# **Supplement material**

# Long non-coding RNA expression patterns in lung tissues of chronic cigarette smoke induced COPD mouse model

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Quality evaluation of RNA sequencing data. (a) Classifications of raw reads. (b) Distributions of the effective reads on the location of genes. (c) Distributions of the effective reads on the genomes. Sample1, sample2 and sample3 are belonged to control group, whereas the other samples are belonged to the chronic CS-induced COPD mouse model group.



Unsupervised hierarchical clustering analyses of (a) lncRNAs and (b) mRNAs in lungs of chronic CS-induced COPD model mice and control animals. RNA sequencing data are obtained from 3 mice per group. Red blocks indicate high expression levels of lncRNAs or mRNAs in each sample, whereas green blocks indicate low expression levels of lncRNAs or mRNAs.



Volcano plots of (a) lncRNAs and (b) mRNAs in lungs of chronic CS-induced COPD model mice and control animals. Red plots indicate significantly differential expressed lncRNAs and mRNAs between these two groups.



Venn diagram depicting the overlaps of lncRNAs, lncRNA potential target protein coding genes, and connections between lncRNAs and their associated protein coding genes in lncRNA cis- and trans- regulation patterns.(a) Overlap of lncRNAs.(b) Overlap of lncRNAs potential target protein-coding genes.(c) Overlap of connections between lncRNAs and their potential target protein coding genes.



Correlation analysis of fold change data between qRT-PCR and RNA sequencing in mouse. (a) Up- and down- regulated lncRNAs selected for qRT-PCR validation. (b) Up- and down- regulated mRNAs selected for qRT-PCR validation. Black plots indicate lncRNAs or mRNAs. R represents correlation coefficient.

|          |   | Raw reads |          | Total roxy   | Reads wa | ith    | Total               | Reads co<br>N | ontaining | Total reads     | Low qual    | lity reads  | Total low        | Other reads               | Reads<br>containi      | The                |
|----------|---|-----------|----------|--------------|----------|--------|---------------------|---------------|-----------|-----------------|-------------|-------------|------------------|---------------------------|------------------------|--------------------|
| ID       | Group   | Read1     | Read2    | reads        | Read1    | Read2  | reads with adapters | Read1         | Read2     | containing<br>N | Read1       | Read2       | quality<br>reads | removed from<br>analysis* | ng<br>ribosom<br>e RNA | effective<br>reads |
| Sample 1 | Control<br>animals                              | 80093321  | 80093321 | '160,186,642 | 46,697   | 46,453 | '93,150             | 78558         | 89768     | '168,326        | 221570<br>0 | 408372<br>1 | '6,299,421       | '3,462,719                | '2,310,63<br>0         | '147,852,3<br>96   |
| Sample 2 | Control<br>animals                              | 72307427  | 72307427 | '144,614,854 | 606340   | 599237 | '1,205,577          | 70386         | 80520     | '150,906        | 203802<br>5 | 361644<br>8 | '5,654,473       | '3,129,488                | '10,451,5<br>30        | '124,022,8<br>80   |
| Sample 3 | Control<br>animals                              | 69158955  | 69158955 | '138,317,910 | 36624    | 36368  | '72,992             | 68331         | 77775     | '146,106        | 188833<br>9 | 303015<br>0 | '4,918,489       | '2,708,761                | '3,983,55<br>6         | '126,488,0<br>06   |
| Sample 4 | Chronic<br>CS-induced<br>COPD<br>mouse<br>model | 77890883  | 77890883 | '155,781,766 | 342395   | 334134 | '676,529            | 76107         | 86940     | '163,047        | 221512<br>5 | 470669<br>6 | '6,921,821       | '3,876,319                | '8,998,89<br>4         | '135,145,1<br>56   |
| Sample 5 | Chronic<br>CS-induced<br>COPD<br>mouse<br>model | 84100609  | 84100609 | '168,201,218 | 392899   | 382975 | '775,874            | 82431         | 93808     | '176,239        | 238617<br>2 | 501380<br>7 | '7,399,979       | '4,186,832                | '9,203,03<br>4         | '146,459,2<br>60   |
| Sample 6 | Chronic<br>CS-induced<br>COPD<br>mouse<br>model | 71413600  | 71413600 | '142,827,200 | 317908   | 310309 | '628,217            | 69695         | 79871     | '149,566        | 203550<br>8 | 537620<br>6 | '7,411,714       | '4,358,709                | '10,060,1<br>78        | '120,218,8<br>16   |

RNA sequencing reads of chronic CS-induced COPD mouse model and control animals.

\*Other reads needed to be removed from analysis, such as reads without 3' adapter reads without judgment sequences, reads with 5' adapter contamination and so on.

| ID       | Crown           | The offective mode  | Total manual made  | Deads man to evens | Reads map to     | Reads map to | Reads map to       |
|----------|-----------------|---------------------|--------------------|--------------------|------------------|--------------|--------------------|
| ID       | Group           | The effective reads | Total mapped reads | Reads map to exons | splicing regions | introns      | intergenic regions |
| Sample 1 | Control animals | 147,852,396         | '140,574,061       | '108,993,577       | '433,245         | '25,065,773  | '6,081,466         |
| Sample 2 | Control animals | '124,022,880        | '115,836,570       | '86,041,686        | '346,303         | '23,992,414  | '5,456,167         |
| Sample 3 | Control animals | '126,488,006        | '119,128,122       | '92,205,678        | '350,935         | '19,394,919  | '7,176,590         |
|          | Chronic         |                     |                    |                    |                  |              |                    |
| Sample 4 | CS-induced COPD | '135,145,156        | '125,783,965       | '98,870,957        | '385,381         | '20,087,387  | '6,440,240         |
|          | mouse model     |                     |                    |                    |                  |              |                    |
|          | Chronic         |                     |                    |                    |                  |              |                    |
| Sample 5 | CS-induced COPD | '146,459,260        | '136,097,519       | '97,391,052        | '389,428         | '29,087,258  | '9,229,781         |
|          | mouse model     |                     |                    |                    |                  |              |                    |
|          | Chronic         |                     |                    |                    |                  |              |                    |
| Sample 6 | CS-induced COPD | '120,218,816        | '112,272,198       | '85,544,144        | '331,616         | '21,997,497  | '4,398,941         |
|          | mouse model     |                     |                    |                    |                  |              |                    |

RNA sequencing data analysis: mapping of RNA sequencing reads to exons, introns, splicing regions and intergenic regions in chronic CS-induced COPD mouse model and control animals.

Top 20 significantly up- and down- regulated lncRNAs in lungs of chronic CS-induced COPD mouse model compared with control animals.

| Gene               | Transcript | Position                 | Strand | Fold<br>Chang<br>e | P Value |
|--------------------|------------|--------------------------|--------|--------------------|---------|
| Up-regulated       |            |                          |        |                    |         |
| Fantom3_2810049006 | AK012936   | chr4:151003658-151004621 |        | 6.72               | < 0.001 |
| Fantom3_C130011B08 | AK081361   | chr4:151042408-151043788 |        | 6.49               | < 0.001 |
| Fantom3_D330021G15 | AK084610   | chr4:151011436-151031497 |        | 6.40               | < 0.001 |
| Fantom3_5330405H16 | AK030382   | chr4:151033075-151036561 |        | 6.29               | < 0.001 |
| Fantom3_7420409G12 | AK135741   | chr4:151018475-151021895 | +      | 5.75               | < 0.001 |
| Fantom3_F830212L20 | AK157369   | chr8:107385117-107388684 | +      | 4.67               | < 0.001 |
| Fantom3_2900002P20 | AK013478   | chr5:120940505-120941428 |        | 4.64               | 0.035   |
| Fantom3_9530016F16 | AK035325   | chr1:127983186-127984687 |        | 4.46               | < 0.001 |
| Fantom3_A930002I24 | AK044236   | chr11:90336537-90338283  |        | 4.15               | < 0.001 |
| Fantom3_A630036C12 | AK041770   | chrX:162628954-162629652 | —      | 4.06               | 0.036   |
| Fantom3_6230411F15 | AK134477   | chr6:126708330-126736811 |        | 3.93               | 0.013   |
| Fantom3_C130085H20 | AK081893   | chr7:110120216-110121740 | —      | 3.91               | < 0.001 |
| Fantom3_A630032O12 | AK041731   | chr1:127982282-127983640 | —      | 3.72               | < 0.001 |
| Fantom3_D630024P09 | AK085437   | chr15:81825471-81826859  | +      | 3.64               | < 0.001 |
| Fantom3_2310028D20 | AK009518   | chr15:81825121-81826859  | +      | 3.62               | < 0.001 |
| Fantom3_2310076L22 | AK010205   | chr15:81826045-81826859  | +      | 3.61               | < 0.001 |
| Fantom3_B230316C23 | AK045874   | chr11:90337983-90339337  | —      | 3.61               | < 0.001 |
| Fantom3_9430099M06 | AK020530   | chr8:102706048-102706790 | —      | 3.56               | 0.034   |
| Fantom3_9930123J05 | AK037130   | chr1:127978904-127981691 | —      | 3.39               | < 0.001 |
| Fantom3_D630021F02 | AK085396   | chr11:95961598-95964859  | —      | 3.19               | < 0.001 |
| Down-regulated     |            |                          |        |                    |         |
| Fantom3_7330403C04 | AK078618   | chr17:34957618-34959819  | +      | 0.04               | < 0.001 |
| Fantom3_E430013E17 | AK088332   | chr7:113219369-113220523 | +      | 0.12               | < 0.001 |
| Fantom3_4732480P20 | AK076384   | chr2:126600233-126618661 | —      | 0.15               | 0.001   |
| Fantom3_A530079J17 | AK080197   | chr5:134738232-134738818 |        | 0.22               | < 0.001 |
| Fantom3_1200007C13 | AK004627   | chr2:167827692-167833646 |        | 0.24               | < 0.001 |
| Fantom3_D430030N05 | AK052469   | chr11:58202414-58204772  | +      | 0.25               | 0.016   |
| Fantom3_F830218D03 | AK172595   | chr6:29853890-29867419   | +      | 0.26               | < 0.001 |

| Fantom3_B930085K01 | AK081095  | chr11:43561869-43564424   | + | 0.31 | 0.039   |
|--------------------|-----------|---------------------------|---|------|---------|
| NR_033355          | NR_033355 | chr4:43730033-43734534    | + | 0.32 | < 0.001 |
| Fantom3_F830208D04 | AK157250  | chr11:20461258-20464664   |   | 0.33 | 0.001   |
| Fantom3_8030479C08 | AK033265  | chr15:101931536-101933987 | + | 0.35 | < 0.001 |
| Fantom3_E030001B03 | AK086777  | chr5:134744725-134747253  | _ | 0.35 | < 0.001 |
| Fantom3_E030024M20 | AK087068  | chr5:134725602-134729106  |   | 0.35 | < 0.001 |
| Fantom3_2900019G23 | AK132033  | chr2:23012822-23014153    |   | 0.36 | 0.007   |
| Fantom3_1700030C12 | AK006530  | chr11:23497756-23499640   | + | 0.36 | < 0.001 |
| Fantom3_A430043G10 | AK040013  | chr12:104247895-104248893 | + | 0.36 | 0.004   |
| Fantom3_F630314A02 | AK155529  | chr5:43784045-43786115    |   | 0.37 | < 0.001 |
| Fantom3_A730094A05 | AK139286  | chr4:40720058-40722867    | _ | 0.38 | < 0.001 |
| Fantom3_A430085D10 | AK079839  | chr6:29876678-29879068    | + | 0.38 | < 0.001 |
| NR_033450          | NR_033450 | chr12:104247895-104254405 | + | 0.39 | < 0.001 |

Top 20 significantly up- and down- regulated mRNAs in lungs of chronic CS-induced COPD mouse model compared with control animals.

| Gene symbol  | Gene Name   | Transcript       | Position                     | Strand | Fold<br>Change | P Value |
|--------------|---|------------------|------------------------------|--------|----------------|---------|
| Up-regulated |   |                  |                              |        |                |         |
| Dbp          | D site albumin promoter binding protein                     | NM_016974        | chr7:45705247-4<br>5710203   | +      | 21.16          | < 0.001 |
| Ces1g        | carboxylesterase 1G   | NM_021456        | chr8:93302369-9<br>3337209   |        | 9.83           | < 0.001 |
| Cyp2a5       | cytochrome P450, family<br>2, subfamily a,<br>polypeptide 5 | NM_007812        | chr7:26835339-2<br>6843264   | +      | 9.07           | < 0.001 |
| Necab1       | N-terminal EF-hand<br>calcium binding protein 1             | NM_178617        | chr4:14952245-1<br>5149131   | —      | 7.91           | < 0.001 |
| Per3         | period circadian clock 3                                    | NM_011067        | chr4:151003655-<br>151044622 | _      | 6.37           | < 0.001 |
| Olfr1342     | olfactory receptor 1342                                     | NM_146713        | chr4:118689503-<br>118690450 |        | 6.25           | < 0.001 |
| Ahrr         | aryl-hydrocarbon receptor repressor                         | NM_009644        | chr13:74211118-<br>74292309  | —      | 6.04           | < 0.001 |
| Bpifc        | BPI fold containing family C                                | NM_177772        | chr10:85959691-<br>86011860  |        | 5.33           | 0.003   |
| Nr1d2        | nuclear receptor<br>subfamily 1, group D,<br>member 2       | NM_011584        | chr14:18204056-<br>18239106  | _      | 5.21           | < 0.001 |
| Nqo1         | NAD(P)H<br>dehydrogenase, quinone<br>1                      | NM_008706        | chr8:107388225-<br>107403205 | _      | 5.11           | < 0.001 |
| Mogat2       | monoacylglycerol<br>O-acyltransferase 2                     | NM_177448        | chr7:99219084-9<br>9238611   |        | 4.61           | 0.008   |
| Enthd1       | ENTH domain containing                                      | NM_0011631<br>89 | chr15:80452240-<br>80560470  | —      | 4.37           | 0.032   |
| Npy          | neuropeptide Y  | NM_023456        | chr6:49822729-4<br>9829505   | +      | 4.36           | < 0.001 |
| Tcfl5        | transcription factor-like 5 (basic helix-loop-helix)        | NM_178254        | chr2:180621957-<br>180642691 | —      | 4.27           | 0.033   |
| Oxct2a       | 3-oxoacid CoA<br>transferase 2A                             | NM_022033        | chr4:123321875-<br>123323679 |        | 4.25           | 0.014   |
| D7Ertd443e   | DNA segment, Chr 7,<br>ERATO Doi 443,<br>expressed          | NM_0010813<br>31 | chr7:134266262-<br>134376828 | _      | 4.16           | 0.037   |
| Spag11b      | sperm associated antigen 11B                                | NM_0010395<br>63 | chr8:19140759-1<br>9143007   | +      | 3.87           | < 0.001 |

| Hlf            | hepatic leukemia factor  | NM_172563        | chr11:90336535-<br>90390917   |   | 3.84 | < 0.001 |
|----------------|--|------------------|-------------------------------|---|------|---------|
| Sult1d1        | sulfotransferase family 1D, member 1                               | NM_016771        | chr5:87554650-8<br>7569006    | _ | 3.78 | 0.049   |
| Igfbp2         | insulin-like growth factor<br>binding protein 2                    | NM_008342        | chr1:72824480-7<br>2852471    | + | 3.74 | < 0.001 |
| Down-regulated | or or  |                  |                               |   |      |         |
| Hspa1b         | heat shock protein 1B  | NM_010478        | chr17:34956429-<br>34959238   |   | 0.04 | < 0.001 |
| Hspa1a         | heat shock protein 1A  | NM_010479        | chr17:34969359-<br>34972156   | — | 0.07 | < 0.001 |
| Spon2          | spondin 2, extracellular<br>matrix protein                         | NM_133903        | chr5:33213518-3<br>3218238    | _ | 0.08 | < 0.001 |
| Gbp10          | guanylate-binding<br>protein 10                                    | NM_0010396<br>46 | chr5:105215699-<br>105239533  | — | 0.08 | 0.049   |
| Arntl          | aryl hydrocarbon receptor<br>nuclear translocator-like             | NM_007489        | chr7:113207465-<br>113314126  | + | 0.09 | < 0.001 |
| Mucl1          | mucin-like 1   | NM_009268        | chr15:103751923<br>-103899300 | — | 0.10 | 0.008   |
| Fga            | fibrinogen alpha chain   | NM_0011110<br>48 | chr3:83026153-8<br>3033617    | + | 0.11 | < 0.001 |
| Npas2          | neuronal PAS domain protein 2                                      | NM_008719        | chr1:39194272-3<br>9363240    | + | 0.15 | < 0.001 |
| Nfil3          | nuclear factor, interleukin<br>3, regulated                        | NM_017373        | chr13:52967209-<br>52981039   | — | 0.17 | 0.002   |
| Avpr1a         | arginine vasopressin<br>receptor 1A                                | NM_016847        | chr10:122448499<br>-122453453 | + | 0.17 | < 0.001 |
| Gm12250        | predicted gene 12250   | NM_0011351<br>15 | chr11:58183843-<br>58190198   | + | 0.17 | < 0.001 |
| Gbp6           | guanylate binding protein<br>6                                     | NM_194336        | chr5:105270702-<br>105293699  | — | 0.22 | 0.020   |
| Hdc            | histidine decarboxylase  | NM_008230        | chr2:126593659-<br>126624024  | — | 0.24 | < 0.001 |
| Cd209a         | CD209a antigen   | NM_133238        | chr8:3743395-37<br>48984      |   | 0.24 | < 0.001 |
| Hsph1          | heat shock<br>105kDa/110kDa protein 1                              | NM_013559        | chr5:149616845-<br>149636315  |   | 0.24 | < 0.001 |
| Fam124b        | family with sequence<br>similarity 124, member B                   | NM_173425        | chr1:80198699-8<br>0213944    | _ | 0.25 | < 0.001 |
| Ccnjl          | cyclin J-like  | NM_0010455<br>30 | chr11:43528749-<br>43586999   | + | 0.26 | < 0.001 |
| Serpina3f      | serine (or cysteine)<br>peptidase inhibitor, clade<br>A, member 3F | NM_0011682<br>94 | chr12:104214544<br>-104221129 | + | 0.26 | 0.007   |

| Tgtp2 | T cell specific GTPase 2                                      | NM_0011451<br>64 | chr11:49057196-<br>49064212  | — | 0.26 | < 0.001 |
|-------|---|------------------|------------------------------|---|------|---------|
| Klra7 | killer cell lectin-like<br>receptor, subfamily A,<br>member 7 | NM_014194        | chr6:130218605-<br>130231687 | _ | 0.27 | 0.005   |

| Experiment<br>ID in GEO<br>database | Authors                                      | Study<br>design  | Study<br>type | Organism        | Platform                            | Samples |
|-------------------------------------|--|--|---------------|-----------------|-------------------------------------|---------|
| GSE475                              | Rubinstein<br>NA<br>Carolan B                | case control<br>study                                  | in vivo       | Homo<br>sapiens | HS_AFFY_U<br>133A <sup>*</sup>      | 7       |
| GSE10006                            | et al. /<br>Crystal<br>RG                    | case control<br>study                                  | in vivo       | Homo<br>sapiens | HS_AFFY_U<br>133PLUS_2 <sup>*</sup> | 84      |
| GSE22148                            | Singh D et<br>al. / Celli<br>B               | clinical<br>history<br>study                           | in vivo       | Homo<br>sapiens | HS_AFFY_U<br>133PLUS_2              | 136     |
| GSE13896                            | R et al. /<br>Crystal<br>RG                  | case control<br>study                                  | in vivo       | Homo<br>sapiens | HS_AFFY_U<br>133PLUS_2              | 46      |
| GSE42057                            | Bowler<br>RP et al. /<br>Hughes<br>GJ        | case control<br>study,<br>clinical<br>history<br>study | in vivo       | Homo<br>sapiens | HS_AFFY_U<br>133PLUS_2              | 131     |
| GSE47460                            | Tedrow J<br>et al. /<br>Schwartz<br>DA       | case control<br>study                                  | in vivo       | Homo<br>sapiens | HS_AGIL_4x<br>44K <sup>#</sup>      | 151     |
| GSE47460                            | Tedrow J<br>et al. /<br>Schwartz<br>DA       | case control<br>study,<br>clinical<br>history<br>study | in vivo       | Homo<br>sapiens | HS_AGIL_8x<br>60K <sup>§</sup>      | 424     |
| GSE22047                            | Butler<br>MW et al.<br>/ Crystal<br>RG       | case control<br>study                                  | in vivo       | Homo<br>sapiens | HS_AFFY_U<br>133PLUS_2              | 125     |
| GSE8581                             | Bhattachar<br>ya S et al.<br>/ Mariani<br>TJ | clinical<br>history<br>study                           | in vivo       | Homo<br>sapiens | HS_AFFY_U<br>133PLUS_2              | 53      |
| GSE11784                            | et al. /<br>Crystal<br>RG                    | case control<br>study                                  | in vivo       | Homo<br>sapiens | HS_AFFY_U<br>133PLUS_2              | 110     |

**Supplementary Table S5** High throughput studies about patients with COPD from GEO datasets.

|          | Shaykhiev  |              |          |         |                    |     |  |
|----------|------------|--------------|----------|---------|--------------------|-----|--|
| GSE20257 | R et al. / | case control | in vivo  | Homo    | HS_AFFY_U          | 76  |  |
| 00120207 | Crystal    | study        | III 1110 | sapiens | 133PLUS_2          | 10  |  |
|          | RG         |              |          |         |                    |     |  |
| GSE20123 | Fujino N / | case control | in vivo  | Homo    | HS_AFFY_U          | 6   |  |
| 03E29133 | Kubo H     | study        |          | sapiens | 133PLUS_2          | 0   |  |
|          | Bastos R   | anna control |          | Uomo    | US AFEV II         |     |  |
| GSE37768 | et al. /   |              | in vivo  |         | 122DLUG 2          | 37  |  |
|          | Kalko SG   | study        |          | sapiens | 133PLUS_2          |     |  |
| CSE56241 | Vuoio EA   | case control | in vivo  | Homo    | HS_AFFY_S          | 22  |  |
| USE20341 | VUCIC EA   | study        |          | sapiens | T1_0 <sup>**</sup> | LL  |  |
| CSE27147 | Steiling K | case control | in vivo  | Homo    | HS_AFFY_S          | 244 |  |
| USE3/14/ | / Spira A  | study        |          | sapiens | T1_0               | 244 |  |
|          |            | case control |          |         |                    |     |  |
|          | Kim WJ et  | study,       |          | 11      | HS_mRNASe          |     |  |
| GSE57148 | al. / Lee  | clinical     | in vivo  | Homo    | q_HUMAN_           | 165 |  |
|          | SD         | history      |          | sapiens | GL                 |     |  |
|          |            | study        |          |         |                    |     |  |
|          |            |              |          |         |                    |     |  |

\*HS\_AFFY\_U133A: Affymetrix Human Genome U133A Array.

<sup>\*</sup>HS\_AFFY\_U133PLUS\_2: Affymetrix Human Genome U133 Plus 2.0 Array.

<sup>#</sup>HS\_AGIL\_4x44K: Agilent-014850 Whole Human Genome Array 4x44K G4112F.

<sup>§</sup>HS\_AGIL\_8x60K: Agilent-028004 SurePrint G3 Human GE 8x60K Array.

\*HS\_AFFY\_ST1\_0: Affymetrix Human Gene 1.0 ST Array.

| Gene name              | Tran<br>script    | Forward $(5' \rightarrow 3')$ | Reverse $(5' \rightarrow 3')$ | Product<br>length<br>(bp) | Tm<br>(°C) |
|------------------------|-------------------|-------------------------------|-------------------------------|---------------------------|------------|
| Up-regulated           |                   |                               |                               | × 17                      |            |
| Fantom3_A9300<br>02I24 | AK0<br>4423<br>6  | TTCAACTCCAGGTG<br>TTCGGT      | CCCCAACACA<br>GATTTTGGCA      | 122                       | 60         |
| Fantom3_95300<br>16F16 | AK0<br>3532<br>5  | CCTGGTCTGTTGTG<br>GTGAGA      | CAAGTCCCAC<br>CCACCTCTAG      | 192                       | 60         |
| Fantom3_C1300<br>11B08 | AK0<br>8136<br>1  | AAGCCCAGTACCC<br>TAGATGC      | TTCCACTGCAC<br>ATGAGGACT      | 115                       | 60         |
| Fantom3_F8302<br>12L20 | AK1<br>5736<br>9  | TTGGAATGCTGAG<br>ACCCTGT      | GGAGTGAAAA<br>CACGTGGCTT      | 173                       | 60         |
| Fantom3_74204<br>09G12 | AK1<br>3574<br>1  | TCTGCTGATAGGA<br>CGAGCTG      | TTCTCACTAGC<br>TGCCGAACA      | 163                       | 60         |
| Fantom3_28100<br>49006 | AK0<br>1293<br>6  | TGAAGTGATTTGG<br>GAGGCCT      | AGCAGGAACC<br>AGAGACCATC      | 112                       | 60         |
| NR_102714              | NR_<br>1027<br>14 | GCAGAGAGGGAGA<br>CCATCAG      | TGTAGCGTAC<br>CATCCATCCA      | 145                       | 60         |
| Fantom3_D3300<br>21G15 | AK0<br>8461<br>0  | CCTGTGTTTCAAGG<br>GTCCACT     | ACAGGTGCTG<br>GCAACTTCTT      | 88                        | 60         |
| Down-regulated         |                   |                               |                               |                           |            |
| NR_033355              | NR_<br>0333<br>55 | CAGAAATCATGGA<br>GACCGCG      | GATGCAGGTA<br>ATGGCCATGG      | 73                        | 60         |
| NR_028593              | NR_<br>0285<br>93 | AGGGTACTGGAGT<br>GGTTTGG      | GGCCATCAAC<br>CAGAAAAGCA      | 75                        | 60         |
| Fantom3_A4300<br>43G10 | AK0<br>4001<br>3  | GGACCCCACTTCCC<br>TTGTAA      | AGTGTCTGAG<br>CAGGTGTCTC      | 89                        | 60         |
| NR_033450              | NR_<br>0334<br>50 | GCATCTGAAACAC<br>TTGACGCC     | CCATGCATTTG<br>CAGGGTTGAG     | 136                       | 60         |
| Fantom3_12000          | AK0               | TACAAACCTGGGC                 | AAGCAGAGGC                    | 103                       | 60         |

| 07C13            | 0462 | TCACCAC        | TAACGGTGTC  |     |    |
|------------------|------|----------------|-------------|-----|----|
|                  | 7    |                |             |     |    |
| Fantom3_D8300    | AK0  | TGGTCTATACCCGC | CTTTCCTCAGC | 108 | 60 |
| 09E10            | 8578 | TGACCT         | GAGGGATGT   |     |    |
|                  | 8    |                |             |     |    |
| Internal control |      |                |             |     |    |
| 18s              | 18s  | GCAATTATTCCCCA | GGCCTCACTA  | 123 | 60 |
|                  |      | TGAACG         | AACCATCCAA  |     |    |

| Primers used for quantitative RT-PCR validation of 6 up-and down-regulated mRNAs in mouse. |                      |                               |                               |                           |            |  |  |  |
|--|----------------------|-------------------------------|-------------------------------|---------------------------|------------|--|--|--|
| Gene name  | Transc<br>ript       | Forward $(5' \rightarrow 3')$ | Reverse $(5' \rightarrow 3')$ | Product<br>length<br>(bp) | Tm<br>(°C) |  |  |  |
| Up-regulated   |                      |                               |                               |                           |            |  |  |  |
| Per3   | NM_0<br>11067        | GAAGCAGTGCCA<br>GCAGTATA      | AAGGGCTTCGTC<br>TCTCTGTC      | 101                       | 60         |  |  |  |
| Nqo1   | NM_0<br>08706        | GGAAGCTGCAGA<br>CCTGGTGA      | CCTTTCAGAATG<br>GCTGGCA       | 69                        | 60         |  |  |  |
| Hlf  | NM_1                 | GACAGCTCCCCT                  | CTGCTGCTCTCA                  | 151                       | 61         |  |  |  |
| Ggt1   | NM_0<br>08116        | TTTGTCATCATC                  | CCCGTCCAATCT                  | 115                       | 61         |  |  |  |
| Ahrr   | NM_0<br>09644        | GTGGTTACGATG<br>GACTCAAGG     | GTCCCCTGAACA<br>GTGAAATGC     | 124                       | 60         |  |  |  |
| Nr1d2  | NM_0<br>11584        | TGAACGCAGGAG<br>GTGTGATTG     | GAGGACTGGAA<br>GCTATTCTCAGA   | 100                       | 62         |  |  |  |
| Uch11  | NM_0<br>11670        | AGGGACAGGAA<br>GTTAGCCCTA     | AGCTTCTCCGTT<br>TCAGACAGA     | 160                       | 60         |  |  |  |
| Down-regulated   |                      |                               |                               |                           |            |  |  |  |
| Serpina3f  | NM_0<br>01168<br>294 | TGGGAGATGCCC<br>TTTGATCC      | AGTAGGGTGTCG<br>TCAGGTTATTA   | 112                       | 60         |  |  |  |
| Ggt5   | NM_0<br>11820        | TTCAATGGGACA<br>GAAACCTTGAG   | TCCCTGTGTATA<br>AGACCTCCG     | 109                       | 61         |  |  |  |
| Dnaja1   | NM_0<br>08298        | ACCACTTACTAC<br>GATGTTTTGGG   | GCCCTCTTTAAT<br>CGCCTGCT      | 213                       | 61         |  |  |  |
| Hspa5  | NM_0<br>01163<br>434 | GCATCACGCCGT<br>CGTATGT       | ATTCCAAGTGCG<br>TCCGATGAG     | 134                       | 61         |  |  |  |
| Fkbp4  | NM_0<br>10219        | CCTCTCGAAGGA<br>GTGGACATC     | TCCCCGATCATG<br>GGTGTCT       | 98                        | 61         |  |  |  |
| Hspala   | NM_0<br>10479        | TGGTGCAGTCCG<br>ACATGAAG      | GCTGAGAGTCGT<br>TGAAGTAGGC    | 219                       | 61         |  |  |  |
| II1rl1   | NM_0<br>01025<br>602 | TGACACCTTACA<br>AAACCCGGA     | AGGTCTCTCCCA<br>TAAATGCACA    | 178                       | 61         |  |  |  |
| Internal control   |                      |                               |                               |                           |            |  |  |  |
| 18s  | 18s                  | GCAATTATTCCC<br>CATGAACG      | GGCCTCACTAAA<br>CCATCCAA      | 123                       | 60         |  |  |  |

Nucleotide homology, gene loci and primers used for quantitative RT-PCR validation of human homologue of the differential expressed lncRNAs in chronic CS-induced COPD mouse model versus control animals.

| The equivalent<br>lncRNAs in<br>human     | Nucleotide<br>homology<br>between<br>mouse and<br>human (%) | Gene loci                       | Strand | Forward $(5' \rightarrow 3')$     | Reverse<br>(5'→3')                           | Product<br>length<br>(bp) | Tm (°C) |
|---|---|---------------------------------|--------|-----------------------------------|--|---------------------------|---------|
| Fantom3A930002<br>I24 human<br>homologue  | 80  | Chr17:<br>55324820-5<br>5325059 | +      | TTTTGGC<br>AACACC<br>ACAAAG<br>A  | GATA<br>AAGG<br>TTTGG<br>ACTTA<br>ACAG<br>CA | 116                       | 60      |
| Fantom3_C13001<br>1B08 human<br>homologue | 83  | Chr1:<br>7785438-77<br>85587    | +      | TGAACA<br>GCAAGAT<br>CGAAAC<br>AG | CACA<br>GCGG<br>AGAG<br>CATAG<br>TTG         | 131                       | 60      |
| Fantom3_F83021<br>2L20 human<br>homologue | 73  | chr16:<br>69710466-<br>69710627 | _      | TATGGCA<br>GAAGGG<br>AATTGCT      | GCTTT<br>GTAAT<br>TGAA<br>AGCA<br>AGAA<br>A  | 162                       | 60      |
| Fantom3_7420409<br>G12 human<br>homologue | 88  | chr1:<br>7819372-78<br>19436    | +      | GCACAG<br>CCCATCC<br>TATCAAC      | TTGCG<br>GTCTC<br>ATACC<br>TGATG             | 62                        | 60      |
| Fantom3_2810049<br>O06 human<br>homologue | 66  | chr1:<br>7844617-78<br>45152    | +      | TTCTTTG<br>CCTTAGC<br>ACACGTT     | CIGA<br>CAGTT<br>CTGC<br>GACA<br>AGC         | 82                        | 60      |
| NR_102714<br>human homologue              | 83  | chr4:<br>41256890-4<br>1257009  | +      | CCGCTAG<br>CTGTTTT<br>TCGTCT      | GTTGA<br>TCTCC<br>ATCGG<br>CTTGA<br>GCTC     | 120                       | 60      |
| Fantom3_D33002<br>1G15 human<br>homologue | 81  | Chr1:<br>7803047-<br>7819420    | +      | ATTGGTC<br>GGCATAA<br>AGTTCG      | ACGT<br>GAAC<br>TGGCT<br>GTA                 | 144                       | 60      |

|                              |    |            |   |                              | CAGAT |     |    |
|------------------------------|----|------------|---|------------------------------|-------|-----|----|
| ND 022255                    |    | Chr9:      |   | GCCCTGA                      | TTGG  |     |    |
| NK_033333                    | 78 | 35911116-3 | + | AATTCTG                      | AAAG  | 97  | 60 |
| numan nomologue              |    | 5911574    |   | AAACCA                       | GCCCA |     |    |
|                              |    |            |   |                              | TA    |     |    |
| NR_028593                    | 81 |            |   | GAGGAC<br>CTGTCTG<br>TGGCATC | AGAC  |     |    |
|                              |    | Chr12.     |   |                              | CTGA  |     |    |
|                              |    | 0233455 02 | _ |                              | GTGG  | 101 | 60 |
| human homologue              |    | 32555      |   |                              | AGGA  | 101 | 00 |
|                              |    | 55555      |   |                              | GAAG  |     |    |
|                              |    |            |   |                              | С     |     |    |
|                              | 72 |            |   |                              | GAGT  |     |    |
| NR_033450<br>human analogues |    | Chr14:     |   | CGTGGTG                      | CTCTC |     |    |
|                              |    | 94614589-9 | + | GAGCTG                       | CACC  | 120 | 60 |
|                              |    | 4623819    |   | AAGTACA                      | GCTTC |     |    |
|                              |    |            |   |                              | AG    |     |    |
|                              |    |            |   |                              | ATGCT |     |    |
| Fantom3_D83000               |    | Chr22:     |   | CTCCAAG                      | CTGA  |     |    |
| 9E10 human                   | 81 | 24232825-2 | _ | GTCTGCT                      | GGGT  | 111 | 60 |
| homologue                    |    | 4244755    |   | CGGATA                       | TGAC  |     |    |
|                              |    |            |   |                              | GAC   |     |    |

| No. | Sex  | Age | Smoke | Underlying | FEV <sub>1</sub> /FVC (%) |
|-----|------|-----|-------|------------|---------------------------|
|     |      |     |       | Condition  |                           |
| 1   | Male | 90  | No    | Donor      | >70                       |
| 2   | Male | 80  | No    | Donor      | >70                       |
| 3   | Male | 52  | No    | Donor      | >70                       |
| 4   | Male | 77  | No    | Donor      | >70                       |
| 5   | Male | 61  | No    | Donor      | >70                       |
| 6   | Male | 67  | No    | Donor      | >70                       |
| 7   | Male | 68  | Yes   | COPD       | <70                       |
| 8   | Male | 55  | Yes   | COPD       | <70                       |
| 9   | Male | 68  | Yes   | COPD       | <70                       |
| 10  | Male | 63  | Yes   | COPD       | <70                       |
| 11  | Male | 60  | Yes   | COPD       | <70                       |
| 12  | Male | 73  | Yes   | COPD       | <70                       |
| 13  | Male | 74  | Yes   | COPD       | <70                       |

Clinical characteristics of the donors and patients with COPD. The age variable of two groups fits normal distribution and homogeneity of variance.

Primers used for quantitative RT-PCR validation of significantly differential expressed mRNAs in human bronchial epithelial cells 16HBE cells, human lung carcinoma A549 cells and human PBMC.

| Gene name        | Transc<br>ript       | Forward(5' $\rightarrow$ 3') | Reverse(5' $\rightarrow$ 3') | Product<br>length<br>(bp) | Tm<br>(°C) |
|------------------|----------------------|------------------------------|------------------------------|---------------------------|------------|
| PER3             | NM_0<br>16831        | GCAGAGGAAATT<br>GGCGGACA     | GGTTTATTGCGT<br>CTCTCCGAG    | 123                       | 60         |
| NQO1             | NM_0<br>01025<br>433 | GAAGAGCACTGA<br>TCGTACTGGC   | GGATACTGAAA<br>GTTCGCAGGG    | 196                       | 60         |
| HLF              | NM_0<br>02126        | CTGGGGGCCTACC<br>TTATGGGA    | GGGGAATGCCA<br>TTTTCTGACA    | 103                       | 60         |
| GGT1             | NM_0<br>01288<br>833 | TTCATCGCTGTG<br>GTGCAAGC     | TCTGCTGCTCAC<br>AGGGGAAG     | 194                       | 60         |
| AHRR             | NM_0<br>01242<br>412 | CCCCGCCCTTGG<br>AGACAGGA     | AGTACTCGGTGG<br>GCGTGCCT     | 87                        | 60         |
| NR1D2            | NM_0<br>01145<br>425 | TTTAGTGGCATG<br>GTTCTACTGTG  | AGCCTTCGCAAG<br>CATGAACT     | 82                        | 60         |
| UCHL1            | NM_0<br>04181        | AATGTCGGGTAG<br>ATGACAAGGT   | GGCATTCGTCCA<br>TCAAGTTCATA  | 88                        | 60         |
| SERPINA3         | NM_0<br>01085        | TGCCAGCGCACT<br>CTTCATC      | TGTCGTTCAGGT<br>TATAGTCCCTC  | 167                       | 60         |
| GGT5             | NM_0<br>04121        | GTCAGCCTAGTC<br>CTGCTGG      | GGATGGCTCGTC<br>CAATATCCG    | 157                       | 60         |
| DNAJA1           | NM_0<br>01539        | ACTGGAGCCAGG<br>CGATATTAT    | CTTCAACGAGCT<br>GTATGTCCAT   | 107                       | 60         |
| HSPA5            | NM_0<br>05347        | CATCACGCCGTC<br>CTATGTCG     | CGTCAAAGACC<br>GTGTTCTCG     | 104                       | 60         |
| FKBP4            | NM_0<br>02014        | GAAGGCGTGCTG<br>AAGGTCAT     | TGCCATCTAATA<br>GCCAGCCAG    | 103                       | 62         |
| HSPA1A           | NM_0<br>05345        | GAACAAGCGAGC<br>CGTGAG       | AGGGTGCTTCGG<br>AACAGG       | 177                       | 60         |
| IL1RL1           | NM_0<br>03856        | ATGGGGTTTTGG<br>ATCTTAGCAAT  | CACGGTGTAACT<br>AGGTTTTCCTT  | 138                       | 60         |
| Internal control |                      |                              |                              |                           |            |
| 18S              | 18S                  | GCAATTATTCCC<br>CATGAACG     | GGCCTCACTAAA<br>CCATCCAA     | 123                       | 60         |