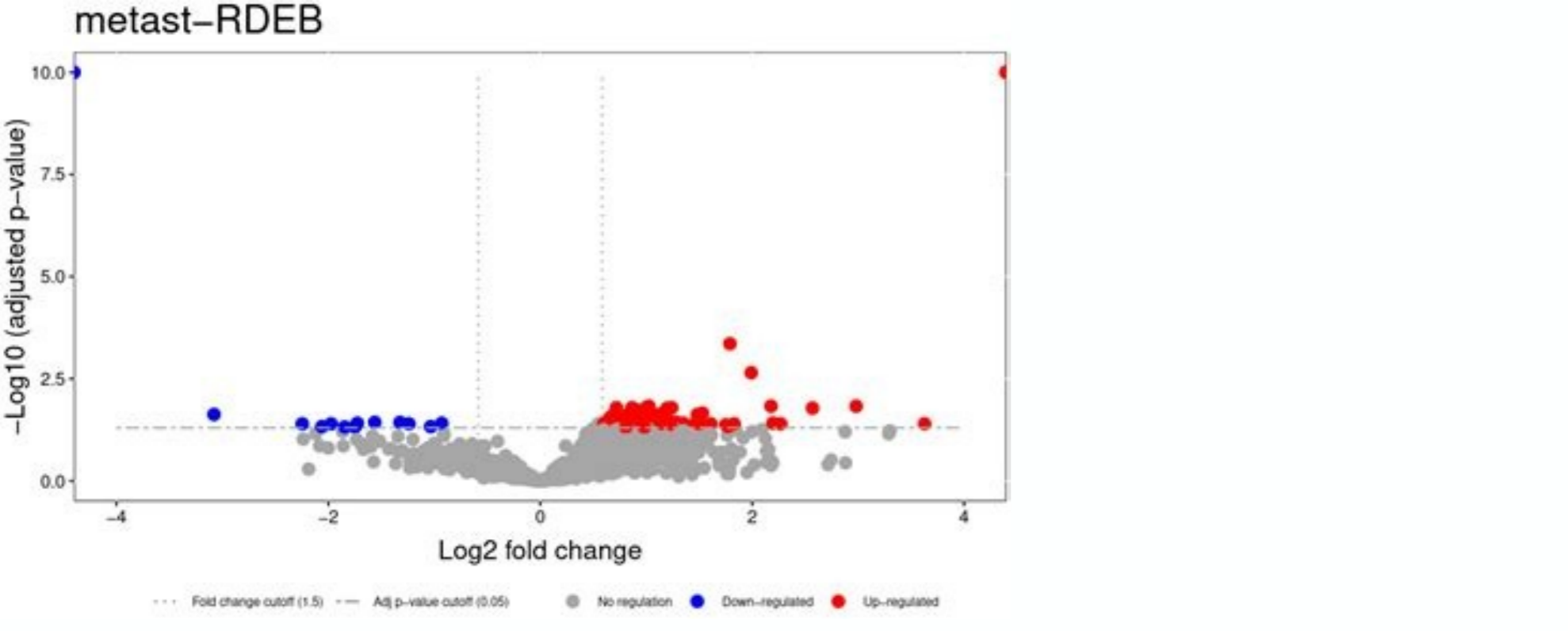
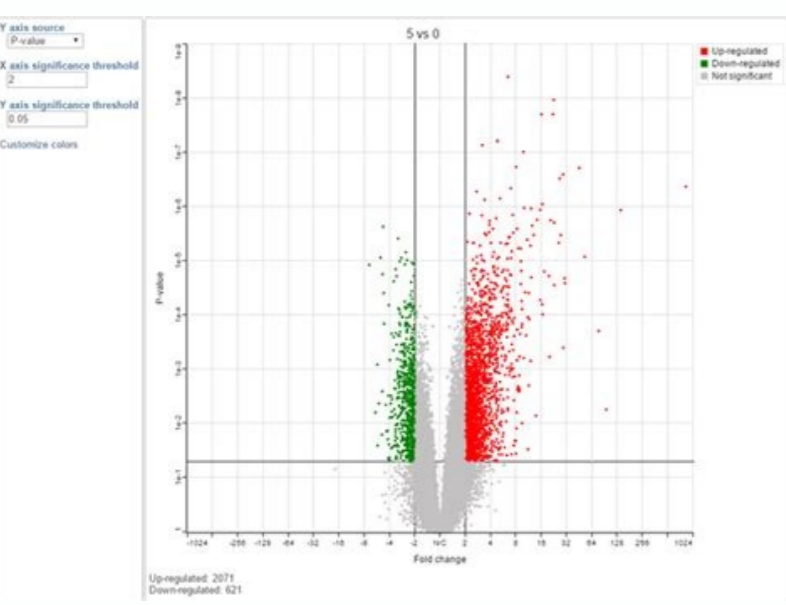
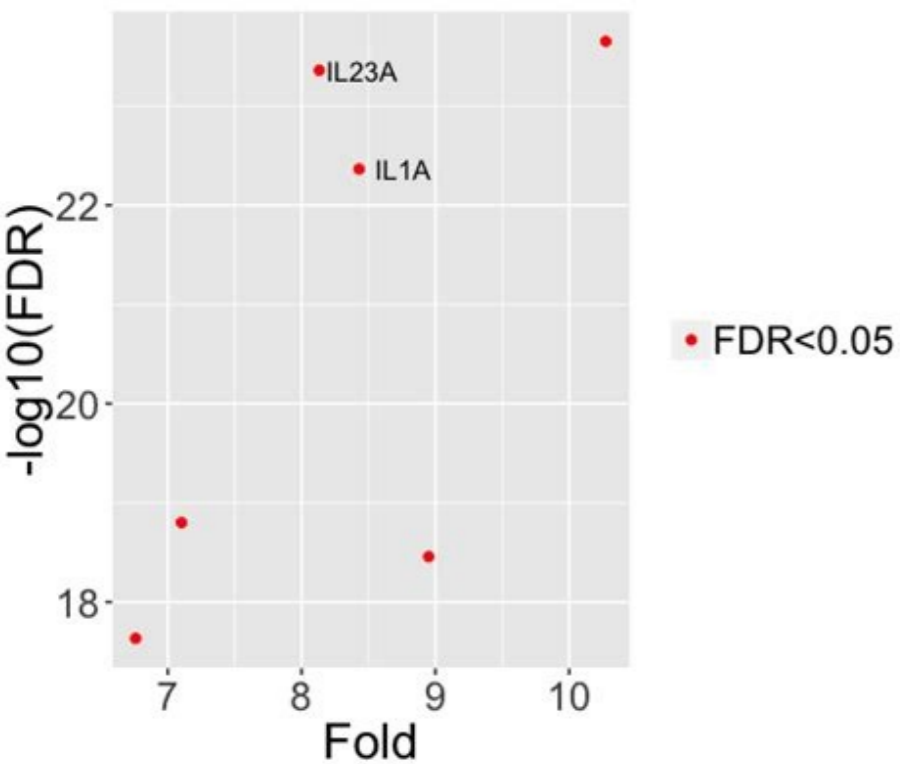
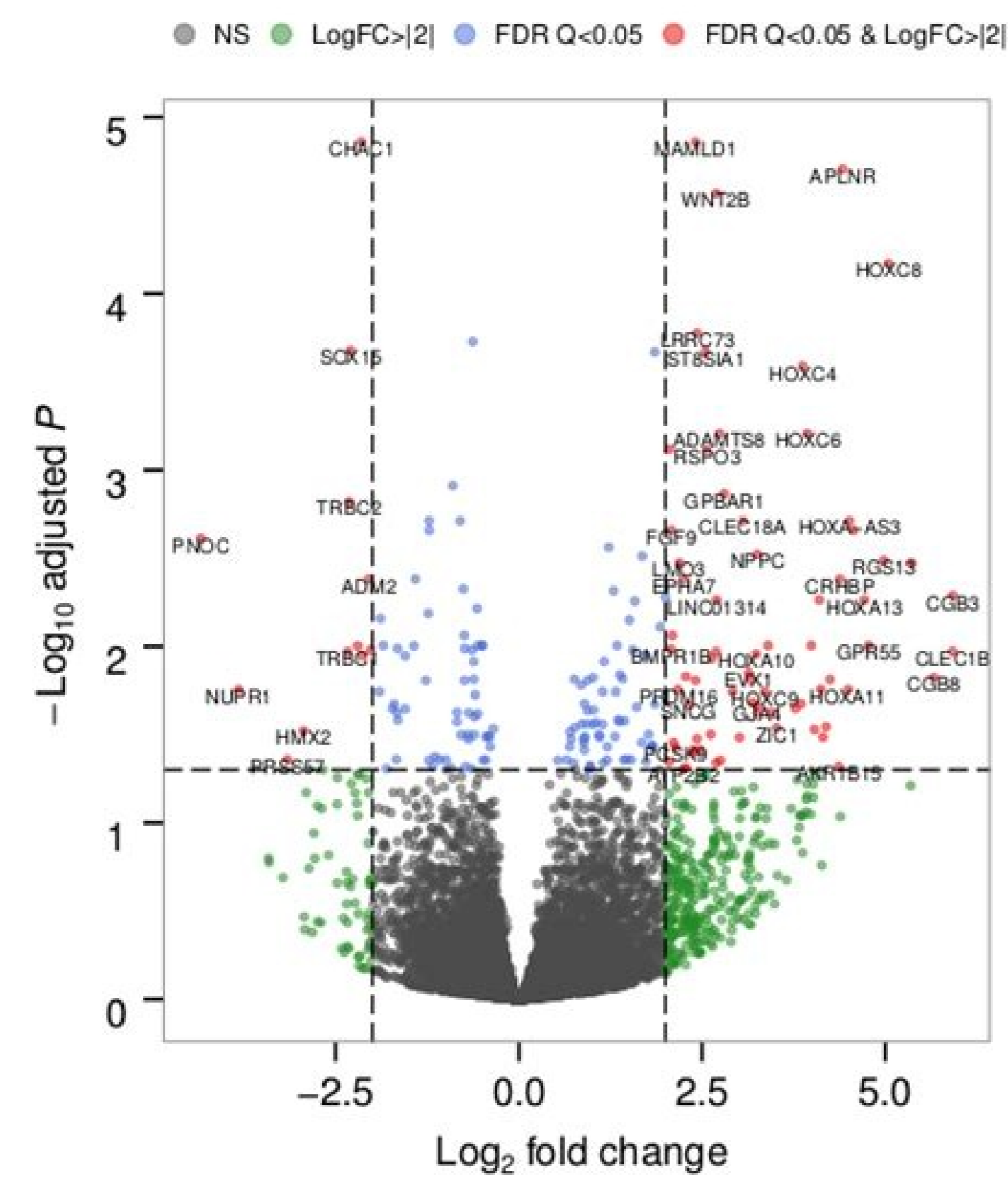
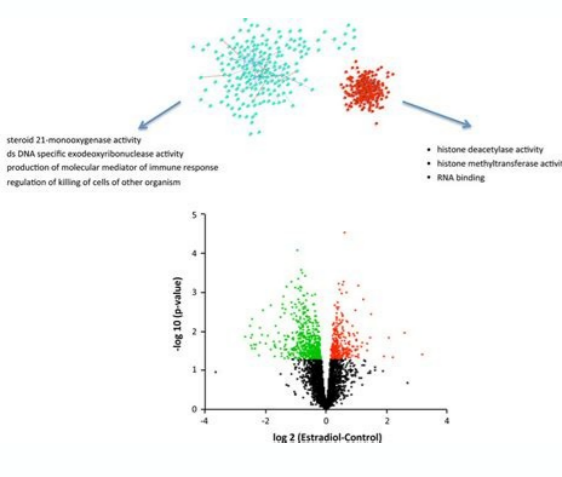


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Volcano plot in r.

In addition, the comparisons between the different experimental settings can be performed to narrow the list of LNCRNA expressed in a differentiated way during fibrosis in different tissues. The RNA-SEQ data were downloaded from the SRA database (Sequence Read Archive) using SRA Toolkit [69]. Due to the ongoing debate on the normalization of the data and expression values of RNA-SEQ [30], the CPM values are used in this study to avoid potential problems relating to the alternative joint and the length of the insert. When the first 20 coding for protein $\hat{c} \hat{c} \hat{c} \hat{c}$ highly express (figure 1B genes are compared) and LNCRNA (Figure 1C), the levels of expression of the LNCRNA genes highly expressed are 40 times lower than those of the coding genes for proteins [Google Scholar] Chang, H.Y.; Who, J.T.; Dudoit, S.; Bondre, c.; Van de Rijn, M.; Botstein, D.; Brown, p.o. Diversity, topographical differentiation and positional memory in human fibroblasts. (C) An example of a volcano diagram for the selected study condition. [Google Scholar] [Crossref] Xie, L.; Wang, y.; Deng, n.; Huang, G.; Taghavifar, F.; Geng, y.; Liu, n.; Kulur, v.; Yao, c.; Chen, p.; Et al. Annu. (E) An example of Venn diagram for the up-regulated genes among the studies recorded in Fibrodb. The extracellular vesicles derived from stem cells derived from the building inhibit the growth of neuroblastoma by regulating the gabbr1 activity through the transcription factor mediated by Linc00622 AR. 2016, 44, W90–W97, False Discovery Tasso (FDR) V-values $\hat{c} \hat{c} \hat{c} \hat{c}$ or have been used for further analyzes, unless otherwise indicated in the text. Only selected genes have been traced as expressed in a differentiated way in the lung fibroblasts (CTEph patients and MRC5 cells treated with TGF- β -ALE). Curr. (A) graphic designer of all genes, including protein coding and LNCRNA coding genes. (B) results of fibrotic marker genes, up-regulated protein encoding and LNCRNA genes. To stimulate fibrosis, the recombinant human TGF- β 21 (derived by HEK293) (Proteintech, Manchester, United Kingdom, #100-21) was added to the medium of growth in the medium of growth in the medium of growth in the medium of growth of 5 ng/mL. They synthesize and secrete extracellular matrix (ECM) proteins and collagens to maintain the tissue structure. As shown in Figure 5B, LINC00622 and LINC01711 were highly up-regulated upon TGF- β 21 stimulation, which confirmed the above selection criteria. Primers 2017, 3, 17074. Climatol. n = 5 biological replicates per anatomical locale, except for soft palate, which is n = 4 biological replicates. Fiji: An open-source platform for biological-image analysis. [Google Scholar] [Crossref] [Omate, N.; Sauler, M. [Google Scholar] [Crossref] [Clark, R.A.; McCoy, G.A.; Folkvord, J.M.; McPherson, J.M. TGF-beta 1 stimulates cultured human fibroblasts to proliferate and produce tissue-like fibroplasia: A fibronectin matrix-dependent event. Differentially expressed genes in TGF- β 21-treated MRC5 lung fibroblastic cell line compared to non-treated MRC5 cells at the threshold of 2-fold (logFC, fold change in logarithm of base 2) and FDR-adjusted p < 0.05 (FDR) (GEO accession number, GSE97829); Supplementary Table S4. RNA 2020, 26, 903eAAA909. 2010, 121, 240eAAA250. Loss-of-function experiments of the candidate lncRNA, LINC00622, in dermal fibroblasts. Clin. Aging 2020, 12, 1512eAAA1526. 2012, 40, e115. Aging 2021, 13, 19776eAAA19788. [Google Scholar] [Crossref] [Rinn, J.L.; Bondre, C.; Gladstone, H.B.; Brown, P.O.; Chang, H.Y. Anatomic demarcation by positional variation in fibroblast gene expression programs. [Google Scholar] [Crossref] [PubMed] [Harris, A.K.; Stopak, D.; Wild, P. enrichR: Provides an R Interface to $\hat{c} \hat{c} \hat{c} \hat{c}$ Enrichment. Version 3.0; 2021. 2016, 30, 1823eAAA1835. License MDPI, Basel, Switzerland. (D,E) Top 10 enriched GO terms (biological process) for shared (D) up- and (E) down-regulated protein-coding genes in two datasets. [Google Scholar] [Crossref] [Abbasi, S.; Sinha, S.; Labi, E.; Rosin, N.L.; Yoon, G.; Rahmani, W.; Jaffer, A.; Sharma, N.; Hagner, A.; Shah, P.; et al. [Google Scholar] [Crossref] [Chen, S.; Zhou, Y.; anicimotports-anilicnep id %1 e) j3157G#_hcidrIA-amgIS (%1 la animatulg-L id enoizulos ,j5417M#_hcidrIA-amgIS (idicaonima id enoizulos elaiNESSe: NON NON NON MEM %1 .j5314F#_hcidrIA-amgIS (%51 la elatof onivob oreis noc otargetni j9722M#_ainamreG_idatmsrAD_hcidrIA-amgIS_MEM) ominim elaiNESSe oidem etenemnoc atiscerc: id onerret len etavitloc etats onis elullec eL_4 arugif_ehcmoneg emmag id enoizatonna'1 e oclac li rep erawtfoS J.V.yeraC ;T.M.nagrom ;R.namelneG.M.noltraC ;P.nuoyobA ;H.enigAP ;W.rebuH ;M.ecnerwaL jfeRssorC jralohcS elgoogG_FGT ateb e elatusis isorbif allen ANRcnL.Y.H.naL ;Y.Y.gnahZ ;M.P.gnat jferrSorC jralohcS elgoogG .9962_74_9102 .883* 083_64_2102 .iranomlop e icaidrac itsalborbif id itad id tes i ert e itttu n italoger-pu ANRcnL ert id erolac id appam)B(.J72l arutloc id aigolodotem al e itusset ied itnaipse ilg rep etazillitu etats onais erudecorp essets el enebbes .) 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[google scholar] [crossref] sharma, s.; hofbauer, T.M.; ondracek, A.S.; chausheva, s.; s.TO.; Artner, t.; Panzenboeck, a.; Redler, J.; Shafran, I.; Mangold, a.; Et al. [Google Scholar] [Crossref] Huang da, W.; Sherman, B.T.; Lempicki, R.A. Bioinformatics enrichment tools: paths towards functional analysis complete with large genes of genes. In use R2 $\hat{c} \hat{c} \hat{c} \hat{c}$ ed ; Springer International Publication; Cham, Switzerland, 2016. enzyme. Figure 4. (C, d) Top 10 enriched GO Terms for (C) Up- and (D) Down-Regulated Genes. In addition, the common-regulated coding genes include the term GO for the WNT signaling pathway (GO: 0016055), such as FRZB (connected protein Fried), an extracellular antagonist of the WNT signal that is known to negatively control fibrosis in vitro [44]. [Google Scholar] [Crossref] Spanier, A.I.; Baarsma, H.A.; Oostenbrink, L.M.; Jansen, s.r.; Kuipers, c.c.; Lindner, m.; Postma, D.S.; Meurs, r.; Et al. Dev. [Google Scholar] [Crossref] De Langhe, e.; Aznar-Lopez, c.; De Vooght, V.; Vanorbeek, J.A.; Luyten, F.P.; Lories, R.J. Related proteins secreted inhibit fibrosis in vitro but appear redundant in vivo. (C) The QRT-PCR results on the simplification of Linc00622. (C) Diagrams of Venn of genes differentially expressed in two data sets: fibroblasts of cteph patients (in pink or yellow) and MRC5 cells treated with TGF- β (in green or light blue). The gene expression changes in the activated fibroblasts, myofibroblasts. [Google Scholar] [Crossref] renew, J.L.; Chang, H.Y. Long Noncoding RNAs: Molecular Modalities to act functions. The Knockdown of Linc01711 in the cell lines of ESCC has induced apoptosis, inhibited the proliferation, migration, invasion and growth of cells, while the administration of Linc01711 derived from Esoma promoted the growth of tumor in naked mice. Not surprisingly, the LNCRNA genes are expressed at a much lower level than the protein coding genes (Figure 3B), with our observations in previous data sets (Figure 1 and Figure 2), when the two data comesthe above fibroblasts were compared, there were 85 up-regulated protein-coding and 24 lncrna genes as well as 76 down-regulated protein-coding and 25 lncrna genes shared between the two datasets: fibroblasts of cteph patients and mrc5 cells treated with TGF- β (figure 3c; complementary table s4). (E,F) top 10 enriched go terms for (e) up- and (f) down-regulated genes. to understand the process of stimulated fibrosis TGF- β , a recent study conducted a RNA-seq of the lung fibroblastic cell line mrc5 treated with TGF- β [43]. the average cpm values of each anatomical locale are shown for each gene; Supplementary table s2, twenty-four hours after the addition of sirna to the medium of growth, cells were herose hungry for one day and stimulated with TGF- β for 24 h in presence of sirnas. n = 6 biological replicates by condition. For AL121749.2, it is not expressed in both non-stimulated and TGF- β -stimulated dermal fibroblasts. 2016, 54, 1 30 31–31 30 33. pharmacol. in the case of siRNA-based knockdown, sirna was added to the medium of culture at the time of average change. the images obtained were melted using the Fiji image processing package [79]. the non-directional RNA-seq was performed at novogene (cambridge, uk) using the next ultra rna library prep kit for preparation of the mRNA-seq library followed by sequencing with the platform illumina novaseq 6000 with a sequencing strategy pe150. the web application fibrodb is based on the r package, shiny [80]. [google scholar] [Crossref] [Barrett, t.; whitte, S.E.; ledoux, p.; evangelist, c.; kim, I.F.; tomashevsky, m.; marshall, K.A.; phillippy, K.H.; sherman, P.M.; holko, m.; this pattern is linked to the user. that suggests that it will be difficult etneibma etneibma etnatsoc anu id asuac A .acineg enoisserrp'lus itasab etenemclipms icificeps-itsalborbif ineg i To the lungs (for

example, dust, viruses) [31,32], the fibroblasts are exposed to various stress conditions, which are activated to support the remodeling during injury [33]. Using fibroblasts and changes in their expression profiles during fibrosis as a model system, we show that the general level of expression of LNCRNA genes is significantly lower than that of the protein coding genes. (F) QRT-PCR results of differentially expressed genes. Alveolar fibroblasts in acute lung lesions: biological behavior and clinical relevance. To obtain the readings for the kilo of transcription for million readings (RPKM) and transcriptions for kilobase values (TPM), the R_genomicfeatures packages were used [29] and EdgeR. Another study discovered that Linc01711 is contained in the Esophageal Squamous Cell (ESCC) carcinoma exofs [50]. After three washes with 0.1% Triton-X 100 in PBS, the secondary antibody was diluted in 0.1% Triton-X 100 in PBS for staining at room temperature (RT) for an hour: GOAT Anti-Rabbit IgG (H + L) Cross-Adsorbed ReadyProbes Secondary Antibody, Alexa Fluor 488 (Thermo Fisher Scientific, #R37116). Containment of the spinal apparatus in the cultures lymphocytes and human fibroblasts. The set data used in this study are indicated in the results section with the corresponding membership numbers from the Gene Expression Omnibus (Geo) database. [Google Scholar] [Crossref] Bochenek, M.L.; Rosinus, n.s.; Lankeit, m.; Hohohm, L.; Bremmer, F.; Schutz, E.; Klok, F.A.; Horke, S.; Wiedenroth, C.B.; Munzel, L.; Et al. 2020, 21, 56. The application provides three main characteristics: (1) Exploration of the results (Explore), (2) Download and (3) Documentation. When this dataset was analyzed using the latest annotation file provided by the Ensembl database [28] (GRC38.103), 2405 coding genes (out of 19,796 protein coding genes without transcriptions of reading registered under the GRC38.103 annotation file) and 8133 LNCRNA LNCRNA (out of 16.593 lncRNA genes without reading transcriptions) were found to be expressed in at least one fibroblast cell line based on normalized values, counts per million (CPM > 0; Supplementary Table S1). Secondly, we focused only on the known lncRNA genes based on the latest annotation provided by the Ensembl database. Voice-fold fibroblasts have been chosen because they are in a more stressful environment than in other parts of the body, leading to gene expression differences triggered by mechanical stress in the vocal fold [27]. The average CPM values (million accounts) for each anatomical locale were used to draw a violin diagram for protein coding and lncRNA genes based on the annotation (biotype) provided by the Ensembl database (GRC38.103). Since there are no lncRNA databases focused on fibroblasts and fibrosis, we have built a web application, FibroDB, to further promote functional and mechanical studies of fibrotic lncRNAs. Fibroblasts are the most common cell type in connective tissue and are found throughout the mammal body [1,2]. 2019, 9, 9580. 2021, 1, e90. FASTQ files were pre-processed with fasting [70] (versions 0.21.0 and 0.22.0) using predefined settings to perform quality control, adaptor filtration, quality filtration and reading pruning. Gene Med. [Google Scholar] [CrossRef]Muller, R.; Weirick, T.; John, D.; Militello, G.; Chen, W.; Dimmeler, S.; Uchida, S. 1997, 170, 69–80. However, there is no lncRNA database focused on fibroblasts currently available. Due to increased interest in fibrosis study, a number of RNA-seq data were deposited in public domain, such as Gene Expression Omnibus (GEO) and ArrayExpress. Category column is based on RNA-seq fibroblasts data id id atla 'Aip enoisserpse'nu ereva orebbertop illevon ANRcnl id ineq i ehc ellbissop 'Á, ~ÁsoC .R rep beW enoizacilppa id ordauQ .ynihS .M .renselhS ;.R .sliE ;.Z .uG]ralohcS elgooG] .loM lleC .]94[]077731CA dna .540780CA .RRDNEF .79410CNIL .29510CNIL .799110CA .784000PAI .sANRcnl rehto neves htw gnola amonicrac illec suomaugš laegahpöse rof rekramoib citsonorp a sa desu eb dluoc 11710CNIL taht detropre yduts tnecer A .X .gnoS ;.C .vl ;.s.t .llewkcalb ;d .euy .h .nehc ;s .gnah]Ferssorç]ralohcs elgoog[.sisorbif yranomlup cihtapoin .sllaw ;.names .l .idlehcir ;.g .uhgar ;.a .drap ;.W .DIAWAJ]Dembupl]ralohcs elgoog[.elprup ni Anr Rehto DNA .Nwohs Era Seneg-Nic-Wowsan GnicneuqneuQ .tuaebiht ;.X-notirt %1.0 htw Dezlibaemrep Erew Sillec .SBP DL OC-ECI Htiw Sehsaw eerht .Retfa .Jd3 edigann(stsalborbif detavitca Fo sitsiretcarahc era .Dehcirne Era)8 dewohs seneg gnidoc-nietorp desserpæ yllaitnerreffid derahs fo sisylana JOG(ygolotno eneG .740306 .7 .0202 .stnemirepxe noitcnuif-fo-ssol mrofrep ot yrassedecn si ti .sANRcnl cificeps fo ecnatropmi lanoitcnuif eht revocnu oT.stsalborbif lamred detalumits-1ÁÁ .FGT ni ron detalumitsu ni desserpæ ton saw .2.947121LA .eneg etadidnac ANRcnl eht .eton fo .esasesid gmul laittisretni detaicossa-sisorelcs cimetsys ni stsalborbifoyem dna ytienegoreteh tsalborbif slaeveer sisylana illec-elgnoS .la te ;.C .auf' naj ;.M.N ., efaug ;.m .gnaw ;.Ediganf .Dig .Seeg Gnidoc-NIDOC-NIDOP FO Scholar] [CrossRef] [PubMed]Quesnel, C.; Nardelli, L.; Piednoir, P.; Lecon, V.; Marchal-Somme, J.; Lasocki, S.; Boudima, L.; Philip, I.; Soler, P.; Crestani, B.; et al. Figure 5. To calculate counts per million (CPM) values and derive differentially expressed genes, the R package, edgeR [72] (versions 3.30.3 and 3.32.1), was used. n = 6 biological replicates per condition. When the differentially expressed genes were analyzed for KEGG pathways, the cytokineÁÁÁcytokine receptor interaction (hsa04060) and the TNF signaling pathway (hsa04668) were enriched (Figure 6E,F), suggesting that LINC01711 is involved in regulating inflammatory responses of fibroblasts.As a large number of RNA-seq data were analyzed in this study, focusing especially on lncRNA genes, we have built a web application, FibroDB, to disseminate the obtained information (Figure 7A). 2020, 16, 11eÁÁÁ31. Transient siRNA transfection (100 nM final concentration) was carried out using RNAiMax (Life Technologies, Carlsbad, CA, USA) according to the manufacturer'sÁÁÁ protocol. When the differentially expressed genes were analyzed for KEGG pathways, the mitogen-activated protein kinase (MAPK) signaling pathway (hsa04010) (Figure 5G,H), which plays an important role in the profibrotic processes in various diseases [52,53,54,55], was enriched. 2014, 5, 123. With the threshold values of 2-fold and p < 0.05, there are 913 up- and 712 down-regulated genes in thrombus compared to pulmonary artery adventitia (control) of CTEPH patients (n = 4 biological replicates). Enrichr: Interactive and collaborative HTML5 gene list enrichment analysis tool. To solve this problem, two databases that focus on a specific cell type is available: ANGIOGENES for endothelial cells [67] and RenalDB for cells in kidneys [68]. FibroDB will be updated twice a year to include the latest publicly available RNA-seq datasets after manual search via the GEO database.Data are presented as the Flaf with the hellow nuffe Sttuk Reputuations) Decanacan Vanean Seanean Sekuadezer mertubrase mertubate ymbocsko hank mant .4il man. There is piclalial platu-tucktuetan Lat succutates embrame 4002 miom 42 , 4 , 20 , 20 , 20 2-4 , . There is no . See Sanana and Sccor correct Rott taneo yoves : Aleant yogine s. Mar.s .Nighte; gnigreme fo notaulave evitarpomc A :sANRcnl rof sesabataD .])54[;810321ESG .rebmun noissecca OEG(dezyilana erew noitalumits ÁÁÁ-FGT fo atad qes-ANR fo tes rehtona .sANRcnl 42 detatuger-pu derahs eht eziretcarahc rehtruf oT.gnlangis ÁÁÁ Seay-grit is a red. "Meo tan .23 23, "Oey eudiate edion edive ,1222 mum , kmern , kabower sume: Elter to Getcipal Centrance , SThyy ...tylmy Fold the change in the logarithm of the base 2) and P



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