

Accepted Manuscript

Transcriptional profiling identifies the lncRNA PVT1 as a novel regulator of the asthmatic phenotype in human airway smooth muscle

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PII: S0091-6749(16)30571-1

DOI: [10.1016/j.jaci.2016.06.014](https://doi.org/10.1016/j.jaci.2016.06.014)

Reference: YMAI 12203

To appear in: *Journal of Allergy and Clinical Immunology*

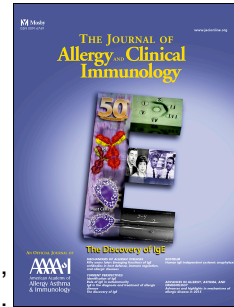
Received Date: 5 April 2016

Revised Date: 24 May 2016

Accepted Date: 13 June 2016

Please cite this article as: Austin PJ, Tsitsiou E, Boardman C, Jones SW, Lindsay MA, Adcock IM, Chung KF, Perry MM, Transcriptional profiling identifies the lncRNA PVT1 as a novel regulator of the asthmatic phenotype in human airway smooth muscle, *Journal of Allergy and Clinical Immunology* (2016), doi: 10.1016/j.jaci.2016.06.014.

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1 **Transcriptional profiling identifies the lncRNA PVT1 as a novel**
2 **regulator of the asthmatic phenotype in human airway smooth muscle**

3

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32 ***Funding bodies***

33 This work was supported by a fellowship from Imperial College London (JRF), grants
34 from Asthma UK (08/041) and The Wellcome Trust (085935) (KFC). This project was
35 supported by the NIHR Respiratory Disease Biomedical Research Unit at the Royal
36 Brompton and Harefield NHS Foundation Trust and Imperial College London. The
37 views expressed in this publication are those of the authors(s) and not necessarily
38 those of the NHS, The National Institute for Health Research or the Department of
39 Health. KFC is a Senior Investigator of NIHR, UK. MMP was an Imperial College
40 Research Fellow. MMP, IMA and KFC are members of Interuniversity Attraction
41 Poles Program-Belgian State-Belgian Science Policy- project P7/30.

42

43 ***Contributors***

44 MP, ML, IA and KFC were responsible for preparation of the manuscript; MP, PA
45 and CB conducted *in-vitro* experiments; ET conducted microarrays; MP, SJ and ML
46 analysed microarrays and undertook statistical analysis.

47 **Abstract**

48 *Background:* The mechanism underlying non-severe and severe asthma remains
49 unclear although it is commonly associated with increased airway smooth muscle
50 (ASM) mass. Long non-coding RNAs (lncRNAs) are known to be important in
51 regulating healthy primary ASM cells whilst changed expression has been observed in
52 CD8 T-cells from patients with severe asthma.

53 *Methods:* Primary ASM cells were isolated from healthy individuals ($n=9$), patients
54 classified as having non-severe asthma ($n=9$) or severe asthma ($n=9$). ASM cells were
55 exposed to dexamethasone and fetal calf serum (FCS). mRNA and lncRNA expression
56 was measured by microarray and quantitative real-time PCR. Bioinformatic analysis
57 was used to examine for relevant biological pathways. Finally, the lncRNA;
58 Plasmacytoma Variant Translocation (*PVT1*) was inhibited by transfection of primary
59 ASM cells with siRNAs, and the effect upon ASM cell phenotype was examined.

60 *Results:* The mRNA expression profile was significantly different between patient
61 groups following exposure to dexamethasone and FCS and these were associated with
62 biological pathways that may be relevant to the pathogenesis of asthma including
63 cellular proliferation and pathways associated with glucocorticoid activity. We also
64 observed a significant change in the expression of lncRNAs, yet only one (*PVT1*) is
65 decreased in expression in the corticosteroid sensitive non-severe asthmatics, and
66 increased in expression in the corticosteroid-insensitive severe asthmatics. Subsequent
67 targeting studies demonstrated the importance of this lncRNA in controlling both
68 proliferation and IL-6 release in ASM cells from patients with severe asthma.

69 *Conclusions:* lncRNAs are associated with the aberrant phenotype observed in ASM
70 cells from patients with asthma. Targeting of *PVT1* may be effective in reducing
71 airway remodelling in asthma.

72

73 ***Capsule Summary***

74 Our data suggest that lncRNA patterns are differentially dysregulated in non-severe
75 asthmatic patients and severe asthmatic patients, and that targeting the lncRNA; *PVT1*
76 may provide a treatment for asthma.

77

78 ***Key Words:*** Asthma, Airway Smooth Muscle, Proliferation, IL-6, Transcriptome,
79 Long noncoding RNA, *PVT1*

80

81 ***Abbreviations used:***

82 ASMC: Airway Smooth Muscle Cell

83 CS: Corticosteroids

84 lncRNA: Long non-coding RNA

85 miRNA: microRNA

86 PVT1: Plasmacytoma Variant Translocation

87

88 ***Key Messages:***

- 89 • Severe asthma is a worldwide health issue that is mostly unresponsive to
90 existing therapy.
- 91 • lncRNAs are differentially expressed between ASM cells from patients with
92 non-severe and severe asthma.
- 93 • Targeting of the lncRNA; *PVT1*, can reduce the increased cellular proliferation
94 and IL-6 release from ASM cells in severe asthma.

95 **Introduction**

96 Asthma is characterized by airflow obstruction and chronic airway inflammation and
97 remodeling⁽¹⁾. Airway smooth muscle (ASM) hyperplasia and hypertrophy leads to
98 increased airway wall thickening and airway narrowing, contributing to the airway
99 obstruction and inflammation. Epigenetic mechanisms are key regulators of ASM
100 function⁽²⁾. We have reported that the aberrant phenotype of ASM cells (ASMCs) from
101 patients with asthma is under the negative regulation of cyclin inhibitors, p21^{WAF1} &
102 p27^{kip1}, which are controlled by microRNA-221⁽³⁾. Furthermore, by utilizing a
103 transcriptomic-based approach, we identified potential miRNA targets and pathways
104 in activated human ASMCs and observed changes in expression of lncRNAs,
105 including natural antisense, pseudogenes, intronic lncRNAs, and intergenic
106 lncRNAs⁽⁴⁾.

107

108 Having reported the results of the healthy, (or ‘non-asthmatic’) ASMCs in 2014⁽⁴⁾, we
109 now report upon the asthmatic ASMCs that were studied at the same time.
110 Specifically, we report upon the differential expression of mRNAs and lncRNAs in
111 ASMCs isolated from non-severe and severe asthmatic individuals, and treated with
112 dexamethasone before subsequent activation with the growth medium, fetal calf serum
113 (FCS). We have then focused upon the only lncRNA found to be *decreased* in
114 expression in the corticosteroid sensitive non-severe asthmatics, and *increased* in
115 expression in the corticosteroid-insensitive severe asthmatics; plasmacytoma variant
116 translocation (*PVT*)1, and performed targeting studies to examine its role in a
117 corticosteroid insensitivity model in these cells induced by the combination of TGF- β
118 and FCS.

119

120 **Methods**

121 Full methodology is available in the **Supplemental data file**.

122

123 **Subject selection and ASMC culture**

124 Primary ASMCs from healthy individuals, non-severe asthmatics and severe
125 asthmatics were treated as described previously⁽⁴⁻⁷⁾. Patient characteristics are in **Table**
126 **1**.

127

128 **RNA extraction**

129 RNA was extracted using the *mirVana*TMmiRNA isolation kit, as previously
130 described⁽⁴⁻⁸⁾.

131

132 **Microarray Analysis**

133 LncRNA and mRNA expression was determined using the Agilent SurePrint G3
134 Human GE microarrays following the manufacturer's instructions, and as previously
135 described⁽⁴⁾. Total RNA samples (50 ng) used in lncRNA and mRNA microarrays
136 were initially labelled with Spike-In control A (for Cyanine 3-CTP) or B (for Cyanine
137 5-CTP). Labelled samples were then used for cDNA synthesis using the cDNA Master
138 Mix (Agilent) and were incubated for 2 h at 40°C followed by 15 min at 70°C to
139 inactivate the Affinity-Script enzyme. The synthesized cDNA was then used for cRNA
140 synthesis and amplification using the Transcription Master Mix with either Cyanine 3
141 or Cyanine 5 and incubated at 40°C for 2 h. Labelled and amplified RNA was then
142 purified using the RNeasy Mini Kit (Qiagen) and quantified using the NanoDrop
143 Spectrophotometer's Microarray Measurement function. The Cyanine 3 or Cyanine 5
144 concentrations and the cRNA concentration were used to calculate the yield (μg) and

145 the specific activity (pmol Cy3 or Cy5 per μg cRNA) of each sample. For each
146 microarray reaction, 300 ng of Cyanine 3- and 300 ng of Cyanine 5-labelled, linearly
147 amplified cRNA samples were mixed and incubated together with Fragmentation
148 buffer for 30 min, followed by the addition of Hybridization buffer. Samples were
149 loaded onto SurePrint G3 (8 \times 60 K) microarray slides (Agilent) and hybridized at
150 65°C for 17 h at 10 rpm using Agilent's Hybridization oven and SureHyb chamber.
151 The microarrays were then disassembled and washed in GE Wash Buffer 1 (Agilent)
152 for 60 sec at RT, followed by GE Wash Buffer 2 for 60 sec at 37°C, followed by an
153 acetonitrile wash (10 sec at RT) and the final wash in Stabilization and Drying
154 solution for 30 sec at RT, to improve microarray results by preventing ozone-mediated
155 fluorescent signal degradation. The microarrays were scanned with the Agilent
156 Microarray Scanner G2565BA using the profile for 2-colour microarrays
157 (AgilentG3_GX_2Color) at 5 μm resolution, dyes channel Red&Green, Scan Area 61
158 \times 21.6 mm. Following normalization against internal controls provided within the
159 labelling kits, probes which had background expression (signal value of mRNA < 4.5)
160 were removed. The threshold of background expression was determined using samples
161 that processed but which contained no RNA. Since initial analysis of mRNA and
162 lncRNA between baseline and FCS-treated cells or dexamethasone + FCS-treated cells
163 showed none that gave a FDR < 0.1, differential expression (p value) was determined
164 by 3-way ANOVA using the Partek Genomics Suite. We report changes in expression
165 with $p < 0.05$.

166

167 **Pathway Analysis**

168 Differentially expressed mRNAs from each dataset were further analysed using the
169 bioinformatics software application "Ingenuity Pathway Analysis" application

170 (www.ingenuity.com). A "Core Functional Analysis" was performed to identify
171 canonical pathways, predicted upstream regulators and gene networks most
172 significantly associated with the differentially expressed mRNAs.

173 The significance of the association of a given canonical pathway with the differentially
174 expressed mRNAs was measured in two ways. Firstly, by the ratio of the number of
175 differentially expressed mRNAs in the dataset that mapped to the canonical pathway
176 divided by the total number of genes that map to the canonical pathway. Secondly,
177 Fisher's exact test was used to calculate a P-value of the association between the
178 mRNA and the network/canonical pathway.

179

180 **Quantitative PCR measurement of miRNA and mRNA expression**

181 lncRNA and mRNA expression was measured as previously described⁽⁴⁾.

182

183 **Transfection with siRNAs that target *PVT1***

184 ASMCs were transfected as previously described^(3;5;9). siRNAs designed to target
185 *PVT1* and *IL6* were purchased from Ambion/Applied Biosystems, Ltd. ASMCs were
186 transfected with *PVT1* inhibitor (30, 100, 300 nM), *IL6* inhibitor (100 nM), or
187 Silencer[®] Negative Control #1 (100 nM) and no siRNA (mock transfection).

188

189 **Data and statistical analysis**

190 Data were analysed using GraphPad Prism, version 5.03. Data were not normally
191 distributed (as assessed by the Kolmogorov- Smirnov test), and therefore groups were
192 compared using the Dunn nonparametric test. All data are expressed as means \pm
193 SEMs.

194

195 **Results**

196 **mRNAs are differentially expressed between non-severe and severe asthmatic**
197 **ASMCs, and are responsible for different pathway activation**

198 Comparison of mRNA expression healthy ASMCs and non-severe or severe
199 asthmatics showed differential expression ($p < 0.05$) of different gene sets depending
200 upon the status of the cells being at a 'baseline' state, following stimulation with FCS,
201 and those pre-treated with dexamethasone, before stimulation with FCS. Full gene lists
202 are in the **Supplemental Data File, Tables 1-9**.

203 To identify the pathways that these mRNAs are involved in, we analyzed each dataset
204 using the bioinformatics software application "Ingenuity Pathway Analysis"
205 application. At 'baseline', those mRNAs that were increased in expression compared
206 to healthy ASMCs, in the non-severe asthmatic cohort are proposed to be important in
207 hydrolase activity. Those decreased in expression are involved in the extracellular
208 matrix, and the whole profile is important for cellular assembly (**Figure 1A**).
209 Interestingly, hydrolase activity is known to be important for calcium signaling in
210 ASM⁽¹⁰⁾, and the extracellular matrix is involved in asthmatic airway remodeling⁽¹¹⁾. In
211 the ASMCs from the patients with severe asthma, these profiles changed to an increase
212 in genes necessary for arachidonic acid metabolism and a decrease in those required
213 for multicellular organismal process, and the whole profile is involved in gene
214 expression and organ morphology. Once again, this follows our current knowledge of
215 ASM function, and the fact that arachidonic acid induces a calcium influx in human
216 airway smooth muscle, which has been proposed to contribute to increased influx in
217 asthma⁽¹²⁾, and previous methylation profiling of the bronchial mucosa of asthmatics,
218 has demonstrated a positive relationship to atopy for the multicellular organismal
219 process⁽¹³⁾. Following stimulation with FCS, those mRNAs increased in expression in

220 the non-severe ASM are associated with the intracellular organelle lumen, those
221 decreased are involved in single-organism development, and together the profile is
222 important in the inflammatory response which is well documented in human ASM⁽¹⁴⁾
223 (**Figure 1B**). In the severe asthma ASMCs, those increased are involved in respiratory
224 tube development, and those decreased in signaling. However, together the mRNAs
225 are proposed to be important in immunological disease which helps explain how ASM
226 is important for immunomodulation in acute exacerbations of airway disease,
227 including asthma⁽¹⁵⁾. When these same ASM cohorts were pretreated with
228 dexamethasone, before stimulation with FCS (**Figure 1C**), those pathways activated in
229 the non-severe ASMCs were associated with glucocorticoid activity, such as
230 macrophage activation, the inflammatory response⁽¹⁶⁾, and phospholipase activity⁽¹⁷⁾.
231 The severe asthmatic ASMCs, however, responded by activating genes associated with
232 cellular growth and proliferation, a phenotype well documented as being aberrant⁽⁴⁻⁷⁾.
233 The levels of *NAV2*, *NFIB*, *PTGIS*, *CHI3L1*, *NOVA1*, *PTPRD*, *IL6*, *PGM5* and *NNAT*
234 were selected to be verified by qRT-PCR (**Figure 1D**). For each of these, FCS caused
235 a significant increase in expression in both the non-severe and severe ASMCs
236 ($p < 0.05$). Pre-treatment of the non-severe ASMCs with dexamethasone inhibited this
237 increase in expression in all mRNAs, apart from *NAV2*. In the severe ASMCs,
238 dexamethasone caused a further increase in *NAV2* and *PTGIS* expression ($p < 0.01$) in
239 all other instances, dexamethasone only slightly inhibited the FCS-induced mRNA
240 expression, to levels that were not comparable to the non-severe ASMCs.

241

242 **lncRNAs are differentially expressed between in non-severe and severe asthmatic**
243 **ASMCs**

244 We have previously shown that more than 30 long noncoding RNAs (lncRNAs) are
245 increased in expression in healthy primary ASMCs following treatment with
246 dexamethasone and stimulation with FCS⁽⁴⁾. Hence, to identify novel lncRNAs in our
247 asthmatic ASMCs, we used ENSEMBLE (www.ensembl.org/index.html) to determine
248 the genomic position of those probe sets from the microarray that did not match
249 known protein coding genes.

250 At baseline, 21 lncRNAs were differentially expressed in ASMCs from non-severe
251 asthmatics (15 increased and 6 decreased) when compared to the healthy individuals
252 (**Supplemental Table 10**). The severe asthmatic ASMCs differentially expressed 19
253 lncRNAs (13 increased, and 6 decreased) when compared to the healthy individuals
254 (**Supplemental Table 11**)⁽⁴⁾. Interestingly, 4 lncRNAs were altered in expression in
255 both disease phenotypes (*RP5-1158E12.3*, *FKBP1A-SDCBP2*, *LINC00472*, and
256 *PVT1*), and *PVT1* was also differentially expressed in the healthy ASMCs⁽⁴⁾.
257 Following stimulation with FCS, the non-severe ASMCs expressed a completely
258 different set of lncRNAs (15 increased and 16 decreased), with the exception of *PVT1*
259 and *RP11-141M1* (**Supplemental Table 12**). A similar pattern was observed in the
260 FCS stimulated severe asthmatic ASMCs; of the 32 lncRNAs changed in expression,
261 only 2 (*LINC00940* & *RP11-120D5.1*) were the same as seen in the baseline non-
262 severe ASMCs (**Supplemental Table 14**). Furthermore, when the severe asthmatic
263 ASMCs were treated with dexamethasone before subsequent stimulation with FCS,
264 the number of differentially expressed lncRNAs doubled (36 increased and 38
265 decreased in expression) (**Supplementary Table 15**).

266 Of those lncRNAs that were expressed in the asthmatic ASMCs, only *PVT1* was found
267 to be decreased in expression in the corticosteroid sensitive non-severe asthmatics,
268 and increased in expression in the corticosteroid-insensitive severe asthmatics

269 (Supplemental Tables 10&11). Therefore we further examined the function of this
270 lncRNA.

271

272 **Effect of FCS and TGF- β on *PVT1* lncRNA expression in asthmatic ASMCs**

273 We have previously demonstrated that to induce a differential response in both cellular
274 proliferation and cytokine release in ASMCs from asthmatic individuals, a combined
275 stimulation of FCS (2.5%) and TGF- β (1ng/ml) is required^(3;5). To determine the
276 potential role of *PVT1* in this proliferative and inflammatory response, we examined
277 the time course of its expression in the presence of FCS and TGF- β . FCS+TGF- β did
278 not change the expression of *PVT1* up to 24h in the healthy ASMCs (**Figure 2A**),
279 while at 24h, there was a significant reduction in the expression of *PVT1* in the non-
280 severe ASMCs ($p < 0.01$ vs. unstimulated control). Furthermore, FCS+TGF- β led to ~3-
281 fold increase ($p < 0.01$ vs. unstimulated control) in the expression of *PVT1* that reached
282 a plateau at 3h in the severe ASMCs, and remained elevated at 24h (**Figure 2A**).

283 At 24h, dexamethasone had no effect upon *PVT1* expression in the healthy ASMCs
284 (**Figure 2B**). However, the FCS+TGF- β -induced reduction of *PVT1* in non-severe
285 ASMCs returned to basal levels in the presence of dexamethasone ($p < 0.01$).
286 Furthermore, dexamethasone alone increased *PVT1* expression in the severe ASMCs
287 (~4-fold; $p < 0.001$), and when these cells were subsequently stimulated with
288 FCS+TGF- β , an even greater increase in expression was observed (~8-fold; $p < 0.001$)
289 (**Figure 2B**).

290

291 **Inhibition of *PVT1* with siRNAs on ASMC proliferation and IL-6 release**

292 To elucidate the role of *PVT1*, we examined the action of siRNA-mediated inhibition
293 of *PVT1* on dexamethasone-exposed [FCS+TGF- β] induced BrdU incorporation and

294 IL-6 release. As previously reported^(3;5), a significant increase in BrdU incorporation
295 and IL-6 release was observed in both healthy and severe asthmatic subjects following
296 stimulation with FCS+TGF- β ($p < 0.001$ vs. unstimulated control) (**Figure 3C-F**).
297 Dexamethasone inhibited BrdU incorporation and IL-6 release in the healthy ASMCs,
298 but had no effect upon the BrdU incorporation in the severe ASMCs, and a limited
299 effect upon IL-6 release (**Figure 3C-F**). These results also demonstrate the relative
300 corticosteroid insensitivity of the cells from severe asthma compared to healthy
301 subjects with respect to BrdU incorporation and IL-6 release.

302 Transfection using Amaxa electroporation with siRNAs designed to target *PVT1*
303 (300nM), knocked-down expression of *PVT1* in healthy ASMCs both at baseline and
304 following stimulation with FCS+TGF- β ($p < 0.01$) (**Figure 3A**). When the same cells
305 were exposed to dexamethasone before stimulation with FCS+TGF- β , a reduction was
306 still observed, but not to the same level as without dexamethasone ($p < 0.05$). When
307 *PVT1* was targeted with siRNAs in the severe ASMCs, the FCS+TGF- β and
308 Dex+[FCS+TGF- β]-induced *PVT1* was returned to basal levels (**Figure 3B**).

309 Knocking down *PVT1* had no effect upon BrdU incorporation induced by FCS+TGF- β
310 in either cohort of ASMCs (**Figure 3C&D**). However, *PVT1* knock-down increased
311 BrdU incorporation in the severe ASMCs when they were exposed to dexamethasone
312 before stimulation with FCS+TGF- β ($p < 0.01$ vs. Dex+[FCS+TGF- β]) (**Figure 3D**).

313 Furthermore, siRNA targeted inhibition of *PVT1* resulted in both an increase in
314 FCS+TGF- β -induced IL-6 release ($p < 0.01$ vs. FCS+TGF- β), and reversed the
315 inhibitory action of dexamethasone in the ASMCs from healthy individuals ($p < 0.01$ vs
316 Dex+[FCS+TGF- β]) (**Figure 3E**). This suggests that inhibiting expression of *PVT1*
317 increases CS insensitivity in ASMCs, however, there was no effect observed upon IL-

318 6 release in the severe asthma ASMCs when *PVT1* was targeted, but this is possibly
319 due to the IL-6 release already being at maximal levels (**Figure 3F**).

320 A non-targeting negative control (30-300nM) demonstrated no effect upon either
321 BrdU incorporation or IL-6 release in either cohort, as previously shown^(5;7;9) (*data not*
322 *shown*). To demonstrate evidence of efficient transfection, concurrent studies were
323 performed to examine the effect of siRNAs (100nM) targeted to *IL6* mRNA. A
324 reduction in IL-6 release induced by FCS+TGF- β stimulation in ASMCs from healthy
325 subjects ($p < 0.001$) and those from severe asthma ($p < 0.01$) was observed, as previously
326 described^(3;9) (**Supplemental Figure 2A&B**). Furthermore, to demonstrate that
327 electroporation had no adverse effect upon cellular viability, MTT assays were
328 performed both before stimulation with FCS+TGF- β (**Supplemental Figure 2C&D**),
329 and after stimulation (**Supplemental Figure 2E&F**). In either situation, transfection
330 using Amaxa electroporation had no effect upon cellular viability.

331

332 **Effect of *PVT1* inhibition on *IL6* mRNA in asthmatic ASMCs**

333 In a similar pattern to that seen in the increasing IL-6 protein release induced by
334 FCS+TGF- β in these ASMCs⁽³⁾, *IL6* mRNA expression is increased in expression in
335 the healthy cells (~15-fold), greater still in the non-severe asthmatics (~20-fold) and to
336 the highest degree in the severe ASMCs (~45-fold), when these cells are stimulated
337 with FCS+TGF- β ($p < 0.01$ vs. unstimulated control) (**Figure 4A**). Incubation with
338 dexamethasone before stimulation with FCS+TGF- β resulted in inhibition of *IL6*
339 mRNA expression in the healthy and non-severe ASMCs ($p < 0.001$ and $p < 0.01$,
340 respectively), with no significant effect in the severe ASMCs (**Figure 4A**).

341 The effect of *PVT1* targeting by siRNAs upon *IL6* mRNA was then examined. In the
342 healthy ASMCs, the FCS+TGF- β induced expression of *IL6* was similar to that

343 observed in **Figure 4A**, when the cells were either mock transfected or transfected
344 with 100nM of negative control siRNA (**Figure 4C**). When the healthy ASMCs were
345 transfected with a siRNA designed to target *IL6* mRNA, the expression of this mRNA
346 was almost completely attenuated ($p<0.001$) (**Figure 4C**). However, when the basal
347 expression of *PVT1* (as described in **Figure 2B**), was inhibited in these ASMCs with
348 300nM of siRNA, a significant increase in *IL6* mRNA expression was observed, when
349 the cells were stimulated with FCS+TGF- β ($p<0.05$) (**Figure 4C**). Addition of
350 dexamethasone prior to FCS+TGF- β , resulted in a decrease in *IL6* mRNA levels in the
351 mock and negative siRNA transfected cells, and IL-6 siRNA transfection resulted in
352 inhibition of *IL6* mRNA expression (**Figure 4C**).

353 *IL6* mRNA expression was similarly affected by the different transfection variables in
354 the ASMCs from the severe asthmatics (**Figure 4E**). Either mock transfection or
355 transfecting with a negative control siRNA had no effect upon the *IL6* mRNA
356 expression. Transfecting with a siRNA designed to target *IL6*, inhibited the expression
357 of *IL6* mRNA (**Figure 4E**). However, inhibiting the expression of *PVT1* with siRNAs
358 reduced the expression of *IL6* mRNA expression following stimulation with
359 FCS+TGF- β , both with and without exposure to dexamethasone ($p<0.001$) (**Figure**
360 **4E**).

361

362 **Effect of *PVT1* inhibition on *c-MYC* mRNA in asthmatic ASMCs**

363 *PVT1* is transcriptionally activated by the oncogene *c-MYC*^(4;18) and, we have
364 previously reported that *c-MYC* is important in controlling ASMC proliferation, but
365 not cytokine release⁽⁵⁾, we therefore examined the effect of targeting *PVT1* with
366 siRNAs upon *c-MYC* mRNA expression. Stimulation with FCS+TGF- β induced an
367 increase in *c-MYC* mRNA expression in ASMCs from the severe asthmatics ($p<0.01$),

368 with no effect seen in the healthy or non-severe ASMCs (**Figure 4B**). Exposure of the
369 severe asthmatic ASMCs with dexamethasone, either on its own, or before stimulation
370 with FCS+TGF- β , resulted in a larger increase in *c-MYC* mRNA expression (both
371 $p < 0.001$) (**Figure 4B**).

372 Transfecting siRNAs designed to target *PVT1* (300nM), knocked-down expression of
373 *c-MYC* in healthy ASMCs both at baseline and following stimulation with FCS+TGF-
374 β ($p < 0.01$) (**Figure 4D**). When *PVT1* was targeted with siRNAs in the severe ASMCs,
375 the FCS+TGF- β and Dex+[FCS+TGF- β]-induced *c-MYC* expression was returned to
376 basal levels (**Figure 4F**).

377 In summary, these results show that in primary ASMCs from non-asthmatic
378 individuals, inhibiting the endogenous expression of *PVT1*, results in a reversal of the
379 inhibitory action of dexamethasone upon the FCS+TGF- β -induced *IL6* mRNA
380 expression and protein release. Furthermore, in ASMCs from patients with severe
381 asthma, dexamethasone increases the expression of *PVT1*, and inhibition of this with
382 siRNAs, results in an increase in FCS+TGF- β -induced cellular proliferation by
383 targeting of the transcription factor *c-MYC*.

384

385 *Discussion*

386 Utilizing a transcriptomic-based approach, we have examined the expression of
387 RNAs (mRNA, miRNA and lncRNA) in primary ASMCs isolated from non-
388 asthmatic, non-severe asthmatics and severe asthmatics. We published the results of
389 the non-asthmatics in 2014⁽⁴⁾, and now, following some additional functional studies,
390 report upon the non-severe asthmatics and severe asthmatics.

391 Of the mRNAs that we examined, we found that the mRNA profile differentially
392 regulated in the non-severe ASMCs is important in ASMC calcium signalling⁽¹⁰⁾,

393 airway remodelling⁽¹¹⁾, the inflammatory response⁽¹⁴⁾, and the activity of
394 glucocorticoids^(16;17). Interestingly, the mRNA profile in ASMCs from severe asthma
395 appears to be important in increased calcium influx in the smooth muscle⁽¹²⁾, atopy⁽¹³⁾,
396 and possible immunomodulation in acute exacerbations of airway disease, including
397 asthma⁽¹⁵⁾. Furthermore, when confirming our array results with RT-PCR, we
398 described mRNAs that have previously been shown to be increased in response to
399 dexamethasone (*NAV2*)⁽¹⁹⁾, to regulate cell viability, cell growth, cellular proliferation
400 and/or airway remodeling (*NFIB*, *NOVA1*, *PTPRD*, *PGM5*)⁽²⁰⁻²³⁾, and those acting as
401 potential tumor suppressors in lung carcinoma (*PTPRD* & *NNAT*)^(24;25). Furthermore,
402 we describe a large increase in *CHI3L1*, which has not only been reported in a number
403 of inflammatory diseases and cancer, but has been implicated in asthma, with the
404 discovery of an allele that doubles the risk⁽²⁶⁾. However, *PTGIS* is the only one of
405 these mRNA targets to have been associated with ASM and can induce both
406 bronchodilation and reverse ASMC remodeling in a mouse model of asthma⁽²⁷⁾.

407 We also measured the expression of lncRNAs in our patient cohorts. A large number
408 of lncRNAs were differentially expressed, under all situations (baseline, corticosteroid
409 treatment, and mitogen stimulation). Interestingly, only *PVT1* was found to be
410 decreased in the non-severe ASMCs, and increased in the severe ASMCs, and so we
411 performed functional studies upon this lncRNA in our model of asthmatic
412 hyperproliferation and corticosteroid insensitivity^(3;5). The action of *PVT1* in our
413 asthmatic ASMCs was complex. As such, we have proposed a figure that shows
414 potential mechanisms for *PVT1* in ASMC proliferation and IL-6 release (**Figure 5**). In
415 the non-asthmatic 'healthy' ASMC, [TGF- β +FCS] induces *IL6* mRNA expression,
416 which translates into IL-6 protein release. Interestingly, the addition of dexamethasone
417 results in an increase in expression of *PVT1*, which, when inhibited by siRNAs

418 **(Figure 5A)**, induces greater *IL6* mRNA expression and more IL-6 protein released. In
419 the ASMCs from patients with severe asthma, [TGF- β +FCS] not only induces *IL6*
420 mRNA expression and protein release, but also the expression of *PVT1*. The effect of
421 dexamethasone was the same, and when we inhibited *PVT1* in these ASMCs with
422 siRNAs **(Figure 5B)**, a decrease in *IL6* mRNA and IL-6 protein release was observed,
423 along with a concurrent increase in cellular proliferation. The mechanism of action of
424 *PVT1* in human primary ASM is clearly complex. Very little is known about the role
425 of *PVT1* in human pathologies. *PVT1* is frequently expressed in numerous cancers
426 (including lung)⁽²⁸⁻³²⁾ and diabetes⁽³³⁻³⁵⁾. Furthermore, targeting of *PVT1* in these
427 pathologies has been shown to have a range of effects including decreasing
428 proliferation and increasing apoptosis^(29;36), decreasing resistance to gemcitabine (a
429 chemotherapy drug)⁽³⁷⁾, and regulation of genes and proteins involved in ECM
430 deposition⁽³³⁾. We have demonstrated, for the first time, the novel way in which
431 targeting *PVT1* in human primary ASMCs can affect phenotype.

432 The variable mechanism of action of *PVT1* could simply be a consequence of different
433 cells, tissues and pathologies examined; however, it may also be due to the action, and
434 configuration of *PVT1* itself. *PVT1* is a downstream target of *c-MYC* that targets and
435 binds *PVT1* driving its transcription⁽¹⁸⁾. We show that in our severe asthmatic ASMC
436 cohorts; dexamethasone increases the expression of *PVT1*, and inhibition of this
437 results in an increase in FCS+TGF- β -induced cellular proliferation, possibly by
438 targeting of *c-MYC*.

439 Finally, *PVT1* is unlikely to be the only ncRNA acting in our ASMC model. We have
440 previously reported upon the role of miRNAs in these cells following stimulation with
441 [TGF- β +FCS]⁽³⁾, and now it is known that *PVT1* can express a cluster of 6 miRNAs
442 such as miR-1207-5p (of which we discussed previously⁽⁴⁾). Although these ncRNAs

443 are co-expressed, regulation of *miR-1207-5p* expression by TGF- β is independent of
444 *PVT1*⁽³⁴⁾.

445

446 In conclusion, we have demonstrated a large difference in ncRNA expression profiles
447 (including miRNAs, and lncRNAs), in primary human ASMCs from patients with
448 non-severe and severe asthma and the differential effects of adding corticosteroids and
449 mitogen. Furthermore we have found that *PVT1* regulates both IL-6 release and
450 proliferation in ASMCs from individuals with severe asthma.

451 *Tables*452 **Table 1: Characteristics of subjects**

	Non-Asthmatics	Non-Severe Asthma	Severe Asthma
<i>n</i>	9	9	9
Age (yrs.)	36.4 ± 12.7	42.4 ± 16.2	48.9 ± 11
Sex (♂ / ♀)	7 / 2	6 / 4	3 / 6
Duration of asthma (yrs.)	N/A	22.2 ± 16.8	25.6 ± 13.2
Inhaled corticosteroid dose (µg BDP equivalent)	N/A	580 ± 576.9	1688.9 ± 176.4
Atopy (<i>n</i>)*	0	8	8
Receiving oral corticosteroids (<i>n</i>)	0	0	7
FEV ₁ (L)	4.02 ± 0.48	2.81 ± 0.71	2.7 ± 0.82
FEV ₁ (% Predicted)	104.23 ± 7.28	84.68 ± 12.31	80.48 ± 12.34
FEV ₁ /FVC (%)	78.79 ± 5.98	69.87 ± 9.27	63.98 ± 9.68
β-agonist reversibility (%) [#]	N/A	12.3 ± 11.9	19.54 ± 14.56
PC ₂₀ (mg/ml)	> 16	0.69 ± 0.64	0.2 ± 0.39

453 BDP, beclomethasone dipropionate; FEV₁, forced expiratory volume in 1s; FVC,
 454 forced vital capacity; PC₂₀, provocative concentration of methacholine causing a 20%
 455 fall in FEV₁; N/A: not available. * Defined as positive skin prick tests to one or more
 456 common aeroallergens. # measured as percent increase in FEV₁ after 400 µg
 457 salbutamol. Data shown as mean ± SEM.

458

459 **Figure Legends**

460 **Figure 1: Venn diagrams showing pathway analysis of differentially expressed**
 461 **mRNAs in asthmatic ASM**

462 Pathway analysis showing inter-group comparisons at baseline [A], following
 463 stimulation with FCS (2.5%) [B] and FCS (2.5 %) + TGF-β (1 ng/ml) [C]. Data
 464 represents *n* = 9 for each patient type. To validate the array data, the expression of 9
 465 mRNAs were confirmed by TaqMan RT-PCR [D]. Bars represent mean ± SEM from 9
 466 primary ASM cell donors. * *p* < 0.05; ** *p* < 0.01; *** *p* < 0.001.

467

468 **Figure 2: Effect of dexamethasone and [FCS+TGF- β] on *PVT1* lncRNA**
469 **expression in asthmatic ASM cells.** [FCS+TGF- β] induced *PVT1* lncRNA expression
470 was measured by qRT-PCR, over 1, 3, 6 and 24 h [A]. Dexamethasone and
471 [FCS+TGF- β] induced *PVT1* expression was measured by qRT-PCR at 24 h [B]
472 Points/bars represent mean \pm SEM of 9 ASM cell donors. ** $p < 0.01$; *** $p < 0.001$.

473

474 **Figure 3: Effect of targeting *PVT1* with siRNAs upon IL-6 release and BrdU**
475 **incorporation in ASM cells from healthy subjects and those with severe asthma.**
476 *PVT1* lncRNA expression was measured by RT-PCR after healthy and severe asthma
477 ASM were transfected with siRNA (300 nM), designed to target *PVT1* (A&B). BrdU
478 incorporation (C&D) and IL-6 release (E&F) were measured by BrdU ELISA and
479 DuoSet ELISA Assay, respectively, at 8 days. Bars/points represent the means \pm SEM
480 of 9 ASM cell donors. */# $p < 0.05$; ##/++ $p < 0.01$; ***/#### $p < 0.001$.

481

482 **Figure 4: Effect of targeting *PVT1* with siRNAs upon *IL6* and *c-MYC* mRNA in**
483 **ASM cells from healthy subjects and those with severe asthma.** *IL6* and *c-MYC*
484 mRNA expression was measured by RT-PCR after exposure to dexamethasone (10^{-7}
485 M) and stimulation with FCS (2.5 %) + TGF- β (1 ng/ml) for 24 h (A&B). Healthy and
486 severe asthmatic ASM cells were transfected with siRNAs designed to target *PVT1*,
487 and the expression of *IL6* (C&E) and *c-MYC* (D&F) mRNA was measured by RT-
488 PCR. Bars represent the means \pm SEM of 9 ASM cell donors. # $p < 0.05$; */##/++ $p <$
489 0.01 ; ***/####/+++ $p < 0.001$.

490

491 **Figure 5: Potential mechanisms for *PVT1* contribution to ASM cells proliferation**
492 **and IL-6 release in asthma.**

References

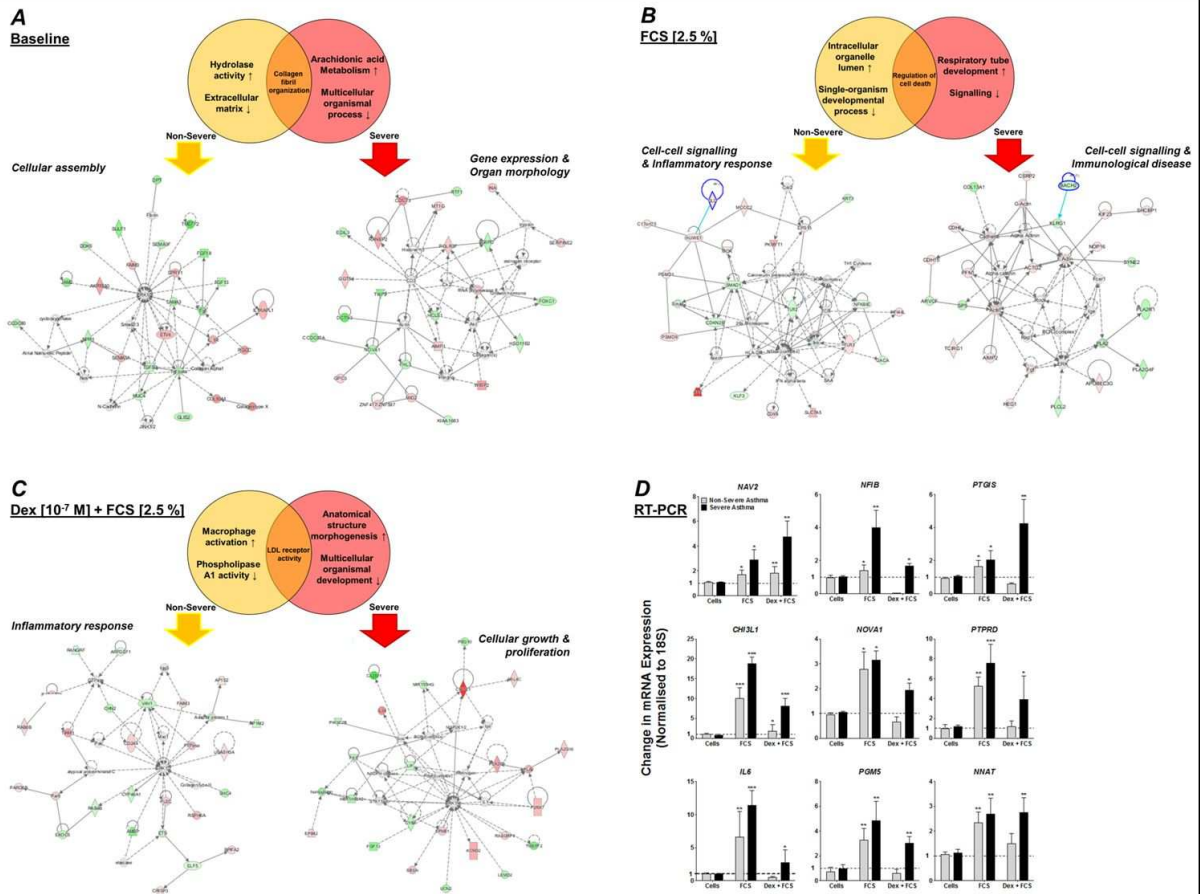
- 493
494
495 (1) Bousquet J, Jeffery PK, Busse WW, Johnson M, Vignola AM. Asthma.
496 From bronchoconstriction to airways inflammation and remodeling. *Am J Respir*
497 *Crit Care Med* 2000; 161(5):1720-45.
- 498 (2) Clifford RL, Singer CA, John AE. Epigenetics and miRNA emerge as
499 key regulators of smooth muscle cell phenotype and function. *Pulmonary*
500 *Pharmacology & Therapeutics* 2013; 26(1):75-85.
- 501 (3) Perry MM, Baker JE, Gibeon DS, Adcock IM, Chung KF. Airway
502 Smooth Muscle Hyperproliferation Is Regulated by MicroRNA-221 in Severe
503 Asthma. *Am J Respir Cell Mol Biol* 2013; 50(1):7-17.
- 504 (4) Perry M, Tsitsiou E, Austin P, Lindsay M, Gibeon D, Adcock I et al.
505 Role of non-coding RNAs in maintaining primary airway smooth muscle cells.
506 *Respiratory Research* 2014; 15(1):58.
- 507 (5) Perry MM, Durham AL, Austin PJ, Adcock IM, Chung KF. BET
508 bromodomains regulate TGF-beta-induced proliferation and cytokine release in
509 asthmatic airway smooth muscle. *J Biol Chem* 2015.
- 510 (6) Perry MM, Hui CK, Whiteman M, Wood ME, Adcock I, Kirkham P et
511 al. Hydrogen Sulfide Inhibits Proliferation and Release of IL-8 from Human
512 Airway Smooth Muscle Cells. *Am J Respir Cell Mol Biol* 2011; 45(4):746-52.
- 513 (7) Perry MM, Baker JE, Gibeon DS, Adcock IM, Chung KF. Airway
514 Smooth Muscle Hyperproliferation Is Regulated by MicroRNA-221 in Severe
515 Asthma. *Am J Respir Cell Mol Biol* 2013; 50(1):7-17.
- 516 (8) O'Leary L, Sevinc K, Papazoglou IM, Tildy B, Detillieux K, Halayko
517 AJ et al. Airway Smooth Muscle Inflammation Is Regulated by MicroRNA-145 in
518 COPD. *FEBS Lett* 2016.
- 519 (9) Lerner-Svensson HM, Williams AE, Tsitsiou E, Perry MM, Jiang X,
520 Chung KF et al. Pharmacological studies of the mechanism and function of
521 interleukin-1beta-induced miRNA-146a expression in primary human airway
522 smooth muscle. *Respir Res* 2010; 11:68.
- 523 (10) Jude JA, Wylam ME, Walseth TF, Kannan MS. Calcium signaling in
524 airway smooth muscle. *Proc Am Thorac Soc* 2008; 5(1):15-22.
- 525 (11) Kumawat K, Koopmans T, Gosens R. beta-catenin as a regulator
526 and therapeutic target for asthmatic airway remodeling. *Expert Opin Ther*
527 *Targets* 2014; 18(9):1023-34.
- 528 (12) Thompson MA, Prakash YS, Pabelick CM. Arachidonate-regulated
529 Ca(2+) influx in human airway smooth muscle. *Am J Respir Cell Mol Biol* 2014;
530 51(1):68-76.

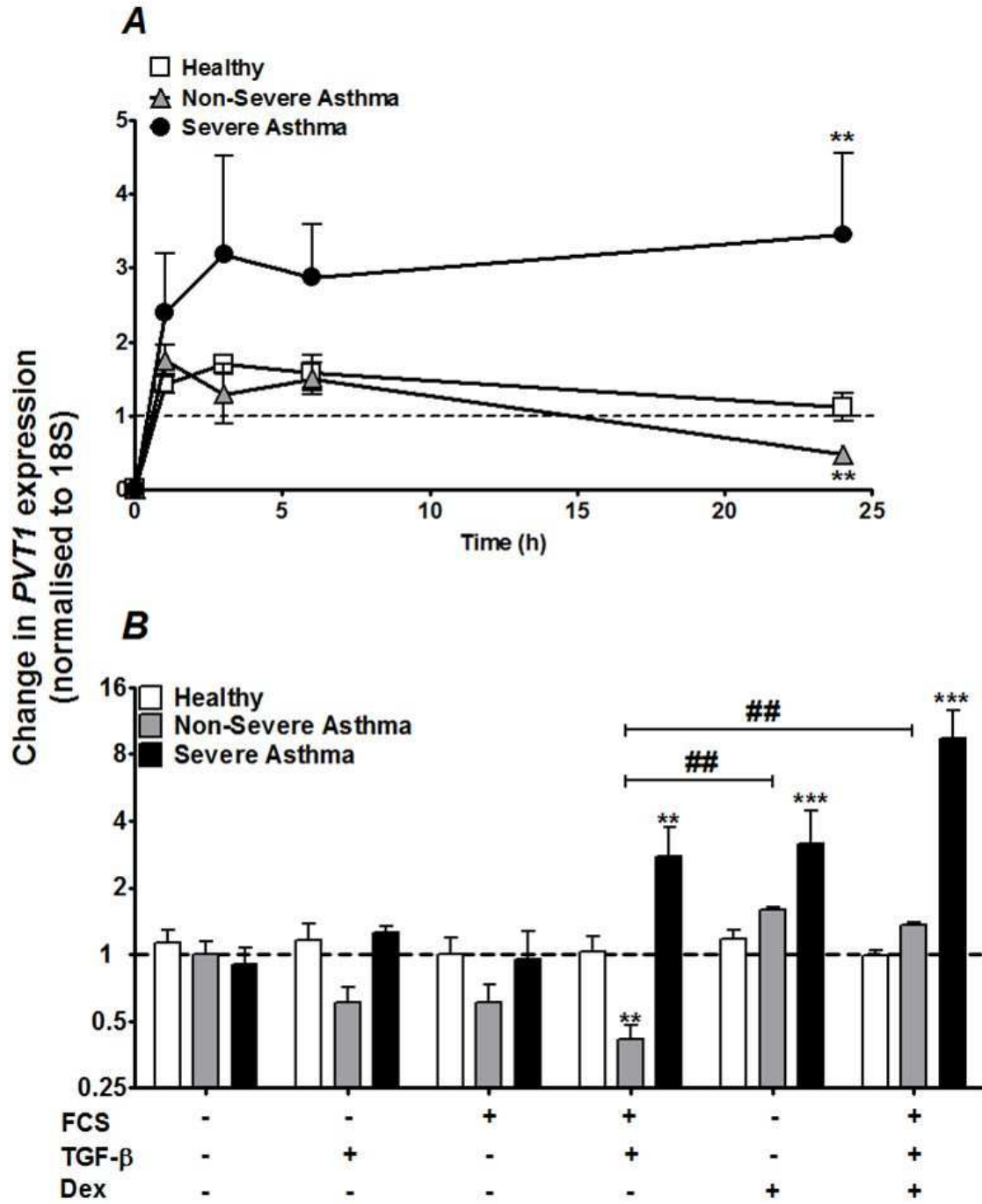
- 531 (13) Kim YJ, Park SW, Kim TH, Park JS, Cheong HS, Shin HD et al.
532 Genome-wide methylation profiling of the bronchial mucosa of asthmatics:
533 relationship to atopy. *BMC Med Genet* 2013; 14:39.
- 534 (14) Chung KF. Airway smooth muscle cells: contributing to and
535 regulating airway mucosal inflammation? *Eur Respir J* 2000; 15(5):961-8.
- 536 (15) Koziol-White CJ, Panettieri Jr RA. Airway smooth muscle and
537 immunomodulation in acute exacerbations of airway disease. *Immunological*
538 *Reviews* 2011; 242(1):178-85.
- 539 (16) Boardman C, Chachi L, Gavrila A, Keenan CR, Perry MM, Xia YC et
540 al. Mechanisms of glucocorticoid action and insensitivity in airways disease.
541 *Pulmonary Pharmacology & Therapeutics* 2014;(0).
- 542 (17) Perretti M, Ahluwalia A. The microcirculation and inflammation:
543 site of action for glucocorticoids. *Microcirculation* 2000; 7(3):147-61.
- 544 (18) Carramusa L, Contino F, Ferro A, Minafra L, Perconti G, Giallongo A
545 et al. The PVT-1 oncogene is a Myc protein target that is overexpressed in
546 transformed cells. *J Cell Physiol* 2007; 213(2):511-8.
- 547 (19) Liu L, Walker EA, Kissane S, Khan I, Murray PI, Rauz S et al. Gene
548 Expression and miR Profiles of Human Corneal Fibroblasts in Response to
549 Dexamethasone. *Investigative Ophthalmology & Visual Science* 2011;
550 52(10):7282-8.
- 551 (20) Buckanovich RJ, Yang YY, Darnell RB. The onconeural antigen
552 Nova-1 is a neuron-specific RNA-binding protein, the activity of which is
553 inhibited by paraneoplastic antibodies. *J Neurosci* 1996; 16(3):1114-22.
- 554 (21) Dooley AL, Winslow MM, Chiang DY, Banerji S, Stransky N, Dayton
555 TL et al. Nuclear factor I/B is an oncogene in small cell lung cancer. *Genes &*
556 *Development* 2011; 25(14):1470-5.
- 557 (22) Shyur SD, Wang JY, Lin CG-J, Hsiao YH, Liou YH, Wu YJ et al. The
558 polymorphisms of protein-tyrosine phosphatase receptor-type delta gene and its
559 association with pediatric asthma in the Taiwanese population. *Eur J Hum Genet*
560 2008; 16(10):1283-8.
- 561 (23) Moiseeva EP, Critchley DR. Characterisation of the Promoter which
562 Regulates Expression of a Phosphoglucomutase-Related Protein, a Component of
563 the Dystrophidutrophin Cytoskeleton Predominantly Expressed in Smooth
564 Muscle. *European Journal of Biochemistry* 1997; 248(3):634-43.
- 565 (24) Kohno T, Otsuka A, Girard L, Sato M, Iwakawa R, Ogiwara H et al. A
566 catalog of genes homozygously deleted in human lung cancer and the candidacy
567 of PTPRD as a tumor suppressor gene. *Genes Chromosom Cancer* 2010;
568 49(4):342-52.

- 569 (25) Okubo C, Minami Y, Tanaka R, Uchihara T, Anami Y, Furuya S et al.
570 Analysis of differentially expressed genes in neuroendocrine carcinomas of the
571 lung. *J Thorac Oncol* 2006; 1(8):780-6.
- 572 (26) Ober C, Tan Z, Sun Y, Possick JD, Pan L, Nicolae R et al. Effect of
573 Variation in CHI3L1 on Serum YKL-40 Level, Risk of Asthma, and Lung Function.
574 *New England Journal of Medicine* 2008; 358(16):1682-91.
- 575 (27) Yamabayashi C, Koya T, Kagamu H, Kawakami H, Kimura Y,
576 Furukawa T et al. A Novel Prostacyclin Agonist Protects against Airway
577 Hyperresponsiveness and Remodeling in Mice. *Am J Respir Cell Mol Biol* 2012;
578 47(2):170-7.
- 579 (28) Iwakawa R, Takenaka M, Kohno T, Shimada Y, Totoki Y, Shibata T
580 et al. Genome-wide identification of genes with amplification and/or fusion in
581 small cell lung cancer. *Genes Chromosom Cancer* 2013; 52(9):802-16.
- 582 (29) Takahashi Y, Sawada G, Kurashige J, Uchi R, Matsumura T, Ueo H et
583 al. Amplification of PVT-1 is involved in poor prognosis via apoptosis inhibition
584 in colorectal cancers. *Br J Cancer* 2014; 110(1):164-71.
- 585 (30) Kim HP, Cho GA, Han SW, Shin JY, Jeong EG, Song SH et al. Novel
586 fusion transcripts in human gastric cancer revealed by transcriptome analysis.
587 *Oncogene* 2013.
- 588 (31) Bisio A, De Sanctis V, Del Vescovo V, Denti M, Jegga A, Inga A et al.
589 Identification of new p53 target microRNAs by bioinformatics and functional
590 analysis. *BMC Cancer* 2013; 13(1):552.
- 591 (32) Zhang Z, Zhu Z, Zhang B, Li W, Li X, Wu X et al. Frequent Mutation
592 of rs13281615 and Its Association with PVT1 Expression and Cell Proliferation
593 in Breast Cancer. *Journal of Genetics and Genomics* 2014; 41(4):187-95.
- 594 (33) Alvarez ML, DiStefano JK. Functional Characterization of the
595 Plasmacytoma Variant Translocation 1 Gene (PVT1) in Diabetic Nephropathy.
596 *PLoS ONE* 2011; 6(4):e18671.
- 597 (34) Alvarez ML, Khosroheidari M, Eddy E, Kiefer J. Role of MicroRNA
598 1207-5P and Its Host Gene, the Long Non-Coding RNA Pvt1, as Mediators of
599 Extracellular Matrix Accumulation in the Kidney: Implications for Diabetic
600 Nephropathy. *PLoS ONE* 2013; 8(10):e77468.
- 601 (35) Alwohhaib M, Alwaheeb S, Alyatama N, Dashti AA, Abdelghani A,
602 Hussain N. Single nucleotide polymorphisms at erythropoietin, superoxide
603 dismutase 1, splicing factor, arginine/serin-rich 15 and plasmacytoma variant
604 translocation genes association with diabetic nephropathy. *Saudi J Kidney Dis*
605 *Transpl* 2014; 25(3):577-81.
- 606 (36) Guan Y, Kuo WL, Stilwell JL, Takano H, Lapuk AV, Fridlyand J et al.
607 Amplification of PVT1 Contributes to the Pathophysiology of Ovarian and Breast
608 Cancer. *Clinical Cancer Research* 2007; 13(19):5745-55.

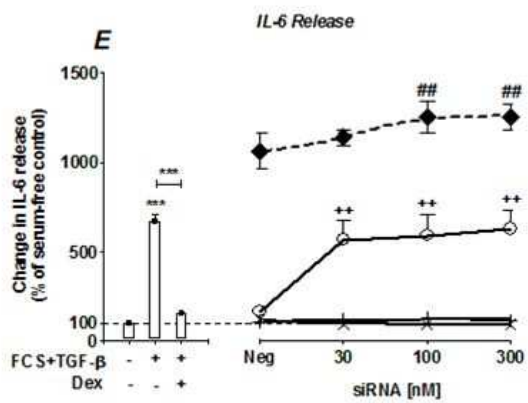
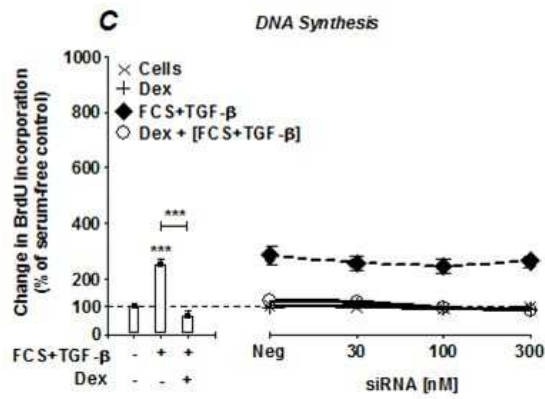
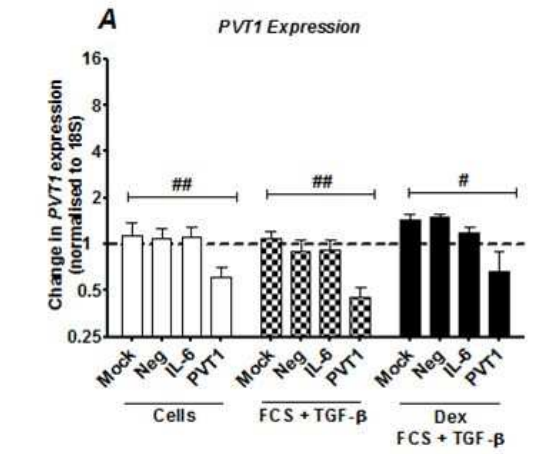
609 (37) You L, Chang D, Du HZ, Zhao YP. Genome-wide screen identifies
610 PVT1 as a regulator of Gemcitabine sensitivity in human pancreatic cancer cells.
611 Biochemical and Biophysical Research Communications 2011; 407(1):1-6.
612
613

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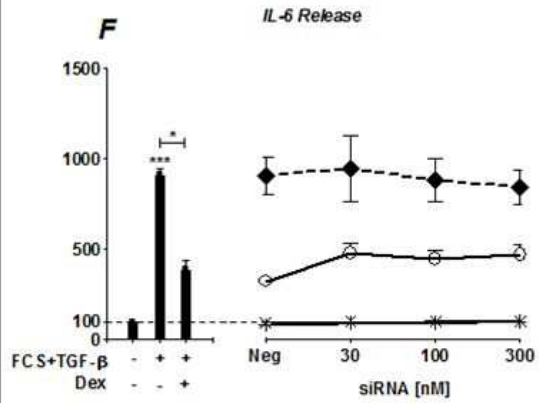
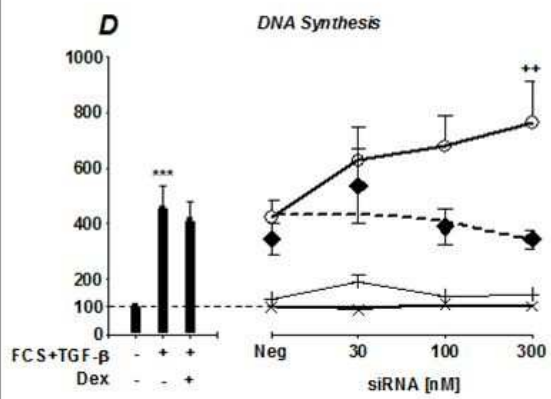
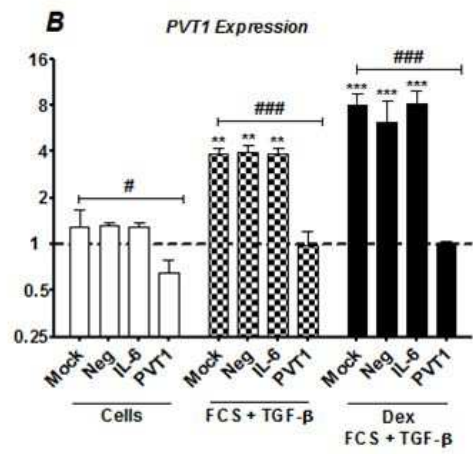


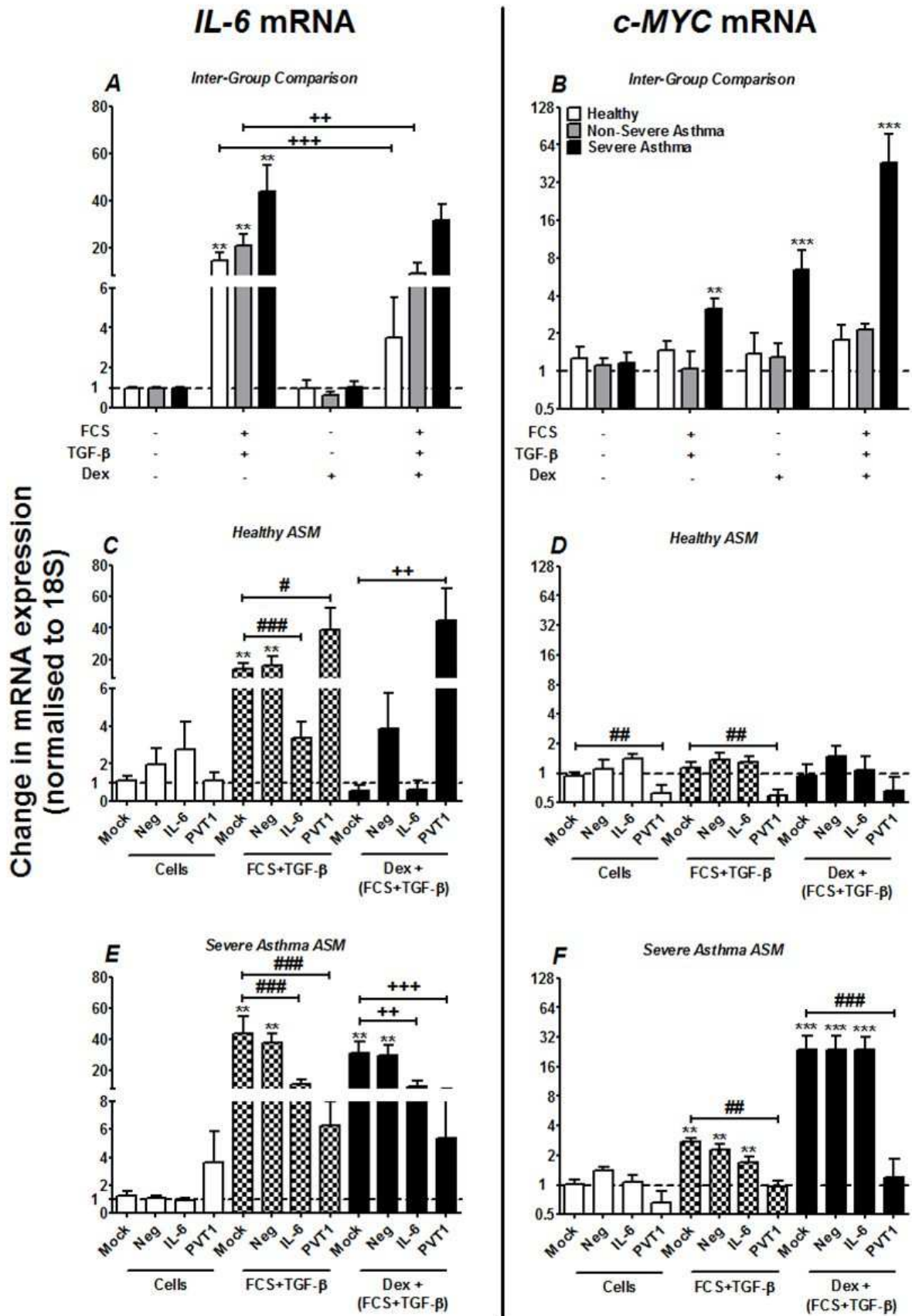


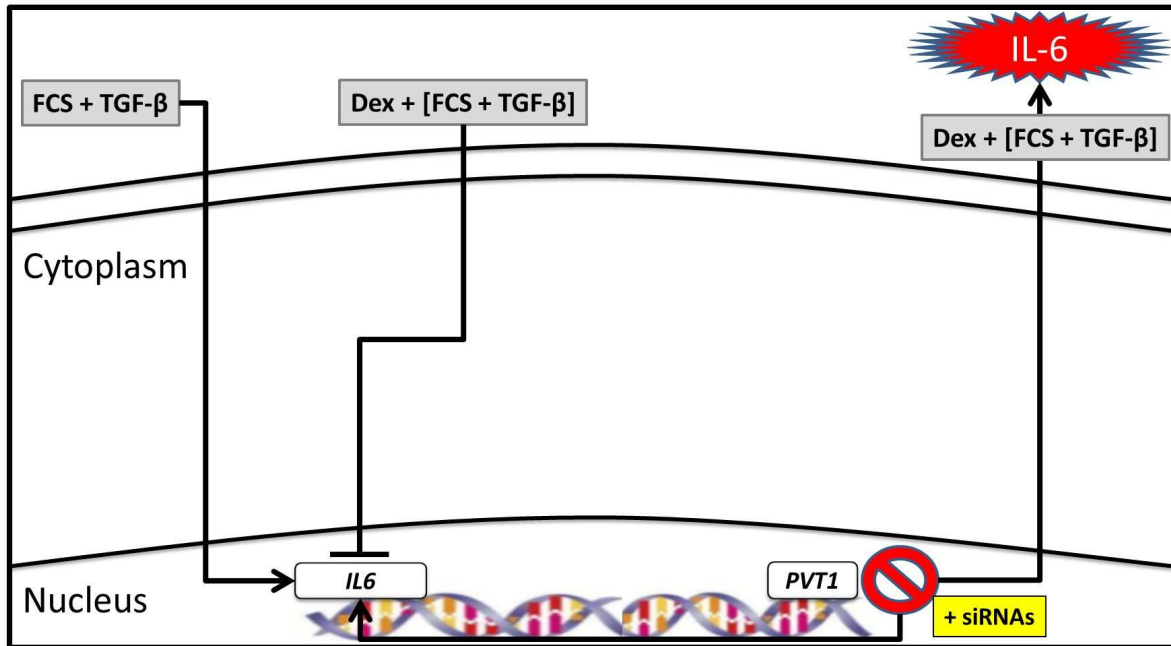
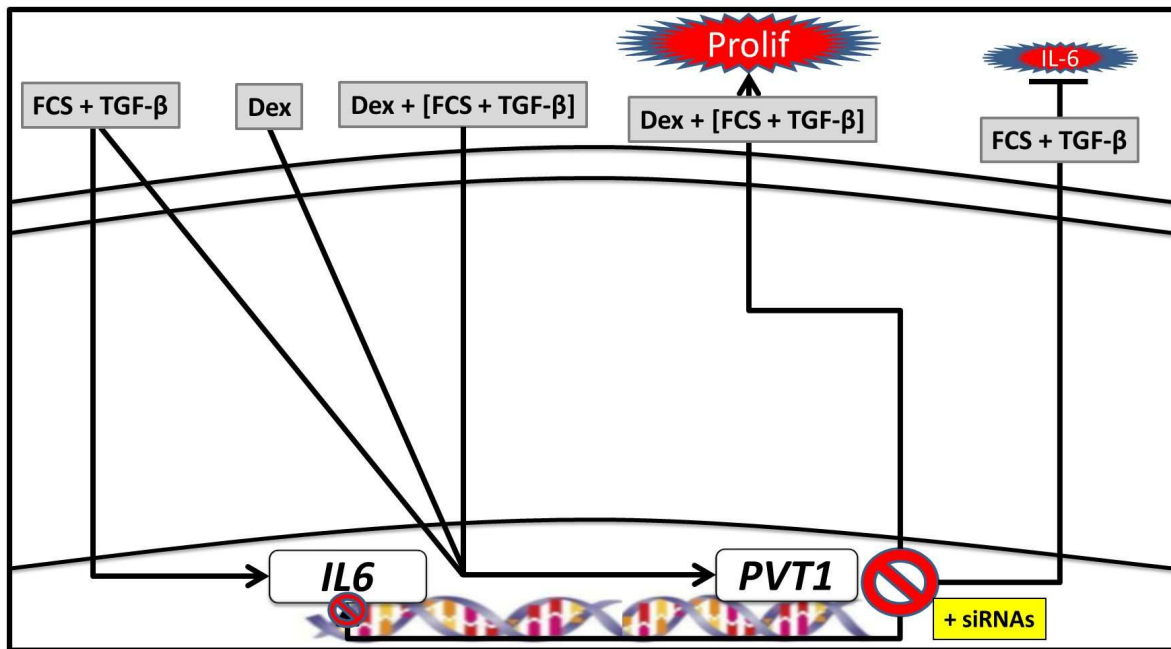
Healthy ASM



Severe Asthma ASM





A. Healthy ASM**B. Severe Asthma ASM**

*Online Repository***Transcriptional profiling identifies the lncRNA *PVT1* as a novel regulator of the asthmatic phenotype in human airway smooth muscle**

Phillip J. Austin¹, Eleni Tsitsiou², Charlotte Boardman¹, Mark A. Lindsay^{1,2,3}, Ian M. Adcock¹, Kian Fan Chung¹ and Mark M. Perry⁴

Methods**Subject selection**

Patients with non-severe and severe asthma as defined by European Respiratory Society/American Thoracic Society Workshop on Severe Asthma⁽¹⁾ were recruited. Current smokers and former smokers with greater than 5 pack-year history were excluded. Non-asthmatic normal subjects with no previous history of asthma and a PC₂₀ >16 mg/ml were also recruited. The subject characteristics are shown in **Table 1**. Each subject underwent a fiberoptic bronchoscopic study under sedation with midazolam and topical anaesthesia to the airways with lidocaine. Airway biopsies were taken from segmental and sub-segmental airways of the right lower lobe. This study was approved by the Ethics Committee and all subjects gave written informed consent.

ASM cell culture and stimulation

ASM cells were cultured as previously described⁽²⁻⁶⁾. Confluent cells were growth-arrested by FCS deprivation for 24 h in Dulbecco's Modified Eagle's Medium supplemented with sodium pyruvate (1 mM), L-glutamine (2 mM), non-essential amino acids (1:100), penicillin (100 U/ml)/streptomycin (100 mg/ml), amphotericin B (1.5 mg/ml), and BSA (0.1 %). Human

26 airway smooth muscle cells at passages 3–4 from nine different donors were used. Cells were
27 pre-treated with dexamethasone (10^{-7} M) for 1 h, before being stimulated with 2.5 % FCS for
28 24 h. The supernatants were removed and IL-6 levels were determined by DuoSet ELISA
29 (R&D Systems, Abingdon, UK) as a measure of ASM cell activation (**Supplementary Data**
30 **File 1**). Cell proliferation was measured by the Cell Proliferation ELISA BrdU kit (Roche
31 Applied Science), an assay comparable to cell counting as confirmed by flow cytometry⁽²⁻⁵⁾.
32 Cellular viability was assessed by MTT assay⁽⁷⁾. Each patient sample was replicated over 3
33 wells.

35 **RNA extraction**

36 Total RNA was extracted using the *mirVana*TMmiRNA isolation kit (Ambion Europe). RNA
37 was eluted in 50 μ l RNase-free water (Promega UK, Southampton, UK) and stored at -70 °C.
38 RNA content and purity was measured using a BioTek PowerWave XS (SSi Robotics, Tustin,
39 CA, U.S.A.) spectrophotometer (yield (\pm SD): 1.1 ± 0.3 mg/ml; purity (A_{260}/A_{280}): 2.0 ± 0.1).

41 **Microarray Analysis**

42 LncRNA and mRNA expression was determined using the Agilent SurePrint G3 Human GE
43 microarrays, as previously described⁽³⁾.

45 **Pathway Analysis**

46 Differentially expressed mRNAs from each dataset were further analysed using the
47 bioinformatics software application "Ingenuity Pathway Analysis" application
48 (www.ingenuity.com). A "Core Functional Analysis" was performed to identify canonical
49 pathways, predicted upstream regulators and gene networks most significantly associated
50 with the differentially expressed mRNAs.

51 The significance of the association of a given canonical pathway with the differentially
52 expressed mRNAs was measured in two ways. Firstly, by the ratio of the number of
53 differentially expressed mRNAs in the dataset that mapped to the canonical pathway divided
54 by the total number of genes that map to the canonical pathway. Secondly, Fisher's exact test
55 was used to calculate a P-value of the association between the mRNA and the
56 network/canonical pathway.

57

58 **Quantitative PCR measurement of miRNA and mRNA expression**

59 miRNA expression was undertaken with the 2-step Applied Biosystems TaqMan RT-PCR
60 protocol (Applied Biosystems) and normalized to 18S, as previously described^(2;3;8). mRNA
61 expression was determined using TaqMan RT-PCR with Assays on Demand (Applied
62 Biosystems). The separate-well $2^{-(\Delta\Delta Ct)}$ method was used to determine relative quantitative
63 levels of individual miRNAs and mRNAs.

64

65 **Transfection with siRNAs that target *PVT1***

66 ASMCs were transfected as previously described^(2;9;10). siRNAs designed to target *PVT1* and
67 *IL6* were purchased from Ambion/Applied Biosystems, Ltd. ASMCs were transfected with
68 *PVT1* inhibitor (30, 100, 300 nM), *IL6* inhibitor (100 nM), or Silencer[®] Negative Control #1
69 (100 nM) and no siRNA (mock transfection).

70

71 **Data and statistical analysis**

72 Data were analysed using GraphPad Prism, version 5.03. Data were not normally distributed
73 (as assessed by the Kolmogorov- Smirnov test), and therefore groups were compared using
74 the Dunn nonparametric test. All data are expressed as means \pm SEMs.

75

76
77**Supplemental Table 1: Baseline mRNA expression in non-severe ASM compared to healthy ASM cells**

Gene	P value	FC	Gene	P value	FC
ERCC8	0.00256679	8.12903	GAL	0.0394773	2.1095
SLC16A6	0.0166426	4.65081	AKR1B10	0.0449671	2.07792
HMSD	0.00663085	4.3893	FITM2	0.0183232	2.07506
HSD17B2	0.0443303	3.89864	SYTL2	0.0198481	2.06856
IGDCC4	0.0465114	3.6928	FLYWCH2	0.0121742	2.06587
MMP1	0.0259227	3.35243	EVI2A	0.0277221	2.06063
MMP3	0.0304801	3.22102	SLC7A14	0.0383132	2.03911
TRPA1	0.01778	3.13945	GNASAS	0.0482069	2.03829
SALL1	0.0052357	2.99666	RAB30	0.0289699	2.03204
RGS2	0.00555875	2.95017	KIAA1217	0.0265248	2.01769
FLI1	0.00364385	2.8631	PTH1R	0.0329649	1.97698
HRK	0.0429068	2.83682	C4orf36	0.0290853	1.96317
UCP2	0.00851212	2.79613	EID2B	0.00613632	1.96143
RARRES2	0.020582	2.77563	ARRDC4	0.0328818	1.95579
CLEC2B	0.00642905	2.77082	PAX4	0.0409322	1.95439
CARD17	0.00592314	2.70494	KCNN2	0.0242211	1.95348
TSHZ2	0.0134582	2.6941	SNORA53	0.0220681	1.94978
RNMT	0.00515799	2.63754	ARHGAP18	0.0106662	1.93914
C20orf196	0.0479645	2.62389	TBPL1	0.00781103	1.93791
CARD16	0.00841454	2.61194	TMEM97	0.00858623	1.93744
C9orf110	0.043834	2.55355	LRP8	0.0443823	1.93136
C17orf60	0.0267141	2.5307	SIPA1L3	0.00637892	1.91352
ICAM4	0.0437101	2.40862	NR_024569	0.0186056	1.90429
HMGCS1	0.0424883	2.39058	SAR1P3	0.00898055	1.89096
CCDC68	0.0233077	2.37967	C17orf86	0.00453316	1.88747
COL10A1	0.0250919	2.35495	CKS2	0.0142289	1.87502
EPHX4	0.00462827	2.34974	CDK17	0.020251	1.872
CST2	0.0389638	2.34496	C8orf41	0.00323954	1.856
CDYL2	0.00955754	2.34042	SEMA3A	0.0369473	1.85269
LCE2A	0.0266531	2.32617	COQ3	0.0370812	1.84123
TNFSF4	0.0253868	2.31612	GLRX	0.0111158	1.82913
IL7R	0.0408885	2.2781	GIT1	0.00646277	1.81225
NES	0.00362585	2.27808	C13orf1	0.0333645	1.80632
SC4MOL	0.0481442	2.26589	STMN3	0.0166473	1.80345
CCDC102B	0.0140359	2.21734	SPRY1	0.032023	1.79181
LOC100130938	0.00548399	2.20849	FANCA	0.00139521	1.78639
ADAMTS9	0.0199445	2.20162	PPP1R2P3	0.030498	1.78449
TTC12	0.00392433	2.18397	LOC728353	0.0144362	1.76044
LYN	0.0191528	2.17462	FAIM3	0.0129136	1.75518
LPPR3	0.0220692	2.17076	COPG2	0.00572741	1.75405
C13orf15	0.0234561	2.13801	KIR3DL3	0.035418	1.74011
SATB2	0.012104	2.13354	ATG9B	0.0388154	1.73542
SNORA74B	0.041715	2.12524	LOC100128340	0.0329169	1.73146
MRPS23	0.0117045	2.12179	RIPK3	0.0234775	1.73035
ATP2A2	0.0172857	2.11786	TMC4	0.00187281	1.72712
PTGES	0.0464004	1.72193	LPO	0.0312946	1.51464

SGIP1	0.0427581	1.71441	C1orf97	0.0127892	1.51182
C11orf85	0.022358	1.70651	TCERG1	0.0210095	1.50193
LY6G5B	0.0323101	1.70556	C11orf94	0.03963	1.50051
PDCD1LG2	0.0460351	1.69217	C12orf34	0.0134796	-1.50109
MOGAT2	0.0454009	1.6802	OLFML2B	0.00965737	-1.50279
ITIH1	0.0179354	1.67862	GAA	0.027051	-1.5045
DGCR11	0.0295952	1.67359	SLC13A3	0.0227501	-1.51245
LOC374443	0.0248206	1.6646	IQCE	0.031671	-1.51583
DUSP18	0.0406348	1.65337	SLIT3	0.0098095	-1.51648
ETV4	0.0257434	1.64981	COL16A1	0.0296194	-1.51924
CD99	0.0252357	1.64791	METRNL	0.0290532	-1.51963
R3HDML	0.0197006	1.64091	CLDN15	0.0472718	-1.53115
APIP	0.0293658	1.62597	MUC4	0.0243439	-1.5319
ICAM5	0.0162558	1.62544	LAMB2	0.027407	-1.53783
KLHL7	0.0397881	1.62432	KCND3	0.017771	-1.5382
FBXO3	0.0496671	1.61443	PBX3	0.00198743	-1.53883
TGDS	0.00616609	1.61348	RN18S1	0.0385365	-1.54727
C2orf135	0.0285209	1.61253	SH3BP5	0.00623863	-1.56086
IL1RAPL1	0.00713879	1.61077	CAND2	0.0156141	-1.5663
AX748082	0.0126975	1.60578	SYNE2	0.0382512	-1.59534
CEPT1	0.040725	1.60157	P2RY11	0.0449651	-1.60603
LRP11	0.0436053	1.59635	CCDC19	0.0123329	-1.6178
WNT6	0.0235748	1.59304	TGFB3	0.0278389	-1.62348
NAAA	0.0289171	1.58906	ZNF230	0.0114767	-1.63745
ASB8	0.027996	1.58609	NPIPL3	0.0361165	-1.63849
ZNF222	0.0223744	1.58609	KCNG1	0.031928	-1.64202
S100P	0.0345147	1.58354	FAT4	0.0394372	-1.65585
HTR7	0.0486079	1.58315	GMDS	0.010624	-1.65937
FAM176A	0.0455432	1.58124	PIP5KL1	0.0423751	-1.6623
ATL1	0.0229584	1.56837	AQP3	0.0283477	-1.6645
ARSG	0.0105803	1.5673	FBXO32	0.0433856	-1.6664
ADAM9	0.0375495	1.55888	DIRAS1	0.038796	-1.66986
LOC442572	0.0258556	1.5564	GYPA	0.0230486	-1.68431
ZNF789	0.0282785	1.5487	GLIS2	0.0127594	-1.68923
LIPT1	0.0292182	1.54776	PBX1	0.00848981	-1.69002
ASL	0.0349748	1.5466	ATP1B1	0.045649	-1.69544
GALNT4	0.00944573	1.54382	DMD	0.0497104	-1.69705
MGC16703	0.0079992	1.54334	NEK10	0.0329041	-1.6991
VWA2	0.00431907	1.54086	TLX2	0.00613515	-1.70613
TATDN1	0.0400969	1.53946	CCDC80	0.0452328	-1.71459
CNR2	0.0366879	1.53872	NPR1	0.00816906	-1.71749
CASS4	0.0270782	1.52985	NNAT	0.0314012	-1.72845
OSGIN1	0.0088119	1.52734	GHR	0.0306231	-1.73155
ZNF195	0.00969063	1.52537	NAV2	0.0113647	-1.73644
OSTF1	0.0349153	1.52403	CACNB2	0.0467284	-1.74416
ZNF417	0.0383173	1.52402	ZNF503	0.00907856	-1.74658
RAD51	0.0388823	1.52261	C9orf96	0.0105939	-1.74742
S100A3	0.0113228	1.51853	DACT1	0.023388	-1.75241
ZNF107	0.0215264	-1.76592	ACCN1	0.0331635	-2.10818

GKAP1	0.0490861	-1.76878	C5orf39	0.0450539	-2.11464
SNAR-G1	0.0383436	-1.77303	PRKCH	0.00336745	-2.13392
SHANK2	0.048114	-1.783	TMEM151B	0.0380533	-2.13457
DOK5	0.0136432	-1.78756	CRL2	0.00269115	-2.16473
SEMA3F	0.0276809	-1.79524	ANGPTL1	0.0236193	-2.18693
PGM5	0.00393577	-1.80463	CMYA5	0.000900832	-2.19022
PEG10	0.0233929	-1.81285	PPL	0.0122776	-2.19369
OR2A9P	0.0494225	-1.81684	KIAA1644	0.0292289	-2.21229
LOC388242	0.00329465	-1.81988	NOVA1	0.0146329	-2.21791
REP15	0.00864225	-1.8237	STAC	0.0195427	-2.23498
PDE8B	0.035244	-1.82845	KCNJ8	0.00643319	-2.28672
HTRA1	0.0112554	-1.83021	PDLIM4	0.0041358	-2.29975
CCDC151	0.00528945	-1.832	NR3C2	0.0201973	-2.30728
HLX	0.0257786	-1.8349	KLHDC7B	0.00447221	-2.31489
SPTLC3	0.0129416	-1.83967	C10orf11	0.0397767	-2.32799
BEST4	0.0010698	-1.84151	SLC39A5	0.01412	-2.3978
NFIA	0.0218309	-1.87978	CYP2J2	0.0314292	-2.4092
SLC6A9	0.0234398	-1.8842	GALNT12	0.00283954	-2.445
FNBP1L	0.0286074	-1.88962	GDF10	0.0227301	-2.45552
MFAP4	0.0489281	-1.9139	EPHA5	0.00717682	-2.54064
L2HGDH	0.00913428	-1.9146	TNNT2	0.0353226	-2.54526
CLU	0.00740704	-1.92507	CGNL1	0.023339	-2.56621
NLGN1	0.0099885	-1.92683	C10orf10	0.0327907	-2.57199
TMEM59L	0.00108387	-1.93338	IGF1	0.0103895	-2.58664
DIRC3	0.0470113	-1.93538	NRCAM	0.00254471	-2.60154
MATN2	0.0142377	-1.93694	DPT	0.00643853	-2.60339
ABCC9	0.0358009	-1.94478	MFAP5	0.044958	-2.61452
ZFPM2	0.0194637	-1.94683	SULF1	0.00534576	-2.66216
TMOD4	0.00319358	-1.95017	COL14A1	0.000357204	-2.66577
ABLIM1	0.00177999	-1.96815	KIAA1324L	0.0359039	-2.67384
FUCA1	0.0405767	-1.97474	DHRS3	0.00774106	-2.75273
SLIT3	0.0398184	-1.98453	FGF18	0.000896677	-2.80081
VWCE	0.0312087	-1.98542	JAM2	0.00305768	-2.80562
FGF13	0.0138649	-1.99866	GPER	0.000233449	-2.84791
LAMA3	0.0341782	-2.00515	COL6A6	0.0472692	-2.92356
OR10G3	0.00739	-2.01027	EPHB6	0.0216317	-2.92423
TACSTD2	0.0488225	-2.01974	CHRD1	0.012315	-2.92678
SCN2A	0.00858522	-2.02318	GPR68	0.0122055	-3.02474
C8orf46	0.00669657	-2.03351	FLJ41603	0.00358055	-3.02479
ITIH3	0.0435118	-2.03558	PTGIS	0.0300997	-3.05012
ADAMTS3	0.00983634	-2.03924	GNAZ	0.031785	-3.07734
HTRA3	0.0243531	-2.04246	C7orf69	0.0411363	-3.09401
SERPINA3	0.0225425	-2.05235	NEFM	0.00778604	-3.13218
LIF	0.00101274	-2.06048	FNDC1	0.0119883	-3.2049
SLC4A4	0.0246772	-2.08013	OGN	0.00233206	-3.27812
FOXC1	0.015423	-2.08185	SCN4B	0.0159437	-3.38216
COBL1	0.0270806	-2.10497	C13orf33	0.0265376	-3.4087
AKAP12	0.0137054	-2.10649	TMEM30B	0.00673075	-3.61571
CRLF1	0.00736869	-3.6385	PTPRD	0.00132004	-4.4638

AGT	0.020381	-3.64996	TMEFF2	8.25E-06	-4.54125
CCDC3	0.0117285	-3.7839	PI16	0.0304839	-4.90266
CXCR7	0.0178151	-3.94469	NFIB	0.0111192	-4.94463
MGP	0.000631693	-3.97238	SCN2B	0.000479454	-7.85751
CKAR	0.00487403	-4.32258			

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Supplemental Table 2: Baseline mRNA expression in severe ASM compared to healthy ASM cells

Gene	P value	FC	Gene	P value	FC
CHI3L1	0.00322219	6.61982	SYTL2	0.0328305	1.96693
TRIM63	0.0231446	4.09239	ENTPD7	0.0257107	1.96311
APBA2	0.0445882	3.82477	LPPR3	0.0489578	1.9601
IL34	0.0191848	3.69834	COQ3	0.026979	1.95358
CDC73	0.0269521	3.68601	CES1	0.0362807	1.89267
HRK	0.0211963	3.44723	EFNB1	0.0338861	1.87755
KIAA1199	0.0148091	3.38659	INA	0.019085	1.81494
LRRC15	0.0295012	3.24591	FLJ31715	0.0352514	1.81384
WISP2	0.0258918	3.08252	GGT5	0.0384159	1.79639
HLA-DRB3	0.0241551	3.0408	UPF0621	0.0193493	1.79492
PLA2G5	0.0270857	3.02936	LOC390251	0.0129469	1.76937
FCRL1	0.0229921	2.81958	B3GALTL	0.0357022	1.76502
BOC	0.0496743	2.69953	PLA2G16	0.0429882	1.76186
RANBP2	0.0213297	2.67464	ST3GAL5	0.0351087	1.7441
KCND2	0.0474138	2.63907	ZNF91	0.0336617	1.73603
SERPINB9	0.0267262	2.36852	CDK17	0.0436539	1.73378
AQP11	0.00276018	2.32601	PIGZ	0.0496192	1.72694
ASB2	0.0247058	2.25971	SERPINE2	0.0453189	1.72255
CCL28	0.0294344	2.18907	MT1G	0.0347974	1.71768
P2RX7	0.0176809	2.18229	POLR2F	0.0103218	1.69222
LOC649941	0.00266206	2.13469	C4orf22	0.0364316	1.69198
PLXDC2	0.0285438	2.07502	TRIM78P	0.0377634	1.68077
SCUBE3	0.00809742	2.06145	GNPTAB	0.00505003	1.67564
SLC30A3	0.0191482	2.05979	ELOVL4	0.0384621	1.67198
LOC645431	0.00327623	2.04048	MID2	0.0272579	1.66531
PLXNC1	0.03469	2.00889	MYO1E	0.00629935	1.64458
TSKS	0.0404227	2.00233	DA992326	0.0232459	1.63417
ARRDC4	0.0322396	1.99718	FAM179A	0.016525	1.62278
SBSN	0.0333072	1.98322	ARL4C	0.0299183	1.61076
GPRC5C	0.00819651	1.97791	RGNEF	0.0401281	1.60602
FZD8	0.0445338	1.97657	AIMP1	0.0260581	1.59682
OR6N1	0.0459387	1.97118	ZNF850P	0.0490557	1.59094
GPC3	0.0416173	1.5907	TMOD4	0.0126156	-1.75445
CU678159	0.0435196	1.58094	FHL3	0.00232316	-1.76187
MAF	0.0488807	1.5683	KCNMB4	0.044772	-1.76424
PCOTH	0.0189505	1.56159	NLGN1	0.0257432	-1.76981
FAM107B	0.0134004	1.5443	LOC100128340	0.0273873	-1.79563
RASGRP4	0.0091248	1.53014	TMSB15A	0.0472232	-1.80402
ZC3H12C	0.0366664	1.52823	G6PD	0.0143391	-1.80527
ALX3	0.01248	1.52661	PGA3	0.029713	-1.82591
EPB42	0.0404321	1.52063	GSTM2	0.00624907	-1.83722
SOAT1	0.0465077	1.51478	RTF1	0.0342033	-1.83891
ZNF417	0.0468942	1.51189	MIR155HG	0.0463894	-1.84051
SUSD2	0.0267075	1.50014	EDIL3	0.00907355	-1.846
EID1	0.0372519	1.5	FOXC1	0.0436204	-1.84634

RXRB	0.0192761	-1.51577	BC013171	0.0176268	-1.85591
COL9A3	0.0275545	-1.52281	LEMD2	0.0283376	-1.87251
THC2551759	0.025643	-1.5293	TEKT4	0.0253215	-1.87611
LIF	0.0360369	-1.54658	MATN2	0.0206684	-1.88823
DNAJC4	0.0231423	-1.55047	GLIS1	0.0160045	-1.90408
LOC100129721	0.0389218	-1.55148	UCN2	0.00691849	-1.93071
PARVB	0.0485998	-1.56027	NOVA1	0.041179	-1.95198
KIAA1683	0.030854	-1.57456	HBA2	0.00836222	-1.9605
OLFML3	0.0229235	-1.58161	EDNRA	0.00849789	-1.98684
LOC606724	0.0305021	-1.58414	HCLS1	0.0126303	-2.01169
CMYA5	0.0382822	-1.58529	CCDC36	0.0361258	-2.03234
AF495723	0.0197298	-1.5889	COL7A1	0.00806561	-2.03399
PIWIL4	0.00386534	-1.59655	C8orf46	0.00705425	-2.06141
FES	0.013501	-1.59932	DPT	0.0325449	-2.10323
AK124041	0.0098982	-1.6135	TMEM151B	0.0410405	-2.15069
HSD11B2	0.0361224	-1.61447	PEG10	0.00432019	-2.2238
LOC100130557	0.0223642	-1.63702	EPHA5	0.0167505	-2.30662
BHLHE23	0.0374452	-1.642	CCDC85A	0.0364354	-2.32329
DCHS1	0.0245409	-1.6444	ZNF462	0.0207553	-2.35787
SH3GL1P3	0.00380501	-1.64995	WBSCR27	0.0236313	-2.39805
COL14A1	0.0445964	-1.65881	KIAA0430	0.037571	-2.52596
CYBA	0.0107948	-1.65884	FLRT3	0.0499926	-2.55809
BAT2	0.0467807	-1.67443	KIAA1324L	0.0370802	-2.72654
PIK3C2B	0.0268458	-1.71271	FGF13	0.000851033	-2.79977
LGI4	0.027596	-1.71907	POMC	0.0269916	-2.89054
PRR16	0.0161184	-1.73578	PSKH1	0.0218528	-2.97571
LOC100130713	0.0158694	-1.73869	BCHE	0.0043359	-3.02392
RAX2	0.0264997	-1.74198	TWF2	0.0336147	-3.03413
PTPRD	0.0128931	-3.08855	ACBD6	0.0498267	-3.4529
TMEFF2	0.000287566	-3.16613	DCTN3	0.0201069	-3.82185
RNF216L	0.0428454	-3.20267	CCKAR	0.00317157	-4.91171
NUDT22	0.0286962	-3.40754	CADM1	0.00090556	-5.16425

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Supplemental Table 3: Common baseline mRNA expression changes in ASM cells from patients with non-severe or severe asthma vs. healthy

Gene Symbol	Gene Name	Non-Severe Asthma	Severe Asthma
		Microarray (FC)	Microarray (FC)
ARRDC4	Arrestin domain containing 4	2.0 (p < 0.01)	2.0 (p < 0.01)
C8orf46	Chromosome 8 open reading frame 46	-2.0 (p < 0.01)	-2.1 (p < 0.01)
CCKAR	Cholecystokinin A receptor	-4.3 (p < 0.01)	-4.9 (p < 0.01)
CDK17	Cyclin-dependent kinase 17	1.9 (p < 0.01)	1.7 (p < 0.01)
CMYA5	Cardiomyopathy associated 5	-2.2 (p < 0.01)	-1.6 (p < 0.01)
COL14A1	Collagen, type XIV, alpha 1	-2.7 (p < 0.01)	-1.7 (p < 0.01)
COPG2	Coatomer protein complex, subunit γ -2	1.8 (p < 0.01)	1.5 (p < 0.01)
COQ3	Coenzyme Q3 homolog	1.8 (p < 0.01)	2.0 (p < 0.01)
DPT	Dermatopontin	-2.6 (p < 0.01)	-2.1 (p < 0.01)
EPHA5	EPH receptor A5	-2.5 (p < 0.01)	-2.3 (p < 0.01)
FGF13	Fibroblast growth factor 13	-2.0 (p < 0.01)	-2.8 (p < 0.01)
FOXC1	Forkhead box C1	-2.1 (p < 0.01)	-1.8 (p < 0.01)
HRK	Harakiri, BCL2 interacting protein	2.8 (p < 0.01)	3.4 (p < 0.01)
KIAA1324L	Estrogen-induced gene 121-like protein	-2.7 (p < 0.01)	-2.7 (p < 0.01)
LIF	Leukemia inhibitory factor	-2.1 (p < 0.01)	-1.5 (p < 0.01)
LPPR3	Lipid phosphate protein type 3	2.2 (p < 0.01)	2.0 (p < 0.01)
MATN2	Matrilin 2	-1.9 (p < 0.01)	-1.9 (p < 0.01)
NLGN1	Neurologin 1	-1.9 (p < 0.01)	-1.8 (p < 0.01)
NOVA1	Neuro-oncological ventral antigen 1	-2.2 (p < 0.01)	-2.0 (p < 0.01)
PBX3	Pre-B-cell leukemia homeobox 3	-1.5 (p < 0.01)	-1.4 (p < 0.01)

PEG10	Paternally expressed 10	-1.8 (p < 0.01)	-2.2 (p < 0.01)
PTPRD	Protein tyrosine phosphatase, receptor type, D	-4.5 (p < 0.01)	-3.1 (p < 0.01)
SYTL2	Synaptotagmin-like 2	2.1 (p < 0.01)	2.0 (p < 0.01)
TMEFF2	Transmembrane protein with EGF-like and two follistatin-like domains 2	-4.5 (p < 0.01)	-3.2 (p < 0.01)
TMEM151B	Transmembrane protein 151B	-2.1 (p < 0.01)	-2.2 (p < 0.01)
TMOD4	Tropomodulin 4 (muscle)	-2.0 (p < 0.01)	-1.8 (p < 0.01)
ZNF417	Zinc finger protein 417	1.5 (p < 0.01)	1.5 (p < 0.01)

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88**Supplemental Table 4: mRNAs in non-severe ASM changed in expression following stimulation with FCS (2.5 %)**

Gene	P value	FC	Gene	P value	FC
HIST1H2AL	0.042169	15.2972	LOC644662	0.0433908	3.00074
AFP	0.045175	13.6111	RNFT2	0.0460387	2.99992
KIF2C	0.0179581	12.5638	GAPDHP32	0.0409119	2.98881
TACC3	0.00420819	10.3329	LHFPL4	0.0125018	2.96321
HIST1H2BE	0.0237102	9.36812	C14orf145	0.0256065	2.95993
UBE2C	0.0492036	8.21674	CLN6	0.00278737	2.95722
KRTAP1-5	0.0103114	8.12693	ASF1B	0.0246229	2.92533
CENPL	0.0417908	7.93986	MTHFD2	0.0292476	2.92091
ACTG2	0.0226104	7.84917	CECR3	0.00506878	2.88227
FAM64A	0.0385425	6.96685	PPIL5	0.0235481	2.83299
CENPF	0.0256589	6.85437	GINS4	0.0189066	2.78582
GINS1	0.0236215	6.52347	PPP1R12B	0.0369438	2.76528
CENPM	0.046922	5.98313	MS4A18	0.0105	2.71174
DGCR14	0.0340715	5.74079	DONSON	0.00280379	2.62237
DTL	0.0424873	5.71324	PPIH	0.0486878	2.54108
PKMYT1	0.0467408	5.32092	NEK10	0.0372871	2.53094
PSG5	0.0411558	5.0389	TRMT11	0.0143645	2.52293
NRP1	0.0207293	4.99781	DARS2	0.0384515	2.52127
PSG3	0.0430847	4.96387	PPPDE2	0.0226035	2.5107
SLC7A5	0.0168647	4.91765	CLEC4A	0.0271478	2.50964
RP11-717D12	0.0125387	4.74994	UHRF1	0.0114807	2.5059
SNORA62	0.0480651	4.53985	FAM183A	0.0115952	2.50458
BLM	0.0359356	4.47101	OSGEPL1	0.0055552	2.50087
DHFR	0.0362396	4.38697	MCM8	0.0046727	2.48865
TPX2	0.0236064	4.36345	ZNF761	0.0124803	2.48471
RP11-631M21.2	0.0391902	4.32804	CD99	0.0476624	2.48135
PSAT1	0.00586812	4.21463	PSMD9	0.0224133	2.44675
C6orf173	0.0116616	4.19215	SFRS7	0.0198257	2.44667
C12orf48	0.0150602	4.152	C2orf63	0.00306824	2.4222
COMP	0.0417089	4.04159	C22orf23	0.00530128	2.41289
FGD2	0.00851702	4.00545	MCOLN2	0.0355785	2.39538
HIST1H3G	0.0346906	3.91419	IFI44L	0.00670638	2.39198
E2F2	0.0170241	3.75432	MAGOHB	0.0143099	2.36689
C7orf69	0.0423192	3.69353	SLC25A19	0.0401612	2.32236
DNMT3B	0.0019108	3.60621	CALML4	0.020143	2.31044
HPVC1	0.00500671	3.57815	C1orf135	0.000107269	2.30686
POLQ	0.00972538	3.53489	AK310642	0.0129591	2.29593
SLC4A4	0.0457484	3.46774	SFRS1	0.00309224	2.2717
MPP2	0.0203948	3.46566	THC2698732	0.014244	2.26837
SLC12A8	0.0148354	3.41566	MCCC2	0.0239829	2.25976

CR979835	0.0119406	3.35836	C3orf26	0.000136262	2.24602
PSRC1	0.0319164	3.26343	M27336	0.00519858	2.23891
SEMA3C	0.0277254	3.23105	Uncharacterized	0.0413966	2.23347
LOC100127904	0.0108389	3.19899	KIAA0467	0.0471104	2.19476
HIST1H3E	0.00995016	3.14865	HN1L	0.0115622	2.19265
ZNF286A	0.0106128	3.09122	C1orf88	0.00356268	2.19033
EID3	0.0158955	3.07464	FITM2	0.0276101	2.14598
AX747988	0.0100492	3.02907	TRIM61	0.0214664	2.1356
TLR3	0.0109683	2.13293	TRPC4	0.000482049	1.71844
FBF1	0.00359897	2.13183	FAM163B	0.0238488	1.71416
KPNA2	0.0287595	2.11384	HIF1A	0.0175851	1.71293
TOMM34	0.047636	2.10906	LOC401357	0.0271595	1.70815
PTPLA	0.0216557	2.10699	RXFP3	0.0308157	1.701
SLC7A1	0.00855046	2.10298	FLJ43315	0.00189219	1.6953
ZNF846	0.0485604	2.10036	ANKRD23	0.0327944	1.68543
RNF170	0.0324877	2.09984	RG9MTD2	0.0420216	1.68441
RAD51	0.010671	2.05954	EME1	0.0208152	1.68283
IPMK	0.0462493	2.05872	ZNF773	0.0178852	1.67989
DAZAP1	0.00609129	2.04506	PPT1	0.0113626	1.67657
AC009065.1	0.0220591	2.0435	MTDH	0.0378097	1.67045
DHODH	0.0229538	2.02404	TARS	0.0489756	1.66668
MRPL52	0.0174852	2.00324	LZIC	0.0228597	1.66613
CLDN15	0.00391595	2.00082	ILKAP	0.0466723	1.65865
CBS	0.0320916	1.98625	HUWE1	0.0393995	1.65522
DAD1L	0.0467537	1.98429	DHX32	0.0290673	1.65436
TNC	0.043421	1.978	PSMD1	0.0448396	1.65114
C17orf75	0.0345164	1.96439	C8orf12	0.046566	1.65041
TSR1	0.016276	1.94851	C14orf106	0.0374258	1.64948
TIPIN	0.0119014	1.93712	LOC497257	0.0126151	1.64176
IGHV4	0.0498597	1.9338	CASD1	0.0389019	1.63331
RRP15	0.010714	1.93131	HIST2H4B	0.0278259	1.62088
EIF4E	0.0256744	1.93005	ADAMTS2	0.0346808	1.62082
LRRC23	0.0336998	1.92391	PGAM5	0.00983565	1.61832
ANKFY1	0.00990802	1.9159	AB305862	0.00236905	1.61206
NSFP1	0.0200841	1.90634	RACGAP1P	0.00628056	1.60766
ZNF232	0.0331495	1.89857	DHX34	0.0489499	1.60645
MARS	0.0195536	1.89063	KBTBD2	0.035033	1.60309
LOC388796	0.0490232	1.8668	PIGA	0.0329098	1.59928
GSTCD	0.0129876	1.86522	ZNF259P1	0.0285483	1.59487
DDIT4L	0.0224462	1.86291	CCDC75	0.0261684	1.58904
ATP10A	0.00458931	1.85362	XPO1	0.0481318	1.58287
USP49	0.00316534	1.85184	RAGE	0.00904688	1.57975
PMPCA	0.0361554	1.84998	REP15	0.036773	1.57611
TUBB	0.00098612	1.83791	MGC14436	0.0452944	1.57506
CACYBP	0.0116392	1.83219	FUS	0.022933	1.56518
EPS15	0.0139386	1.81679	ALKBH8	0.0186885	1.56504
DPP3	0.0152883	1.81394	IFRD2	0.0338035	1.55328
LOC100132774	0.0251185	1.80329	PHTF1	0.0213646	1.55108
MKNK2	0.00159673	1.78837	FH	0.0428265	1.55003
DLD	0.00708761	1.78761	SMN2	0.00451399	1.54349
KIAA1310	0.0309488	1.78021	SIL1	0.0137999	1.54321
AIFM2	0.0486621	1.77614	SLC19A3	0.0429533	1.53829

PLA2G16	0.0145217	1.77477	SFRS3	0.0114201	1.53351
ATP6V1C2	0.0241497	1.76747	RNF8	0.044035	1.53324
FASTKD2	0.0189688	1.76226	CDC10L	0.0161337	1.53244
FLVCR1	0.0244468	1.7581	SDS	0.0497296	1.52589
KLHL26	0.0095282	1.75207	GLRX2	0.0337985	1.52024
BLZF1	0.0139667	1.74802	C2orf86	0.030794	1.50989
OGFOD1	0.0492616	1.74646	LRP11	0.0327101	1.50692
TGM2	0.00809875	1.72013	TTC39B	0.0304907	1.50559
PAN3	0.0261818	1.50394	LOC283335	0.0407034	-1.93147
LOC100130093	0.00400245	-1.50118	TMEM158	0.0307114	-1.94396
SLC35B4	0.0420702	-1.50184	FLJ10357	0.0264898	-1.95443
SPINK7	0.00238846	-1.50987	TCF7L1	0.0408114	-1.95539
NFKBIE	0.00217181	-1.51769	SLC37A2	0.0245677	-1.97465
SIX4	0.0455931	-1.52335	PDZD2	0.036989	-1.98523
BTNL8	0.0479463	-1.52593	BC038245	0.00630883	-1.99291
APBA2	0.00966014	-1.53101	CDKN2B	0.0371591	-2.00957
TMTC4	0.0431429	-1.53995	IGKV2D	0.00469022	-2.01651
PIP5K1C	0.0483843	-1.54103	BAI1	0.0245881	-2.05008
COL8A1	0.0391784	-1.5436	TLR2	0.0304678	-2.05671
KLF3	0.0337641	-1.54606	MAF	0.0182159	-2.05987
AK097103	0.0211365	-1.55156	IGDCC4	0.0250946	-2.10885
C1QL1	0.0124643	-1.55905	CCL8	0.0410618	-2.11255
USP7	8.85E-05	-1.56233	C3orf17	0.00177469	-2.16793
B3GNT8	0.0184764	-1.57443	SEZ6L2	0.00263898	-2.20901
GAL3ST4	0.0323236	-1.58089	TMEM100	0.023037	-2.22181
LOC100131831	0.018233	-1.5968	UACA	0.0244656	-2.24136
EGR1	0.0459262	-1.6054	CCDC102B	0.0363297	-2.28346
C21orf7	0.0280334	-1.60858	EMILIN2	0.0240823	-2.32076
EVC2	0.0240317	-1.61969	C14orf138	0.0412158	-2.33047
GLUL	0.010041	-1.62454	ISYNA1	0.0384217	-2.33646
GPC2	0.0302108	-1.62894	ARHGAP26	0.0437545	-2.34708
CYBRD1	0.0271256	-1.63724	CCDC68	0.0399964	-2.34718
TCTE1	0.0489872	-1.64832	APCDD1L	0.0160971	-2.41235
UCN	0.0037761	-1.64946	DCHS1	0.00752015	-2.43273
TMEM86A	0.00964896	-1.64994	KRT3	0.041891	-2.44482
SART3	0.0154546	-1.65959	ADH1C	0.0260881	-2.45803
GOLGA2P2	0.0142093	-1.67088	DLK2	0.040191	-2.47085
TRNP1	0.0439195	-1.67769	GSN	0.0477098	-2.47101
HEPH	0.0381521	-1.68225	FLJ46875	0.0201755	-2.47952
MARVELD2	0.0381364	-1.68234	HMGCS1	0.0499847	-2.575
PLAC9	0.0377636	-1.68649	TRIB2	0.0380756	-2.64709
SH3KBP1	0.0451682	-1.69882	LAG3	0.0398748	-2.68553
HPCAL1	0.0189406	-1.69957	THBS4	0.0256252	-2.7205
SCT	0.0418042	-1.71813	HSD17B2	0.0330886	-2.75754
PRKG1	0.0184531	-1.72592	ABTB1	0.0369234	-2.85716
RADIL	0.00662583	-1.75871	FAM78A	0.038982	-3.11112
C20orf135	0.0309732	-1.76323	FLJ30698	0.0426586	-3.13743
TMEM37	0.0334918	-1.79774	RABL2B	0.00800631	-3.16736
AGER	0.0496659	-1.8104	ETV4	0.0365959	-3.26767
SHROOM3	0.0489757	-1.82287	LOC339192	0.0342404	-3.38369
SMO	0.0380795	-1.823	C13orf16	0.0248009	-3.45668
PLCL2	0.0359885	-1.826	LOC642335	0.0265109	-3.65619

LRRC16B	0.0159671	-1.84618	STMN3	0.0318109	-3.69304
COL14A1	0.0286924	-1.84778	TMEM176B	0.0221529	-3.79105
OGN	0.0368907	-1.85259	C13orf33	0.037319	-4.30016
BFSP1	0.0214947	-1.85693	TRPA1	0.0494467	-4.73558
METTL12	0.003944	-1.86401	HBA2	0.00661282	-5.8041
SMAD1	0.0403424	-1.89878	SIPA1L2	0.0337634	-6.76115
LPIN3	0.0474008	-1.91035	ICOSLG	0.0154353	-6.86364
ARRB1	0.014972	-1.91722	MMP10	0.0472607	-9.51461
TLE2	0.0321331	-9.55024	CYP7B1	0.0270015	-10.1216

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92**Supplemental Table 5: mRNAs in severe ASM changed in expression following stimulation with FCS (2.5 %)**

Gene	P value	FC	Gene	P value	FC
SAE1	0.0315319	28.776	DDN	0.0128671	2.29176
NUDT22	0.0383927	23.1666	EDN1	0.0104384	2.2315
TRIP12	0.0374441	20.7629	TAGLN	0.0487656	2.22898
C6orf108	0.0247918	19.7578	TMEM88B	0.0323484	2.22675
ACBD6	0.0429061	18.8501	LOC389842	0.0454044	2.21946
RNF216L	0.0361313	17.2554	E2F2	0.0165037	2.19929
FAM50A	0.0396457	14.9825	LSR	0.0235457	2.19467
PSKH1	0.0486055	14.7079	ZIC4	0.0429361	2.18695
SDSL	0.0225439	14.5717	DA567289	0.00549359	2.15372
ATAD3A	0.030444	13.8475	NDUFS8	0.00381808	2.14945
SNRNP27	0.0327279	11.8091	ID4	0.0137383	2.1279
ASNSD1	0.0354113	11.2429	PLCB2	0.0184724	2.12514
TULP3	0.0370215	9.8634	FAM54A	0.00265674	2.11959
OXSM	0.0301995	9.78723	AFP	0.0470928	2.11115
RAB21	0.0491913	9.77369	HIST1H1B	0.0116681	2.10204
ARHGEF17	0.0388136	9.28091	ARHGDI1B	0.0162116	2.09234
C7orf50	0.0253458	9.19125	SGOL2	0.00482879	2.0429
RPL10AP6	0.0442215	6.49763	MMP3	0.00927657	2.03684
CAPNS2	0.040892	6.1604	ENST00000404580	0.0151055	2.03313
PIGX	0.0335979	5.642	ACTBL2	0.0165729	2.02833
LOC283761	0.0362225	4.92652	APOBEC3G	0.00703699	2.01329
RELL2	0.0303205	4.52845	LIG3	0.00210713	2.01078
HIST2H3A	0.0116836	4.43854	DKK1	0.00945856	2.00856
NAA50	0.0304966	4.18773	C18orf50	0.0152191	2.00559
ACTG2	0.0118337	4.01062	FMO2	0.0204379	1.98753
COMP	0.0274281	3.84419	LIPN	0.00158453	1.97156
C7orf69	0.000417546	3.39355	WDR85	0.0288708	1.96528
ID1	0.00487957	3.37276	CDCA4	0.0140678	1.95348
ID3	0.000162498	3.15246	BLM	0.00836898	1.95115
SERP2	0.0458915	2.86087	C19orf36	0.0414973	1.93632
ASTN2	0.000738895	2.83591	EIF4EBP1	0.0105519	1.93568
DHRS3	0.000668734	2.7709	CNN1	0.0193895	1.90859
SYT3	0.0318851	2.71504	ACTL9	0.0408739	1.90733
GIYD1	0.0363437	2.70562	TMEM110	0.00729636	1.90372
PHF7	0.024339	2.67045	ULBP1	0.00337033	1.9001
LOC100129324	0.00911405	2.6471	ALDH1B1	0.00183288	1.89709
NPW	0.00445001	2.59169	AC120194.1	0.0421492	1.89433
SNORA74B	0.00355454	2.59106	DONSON	0.00667162	1.89237
CDC45L	0.0219393	2.4589	ELMO3	0.0194432	1.88445

FAM83D	0.0106239	2.45033	PXDN	0.00678331	1.87335
FAM183A	0.034768	2.42204	DGKG	0.0111504	1.87098
PI16	0.0174762	2.39663	CDCA8	0.0434952	1.87042
MMP24	0.00989577	2.37446	KLF7	0.00991614	1.86591
HJURP	0.0491266	2.35793	PSG8	0.0466474	1.85618
SLC7A5	0.0181817	2.332	C14orf138	0.0225217	1.85215
SLC17A9	0.0280329	2.30034	SNAR-A3	0.0274161	1.85096
FAM132A	0.00176382	1.84438	ALPK2	0.021769	1.63973
LOC100128429	0.0289081	1.84399	WARS	0.012276	1.63779
PDLIM7	0.0110294	1.84335	HR	0.010702	1.63613
ACTA2	0.00446266	1.84298	AIFM2	0.0412398	1.63467
NPAS1	0.000454168	1.82921	TCIRG1	0.0178322	1.62906
HMMR	0.0202382	1.82606	TNC	0.00521396	1.62092
CSRP2	0.0249357	1.8154	APOL5	0.042588	1.61928
OIP5	0.0242851	1.81163	PRPS1L1	0.0330893	1.61876
ENPP4	0.000291782	1.80634	HEG1	0.0292205	1.61529
ALDH1A1	0.0155456	1.79998	POTEF	0.0125938	1.6145
NDNL2	0.0407615	1.79555	ODC1	0.0404126	1.61089
ABCC3	0.00528059	1.79542	TGFBI	0.0232463	1.60382
TACC3	0.0146334	1.78537	LOC90246	0.0417054	1.60312
CDK12	0.0403507	1.77716	CDH6	0.0273261	1.60102
CXorf36	0.0399867	1.77386	DKFZp779M0652	0.0369208	1.5986
PPAPDC1A	0.00459146	1.77208	LOC391334	0.0187152	1.59564
KRTAP19-8	0.0111527	1.768	SHCBP1	0.0125923	1.5899
CCNE2	0.040152	1.76776	SRPK3	0.0395365	1.58695
CDH15	0.00514977	1.76617	TUBB2A	0.036036	1.58243
CDRT8	0.0476002	1.76148	KRT18	0.0289952	1.57967
EARS2	0.026841	1.75945	IL6	0.0286464	1.57711
TPM1	0.00128356	1.75561	ZWINT	0.0272534	1.57286
NUAK2	0.0408128	1.75403	ATF6	0.0116662	1.56936
IGKV2D-26	0.0381266	1.73547	TUBGCP4	0.0306173	1.56756
EXO1	0.00344069	1.73461	CHMP5	0.0456459	1.56092
SH2D4A	0.0188817	1.73319	PFN1	0.00875389	1.55958
GPR173	0.0293878	1.73188	ANO7	0.0434326	1.55938
CRYAB	0.000394639	1.72738	ARRDC4	0.042354	1.55865
SQLE	0.0291135	1.72525	PDSS1	0.0327617	1.54896
MCM6	0.00443025	1.72247	PGAM5	0.0237636	1.54858
UCHL3	0.00591859	1.72062	BE897625	0.0450089	1.54428
MTP18	0.0387551	1.71943	IL17REL	0.0244906	1.54247
PKMYT1	0.0442163	1.70402	NOP16	0.0355891	1.53584
FGF1	0.0341872	1.70077	EYA2	0.0304183	1.53301
SDHB	0.0175247	1.6982	URB2	0.00172548	1.53158
MGC31957	0.0441615	1.6915	OR8B8	0.0210497	1.52967
CENPM	0.0455267	1.68005	LOC644686	0.0121129	1.52698
GATA6	0.000328035	1.67938	IL23A	0.0306401	1.5269
C17orf55	0.0317488	1.67516	SNAPC2	0.0493027	1.52311
SLC7A1	0.0277587	1.67209	DLEU1	0.0397625	1.52274
EPHX4	0.0457424	1.66998	CCDC134	0.012816	1.52022
NP511207	0.0470343	1.66315	DHODH	0.0341323	1.5189
BATF3	0.0474352	1.66035	KIF23	0.0385091	1.51864
UXT	0.0200589	1.65571	TUBA1B	0.0485987	1.51811
LOC100133478	0.0162422	1.65485	FABP5	0.0111229	1.51057

MPI	0.013293	1.65459	ANO9	0.0480375	1.50866
PRKCI	0.0103238	1.65242	TNFRSF12A	0.0253343	1.50694
FBXW8	0.00214241	1.65007	ASB2	0.00227959	1.5052
HHEX	0.00717586	1.64445	AIMP2	0.0183562	1.50163
NCL	0.0212408	1.64283	IGJ	0.0277505	1.50158
ZBTB8OSP1	0.00288391	1.64143	CD83	0.0282823	-1.50228
TMEM138	0.00161397	1.64023	SPTBN4	0.0282382	-1.50281
KCNH2	0.0469862	-1.50303	DPT	0.0164097	-1.6272
SPRY1	0.025703	-1.50499	TBC1D22B	0.0116999	-1.6273
NFKBIA	0.0164733	-1.50535	OPN1SW	0.0380872	-1.63001
HEXIM2	0.0265515	-1.50677	ARVCF	0.0097111	-1.63635
KIAA0495	0.0424653	-1.50793	RASA4	0.0404237	-1.63808
PABPC3	0.00939298	-1.50982	ETV1	0.0172944	-1.64143
GFRA1	0.0271806	-1.51225	LOC100132197	0.0017269	-1.64502
KIAA0895L	0.0408107	-1.51644	PLCL2	0.0227026	-1.64503
METTL7A	0.0308474	-1.51819	ZNF29P	0.00222593	-1.64536
BTG1	0.0412704	-1.51955	ADAM8	0.0220746	-1.64573
TRERF1	0.0192006	-1.52049	SCN2A	0.0160161	-1.64932
ZBTB46	0.0406111	-1.52212	OXER1	0.0155099	-1.65046
RAP2B	0.0235145	-1.53124	MXRA5	0.00549818	-1.65166
PDZRN3	0.00504218	-1.53388	ADRBK2	0.036771	-1.65168
EPHB3	0.0281024	-1.53478	PPL	0.0354628	-1.65483
NDRG3	0.0411172	-1.53567	FAM59A	0.0131217	-1.65541
KLRG1	0.00484315	-1.53642	PTPRU	0.000647812	-1.65573
ZMIZ2	0.00599439	-1.5395	PANX3	0.0435711	-1.65639
TMEM120B	0.00832699	-1.54006	CCL27	0.023936	-1.66092
MYOF	0.0140487	-1.54498	CLN8	0.0067489	-1.66444
ANKRD36	0.0342401	-1.54625	NNAT	0.0193647	-1.67641
GAS1	0.0342949	-1.5472	AGER	1.80E-05	-1.6812
UBTF	0.0463208	-1.54893	ARRB1	0.0053879	-1.6816
SNHG7	0.0276343	-1.55065	ARHGAP6	0.0293974	-1.68299
BACH2	0.0422622	-1.55106	PHEX	0.0352096	-1.68449
EHD3	0.017498	-1.55421	IRAK2	0.0133486	-1.68593
MRPS6	0.0102987	-1.55456	SCXA	0.0441773	-1.70553
ZNF596	0.0323015	-1.55726	SGIP1	0.0077103	-1.70833
SNCAIP	0.00703485	-1.55821	NTN1	0.00603033	-1.71195
GRIN3B	0.00278114	-1.56203	CRMP1	0.0402138	-1.71328
DCHS1	0.0493557	-1.56359	C19orf67	0.0442978	-1.71828
LOC91450	0.0149978	-1.56424	SYNE2	0.0164992	-1.73058
C14orf139	0.0111174	-1.56482	CCL15	0.0481097	-1.73132
MAPK10	0.0468834	-1.56652	BC030764	0.0106245	-1.73984
NPR1	0.00656877	-1.5676	USP21	0.000202573	-1.74008
GGTLC1	0.022507	-1.57194	KBTD3	0.0351395	-1.75224
C3orf65	0.00511018	-1.57454	PHLDA1	0.0157209	-1.75268
PLGLB1	0.0230776	-1.57603	LOC92973	0.0467445	-1.75423
OTUD4	0.00801676	-1.58681	SEMA3D	0.0390407	-1.75514
FAM179A	0.0284816	-1.58839	FRMD4A	0.024925	-1.75934
MEG8	0.00128523	-1.59095	CD19	0.0104817	-1.76635
PIK3CA	0.00813475	-1.59644	SH2B2	0.00634026	-1.76713
RNF122	0.0131832	-1.6004	MTVR2	0.0278556	-1.76758
IFIT1	0.0334282	-1.60155	C6orf225	0.0160706	-1.77255
JAK2	0.0363478	-1.60258	KRTAP10-5	0.0170766	-1.77611

C3orf25	0.00786974	-1.60261	AGBL2	0.0258052	-1.80999
DLGAP3	0.0034738	-1.60553	SPTLC3	0.00397278	-1.81215
NKX3-2	0.00942769	-1.60586	AX747836	0.00124121	-1.8345
ZNF263	0.0440153	-1.60785	PDE4D	0.0227853	-1.8369
HBM	0.0225791	-1.6087	NFIA	0.0319257	-1.83882
DYTN	0.021317	-1.61031	PLA2R1	0.0385392	-1.83937
TTLL8	0.00711562	-1.6134	COL4A6	0.0234852	-1.84027
OR4A15	0.0102407	-1.84033	C3orf58	0.0234418	-2.15172
C12orf70	0.0427254	-1.84058	SCN7A	0.00669843	-2.2424
PPP1R1B	0.0456885	-1.84318	FLJ41484	0.0423813	-2.24948
OR52K2	0.0251642	-1.86224	SIPA1L2	0.0388468	-2.25607
LEF1	0.0189959	-1.87785	SYT7	0.00680712	-2.27284
RELB	0.00251178	-1.87954	ZSWIM1	0.0193076	-2.28022
ABCA1	0.0478522	-1.88101	ZNF165	0.0322561	-2.29244
PAX8	0.00654786	-1.88673	CHRD1	0.00714013	-2.33939
PLA2G4F	0.00644873	-1.89378	OLFML2A	0.0368902	-2.36171
C7orf53	0.0175538	-1.8955	AL832161	0.0147706	-2.3768
CRTC1	0.00214418	-1.89906	LRRC66	0.023585	-2.3824
PCDHB9	0.0122211	-1.90041	OR2Y1	0.0424392	-2.38439
KILLIN	0.0391846	-1.91338	AX747124	0.0432925	-2.41574
SLC5A3	0.015224	-1.91469	COL13A1	0.00735126	-2.4369
LOC646936	0.0176281	-1.91957	POLR2F	0.0286454	-2.45184
SP5	0.0380915	-1.92488	HOXA10	0.0173438	-2.46894
GPR115	0.0381257	-1.92707	ZNF606	0.0102262	-2.47866
FLJ38717	0.0172665	-1.92854	KISS1	0.0368085	-2.4838
ENST00000380859	0.0172847	-1.93667	FLJ13197	0.0284087	-2.50724
STON1-GTF2A1L	0.0194851	-1.94012	USP9X	0.0205324	-2.54888
CNIH3	0.00835817	-1.94043	PLAT	0.0247061	-2.56001
ASPRV1	0.00875346	-1.94749	CENPM	0.0453517	-2.605
NXPH3	0.0435522	-1.949	SDCBP2	0.00585325	-2.66208
GRAMD1A	0.00926919	-1.97029	KIAA2026	0.0432449	-2.74054
TUB	0.0369388	-1.98155	OR1K1	0.00985021	-2.84986
C12orf53	0.0234272	-1.9904	CILP	0.00252968	-2.94239
LOC100129888	0.0435407	-1.99092	OR10G9	0.0212547	-3.1438
COL4A5	0.0448822	-1.99106	KRTAP13-2	0.0168551	-3.30306
HBA2	0.0324804	-2.00028	CCL11	0.00678786	-4.09672
SCGBL	0.0444717	-2.00533	OR6N1	0.0249156	-5.33171
MATN2	0.0215137	-2.02372	CHST8	0.0475643	-5.62812
PCDHB5	0.0288846	-2.10017	CD274	0.020515	-5.80621
PRRT2	0.0313314	-2.11684	HLA-DRB3	0.0452149	-11.3561
PPARGC1A	0.0307013	-2.13856			

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Supplemental Table 6: Common mRNA expression changes in ASM cells from patients with non-severe or severe asthma after exposure with FCS (2.5 %)

Gene Symbol	Gene Name	Non-Severe Asthma	Severe Asthma
		Microarray (FC)	Microarray (FC)
AFP	Alpha-fetoprotein	13.6 (p < 0.01)	2.2 (p < 0.01)
TACC3	Transforming, acidic coiled-coil containing protein 3	10.3 (p < 0.01)	1.8 (p < 0.01)
ACTG2	Actin, gamma 2, smooth muscle, enteric	7.9 (p < 0.01)	4 (p < 0.01)
PSG5	Pregnancy specific beta-1-glycoprotein 5	5.0 (p < 0.01)	2 (p < 0.01)

SLC7A5	Solute carrier family 7 (amino acid transporter light chain, L system), member 5	4.9 (p < 0.01)	2.3 (p < 0.01)
BLM	Bloom syndrome, RecQ helicase-like	4.5 (p < 0.01)	2 (p < 0.01)
COMP	Cartilage oligomeric matrix protein	4.0 (p < 0.01)	3.8 (p < 0.01)
E2F2	E2F transcription factor 2	3.8 (p < 0.01)	2.2 (p < 0.01)
C7orf69	Chromosome 7 open reading frame 69	3.7 (p < 0.01)	3.4 (p < 0.01)
DONSON	Downstream neighbour of SON	2.7 (p < 0.01)	1.9 (p < 0.01)
FAM183A	Family with sequence similarity 183, member A	2.5 (p < 0.01)	2.4 (p < 0.01)
SLC7A1	Solute carrier family 7 (cationic amino acid transporter, y+ system), member 1	2.1 (p < 0.01)	1.7 (p < 0.01)
DHODH	Dihydroorotate dehydrogenase (quinone)	2.0 (p < 0.01)	1.5 (p < 0.01)
AIFM2	Apoptosis-inducing factor, mitochondrion-associated, 2	1.8 (p < 0.01)	1.6 (p < 0.01)
AGER	Advanced glycosylation end product-specific receptor	-1.8 (p < 0.01)	-1.7 (p < 0.01)
ARRB1	Arrestin, beta 1	-1.9 (p < 0.01)	-1.7 (p < 0.01)
IGKV2D-26	Immunoglobulin kappa variable 2D-26	-2.0 (p < 0.01)	1.7 (p < 0.01)
C14orf138	Methyltransferase like 21D	-2.3 (p < 0.01)	1.9 (p < 0.01)
DCHS1	Dachsous 1	-2.4 (p < 0.01)	-1.6 (p < 0.01)
HBA2	Hemoglobin, alpha 2	-5.8 (p < 0.01)	-2.0 (p < 0.01)

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Supplemental Table 7: mRNAs in non-severe ASM changed in expression following treatment with dexamethasone (10^{-7} M), before stimulation with FCS (2.5 %)

Gene	P value	FC	Gene	P value	FC
EGFL6	0.0224845	9.85829	CR591103	0.0186415	3.12462
SCN2B	0.0284043	9.27174	BC047615	0.00346642	3.08526
ICAM2	0.0145181	8.29318	CPVL	0.0368554	3.05313
CPXM2	0.0152785	8.15319	GLYATL1	0.00971849	3.04558
C3	0.0319192	7.59113	RSPH6A	0.0132347	3.0372
FOS	0.0326376	6.21901	SLC7A2	0.023903	2.97487
CYP7B1	0.00219021	5.83924	PDGFRL	0.0306045	2.96067
MTPP	4.54E-05	5.79869	UNQ6228	0.0132763	2.93464
CYTL1	0.00570101	5.57193	PAPLN	0.00211136	2.92105
AQP1	0.00918987	5.30482	LOC100128343	0.00424291	2.8933
SHC2	0.0229531	5.13233	LOC145783	0.0100316	2.88
C21orf90	0.0235437	4.95966	BEGAIN	0.017262	2.87315
ITM2A	0.0174152	4.79411	MFSD4	0.00521417	2.8624
NEFH	0.0027194	4.44272	OR8S1	0.0127905	2.8326
AF072164	0.0188097	4.34572	LOC100130218	0.0434096	2.83212
FOSB	0.0225566	4.26843	LOC389831	0.0332219	2.80806
EFHB	0.0107258	4.22377	PACSIN1	0.00266411	2.80071
RNF212	0.0147874	3.82536	LOC100130276	0.0300703	2.79567
SLC17A9	0.0150972	3.80832	MGC20647	0.0488981	2.76145
TIAM1	0.0238606	3.67755	DPRX	0.0382461	2.75117
TMEM211	0.00572655	3.66668	IRAK3	0.0407267	2.74829
UNQ3028	0.0173281	3.59575	GRIA3	0.022389	2.74313
DA759359	0.0115304	3.34984	PCDHGB3	0.0286299	2.73755
MYO15A	0.0312493	3.34296	LOC651900	0.0238231	2.72276
LOC440173	3.07E-05	3.28153	E00167	0.00848514	2.69841
FAM184B	1.01E-05	3.23284	COL4A4	0.049413	2.69739
LOC392335	0.00466136	3.22476	LOC253039	0.0100862	2.69359

LOC100293193	0.0125121	3.17947	DC378344	0.0345073	2.68776
C7orf29	0.0252444	3.17744	CACNG7	0.00858398	2.67851
LOC100132368	0.00272669	3.15585	MORN5	0.0141567	2.67189
GLB1L	0.0341164	3.1296	C9orf96	0.00116525	2.66608
ATP13A1	0.0127753	2.6656	CLDN20	0.0246253	2.31225
CD511677	0.0261348	2.65122	RABGAP1	0.0229787	2.30133
RTP1	0.0420071	2.63694	STK31	0.0399854	2.29911
ARID3C	0.041896	2.62656	LOC100130454	0.0115812	2.29336
C1orf187	0.0354729	2.61687	SOX8	0.0171318	2.27971
LOC100133227	0.0143937	2.60259	SLC35D3	0.00676386	2.27606
FAM110B	0.0152177	2.59557	BX104605	0.0389744	2.27346
LOC730020	0.0204273	2.57775	TRAV7	0.0240724	2.26266
C5ORF56	0.0370495	2.5736	LOC100131744	0.0321835	2.22234
LOC728347	0.0206348	2.56986	SLCO2A1	0.0294004	2.21862
LOC100128019	0.0100883	2.5681	FAM27E1	0.0201259	2.21555
FAM177B	0.00951209	2.56634	PUS7L	0.0101342	2.214
DLX6AS	0.0412825	2.55491	LOC652554	0.0366983	2.21147
FLJ39061	0.00800903	2.54887	BEST3	0.00473454	2.20322
FAM43B	0.0118631	2.53446	RAB17	0.00510537	2.19712
KIAA0485	0.00176249	2.53122	TCN1	0.0107946	2.18241
LOC100132428	0.00528968	2.52949	C4orf47	0.0237212	2.18075
LOC100129292	0.00622093	2.52809	BM930849	0.00261303	2.17787
GJA8	0.0331591	2.52799	ASPHD1	0.0165594	2.17764
ZSWIM5	0.00888449	2.52752	FLJ42220	0.0271359	2.17659
KLKB1	0.0147225	2.50704	LOC100129280	0.0191425	2.17518
KIF26A	0.0390661	2.50692	BCORL2	0.0385956	2.1724
UNQ6494	0.0209033	2.49631	PRKCE	0.00770568	2.16966
C6orf15	0.0465234	2.48525	LOC100129048	0.0468273	2.16744
FLJ42351	0.0305779	2.48101	DLEC1	0.00271548	2.16663
NFE2	0.0161531	2.48053	LMO3	0.000173794	2.16137
RFPL1S	0.0338504	2.47875	DUSP9	0.0414663	2.16082
C12orf50	0.0395112	2.47662	SNAR-E	0.0250995	2.15839
BAIAP2L2	0.00879244	2.46611	FOXE3	0.0292607	2.15296
RGPD1	0.018853	2.46436	BLID	0.0348142	2.15038
ZFR2	0.0407983	2.43805	CCDC110	0.0106732	2.14595
ASTN1	0.000239932	2.43532	D21S2088E	0.0204949	2.14226
PHF7	0.0494961	2.42975	TRIM50	0.0066816	2.13884
ADRA1D	0.0061145	2.4213	RPS15AP10	0.0120046	2.13503
LOC100289418	0.0364615	2.42035	GGT8P	0.0301629	2.13128
SMTNL2	0.00837463	2.41454	HOPX	0.0196611	2.12091
LOC100129380	0.0234232	2.40886	LOC100128562	0.0349627	2.11421
TSPY16P	0.0442626	2.38998	X51791	0.0440148	2.11385
LOC729041	0.0452279	2.38739	CPAMD8	0.024003	2.11303
LOC727844	0.00878575	2.38436	RHPN1	0.0111075	2.10808
STAG3	0.0342446	2.38192	SLC17A1	0.0223298	2.10807
TDRD6	0.0285918	2.3769	CU691765	0.00847318	2.10361
LOC100131608	0.00697544	2.37241	ZNF334	0.017776	2.0923
HEPACAM	0.0243969	2.36755	KCNA6	0.00750647	2.08436
PAQR5	0.0217854	2.35641	TTY7	0.0363452	2.07877

LOC100131657	0.0294199	2.35553	CHDH	0.0363727	2.07317
IGHV1-58	0.028446	2.35106	PLEC	0.0471604	2.06796
C6orf103	0.0106071	2.3392	TCL1B	0.000474969	2.06752
TSSK2	0.0305164	2.32101	PCDHB6	0.0410447	2.06634
LOC401561	0.0419644	2.05753	PIP5K1A	0.00247996	1.79475
UTP23	0.0470728	2.04735	EFR3B	0.0449516	1.78646
LOC439950	0.0105374	2.04028	LOC645146	0.0343767	1.78442
PAIP2B	0.00970691	2.03869	RAB6B	0.00298074	1.77689
C2orf83	0.0229905	2.03791	LOC283911	0.0487751	1.77496
QSOX2	0.0364102	2.03504	TREM2	0.0157232	1.77476
MYL7	0.0495107	2.03266	PROL1	0.0126878	1.76938
IL1B	0.00337457	2.01875	LOC100506302	0.0348837	1.76898
CEACAM7	0.00425023	2.01502	C21orf58	0.0105458	1.75753
CTSL	0.0164967	2.01376	LOC100288412	0.0218689	1.74799
C9orf152	0.0159139	2.00518	SERPINB12	0.0229203	1.74729
GPR123	0.0133016	1.98501	KRTAP10-12	0.0272806	1.74726
FHL1	0.0258499	1.97289	KRT17	0.0331374	1.74684
CACNA1I	0.0177944	1.971	tAKR	0.0171625	1.73752
NET1	0.0022538	1.9696	GBX1	0.0416199	1.73375
CEACAM18	0.0115634	1.96952	KU-MEL-3	0.0443896	1.72162
LOC644075	0.044254	1.96929	NECAB1	0.0262466	1.72067
OLFML1	0.00653956	1.96783	PATE2	0.0012714	1.71786
VMO1	0.0138649	1.96773	LOC100131825	0.00739712	1.71753
MAGEA13P	0.0177464	1.96604	LOC283174	0.0368537	1.71613
C8orf67	0.017583	1.96038	SBNO2	0.0185852	1.71416
INHBC	0.0293898	1.95938	FBXO47	0.0303511	1.71365
ARHGAP26	0.0199751	1.9388	ARHGAP27	0.0453791	1.70604
LOC154860	0.0168305	1.93675	RICH2	0.0455539	1.70033
CU691877	0.00895458	1.93611	CLEC4G	0.00484712	1.69154
IQCH	0.0168583	1.9353	SLCO2B1	0.0350121	1.68995
CD244	0.0146865	1.92737	LOC100130354	0.0499476	1.68954
OLFML2B	0.0121324	1.92565	YIPF3	0.0303159	1.68865
LOC731312	0.0306703	1.92023	TSPAN8	0.0252275	1.68416
TMEM174	0.00551208	1.91576	FAM9A	0.0325952	1.67987
ADAM11	0.0208085	1.91515	MAML1	0.0347817	1.67804
KRTAP23-1	0.031784	1.9062	ZNF445	0.0271602	1.67569
CALML4	0.0287723	1.90351	GPR32	0.0350271	1.67274
SLIT2	0.0498067	1.89512	DA666023	0.0430406	1.67235
LOC339568	0.0215577	1.89024	C6orf195	0.0242215	1.66734
OR6K3	0.036102	1.88625	IFNA2	0.00802891	1.6637
LOC100133089	0.0258844	1.87293	LOC100268168	0.025986	1.65787
PM20D1	0.023256	1.86964	NDRG2	0.0442569	1.65369
ND6	0.0371702	1.86015	LOC389033	0.0217474	1.65276
TPH1	0.0307384	1.85883	LOC100130710	0.0299083	1.65148
RIBC2	0.0029066	1.85262	RAB33B	0.00183748	1.6505
LOC651845	0.0149557	1.85036	KLC2	0.021582	1.64417
TBX10	0.0337038	1.83411	PRODH	0.034482	1.63989
DKFZP586B0319	0.000230914	1.82648	DPYSL5	0.00493524	1.63763
LOC100128747	0.0396306	1.82634	PLD3	0.0463304	1.6364

KCNH6	0.00580284	1.81941	AJAP1	0.0302189	1.63436
LOC729479	7.09E-09	1.81097	FAM81A	0.0439556	1.63142
C10orf67	0.0481221	1.79864	POR	0.0430517	1.62831
C1QL4	0.0146332	1.79761	DKFZP434I0714	5.22E-05	1.62454
LOC340017	0.000930056	1.61948	UBE4B	0.000178117	1.49723
HEPH	0.0291872	1.61907	FLJ39051	0.0207371	1.48876
LOC286058	0.0182636	1.61866	ZNF787	0.0249678	1.47737
CHRNA9	0.0052177	1.61802	STK38L	0.0337557	1.47362
LOC729494	0.0430389	1.61712	ELOVL7	0.0355321	1.47254
C22orf32	0.000799759	1.6171	C20orf70	0.0380086	1.47186
KIR3DL2	0.0476025	1.61614	BCL9L	0.0437571	1.46794
FAM159A	0.0271374	1.61373	ANKRD34B	0.0392712	1.46612
SKCG-1	0.0470318	1.61284	IL11RA	0.0240191	1.46109
ZNF423	0.0359766	1.60837	TRIM29	0.0422691	1.4454
MAF	0.0387875	1.60742	TAF10	0.00373934	1.4429
C9ORF147	0.0275508	1.60594	LOC400756	0.0254187	1.43656
KCNV1	7.01E-06	1.60464	ZNF804B	0.0434655	1.43543
LOC100130456	0.0302841	1.60259	LOC284373	0.0469246	1.42999
FREM2	0.0030197	1.59876	AB305825	0.0266727	1.42943
CRISPLD1	0.011944	1.5938	SLC4A11	0.042295	1.42717
KHK	0.0121562	1.58493	GABRA1	0.0420077	1.42689
NYNRIN	0.0421409	1.58189	COL23A1	0.0474148	1.40249
GOLGA6L2	0.0354207	1.5813	COL11A2	0.0323107	1.39073
PNMA5	0.0164874	1.57732	INSL5	0.00294359	1.38953
C21orf94	0.0351323	1.57598	GALR3	0.0198297	1.37979
SYNGR4	0.030568	1.56816	ETFDH	0.0221111	1.37676
DB335107	0.0215759	1.56787	LOC728875	0.0405595	1.37306
FAIM3	0.0296525	1.56452	PR47	0.0320595	1.36965
TPH2	0.0209772	1.56404	UBASH3A	0.0313047	1.36855
CNFN	0.00969497	1.56004	TOR2A	0.0472085	1.36779
RUSC2	0.0337211	1.55193	ATP8B3	0.00121018	1.36592
SHPK	0.0323088	1.55079	BPIL3	0.000446043	1.36341
LOC100130288	0.000151666	1.54996	LOC100128893	0.0465814	1.35989
LOC440419	0.0122559	1.54553	LST-3TM12	0.0271738	1.35959
PAQR6	0.0409996	1.54483	IL1R2	0.0493842	1.35455
UNQ3104	0.0308211	1.54306	BC038732	0.031831	1.3537
KCNG3	0.0411575	1.54151	TYROBP	0.0460439	1.35297
STAP1	0.0350517	1.53383	ATP1A1	0.0346405	1.35051
LOC388564	0.00360479	1.5331	RAD9B	0.00672859	1.34225
CCNYL3	0.000321594	1.53128	ESYT3	0.0193972	1.33735
LOC283516	0.0138627	1.53019	TLE1	0.0289195	1.33728
HSD17B13	0.0106886	1.53015	MYH16	0.00728031	1.33569
SULT4A1	0.0308749	1.52772	MFSD2A	0.0369064	1.33288
LOC407835	0.0293713	1.52761	RTP3	0.0224333	1.33233
FOXS1	0.0486199	1.52565	LOC100133959	0.00243993	1.32764
RFX2	0.0349621	1.52095	C8orf23	0.000126475	1.3212
LRCH4	0.0418985	1.52027	SARS2	0.0177337	1.32111
ACTR3C	0.0155141	1.51954	LOC100129036	0.0258009	1.31652
ZNF768	0.0263864	1.51948	GPR64	0.0227623	1.30967

HLA-DRB1	0.0496063	1.51891	AP1S2	0.0304579	1.30014
ASB5	0.0321277	1.51685	LOC100129449	0.00127755	1.29849
MAST3	0.0400648	1.51681	CV572371	0.0161569	1.29073
KRT81	0.0261695	1.51343	CRISP3	0.0271476	1.27679
RPE65	0.025819	1.27407	TMPRSS11F	0.0456055	-1.09864
PGLYRP4	0.036499	1.26499	LOC100128889	0.0461903	-1.10646
TMEM44	0.0371009	1.26306	ADH6	0.0281598	-1.12724
MUC21	0.0109483	1.26161	ZSCAN23	0.0368113	-1.12983
TAOK2	0.0325985	1.26161	TIFA	0.033797	-1.13958
MED12L	0.00227837	1.25117	RPP21	0.0496079	-1.18122
POLD4	0.045117	1.25011	TTY12	0.0350541	-1.19127
MRPL55	0.0181834	1.24403	PLA2G4D	0.0346843	-1.20836
HRNR	0.0397009	1.24037	LOC339751	0.0406197	-1.21402
LOC100132972	0.00405942	1.23661	LOC100128477	0.0146921	-1.22535
UNC5CL	0.02062	1.23546	IGLV1-44	0.0283777	-1.22657
PAR6B	0.004883	1.23262	ARFGF1	0.0349307	-1.23045
LOC339260	0.0326179	1.22263	ILF2	0.048405	-1.23527
LRRC70	0.00738901	1.19213	ZC3HC1	0.0166388	-1.23692
WDR55	0.0472904	1.18886	FLJ45721	0.0153009	-1.25978
OR5M1	0.00471608	1.18431	TEX264	0.0234891	-1.27281
FABP9	0.0169342	1.18204	RANGRF	0.0377242	-1.27903
PLD5	0.0443132	1.1777	DTX1	0.0257816	-1.28439
LOC728147	0.0428683	1.17184	ARAPI	0.0164053	-1.29282
MYH4	0.0093955	1.16987	PCDH8	0.0449058	-1.29606
MAPK4	0.000413154	1.16784	RPL14	0.0416995	-1.29855
HCG27	0.0431368	1.15153	EIF3K	0.0327072	-1.30717
ANKRD19	0.0121885	1.14466	COPS6	0.0321624	-1.31843
EXOC6B	0.0481348	1.14053	BF733045	0.00167963	-1.32042
CTCFL	0.0174172	1.12855	NDUFA9	0.0469431	-1.32602
FIGLA	0.0305764	1.12619	PKHD1L1	0.0494912	-1.33834
LOC729409	0.0274765	1.10431	MOBP	0.0170939	-1.34063
CYP27C1	0.0249948	1.09287	ANKRD5	0.0147312	-1.36002
RP11-218C14.6	0.0135067	1.07401	CT45A5	0.0367247	-1.36032
ECHDC1	0.0154592	-1.04898	NEUROD6	0.0261876	-1.36043
LOC401445	0.0146153	-1.05782	C6orf70	0.038348	-1.36457
ELF5	0.00800403	-1.06654	TST	0.0247942	-1.365
TAAR3	0.0233372	-1.06767	BIRC8	0.0113783	-1.3714
SPDYE1	0.0464789	-1.06918	CORO1B	0.0295777	-1.37383
LOC100129717	0.00881801	-1.07103	BAI3	0.0260008	-1.37729
PTCHD1	0.0340978	-1.07122	NSFL1C	0.0241619	-1.37979
IRX1	0.00867645	-1.07144	C11orf48	0.0327563	-1.38163
WDR72	0.0261069	-1.07253	PLG	0.0325968	-1.38824
TMC5	0.011084	-1.07276	MRPL16	0.00522512	-1.39013
TTR	0.0334625	-1.08564	CLNS1A	0.0215771	-1.39112
LOC285965	0.0447548	-1.08603	FLJ45872	0.0380872	-1.39117
PRR23A	0.0488675	-1.08614	LOC100134139	0.0292488	-1.39632
C1orf105	0.0067356	-1.09049	POU3F2	0.0238103	-1.40624
CLEC4GP1	0.0400279	-1.09058	OBFC1	0.0350366	-1.4104
SMEK3P	0.0365378	-1.09113	SLC15A1	0.0245224	-1.43041

OR51B4	0.0416735	-1.09296	C6orf164	0.0463458	-1.43086
MS4A8B	0.0287862	-1.09366	MRPL3	0.028822	-1.43289
PDILT	0.0352373	-1.09781	MRPL12	0.0189764	-1.43367
TNFAIP8L2	0.0415126	-1.09822	CTAGE4	0.0318006	-1.43402
C2orf27B	0.0127679	-1.45544	GPX6	0.0300355	-1.6865
COX5A	0.0203388	-1.45682	SDC2	0.0167533	-1.68738
FUBP1	0.0431114	-1.4631	PCIF1	0.0215369	-1.6876
MYRIP	0.0112902	-1.47356	UBA6	0.0366945	-1.69066
ESD	0.0275872	-1.47665	CDA	0.0424501	-1.69099
TP53TG5	0.0219031	-1.47881	SFTPA1	0.0258629	-1.69425
RSBN1L	0.0265224	-1.48784	ZBTB16	0.0187443	-1.69934
NAA38	0.0380492	-1.48932	FASTKD2	0.0284946	-1.69956
TFAM	0.0067683	-1.49219	BEND6	0.0327597	-1.70459
DUOXA2	0.0347074	-1.49359	IGKV1D-16	0.00625904	-1.71148
MGC15705	0.0364406	-1.49375	PPHLN1	0.0244872	-1.71436
TCFL5	0.0375455	-1.51012	ANKRD34A	0.039789	-1.71619
OTOS	0.016899	-1.52633	MRPL48	0.0392436	-1.72211
DCHS2	0.0253431	-1.53272	SFTA2	0.00982478	-1.7225
SDSL	0.0347529	-1.54678	ABCB7	0.0249674	-1.72458
FAM171A2	0.01809	-1.54799	FLJ37798	0.0473696	-1.72555
USP4	0.00211787	-1.54909	AP1M2	0.0366944	-1.7276
SRRD	0.0168979	-1.55799	TYW3	0.0408083	-1.74336
LOC221710	0.000955977	-1.56203	CAPNS2	0.030342	-1.74481
ABCC6P1	0.0251204	-1.56227	UTP6	0.0309216	-1.75103
SLC12A5	0.0273618	-1.56248	LPO	0.0241068	-1.75458
APOM	0.000720936	-1.56283	STIM2	0.0251011	-1.75954
ARMCX6	0.0399629	-1.56553	ZNF420	0.00769476	-1.76578
LOC100132874	0.0348226	-1.57066	KIF18A	0.0449543	-1.77577
TMEM223	0.0349219	-1.57095	AFMID	0.0381957	-1.77832
NMNAT1	0.01655	-1.57297	GLS2	0.0147042	-1.78134
RAB4B	0.00832978	-1.57885	LOC286299	0.0295837	-1.78713
STYXL1	0.0157409	-1.58396	CYP46A1	0.00876744	-1.79645
RP11-403I13.9	0.0445731	-1.58819	C9orf140	0.008924	-1.79783
CCNH	0.0419571	-1.59265	STAT4	0.0388631	-1.79812
ZNF187	0.0347383	-1.5933	NDUFS3	0.0193552	-1.80603
SIX3	0.0414476	-1.60428	PFKFB1	0.0298504	-1.81156
EAPP	0.0376325	-1.60634	SDHB	0.0100156	-1.81744
TPRKB	0.0366331	-1.6117	SFRS3	0.0402468	-1.81989
FLJ34208	0.0476374	-1.62624	C6orf108	0.0133844	-1.83204
NCRNA00160	0.0401118	-1.63183	C16orf74	0.00862393	-1.83255
B3GALT1	0.0303402	-1.63266	NKD2	0.0348643	-1.83698
C1QTNF3	0.0230505	-1.63381	GUCY1A3	0.0460035	-1.847
PCDH12	0.0248739	-1.63423	LECT2	0.0185627	-1.852
ZNF778	0.0497829	-1.63921	MALT1	0.0234089	-1.854
OSBP2	0.0242293	-1.64528	NLRP10	0.0270145	-1.86595
TRIP12	0.0240859	-1.66324	VAV1	0.0308983	-1.87005
LOC391767	0.04405	-1.66609	VLDLR	0.0487244	-1.87175
FLJ16171	0.0478968	-1.66854	GPR20	0.0442183	-1.87301
ZNF607	0.032604	-1.672	HEBP2	0.0494134	-1.87345

DNAH2	0.044721	-1.67467	LOC100131542	0.00693669	-1.87349
RNASEH2B	0.0370652	-1.67546	LOC150568	0.0468719	-1.87393
TIMM44	0.00107801	-1.67683	TMEM60	0.044222	-1.87516
LOC100133224	0.0132813	-1.6781	NOS1AP	0.0143965	-1.87874
PCDHAC1	0.0263291	-1.89643	RASAL2	0.00892127	-2.18315
CDCA3	0.048928	-1.89865	VN1R1	0.0115255	-2.2053
CR607463	0.0242893	-1.90138	FLJ45950	0.011803	-2.20917
CAB39L	0.0375589	-1.90893	ZNF77	0.0490546	-2.21015
PPM1L	0.0465441	-1.90908	DONSON	0.0208259	-2.22181
SAE1	0.00682671	-1.91643	TADA1	0.0134694	-2.22358
RTF1	0.0359386	-1.91712	LOC100335030	0.0401339	-2.23138
EXOC5	0.0436936	-1.91726	PRINS	0.0294081	-2.25029
OR6A2	0.0373859	-1.92839	DCAF15	0.0335145	-2.25425
C6orf150	0.0255693	-1.93105	DEFB128	0.0332666	-2.28786
STOX1	0.04999	-1.93657	CD36	0.0499506	-2.29363
FCRLB	0.0442974	-1.95086	CHN2	0.0129252	-2.29944
MAP6D1	0.0193414	-1.96376	ECEL1	0.00335713	-2.3002
INPP5B	0.00978147	-1.96507	KCNRG	0.00372492	-2.31241
LOC201477	0.0199036	-1.96661	VILL	0.00186831	-2.3235
KCNU1	0.0186844	-1.97358	LPCAT2	0.00257542	-2.32538
ZNF583	0.0306699	-1.97481	INTS8	0.0396496	-2.33448
DCTN3	0.0218782	-1.97551	LOH12CR1	0.0101759	-2.34799
SUV420H1	0.00836247	-1.98208	AVL9	0.00787749	-2.35523
SCAPER	0.0124862	-1.99993	ILKAP	0.0490355	-2.35916
FASTKD3	0.0240289	-2.00515	ACPP	0.0487522	-2.37048
CENPT	0.0388359	-2.00572	NKX6-1	0.0241127	-2.37093
LCE3B	0.0310833	-2.00984	SHC4	0.035591	-2.39069
ZNF266	0.0156899	-2.01565	CR612090	0.0170573	-2.39411
ANGPT4	0.0425998	-2.02442	KCTD14	0.0232979	-2.40181
SLC27A4	0.0225529	-2.02761	LOC374443	0.0418283	-2.41002
STAMBPL1	0.0425329	-2.02813	DSCC1	0.0445259	-2.41409
OPTC	0.031607	-2.03657	DHDDS	0.00260125	-2.44501
LOC144742	0.0334827	-2.0412	OR4K14	0.0404942	-2.49172
LOC440518	0.0242885	-2.04559	FMN2	0.0380029	-2.52012
TACR3	0.00414029	-2.04981	SHMT1	0.0250764	-2.53136
LOC285740	0.0281476	-2.06003	FLJ33360	0.0307568	-2.55112
LOC727900	0.005461	-2.07472	FAM26E	0.0158991	-2.56312
TDO2	0.0217135	-2.07555	INPP4A	0.0300925	-2.57306
ADCY2	0.014242	-2.0777	GAB1	0.0326721	-2.60154
LOC402377	0.027925	-2.08423	ZNF142	0.0167231	-2.61827
ASNSD1	0.0363381	-2.09126	BTBD19	0.0167944	-2.63699
SNORA59B	0.0178836	-2.1052	CEP97	0.00114581	-2.64601
ASCL1	0.0481069	-2.10654	DBF4	0.023114	-2.67845
C7orf65	0.0471925	-2.11276	CCDC89	0.0461908	-2.69102
GPR183	0.0426155	-2.12437	ZNF208	0.0176612	-2.69905
SLC17A3	0.0139654	-2.12506	FAM83D	0.0444039	-2.74292
ZNF430	0.0478224	-2.12801	POLE2	0.0477631	-2.85062
C9orf125	0.012377	-2.13302	PITPNM2	0.00883297	-2.85263
GYG2	0.040705	-2.13839	LOC100290819	0.0115081	-2.857

PRX	0.0117804	-2.13843	TRMT13	0.0397206	-2.86425
ZNF823	0.0235157	-2.14283	LOC552889	0.041421	-2.88387
CASD1	0.0458806	-2.15138	LOC100132658	0.0040329	-2.91454
PECAM1	0.0389329	-2.18241	COPG2	0.0175791	-2.93662
SLC32A1	0.0118395	-2.93921	ZNF700	0.0127506	-3.53078
CB962925	0.0406413	-2.94258	ZNF660	0.0185591	-3.55258
MIR17HG	0.00503779	-2.96279	KCTD16	0.026767	-3.62981
FGD4	0.00460589	-2.97469	KCNK18	0.0288435	-3.67756
KIAA1383	0.0349422	-2.99342	PLEK2	0.031753	-3.67869
SLA	0.0124339	-2.99922	DEPDC1	0.040848	-3.71229
ACSL6	0.00167299	-3.03124	RGAG1	0.00415394	-3.84478
LOC100130176	0.0285593	-3.0509	CXORF67	0.0146076	-3.87188
CXORF28	0.0288017	-3.05342	C18orf54	0.00363234	-3.87393
SPP1	0.0396132	-3.06286	AMBP	0.0107961	-3.92483
OR11H6	0.00187437	-3.09524	ZNF536	0.0430415	-3.94608
MMP16	0.000340787	-3.10346	USF1	0.0150606	-4.00724
ACTR5	0.00655942	-3.10794	HSF2BP	0.0443773	-4.02576
ABHD3	0.013552	-3.11161	OR10AD1	0.0159812	-4.1007
LOC729983	0.0484273	-3.1273	IGLV3-22	0.00322099	-4.15799
ZNF280A	0.00132765	-3.1666	SOX6	0.0124537	-4.36315
LOC646993	0.0471719	-3.20639	SALL1	0.0120465	-5.30655
EPHX4	0.0273351	-3.23078	SYT1	0.00941826	-5.56205
FLVCR1	0.00126143	-3.33992	MLC1	0.0306403	-6.24952
NCOA2	0.027666	-3.3441	LOC100240735	0.00225577	-6.34631
DKK2	0.0139107	-3.43965	UCP2	0.00701355	-6.60541
GPR37	0.011303	-3.46342	LOC100144602	0.0192818	-7.04829
C14orf50	0.00235508	-3.47589	MND1	0.0128997	-7.28275
SNRNP27	0.00145885	-3.50165			

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Supplemental Table 8: mRNAs in severe ASM changed in expression following treatment with dexamethasone (10^{-7} M), before stimulation with FCS (2.5 %)

Gene	P value	FC	Gene	P value	FC
SAE1	0.0293833	30.8509	COL4A4	0.00861455	5.08209
FKBP5	1.75E-06	25.891	GPM6B	0.0108153	4.98446
NUDT22	0.0357378	24.8109	TIMP4	0.00176917	4.81366
TRIP12	0.0336078	22.9363	WFDC1	0.00892648	4.76096
GGT5	0.000192039	18.7544	ENST00000379816	0.000181883	4.72378
RNF216L	0.0330866	18.6092	SORT1	6.23E-05	4.67066
DCTN3	0.0457529	18.0032	MAP2	0.00126428	4.65171
C6orf108	0.027999	17.8552	KCNK6	0.0139623	4.64616
FAM50A	0.0351623	16.5548	FAM83D	0.00107002	4.60643
ZBTB16	0.00307208	16.2454	RNF144B	0.0151476	4.57625
IGFBP2	0.00274071	15.7287	CDIPT	0.0426481	4.56102
PSKH1	0.0467332	15.2121	PTX3	0.000904222	4.49363
FAM107A	0.00653331	14.7382	INHBB	0.0266491	4.43562
ATAD3A	0.0297641	14.0888	SAMHD1	0.000396778	4.24656
ARHGEF17	0.0272866	11.8389	COL8A1	0.000775198	4.22817
RASL11B	0.00210506	11.7764	ERRFI1	8.50E-06	4.21409
ITGA10	0.0019372	11.7542	MT1X	0.000333054	4.20059

CORIN	0.00111639	11.3277	COMP	0.0219541	4.19289
SNRNP27	0.0348066	11.294	MOBKL2B	0.0457821	4.15896
ASNSD1	0.0364774	11.0048	MT1M	0.000145813	4.13462
TULP3	0.036178	10.0216	RELL2	0.0377615	4.11776
OXSM	0.0312126	9.57611	FOXO1	0.00100229	4.10549
SPARCL1	0.000351684	8.71945	IFI44L	0.00160796	4.10517
SDSL	0.0469366	8.65442	FBN2	0.00045236	4.09649
MAOA	4.71E-05	8.65072	ID3	6.30E-05	4.04241
ID1	0.000380069	8.50726	GABBR2	0.00244403	4.04052
MESDC1	0.0343102	8.06953	MT1H	0.000234725	4.02909
LOC100128054	0.000177149	8.04811	GALNTL2	0.00651786	4.02419
CACNB2	5.95E-05	7.71055	CTGF	0.00172937	4.01877
C7orf50	0.0370643	7.28522	LEMD2	0.0426577	3.97875
C13orf15	0.00154918	6.93071	TSC22D3	1.14E-05	3.93961
ADRA1B	0.00508932	6.89065	DUSP1	0.000455907	3.93387
ACTG2	0.00301672	6.88999	NP274062	0.00209432	3.92619
PIGX	0.0233662	6.82221	FAM196A	0.0393619	3.89455
CAPNS2	0.0353172	6.69009	C10orf10	0.0167328	3.89057
ENST00000399893	0.0441167	6.50664	GADD45B	0.000273981	3.84901
RP3-402G11.5	0.0460247	6.50258	SCRG1	0.0429723	3.83316
GPX3	0.000199301	6.36918	NAA50	0.0379298	3.82847
B3GALT2	0.0181628	6.27837	RASAL2	0.0290488	3.81753
SPINT2	0.0154338	6.07396	PER1	0.000613973	3.75164
GLUL	8.88E-06	6.04048	SUSD2	0.000676035	3.70154
OMD	0.00035564	5.82124	MT1A	0.000541503	3.66803
FLJ37798	0.0408714	5.56809	MT1L	0.000574419	3.62364
RASL11A	0.0003236	5.34133	HSPA2	0.0140091	3.58406
FMO2	0.000465789	5.27339	MT1B	0.000402572	3.55976
HSD11B1	0.000577978	5.14342	TAGLN	0.00998786	3.48216
CCK	0.0357132	3.47118	SNORA74B	0.00309697	2.67189
NEXN	0.000673327	3.45126	MYADM	0.00209306	2.64763
MT1E	0.0001665	3.44808	LOC100129104	0.0379053	2.64592
CDH4	0.0278858	3.44373	YIF1B	0.00912271	2.64548
ADAMTS1	0.00316131	3.38848	STMN2	0.0429079	2.63713
USP53	0.00533808	3.37808	GCNT1	0.000525352	2.6321
ALCAM	0.000415557	3.37174	LOC643650	0.0230739	2.61701
TRNP1	0.000101656	3.36238	CTSC	0.0125391	2.59394
C2orf81	0.0471609	3.36115	SRGN	0.0113194	2.5707
ARHGDI3	0.00210903	3.34564	CRISPLD2	0.0144604	2.56427
FMO3	0.0200423	3.33518	OR1N1	0.0213216	2.55823
PRUNE2	0.00292861	3.33047	C13orf1	0.0216735	2.54744
IMPA2	0.00106513	3.32463	CYR61	0.0149191	2.52572
NEDD9	0.00515643	3.31	EDN1	0.00588036	2.5197
FIBIN	0.000939865	3.28638	TMPPE	0.0427563	2.51672
ASTN2	0.000400936	3.28043	RPS6KA2	0.00023674	2.51198
MMD	0.00132298	3.24091	LOC100130433	0.0277066	2.50269
GIYD1	0.020399	3.23461	ACTBL2	0.00608095	2.485
ID4	0.00231071	3.18559	ENDOD1	0.0212248	2.48295
ITIH3	0.0022738	3.15811	TCEAL4	0.000119079	2.47177

ITGA1	3.24E-05	3.07376	C5orf62	0.00726222	2.46289
OXTR	0.0354296	3.0722	NPW	0.00563788	2.46064
GPC4	0.00987549	3.05569	DNAJB4	0.000156835	2.45446
FBXL16	0.0343697	3.05342	CALCOCO2	8.49E-05	2.43369
DHRS3	0.000445054	3.04017	DUSP5	0.0116667	2.42986
AOX1	0.00432776	3.03646	PTPLB	0.00205711	2.42043
FSTL3	0.00037622	2.93921	C19orf36	0.0149041	2.41685
FAM105A	0.000683306	2.93841	DNAJB13	0.0278071	2.41509
CRYAB	1.55E-05	2.90751	CCDC68	0.00352976	2.39002
ACTN4	0.0071471	2.89902	ANPEP	0.0140188	2.37735
ADARB1	0.0169215	2.89265	ENST00000402541	0.0293413	2.37316
PRODH	0.00432797	2.88292	AB072904	0.0134451	2.37294
SYNPO2	0.00245813	2.86211	C6orf145	0.00378103	2.36902
DNAJC6	0.0174459	2.84397	NNMT	0.00245006	2.36272
ANGPTL1	0.000998193	2.84395	ALDH1A1	0.00328273	2.36271
LOC285300	0.00217058	2.83903	LOC100133047	0.00604439	2.34181
LOC729314	0.0169639	2.83454	ABCC3	0.00102183	2.33761
ACTA2	0.000410772	2.82078	KCNS3	0.00568082	2.332
PLA2G2D	0.0402534	2.81014	APOD	0.00605547	2.33058
MCOLN2	0.0285976	2.77763	COL7A1	0.0112029	2.32901
AX747335	0.0368348	2.77485	CDC45L	0.0276114	2.32437
KLF9	2.05E-05	2.74138	ALDH1B1	0.000519545	2.32301
DDAH1	0.0117291	2.74024	MORF4L2	0.000383087	2.31079
DMD	0.0234342	2.73938	DKFZp686L14188	0.0417111	2.30624
THC2512536	0.0194684	2.73473	MYL9	0.0106104	2.29158
F3	0.0171058	2.72834	CST5	0.015985	2.28543
CLIC3	8.50E-05	2.70758	TEX2	0.00158427	2.27641
VGF	0.00536216	2.70377	SYTL4	0.00441957	2.27422
CDC42EP3	0.0062412	2.70142	ADM	0.00242228	2.27403
TXNRD1	0.0387953	2.26557	RABL2B	0.0304508	2.09569
SLC26A6	0.0030031	2.2592	ENST00000391684	0.0256501	2.09526
PDLIM5	0.00641439	2.2577	COL4A1	0.000461987	2.09426
AKAP2	0.0179959	2.25682	TMEM204	0.0051942	2.09185
CPPED1	4.89E-05	2.2549	HIGD1A	0.00200655	2.09133
SPON1	0.00945096	2.24465	PHF17	0.000722498	2.08993
ENST00000390431	0.0157644	2.23779	NDUFS8	0.00451451	2.0872
ACTN3	0.0342007	2.23762	PDLIM7	0.00526287	2.08165
TMEM88B	0.0321441	2.23007	CORO6	0.00796894	2.07296
MT1G	0.000196228	2.2281	BCAT2	2.85E-05	2.0727
EPSTI1	0.0136577	2.22378	TMEM47	0.00940008	2.07108
ATP10A	0.00434919	2.2225	CITED2	0.00632978	2.07009
ENST00000432803	0.0312689	2.22134	MTP18	0.0135319	2.06869
GDNF	0.00269501	2.21216	HPD	0.00988168	2.06862
ELMO3	0.0081153	2.21138	ZDHHC23	0.00079984	2.06565
SERPINE1	0.00445858	2.20768	ST8SIA3	0.029852	2.0624
ARMC8	3.76E-05	2.20455	TCEAL1	0.000157088	2.05244
NUAK2	0.0120228	2.20189	ZCCHC6	0.00543392	2.05179
ITGA5	0.00848922	2.19775	CFL1	0.00803712	2.05126
DIO3OS	0.042181	2.19679	FGD4	0.000368076	2.05079

SLC17A9	0.034645	2.18829	PFN1	0.00109584	2.05005
DAAM2	0.000143499	2.18418	LDHA	0.00034808	2.04853
MYL2	0.0120666	2.18221	PCDH7	0.0217007	2.04643
METTL7A	0.00263576	2.17311	TXNRD2	0.0432052	2.04268
KIAA0408	0.0299493	2.1718	TBX10	0.00410111	2.04007
MYC	0.00142509	2.16842	KLF7	0.00575005	2.03958
BATF3	0.0105979	2.16133	THBS1	0.021792	2.03869
TLN1	0.00532275	2.15891	BAIAP2L2	0.0460722	2.03592
ASPN	0.0186281	2.15457	MCAM	0.0218424	2.03524
THC2499666	0.0167206	2.14283	PHC2	0.000105738	2.03368
PAWR	0.00517323	2.14082	MGP	0.00528811	2.02627
MT2A	0.0311945	2.13848	PRKAG2	0.00351825	2.02516
PTPRJ	0.000263112	2.13055	CD513837	0.00266014	2.02135
PIK3R1	0.00136677	2.12926	THC2631347	0.046344	2.01857
FAM54A	0.00260018	2.12741	SQLE	0.0114418	2.01714
LMOD1	0.000458295	2.12602	PSME3	0.00232806	2.017
CELF5	0.0318365	2.12593	KLF5	0.0425953	2.01452
FZD6	0.000822425	2.12475	GPD1L	0.000976915	2.01167
C7orf69	0.00373963	2.12408	LOC391334	0.00369431	2.01149
GFPT2	4.69E-05	2.12213	ELANE	0.0498767	2.00882
HIF1A	0.00416025	2.11409	LIPN	0.00140853	2.00722
KIR3DP1	0.0497948	2.10917	STK17B	0.00347825	2.00367
LMCD1	0.00163141	2.10535	PPME1	0.0295785	2.00351
MMP24	0.0178651	2.10029	ING2	0.0094718	2.00301
B3GNT5	0.00443162	2.09994	LOC646048	0.00869057	2.00188
LBH	0.00905975	2.09928	C21orf122	0.00156753	1.99988
UQCRC1	0.000891989	2.09869	ODZ2	0.0350808	1.99767
C5orf58	0.00164073	2.09774	CD302	0.00165848	1.99728
RXFP3	0.0482927	2.09724	HPS5	0.00254274	1.98919
ZNF828	0.00708639	1.98828	TUBB6	0.00762767	1.88766
LOC100129536	0.00144269	1.98684	SYDE1	0.0052336	1.88589
TMEM64	0.00237239	1.9828	C1orf133	0.0334995	1.88411
C14orf56	0.045008	1.97702	NOP16	0.00842041	1.88205
MMP15	0.00054594	1.97466	SEPN1	0.0248979	1.88112
DKK1	0.010454	1.97412	LRRC16A	0.0249664	1.88084
PXDN	0.00486628	1.97317	LOC100129324	0.0443199	1.87754
NFXL1	0.0153216	1.97273	COTL1	0.0173498	1.87628
S100A11	0.00305132	1.96806	HSPB1	0.000119283	1.87343
CTPS	0.00736087	1.96543	BRMS1L	0.0346498	1.87094
ACSS1	0.0184484	1.96488	NFYB	0.00202677	1.8689
HNMT	0.00761871	1.96127	AP1M1	0.00307059	1.86845
TG	0.0107898	1.96093	WEE1	0.00145312	1.8668
AX747582	0.00845319	1.95636	MTMR10	0.00716182	1.86373
GRAMD1C	0.00226138	1.95518	C3orf43	0.0321532	1.86292
OR2AG2	0.0162415	1.95096	SSH2	0.00311066	1.86272
SKP2	0.000752515	1.95061	TMEM110	0.00841112	1.86215
CNN1	0.0172085	1.94926	ACTB	0.0198031	1.85667
CDH15	0.00260405	1.94704	TST	0.00656643	1.85402
NOSTRIN	0.0277534	1.9418	TTC32	0.00535253	1.85333

LIMS2	0.0211709	1.93969	TRIM7	0.00482179	1.85086
HMMR	0.0141799	1.93876	ITGBL1	0.00273311	1.84438
RHOBTB3	0.00270591	1.93864	CCNE2	0.032104	1.83894
CDCA4	0.0148564	1.93506	C9orf3	0.000526926	1.83891
TMTC1	0.00778027	1.93196	GPRC5B	0.0202692	1.83612
THC2539563	0.0165637	1.92263	TRAM1	0.0074447	1.83573
TIMM22	0.00145301	1.92005	RGNEF	0.0416197	1.83562
MRM1	0.00286021	1.91949	MMP19	0.0111424	1.83523
YRDC	0.0375096	1.91836	LOC400743	0.0135742	1.83486
POTEF	0.00355557	1.91792	UBL7	0.0245274	1.83452
WDR1	0.00570827	1.91536	PIK3C2A	0.0187197	1.83449
BANF1	0.00283209	1.91218	CORO1B	0.0452685	1.83428
TMCO6	0.000575061	1.91053	TCF19	0.0310745	1.83413
LOC283663	0.0140178	1.90931	TP53I11	0.00659414	1.83377
NCAPH	0.0212179	1.90562	LRRC42	0.00157328	1.83296
WDR37	0.0198291	1.90296	HEG1	0.0123619	1.83219
LOC100129269	0.0413582	1.90202	STOM	0.000282	1.83158
RRAS2	0.00256184	1.90171	EPHB6	0.00255392	1.83116
SDHB	0.00824247	1.90123	SERPINA3	0.013681	1.82793
NLN	0.0209493	1.89853	TGFBR2	0.000128245	1.82327
BRX1	0.0136274	1.89733	OPN3	0.00906124	1.82318
DCXR	0.00131425	1.89688	RRP9	0.00220878	1.82082
TRAPPC1	0.00530354	1.89552	FJX1	0.0189592	1.82023
ASF1B	0.0469889	1.89282	PRICKLE3	0.0409922	1.81724
SNAR-A3	0.0243274	1.89057	GHR	0.0279752	1.81717
ATOH8	0.00349795	1.88994	RASGRP2	0.0109952	1.81531
LAMA2	0.0118164	1.88945	PLA2G4E	0.030434	1.81343
MT1F	0.00309801	1.88839	SYPL2	0.0302298	1.81236
TACC3	0.0102217	1.88794	SEH1L	0.010897	1.81144
LOC100287322	0.00902287	1.8044	MAP1D	0.000839781	1.74591
ZNF236	0.0353299	1.8036	BC031250	0.0412106	1.744
ATP1B1	0.017102	1.80204	VCL	0.0317248	1.74152
SWAP70	0.00601783	1.80193	UBASH3B	0.012351	1.74036
B3GNT2	0.0334527	1.79871	ADAP1	0.0225462	1.73795
ST6GALNAC2	0.023229	1.79789	FBLN5	0.00390276	1.73776
TUBB2A	0.015036	1.79654	TCEAL6	0.0034694	1.73589
ANXA2	0.00206354	1.7958	ENST00000390268	0.038455	1.73299
UXT	0.0114532	1.79375	INMT	0.0243677	1.73051
ANGPT1	0.0403703	1.79187	PRDX6	0.0449437	1.73049
FERMT2	0.00244785	1.79174	ZFP36	0.00078675	1.72922
MYO1E	0.0262112	1.79133	C20orf134	0.00915441	1.72737
FAM83H	0.0116877	1.7882	P704P	0.0207662	1.72579
KLF6	0.00638809	1.78657	LOC100128934	0.0208209	1.72542
DLK2	0.00350101	1.7864	SMARCD2	0.00092234	1.72355
NCL	0.0117862	1.78619	LOC644538	0.00754975	1.72277
MTRR	0.0117564	1.78587	DONSON	0.0126751	1.7221
AFAP1L1	0.0177821	1.78496	ENST00000434415	0.00520962	1.72199
LOC92249	0.000703134	1.78488	SNRPB	0.0285952	1.72109
KIAA1467	0.0121673	1.7841	GSTT2B	0.00788193	1.71968

MRV11	0.0123391	1.78339	COL5A3	0.0130896	1.71903
ZYX	0.0468308	1.78334	SCAF1	0.0196109	1.71662
ITGA4	0.00513756	1.78021	EARS2	0.0313925	1.71609
LOC100290344	0.00155041	1.77948	MFSD6	0.0161656	1.71476
THC2715632	0.0124454	1.77828	ROR1	0.00506866	1.71476
MGLL	0.0364153	1.77693	ARSK	2.29E-05	1.71455
PUS7	0.0040995	1.77537	APOOL	0.000623268	1.71439
STBD1	0.021483	1.77418	C10orf114	0.0234086	1.71071
SEC14L2	0.0127481	1.77342	CDC42SE2	0.00277149	1.71053
BF515046	0.0214467	1.76782	F12	0.0433054	1.70921
CCDC107	0.00458112	1.76646	PKDCC	0.00412631	1.70851
CTHRC1	0.00325109	1.76522	CCDC69	0.00833739	1.70729
IRS2	4.84E-05	1.76474	ANXA2P3	0.00434377	1.70558
TMEM2	0.016153	1.76296	TAS2R9	0.0452797	1.70384
MFAP5	0.0356614	1.76125	NID1	0.0219034	1.70331
DA567289	0.0184802	1.7595	ARSJ	0.0327042	1.7027
PDLIM1	0.0171536	1.75844	AKAP7	0.00878199	1.70249
SHBG	0.0016997	1.7583	CDK2AP2	0.0234804	1.70193
TACC1	0.00582566	1.75689	C1orf152	0.00119424	1.70175
TPM2	0.00212428	1.75592	SCAMP2	0.0146757	1.7017
COQ2	0.0452233	1.75548	ELN	0.0214547	1.70075
CHST2	0.0152059	1.755	RSPO1	0.0343332	1.70073
PPARG	0.0262484	1.75222	IL1F10	0.0181831	1.70026
HIP1	0.0231741	1.74858	MCM6	0.0049255	1.69953
SYT2	0.0267923	1.74762	LDLR	0.0377244	1.69872
IL18RAP	0.00556959	1.74752	ACER1	0.0150161	1.69818
ARHGAP29	0.00878362	1.7473	C7orf40	0.0137765	1.69793
HIPK2	0.00966278	1.7471	PRRG1	0.00591503	1.69748
CNN2	0.00647049	1.747	MYL12A	0.0156914	1.69725
ECE2	0.0209534	1.69643	TPM1	0.00213395	1.6531
MYL6	0.0117597	1.6956	TLE1	0.00573661	1.65247
PEBP4	0.0364478	1.69473	OR6K2	0.0421191	1.64882
TCEAL2	0.00862442	1.69264	STON1	0.0195369	1.64803
PARVB	0.0271266	1.6916	NAA10	0.00421202	1.64523
UAP1	0.00442433	1.69151	SPOCD1	0.00964886	1.64475
PRPF3	0.0238776	1.69001	SNAPC2	0.028432	1.6437
PLSCR4	0.000556663	1.68971	ENPP4	0.000663693	1.6429
LOC643371	0.0132777	1.68945	DUSP23	0.045555	1.6415
LOC389333	0.0162535	1.68786	FARSB	0.00319796	1.64021
TCIRG1	0.0136844	1.68759	MUC1	0.00419683	1.6393
FABP5	0.00419207	1.68682	LOC100128714	0.000836864	1.639
IGF2	0.00430152	1.68655	FGF1	0.0434016	1.6388
KLHDC3	0.0243576	1.68567	HR	0.0105812	1.63844
ANO9	0.021372	1.68523	CLTB	0.00141911	1.63841
FKBP1B	0.00211799	1.68503	MTSS1L	0.00292838	1.63676
AX746533	0.0395465	1.68485	ADAM19	0.00985981	1.63592
UBE2N	0.00999596	1.68317	AK131288	0.00651412	1.63472
POTEE	0.031172	1.68208	OR2M7	0.029241	1.63449
CENPVL1	0.0146573	1.67962	SLC25A32	0.00479982	1.63413

SRPX	0.00036694	1.67958	LRRC59	0.00615603	1.63396
SHMT1	0.0280122	1.6767	SLC16A3	0.0236032	1.63375
POTEKP	0.0352168	1.6765	PALLD	0.0120431	1.63368
FAM114A2	0.0295041	1.67537	HMHB1	0.0419993	1.63363
DNAJC17	0.00170186	1.67395	PHOSPHO2	0.0247257	1.63363
CD3EAP	0.00513222	1.67367	NANOS1	0.0428206	1.63205
OR10P1	0.0134752	1.67212	MSRB3	0.00357306	1.63186
BC018676	0.00151845	1.6721	DCT	0.00721748	1.63157
C9orf29	0.0294436	1.67129	DSTN	0.00352243	1.6293
KIF17	0.00089881	1.67089	GRAMD3	0.0327261	1.62699
DHCR24	0.0161305	1.66965	FAM198B	0.00097895	1.62566
GPR173	0.0371352	1.66959	CLDN7	0.0322532	1.62537
SHOX	0.00212326	1.66851	RUNX2	0.0268564	1.62489
PCGF5	0.00245105	1.66764	LPIN3	0.0131145	1.62462
ACTN1	0.031856	1.66748	GCHFR	0.0276693	1.6245
CD14	0.00424562	1.66682	CHST15	0.0367848	1.62196
LSM12	0.00186415	1.66515	KRTAP19-8	0.0208002	1.62194
KBTBD11	0.00753394	1.664	DKFZp667E0512	0.0341119	1.62155
ENST00000374441	0.00490774	1.66385	PIP4K2C	0.0176893	1.62
TSEN2	0.00079817	1.66345	CSRP1	0.029417	1.61974
RAI14	0.00725905	1.662	LOC400950	0.0216949	1.61924
KIAA0114	0.00321781	1.66087	OIP5	0.0490564	1.61912
CRHR1	0.0348277	1.66061	TUBA1B	0.0303507	1.61872
SRPX2	0.00241227	1.6606	TIMM16	0.0086793	1.61744
ZRANB1	0.0239837	1.65782	FLNA	0.02978	1.61702
C10orf96	0.0121685	1.65765	PAPSS2	0.0375943	1.61627
NPAS1	0.00104748	1.65599	CGREF1	0.016036	1.61571
COMTD1	0.029183	1.65516	ANXA2P1	0.0195384	1.61496
NRAS	0.00106167	1.655	SERTAD3	0.0146449	1.61403
PNO1	0.0465145	1.61377	SEMA7A	0.00883937	1.57502
SLC30A6	0.000340055	1.61364	BARHL1	0.0389394	1.57497
CYTH3	0.0353411	1.61233	TMEM150A	0.0183261	1.57445
AK123701	0.0279208	1.61074	C6orf150	0.00443606	1.57318
PPP1R13L	0.00364898	1.61034	ATF6	0.0114363	1.57296
AHCTF1	0.018066	1.61025	CYP7B1	0.0120147	1.5722
SCHIP1	0.00872129	1.60964	CPNE7	0.0276006	1.57007
REEP4	0.000543764	1.606	TGIF1	0.0178419	1.57001
ANXA6	0.0339389	1.60521	ZHX3	4.46E-05	1.56993
PRR21	0.0248492	1.6049	AMOTL2	0.0244798	1.56989
TLR4	0.0493724	1.60452	EID3	0.0193207	1.56988
COL4A2	0.00176503	1.60439	GSTT2	0.00137581	1.5697
SSB	0.00617313	1.60385	C5orf25	0.000714449	1.569
COQ3	0.00687164	1.60221	ACSL1	0.00946129	1.56861
PPIAL4A	0.0081133	1.6016	TIPARP	0.000641681	1.56846
FKBP11	0.0163706	1.60132	CBX8	0.0430133	1.56843
ARL4A	0.0302989	1.60103	ARNT2	0.015852	1.56725
ATP13A2	0.0139831	1.59907	TNFRSF12A	0.0182899	1.56607
PVT1	0.00470682	1.5987	LOC646821	0.0265603	1.56384
KLK4	0.0402675	1.59748	STAG3L1	0.00289827	1.56379

USP4	0.0184042	1.59571	AQP8	0.0249671	1.56347
PI3	0.00274427	1.59518	CD200	0.0323791	1.56275
SH3PXD2B	0.0141415	1.59259	H2AFJ	0.0333066	1.56207
UCHL3	0.0110704	1.59221	RBM14	0.000551019	1.55969
MYBBP1A	0.0301502	1.59204	NOL6	0.0114674	1.55958
RAD1	0.0110491	1.59007	RASL10B	0.0107211	1.55778
LHX1	0.0471444	1.58945	C1QTNF5	0.0315733	1.55643
IMPAD1	0.00244333	1.58851	UGP2	0.00902641	1.55609
COL9A3	0.00837941	1.58652	PDSS1	0.0316673	1.55577
NOC3L	0.00583487	1.58609	EEF1E1	0.00844804	1.55479
LOC401557	0.0314518	1.58577	HLA-DPB2	0.0326049	1.55424
KRTAP9L1	0.0296681	1.58468	EYA2	0.0272598	1.55416
REEP1	0.00535273	1.58398	CYP1B1	0.00408749	1.55401
CAV1	0.00317772	1.58333	C8orf85	0.0140055	1.55387
EMP1	0.0344204	1.5828	PTPDC1	0.00293183	1.55347
CLOCK	0.000948691	1.5826	SGK269	0.0157111	1.55303
KANK1	0.0308752	1.58206	RRAS	0.00576408	1.55272
TMOD2	0.0217739	1.58025	UBR3	0.0175791	1.55249
INHBA	0.0185378	1.57967	HHEX	0.0117605	1.5524
SLC35D1	0.00461209	1.57963	VKORC1L1	0.00456739	1.55211
BCL7A	0.0212591	1.57923	PTPLA	0.00786451	1.54888
EIF5A	0.0238916	1.57799	MPP3	0.0390802	1.54885
DHX35	0.00544215	1.5779	RAB5B	0.0120912	1.54728
MSI1	0.00250336	1.57778	CR615613	0.0251841	1.54671
ILK	0.0227481	1.5769	SGTB	0.0169976	1.54639
SLC19A2	0.0336608	1.57651	NCRNA00181	0.011972	1.54357
AGPAT9	0.0457566	1.57627	DIO2	0.0036974	1.54344
GCM1	0.0245097	1.57604	NOP2	0.0178898	1.54297
TEAD3	0.00843151	1.57519	ENST00000395453	0.027586	1.54276
STC2	0.00428328	1.54241	ZNF485	0.0316016	1.52082
DPM2	0.00915178	1.54166	RUNX1	0.0461004	1.52043
OR8B8	0.0196988	1.54159	FAM127B	0.0339392	1.51995
ENST00000342688	0.00519207	1.54061	TWIST2	0.00200376	1.51932
ZBTB7A	0.00788696	1.53949	NAP1L1	0.0121582	1.51875
ZDHHC12	0.00684217	1.53934	TCTE1	0.00719065	1.51819
MPI	0.0238554	1.53787	SH3GL1P3	0.0234892	1.5177
ZWINT	0.0326763	1.53679	RAD51	0.038863	1.51761
SP140L	0.00290213	1.53648	SFPQ	0.000477149	1.51678
D13069	0.00136304	1.53621	ANG	0.00971459	1.51637
LOC401561	0.00702947	1.53594	IGF2BP2	1.69E-05	1.51616
CABIN1	0.00113746	1.53584	C7orf51	0.0468031	1.51615
ACTR3	0.018905	1.53539	IRS1	0.0147083	1.51522
ADAMTS9	0.0182146	1.53538	LOC340515	0.0175562	1.51522
MED8	0.00138042	1.535	REG3A	0.0306929	1.51503
NAA11	0.00473761	1.53474	BLM	0.0474108	1.5138
URB2	0.001694	1.53426	CHCHD7	0.00481288	1.51368
LOC344382	0.0182254	1.53405	FAM166A	0.0205222	1.51338
INHBC	0.00960291	1.53377	REEP3	0.0446637	1.5132
LCE1A	0.00423117	1.53363	TNFSF13	0.0360986	1.51284

TGFB111	0.00153039	1.53354	FN3K	0.00428976	1.51276
GCAT	0.0438546	1.53285	DDX21	0.0144562	1.51194
ENST00000377039	0.0358711	1.53251	SFRS7	0.0389748	1.51147
LOC100009676	0.021047	1.53169	PTS	0.0261883	1.51129
UFSP1	0.00677257	1.53131	ENST00000399730	0.00474636	1.50957
CCND3	0.00263342	1.53086	GRRP1	0.0384513	1.50939
C7orf11	0.00371683	1.53067	SAR1B	0.0164026	1.50891
HPDL	0.0359797	1.53031	ENST00000366413	0.0260504	1.50808
CFLAR	0.0157431	1.53002	NDUFS3	0.0251057	1.50776
OR5L2	0.00382358	1.52988	LOC646576	0.0473773	1.50687
PEA15	0.0158775	1.52966	SAMD4A	0.00270771	1.50563
SGMS2	0.0273588	1.52934	SBDS	0.000455425	1.50489
ENST00000376775	0.0351426	1.52884	LOC128322	0.00954339	1.50443
CDA	2.40E-06	1.52856	TJP2	0.00470322	1.50322
SELS	0.00793408	1.52767	AMD1	0.0163402	1.5032
SPTBN2	0.00634065	1.52673	ERGIC1	0.0131549	1.50037
RABL3	0.0292641	1.52611	DUS2L	0.0306426	1.50003
PTPN18	0.00392213	1.52604	SVIL	3.91E-05	-1.50118
TAF7	0.0244297	1.52481	ENST00000371488	0.018129	-1.50177
PEMT	0.0286748	1.52465	LOC401286	0.0406118	-1.50186
RNGTT	0.00267116	1.52432	PGPEP1	0.00642076	-1.50262
MRPL15	0.00598968	1.52378	LOC84989	0.0255584	-1.50326
PRDM13	0.00945784	1.52289	DSTYK	9.62E-06	-1.50372
TXNIP	0.0110062	1.52264	CDYL	0.0144349	-1.50388
LOC400236	0.0432812	1.52218	CLU	0.0117427	-1.50485
TTC13	0.021895	1.52208	DZIP1	0.0104316	-1.50724
FAM199X	0.0212841	1.52172	KLRG1	0.00584876	-1.50774
RHOB	0.0354701	1.52138	ARHGEF2	0.00433198	-1.50825
TCEAL5	0.0154601	1.52098	JMJD7-PLA2G4B	0.0081886	-1.51007
TRIM22	0.00519648	-1.51009	PAN3	0.0467904	-1.53088
SPATA4	0.0411625	-1.51087	PARP14	0.00361116	-1.53115
FRAT1	0.0170407	-1.51164	CBR3	0.0313695	-1.53126
PSIP1	0.0214491	-1.51176	SLC35E2	0.00766206	-1.53148
UNK	0.00355972	-1.51186	EGFL8	0.0162427	-1.53151
PBX2	0.0399724	-1.51247	C9orf140	0.00410175	-1.53226
NFKBIE	0.0149794	-1.51322	PNPLA7	0.0215441	-1.53357
CCDC102A	0.0326922	-1.51323	PAFAH1B3	0.0206772	-1.53383
ENST00000432854	0.00592678	-1.51355	FAM107B	0.0301075	-1.53401
C20orf177	0.0110692	-1.51368	TMEM121	0.00322258	-1.53422
SNX30	0.0259454	-1.51489	LNP1	0.0368891	-1.53479
NNAT	0.04094	-1.51674	OR4A15	0.0372018	-1.53544
ZMAT3	0.0295509	-1.51674	TP53BP1	0.00357083	-1.53581
ARID5A	0.0188059	-1.51712	DST	0.0182532	-1.53628
LOC100132774	0.0129553	-1.51754	DPP4	0.00596302	-1.53686
LOC100133131	0.00438744	-1.51788	ZNF780B	0.0053232	-1.53694
SLC16A4	0.0245246	-1.518	GPT2	0.0324714	-1.5375
TCF4	0.00422215	-1.51811	RPS6KA3	0.00285817	-1.53772
PSD3	0.0212434	-1.51812	CTSLL2	0.0220518	-1.53788
PRKACB	0.00126809	-1.5183	C1orf96	0.00799625	-1.53825

LOC100130009	0.00414006	-1.51882	DHFRL1	0.00437084	-1.53929
SCARA3	0.00126832	-1.51937	C6orf225	0.043217	-1.53997
ZNF74	0.0418136	-1.5196	LIMA1	0.00164674	-1.54037
SLC45A3	0.0259792	-1.51975	GRAMD4	0.00123944	-1.54154
CTNNBIP1	0.000725854	-1.52066	FANCE	0.00215588	-1.5421
UTS2R	0.0194121	-1.52094	LRRC2	0.00240516	-1.5426
ENST00000439203	0.000861267	-1.52145	PELI1	0.0270355	-1.54307
INSIG1	0.0327888	-1.52223	HCFC1R1	0.00402001	-1.54366
TTLL8	0.0119498	-1.52252	LOC100128416	0.0384879	-1.54451
BAGE4	0.00793398	-1.52366	TIA1	0.0232977	-1.54501
GAMT	0.0020288	-1.52378	USP27X	0.038469	-1.54513
C9orf7	0.00158852	-1.52455	PIK3IP1	0.00770499	-1.54543
MXI1	0.00832321	-1.525	AUTS2	0.010285	-1.54547
ARHGEF6	0.0310599	-1.52589	SLC9A9	0.0108561	-1.54589
KLF11	0.00235205	-1.52623	ZMIZ1	0.00322675	-1.54876
TGFBR3	0.0243335	-1.5267	PLK2	0.0195957	-1.5492
CRBN	0.0141834	-1.52675	ZNRF1	0.00954571	-1.55056
WWC2	0.0451787	-1.52695	STAP2	0.00308432	-1.55117
ACAD11	0.0476931	-1.52701	FES	0.0247493	-1.55169
EPHB2	0.0168057	-1.52702	CARD17	0.0322264	-1.5533
SESN2	0.00128195	-1.52719	RFX7	0.0334087	-1.55383
NISCH	0.0268881	-1.52724	HMGB3L1	0.0115716	-1.55489
KIAA0495	0.0382779	-1.52807	DDAH2	7.24E-05	-1.55491
OCIAD2	0.0145437	-1.52815	PGM5	0.0217452	-1.55499
ADNP	0.00143483	-1.52851	FAM125B	0.00439971	-1.55544
BICC1	0.00733564	-1.52852	LOC283861	0.0216603	-1.55704
OSBPL7	0.00569432	-1.52998	MOXD1	0.026759	-1.55709
FHOD3	0.026902	-1.53069	LIPT1	0.00546301	-1.55854
FYCO1	0.0129197	-1.53088	C6orf134	0.00811826	-1.55858
FAM171A1	0.000119603	-1.55906	CIC	0.00282024	-1.58387
LOC441795	0.0121469	-1.55918	SACS	0.00191987	-1.58394
IGF2R	0.00105074	-1.55968	PRNP	0.00141919	-1.58435
SSX2IP	0.0464588	-1.55989	HSPA12A	0.0109366	-1.58531
TSHZ3	0.00713993	-1.5604	FZD1	0.0252886	-1.5856
CAND2	0.0274221	-1.56079	AX747640	0.00455084	-1.58625
LOC285629	0.0107335	-1.56239	TBC1D2B	0.00222875	-1.58926
HGF	0.00067535	-1.56261	RN5-8S1	0.000105192	-1.59011
NEK10	0.0101658	-1.56262	ARHGAP22	0.0183132	-1.59129
C6orf154	0.0446415	-1.56294	CDKN1A	0.0118619	-1.59219
PTPN13	0.00818166	-1.5656	SPEG	0.0322934	-1.59256
Sep-05	0.00748971	-1.56627	EXT1	0.0124141	-1.59257
OAF	0.0179696	-1.56655	NCRNA00219	0.00648519	-1.5932
EPAS1	0.00121363	-1.56688	KIAA0895L	0.0279553	-1.59322
PGAP1	0.00732748	-1.56794	EYA4	0.0172744	-1.59475
VPS8	0.0466266	-1.56849	PTPRU	0.000925544	-1.59492
PABPC4L	0.0200126	-1.56891	ZNF561	0.0120664	-1.59584
JMY	0.00957186	-1.56926	CFB	0.0492871	-1.59601
MARCKS	0.0220441	-1.5695	HIST1H3J	0.0285744	-1.59676
PCSK4	0.031863	-1.56987	C2orf60	0.0015856	-1.59832

CPZ	0.0060581	-1.57003	TMEFF2	0.0168481	-1.59894
BACH2	0.0386525	-1.57006	LRRC49	0.00267242	-1.60017
NR2F1	0.0252862	-1.57035	PTEN	0.013739	-1.60028
C16orf74	0.0033656	-1.57048	FGF7	0.000138676	-1.60135
LOC554202	0.00469693	-1.57097	CCDC142	0.0156004	-1.60154
EYA1	0.030475	-1.57168	SLC4A4	0.0385978	-1.60178
RFX2	0.00724667	-1.57231	SLC25A29	0.000582752	-1.60207
ZBTB2	0.0272753	-1.57372	IRF2BP2	0.0281924	-1.60393
SLC27A1	0.000601986	-1.57382	C20orf108	0.000778739	-1.604
NTNG2	0.0457537	-1.57412	ANKDD1A	0.00119112	-1.6064
PLEKHN1	0.0381408	-1.57421	BCL9	0.0212728	-1.60678
TIGD1	0.00327985	-1.57507	XPC	0.0384741	-1.60856
C5orf41	0.00619559	-1.57538	MASTL	0.0423368	-1.60881
HIST1H3A	0.00412538	-1.57599	LRRN4CL	0.00487135	-1.60944
LOC375010	0.0383873	-1.57721	BCL2	0.0159714	-1.61054
THAP11	0.010318	-1.57746	KCNE4	0.0201001	-1.61136
HIST1H4B	0.0118353	-1.57778	GLIS2	0.0114409	-1.61181
LOC286161	0.0284388	-1.57806	LONP1	0.0433688	-1.61228
GATAD2B	0.0226438	-1.57909	ABCA7	0.00567939	-1.61241
CCR10	0.00229571	-1.57911	TCF3	0.036804	-1.61336
ERV3	0.0368821	-1.57935	HIST1H3E	0.0233539	-1.61351
IQCD	0.039425	-1.57941	LOC100287428	0.0151964	-1.61445
C14orf37	0.0492402	-1.57951	AK058117	0.0352799	-1.61696
TMEM66	0.01153	-1.57965	HECTD1	0.00289452	-1.61715
LOC100170939	0.0219398	-1.57981	ENST00000367596	0.01976	-1.61751
PCSK5	0.0103333	-1.58082	TUBA4A	0.00111482	-1.61849
SASH1	0.000198955	-1.58196	TOB1	0.000268462	-1.62097
LOC388242	0.0115597	-1.58197	AKD1	0.00166826	-1.62342
SLC37A2	0.0338481	-1.582	PMEPA1	0.0225467	-1.62404
BC043411	0.00463014	-1.62515	MAST4	0.000717315	-1.65826
SOD2	0.0109965	-1.6255	KRTAP4-11	0.0335412	-1.65855
C7orf61	0.00337805	-1.62561	HSPB8	0.00368304	-1.65872
SH3BGR	0.0245866	-1.62585	C8orf47	0.0133066	-1.66033
CD44	0.00616166	-1.62596	DAB2IP	0.0318262	-1.66035
HIST1H4K	0.0158534	-1.62666	HIST2H4B	0.0129093	-1.66159
PPL	0.0396414	-1.62749	PER3	0.0290996	-1.66177
RAPGEF6	0.0499704	-1.62765	C8orf31	0.0211327	-1.662
IFI16	0.00541607	-1.62783	RHOJ	0.0338931	-1.66223
SNHG7	0.0188353	-1.62897	C4orf46	0.0307614	-1.66389
CCNG1	0.013129	-1.63104	TSHZ1	0.0283001	-1.66502
PTPRK	0.00463236	-1.63175	NBEA	0.0017485	-1.66531
CR620599	0.000494353	-1.63331	FRMD4A	0.0354197	-1.66574
SOCS1	0.00656085	-1.63468	PGF	0.0148908	-1.66606
CA11	0.0232012	-1.63497	CASK	0.0059835	-1.66618
BTG2	0.00872136	-1.63624	COLEC12	0.00566187	-1.66626
NAALADL2	0.00430369	-1.6368	GALNT12	0.0414699	-1.66682
RPA4	0.0185263	-1.63774	PBXIP1	0.0114431	-1.66771
AGAP1	0.0029188	-1.64008	CFP	0.000356378	-1.66785
AX747706	0.0042293	-1.64027	PCDHB9	0.0282593	-1.66842

C21orf49	0.00910901	-1.64131	CARD10	0.0262575	-1.66969
SPATA13	0.00279529	-1.64136	PTPRS	0.00361604	-1.66977
LOXL1	0.0224028	-1.64156	XAF1	0.0117507	-1.67157
ACCN2	0.0059297	-1.64164	KIAA1549	0.0163473	-1.67198
KRBA2	0.026965	-1.64187	KCNAB3	0.0381156	-1.67238
C21orf66	0.00185886	-1.64204	METRNL	0.000238882	-1.67329
ZNF667	0.00527452	-1.64351	CEP57	0.00714972	-1.67499
PGBD2	0.0168251	-1.64447	ANGPTL6	0.043869	-1.67641
LOC729175	0.00211095	-1.64581	DTWD1	0.00758613	-1.67643
AGT	0.027293	-1.64589	GRASP	0.00193064	-1.67698
TBX3	0.0172112	-1.64615	DYNLRB2	0.0249205	-1.67826
SCARNA9	0.00113747	-1.64706	MAP1A	0.0123902	-1.67888
IFT88	0.00195007	-1.64851	FAM46A	0.0405706	-1.67908
IFIT3	0.00695599	-1.64925	CENPL	0.0161494	-1.67969
IFI30	0.00140305	-1.64944	AHCYL2	0.0175128	-1.68008
P4HA2	8.84E-05	-1.65031	ADAL	0.0172775	-1.68042
LOC100132891	0.0117061	-1.6522	NDRG3	0.0213009	-1.68045
UCN	0.0135158	-1.65232	TNIK	0.0298829	-1.68131
LOC644925	0.0017931	-1.65258	NFE2L3	0.0145034	-1.68365
ADSSL1	0.042551	-1.65277	NEK11	0.0299512	-1.68536
SYNJ2	0.00265125	-1.65338	SLC43A3	0.0208433	-1.68536
MFAP4	0.00772648	-1.65375	KLF3	0.0179288	-1.68711
PHACTR1	0.0114834	-1.65397	VAMP4	0.0047297	-1.68747
NAF1	0.0186522	-1.65402	GPRASP2	0.00117835	-1.6894
PLCB1	0.00486583	-1.65479	ZCCHC14	0.00195396	-1.69103
BTN3A1	0.0133041	-1.65555	SP4	0.0210173	-1.69166
TBX4	0.0105486	-1.65566	CIDEA	0.00620517	-1.69308
CLSTN3	0.00490672	-1.65616	TNFRSF10B	0.00269714	-1.69333
FAM20A	0.0120662	-1.65618	CYS1	0.00652154	-1.69385
ZMYM3	0.006019	-1.69545	LOC100291791	0.0212388	-1.75355
ANKRD36	0.0172586	-1.69602	PRR3	0.0274573	-1.75369
LHFPL2	0.00110919	-1.69722	ZNF497	0.00480268	-1.75486
FAM155A	0.00346109	-1.69912	MKL2	0.0175421	-1.75511
ARHGEF9	0.0041324	-1.69967	SCN2A	0.0101107	-1.75649
RNF146	0.00551771	-1.69985	NAB1	0.00264615	-1.7566
LOC729595	0.0330492	-1.70081	PRR19	0.0113106	-1.75719
BATF2	0.0353445	-1.70138	VPS37D	0.00121596	-1.75867
MYST2	0.0356337	-1.70279	SORL1	0.0224045	-1.7594
SOX9	0.0398713	-1.70363	MTHFR	0.00074491	-1.76002
THC2620530	0.0178753	-1.70371	SOCS2	0.0293658	-1.76019
LOC100049716	0.0151159	-1.70412	TMEFF1	0.00745907	-1.76084
SLC5A12	0.0490626	-1.70456	RGS10	0.0165217	-1.76131
TEF	0.024159	-1.70601	ZNF653	0.0242651	-1.76346
PFN4	0.00382213	-1.70605	FAM161A	0.00469633	-1.76665
SEC31B	0.000431119	-1.70807	PRTFDC1	0.00643595	-1.7693
NINL	0.00421214	-1.70862	PURG	0.0397532	-1.77074
ING4	0.00133649	-1.71	SELENBP1	0.016457	-1.7712
EDA2R	0.00952513	-1.71049	STARD10	0.00278286	-1.77196
C3orf65	0.0024727	-1.71099	TIMP3	0.00502799	-1.77224

MSX2P1	0.00712371	-1.71314	LOC286367	0.0132135	-1.77311
CARD16	0.0202562	-1.7135	KRTAP10-5	0.017222	-1.7738
THC2655610	0.0036342	-1.71357	RASGEF1A	0.0370069	-1.77429
C20orf132	0.0321411	-1.71594	ANKIB1	0.0140934	-1.77583
BAI2	0.00268282	-1.7167	TMEM88	0.0434898	-1.77783
RASSF5	0.0283061	-1.71883	FCGR2A	0.0441334	-1.77799
KRTAP12-1	0.0136459	-1.71975	SHC2	0.00740202	-1.77841
PPAP2C	0.0107034	-1.72071	SOCS3	0.0226194	-1.77916
LOC100130819	0.00473786	-1.72083	PDE4D	0.0275595	-1.77955
RALGDS	3.43E-05	-1.72118	IFIT2	0.00668926	-1.78029
CASP1	0.0249651	-1.72716	LIF	0.0221744	-1.78151
CAMK4	0.0449033	-1.72745	SERPINE2	0.0027427	-1.78308
LUZP1	0.0281258	-1.72824	MCM7	0.00708165	-1.78447
SSC5D	0.00873221	-1.72928	MYLIP	0.0372086	-1.78476
POU6F1	0.0331716	-1.72947	DLG3	0.00784381	-1.78483
L3MBTL	0.0425477	-1.73008	FAM129A	0.0186803	-1.78573
ENST00000380683	0.0305764	-1.73058	PTPN4	0.013027	-1.78616
IFI44	0.00135842	-1.734	C20orf96	0.0283764	-1.78686
PRKCE	0.0149573	-1.7389	RIBC1	0.0379209	-1.78741
POU2F1	0.0011445	-1.73912	JMJD7	0.0107785	-1.78951
TRIM5	0.000905955	-1.7399	PHKG2	0.000605278	-1.79094
IFFO1	0.000895382	-1.74309	HEXIM2	0.00687816	-1.7913
LOC153684	0.00318901	-1.74384	SNX21	0.000333609	-1.79147
MANBA	0.00149642	-1.74444	STRN3	0.00806945	-1.79592
GYPC	0.00371899	-1.74593	HIST1H2AE	0.0189585	-1.79718
TNFRSF14	0.00281423	-1.74941	FOXP2	0.00878485	-1.79894
TCAP	0.0444795	-1.74962	RBP1	0.0220172	-1.79933
COL6A6	0.0130339	-1.74985	SLC8A1	0.00987762	-1.80136
PIP5KL1	0.0193506	-1.75202	GPR162	0.000634474	-1.80235
ATF5	0.00187252	-1.80327	C4orf38	0.0491376	-1.85925
FLJ10357	0.00515077	-1.80358	TMEM200A	0.000813525	-1.86001
EFCAB7	0.00849823	-1.80586	PPAP2A	0.0157463	-1.86252
LOC100129365	0.0253237	-1.80771	NUMA1	0.0480917	-1.86358
HBP1	6.84E-05	-1.80827	ASPRV1	0.0114617	-1.86435
PARP11	0.0258225	-1.81082	SULF2	0.00131374	-1.86519
GALM	0.003476	-1.81111	MAMSTR	0.0316064	-1.86552
JMJD1C	0.00409768	-1.81133	C14orf79	0.0204964	-1.86717
TCEAL7	0.000978636	-1.81202	POPDC2	0.0164453	-1.86739
VLDLR	0.0107936	-1.81259	CSDC2	0.0323883	-1.86758
LRIG1	0.00421353	-1.81332	TRIM2	0.00120328	-1.87009
SERTAD2	8.93E-06	-1.81362	TMEM132A	0.00860836	-1.87226
LYZL1	0.0140937	-1.81371	LOC282997	0.000162601	-1.87541
FNDC1	0.0124359	-1.81688	ARL4C	0.00639056	-1.87693
OSBPL3	0.00277281	-1.81795	CPEB1	0.00159968	-1.8786
ULK1	0.00718744	-1.81916	ZBED3	0.00796132	-1.88414
PYROXD2	0.00762256	-1.82146	ZNF710	0.0360452	-1.88414
GPC2	0.0261739	-1.8215	PITX1	0.0195004	-1.88446
CD248	0.00174394	-1.82167	CD86	0.00242742	-1.88519
DDIT3	0.000237384	-1.82169	GALNTL1	0.0096522	-1.88647

ENST00000395936	0.0260157	-1.82247	CCDC74B	0.00119343	-1.88889
FLJ90757	0.000294096	-1.8225	ABI3BP	0.0220532	-1.88936
ANK2	0.0111876	-1.82602	PDCD4	0.0170675	-1.89019
FLYWCH1	0.00494036	-1.82749	GPR125	0.0360252	-1.89059
ROBO1	0.00760105	-1.83005	RP1-21O18.1	0.00975741	-1.89328
HIVEP2	6.07E-05	-1.83162	COL15A1	0.0295365	-1.89335
ZNF154	0.0363896	-1.83166	AK074144	0.0223447	-1.89441
SPATA18	0.00511123	-1.83168	C13orf33	0.0305718	-1.89452
AX747437	0.0289977	-1.8326	AHNAK2	0.0049417	-1.89616
CPAMD8	0.0227381	-1.83279	PFKFB3	0.00230741	-1.89647
GXYLT2	0.0120212	-1.83413	PELI2	0.000242001	-1.89671
LIG1	0.00731637	-1.8349	RAVER2	0.0260669	-1.89701
TMEM37	0.0189832	-1.83492	LOC100128163	0.040367	-1.89801
RN18S1	0.00160088	-1.83672	SLURP1	0.0199161	-1.89843
BEND6	0.00650894	-1.83724	FAM161B	0.0294612	-1.89988
ASGR1	0.0128841	-1.83878	CAPS2	0.0472048	-1.90106
NR3C1	0.000498005	-1.84159	TCF7	0.00366817	-1.90161
EFR3B	0.0157715	-1.84229	ST6GAL1	0.0137812	-1.90173
MIR155HG	0.0056669	-1.84519	SPI1	0.0370844	-1.90427
C11orf20	0.020531	-1.84819	CHADL	0.00374819	-1.90464
CCL15	0.0332264	-1.84911	PLCL2	0.00842468	-1.90509
MGC2848	0.0303144	-1.84982	CCDC85C	0.000536567	-1.90607
HIST1H4I	0.0108644	-1.85003	CLIC2	0.00280036	-1.90808
SEMA5A	0.000115808	-1.85342	VEGFA	7.80E-05	-1.90829
PKIA	0.00511557	-1.85379	MALL	0.0265984	-1.90837
PRKG1	0.00150954	-1.85582	RASA4	0.0154752	-1.91052
MCPH1	0.0178924	-1.85766	BCL2L11	0.0182161	-1.91192
ALDH3A2	0.0325662	-1.85835	LARP6	0.00148867	-1.91759
MX2	0.043301	-1.85847	ANKRD10	0.0108932	-1.9192
FAM65B	0.0455055	-1.91935	CLN8	0.00177106	-2.00272
COL21A1	0.0404951	-1.91941	SOBP	0.00246175	-2.00551
C3orf58	0.0405864	-1.92104	KIAA1683	0.0015688	-2.00702
SDCBP2	0.0279108	-1.92118	TCP11L2	0.0100366	-2.00873
PPP1R1B	0.0368319	-1.922	NT5E	0.00138952	-2.01248
PHLDB3	0.00452662	-1.92721	C2orf84	0.017976	-2.01651
C10orf41	0.00603495	-1.93223	PLXNC1	0.00731964	-2.01663
C15orf51	0.000213284	-1.93515	LOC730058	0.0331972	-2.02103
JUN	0.00118891	-1.93669	ADAMTS19	0.0155415	-2.02252
HIST1H4A	0.0129631	-1.93723	DDB2	0.0142488	-2.02277
TRERF1	0.00299111	-1.93972	SLC7A4	0.0360427	-2.02478
ELTD1	0.00306059	-1.94304	C15orf48	0.00237774	-2.02618
TNFRSF11B	0.047084	-1.94468	FAM117B	0.02049	-2.02684
ST3GAL5	0.00717268	-1.94564	GPR179	0.0471732	-2.03225
TNFRSF10C	0.000208728	-1.94574	CDCP1	0.0207959	-2.03703
C12orf70	0.0318504	-1.94742	TP53INP1	0.000192707	-2.03705
GJC2	0.0089249	-1.94782	MAPK10	0.00878403	-2.03901
NDRG4	0.00359485	-1.94904	OR52K2	0.0151664	-2.04112
HIST1H4H	0.00813219	-1.95217	FKBPL	0.00414387	-2.0438
MTMR9L	0.000226335	-1.95239	NINJ1	0.000152413	-2.04386

PTGFR	0.0404748	-1.95551	GPRC5C	0.00673569	-2.04442
CLDN11	0.0101785	-1.95669	RTTN	0.0411547	-2.04525
SC5DL	0.00981905	-1.9592	DQ895628	0.0284148	-2.04585
PDZRN3	0.000667329	-1.96065	DCUN1D2	0.00446433	-2.04922
GNAZ	0.00344932	-1.96067	C3orf71	0.0375797	-2.05171
SGIP1	0.00290057	-1.96324	HTRA3	0.0381453	-2.0537
GPR153	0.0493253	-1.96692	LOC440082	0.0219406	-2.05736
TNXB	0.00405074	-1.96984	CRTC1	0.00123513	-2.06474
HMOX1	0.000217658	-1.9699	TXLNB	0.0137409	-2.06565
CACNA1G	0.0163947	-1.9703	VWF	0.00134621	-2.06973
PHEX	0.0135048	-1.97352	ZNF821	0.0257483	-2.07192
TMEM140	0.00370241	-1.97784	RASL12	0.0151539	-2.07496
AKR1C4	0.0431062	-1.98033	DBNDD1	0.0280648	-2.07513
LOC401357	0.0190159	-1.98697	PLD1	0.0392563	-2.0833
POSTN	0.0243548	-1.98888	CHRDL1	0.0128169	-2.08377
DYTN	0.0050043	-1.98893	HIST1H4E	0.00600529	-2.08387
MRPS6	0.00154995	-1.98902	TNFAIP2	0.00863218	-2.09067
ENC1	0.0245506	-1.98922	ZBTB46	0.00472291	-2.09757
PIK3C2B	0.0242041	-1.98927	CCDC30	0.0259982	-2.09826
C5orf4	0.019397	-1.98959	LAMB3	0.000276104	-2.10045
FLJ41603	0.0211472	-1.99124	IER3	0.00122035	-2.10279
AK123797	0.0200231	-1.99217	FLJ44253	0.0364392	-2.1055
LOC100128055	0.0245863	-1.99254	PER2	0.00463593	-2.1093
MBP	0.00896874	-1.99458	TAC3	0.0150556	-2.11262
AF072164	0.040833	-1.99467	AIF1L	0.0367536	-2.11437
LOC100130996	0.00565763	-1.99496	GGTLC1	0.00294074	-2.11674
UACA	0.00209645	-1.99606	ITGA7	0.000358097	-2.11706
MSR1	0.0123097	-1.99945	USP6NL	0.0209651	-2.1199
TRO	0.000815526	-2.00129	VASH2	0.0274618	-2.12432
SH2B2	0.00188046	-2.12618	SLC5A3	0.00609932	-2.26351
PAQR5	0.00279041	-2.12679	DCHS1	0.00523407	-2.26518
IRAK2	0.00288731	-2.13016	CSGALNACT1	0.0215879	-2.26544
DRAM1	6.05E-05	-2.13031	SMAD1	0.00177219	-2.26762
MGC42105	0.0481199	-2.13361	UNC5B	0.00149188	-2.26793
KRT19	0.0252756	-2.13385	NFATC4	0.00588824	-2.27027
ZNF606	0.0201636	-2.13848	LOC285141	0.0307332	-2.27033
SPTLC3	0.00133782	-2.13921	TNC	0.000485016	-2.27137
DENND5B	0.00502217	-2.14032	CRABP2	0.000284095	-2.27441
ENST00000390301	0.00922738	-2.1436	ITGA11	0.0127115	-2.27469
PRRX1	0.00407039	-2.14525	TNFRSF25	0.00860519	-2.2751
MATN2	0.0160175	-2.14538	AMIGO2	0.0188621	-2.27692
GADD45G	0.00577251	-2.14843	PLA2G4A	0.0178399	-2.28179
HOXA3	0.0293659	-2.14896	RELB	0.000732311	-2.28955
HTR2B	0.0059829	-2.15029	PCNXL2	0.0111275	-2.29363
QPRT	0.000322493	-2.15416	ITPKB	0.00376458	-2.29408
LOC728903	0.0325493	-2.15499	LOC728392	0.0123275	-2.29463
CCRL1	0.0458366	-2.15526	FAIM2	0.00390309	-2.29614
ABCB4	0.025316	-2.16359	OLFML1	0.0146794	-2.2974
SECTM1	0.0056696	-2.164	C14orf132	0.00485107	-2.29851

BC030764	0.00261796	-2.16711	PLEKHG1	0.0105358	-2.30307
TNNC2	0.00433159	-2.17335	PLEKHG4	0.00113659	-2.30361
KILLIN	0.0206867	-2.18127	THC2564554	0.043092	-2.30396
ADAM8	0.00359133	-2.19147	TYMS	0.018108	-2.30487
ENPP2	0.0484056	-2.19226	MAF	0.00262797	-2.30716
CCDC48	0.00484607	-2.19337	FOLR3	0.00112763	-2.30988
RNF122	0.00145982	-2.20561	TCEA3	0.00213543	-2.31001
LOC390251	0.024576	-2.20659	COL4A5	0.0229976	-2.31249
MBD5	0.00217481	-2.20768	ARHGAP28	0.0363884	-2.31275
MAFB	0.0283171	-2.20814	ZNF323	0.0437756	-2.31434
RGS5	0.0197477	-2.21163	HOXA10	0.0222964	-2.32598
LOC157562	0.0223075	-2.22041	PPARGC1A	0.0211435	-2.327
SEMA3B	0.000894984	-2.22444	ETV1	0.00189265	-2.32789
C17orf44	0.0333928	-2.22605	TMEM130	0.00144731	-2.33212
ZFP14	0.0192304	-2.22655	ZNF483	0.017416	-2.335
LOC645431	0.0303829	-2.22744	CIT	0.00783073	-2.33737
ZNF521	0.0048713	-2.22913	ABCA11P	0.0152178	-2.33772
MALAT1	0.0489195	-2.23252	COL14A1	0.00182548	-2.33831
THC2539584	0.049034	-2.23648	LPPR3	0.036024	-2.33837
CD36	0.0109877	-2.23897	HBD	0.0243098	-2.3389
ABCA1	0.0207415	-2.24225	VAT1L	0.0354067	-2.34081
SYTL2	0.00331061	-2.24309	PHGDH	0.0107903	-2.34366
FLJ13197	0.0435998	-2.24525	SPTBN4	0.00138058	-2.34695
GBP2	0.00375895	-2.24538	FAM134B	0.0222865	-2.34911
PLXDC1	0.00825863	-2.25051	C18orf56	0.00985652	-2.35272
ZNF165	0.0347887	-2.25079	CRYM	0.00051315	-2.35813
ZNF221	0.0353176	-2.2514	THC2728054	0.0168281	-2.36191
LRDD	0.00229135	-2.25431	LOC283454	0.00151061	-2.36518
GPR62	0.00734075	-2.26238	IL13RA2	0.0386779	-2.3665
C1orf228	0.00199302	-2.37091	Sep-12	0.017346	-2.61068
LOC203510	0.0105021	-2.37188	GDF10	0.0106163	-2.61162
RGS2	0.0216326	-2.3742	PHLDA1	0.00163238	-2.62249
CA14	0.0109646	-2.37797	FLJ41484	0.0225578	-2.6502
RAP2B	0.0012435	-2.37995	KRTAP13-2	0.0343849	-2.66001
NHS	0.00816653	-2.38049	LRRC25	0.0404329	-2.68019
HSPA4L	0.00502894	-2.38086	FLJ22536	0.0335532	-2.68094
LUM	0.00459266	-2.38331	FAM171B	0.00253607	-2.68106
DACT3	0.00361146	-2.38466	KLF4	0.0263349	-2.686
NEDD4L	0.00340027	-2.39217	OR10G9	0.0347738	-2.70534
RCOR2	0.00273849	-2.39429	CDKN2B	0.00010202	-2.70931
TMEM158	0.0182022	-2.40322	SLC7A14	0.000666958	-2.72656
ADAMTS14	0.0347588	-2.40669	SALL2	0.00557715	-2.72715
RSPO3	0.0135325	-2.4155	TARSL2	0.000528049	-2.72922
FDXR	0.000493899	-2.41657	ENST00000402420	0.0388179	-2.73066
SNCAIP	0.0003216	-2.41885	TMCC2	0.0362454	-2.73384
GRAMD1A	0.00304616	-2.42083	TNFSF13B	0.0457193	-2.75552
FAM102A	6.19E-05	-2.42137	BAALC	0.00914276	-2.76266
FLRT2	0.000293604	-2.42699	GDF15	0.000129115	-2.77627
PRRT2	0.0171098	-2.42928	VWCE	0.0156536	-2.79722

BBC3	0.00116986	-2.43318	C6orf138	0.00222058	-2.79844
PLA2G4C	0.000799513	-2.43367	RAB7B	0.000687243	-2.80818
OXER1	0.00136629	-2.44069	RDH5	0.00231506	-2.81584
KCNMA1	0.0031953	-2.44479	IGDCC4	0.00148491	-2.81815
SH3BP5	0.0181129	-2.45401	EPHB3	0.000703597	-2.82279
CHRD2	0.0260872	-2.4558	RCAN2	0.0011036	-2.82403
CGNL1	0.0134285	-2.46573	CLGN	0.000254954	-2.8298
FST	0.00322235	-2.46728	CNTN3	0.026407	-2.83565
PLAU	0.00127162	-2.47345	OR2Y1	0.022669	-2.83964
C20orf195	0.00312693	-2.47866	DIP2A	0.0212757	-2.85123
GFRA1	0.00105592	-2.48121	LOC100130111	0.00387314	-2.88354
CA12	0.00571127	-2.48146	IGSF10	0.00879671	-2.88593
ZNF846	0.023978	-2.48209	FIGF	0.0321458	-2.89233
SAMD12	0.00558809	-2.48494	P2RX7	0.000988212	-2.90941
SMO	0.00162981	-2.48883	HSD17B2	0.0113764	-2.90988
ACP5	0.000682876	-2.48975	PKP3	0.00291831	-2.94756
DDIT4L	0.0392359	-2.50747	KCTD12	0.0190956	-2.96429
RASSF2	0.0125668	-2.51323	LOC646936	0.00213994	-2.9659
ARVCF	0.000616711	-2.52069	LDB2	0.000510225	-3.00525
GDF1	0.013016	-2.5208	AQP3	0.0357826	-3.00815
ADCY1	0.0106139	-2.54299	RFTN2	0.00133565	-3.02176
IL17RD	0.01906	-2.54413	MIAT	0.00476707	-3.02631
AF359419	0.0315234	-2.55552	LRRC15	0.0244118	-3.04724
LOC100132815	8.29E-05	-2.55603	MX1	0.00333702	-3.05139
LOC729603	0.0119687	-2.55654	KIAA2026	0.0307381	-3.05586
RASGRF2	0.0228091	-2.56552	LASS1	0.00484164	-3.05796
FLJ37644	0.0139146	-2.5689	CTTNBP2	0.0321254	-3.06626
ADAMTSL1	0.0397345	-2.57095	ARSI	0.0070051	-3.07722
GYG2	0.0377113	-2.5869	RAB33A	0.000675221	-3.0787
PCDHB5	0.00579755	-3.08415	FGF13	0.00643471	-3.76609
ENST00000423322	0.0136764	-3.08419	E2F7	0.000767994	-3.78745
PRKCG	0.00417623	-3.09221	SOX4	0.0153381	-3.82857
C17orf76	0.000836986	-3.11032	MEX3A	0.00161493	-3.8398
TMEM35	0.00311096	-3.13942	TNFAIP6	0.00422564	-3.87415
ANGPTL2	5.47E-05	-3.13951	TRIM45	0.000116789	-3.92432
DCLK1	0.0241395	-3.18545	SYT7	0.000705314	-3.94339
MEX3B	0.0441479	-3.19048	GLI1	0.00714094	-3.95142
TMEM217	0.000680899	-3.20839	CXCL12	0.00359088	-3.96001
FSTL5	0.0432873	-3.2283	MXRA5	5.14E-05	-3.96914
GPER	0.00214358	-3.23689	GPR68	0.00266368	-4.32065
MYBPH	0.0398398	-3.23747	PDE4B	0.0199266	-4.39107
EVI2A	0.00133385	-3.25217	CCL11	0.00543929	-4.42498
DACH1	0.0308535	-3.25745	RRAD	0.00650411	-4.68968
AMOT	0.00728667	-3.26956	LRRN3	0.0207673	-4.70784
IFIT1	0.000709866	-3.31245	RAB26	0.00377299	-4.96857
LRRC17	0.0307473	-3.32752	FAM46C	0.00140449	-5.03319
LOC375196	0.0328343	-3.35661	CD274	0.0269718	-5.10222
OR1K1	0.00541602	-3.35979	BDKRB1	0.000679002	-5.22339
ENST00000331733	0.0103568	-3.36124	GPR56	0.00348262	-5.43723

LOC283070	0.0138072	-3.36408	LOC649941	0.0373539	-5.4505
SLC6A9	0.0001186	-3.4027	CNIH3	0.000112112	-5.56423
BDKRB2	0.000469808	-3.43774	NR0B1	0.0043313	-5.78435
LOC100132167	0.0226973	-3.44223	MMP10	0.0199715	-5.85228
ISG20	0.00891136	-3.47533	NOV	2.59E-05	-6.38307
SEMA3A	0.00853538	-3.48542	SIPA1L2	0.00144401	-6.38375
NFE2	0.000617891	-3.5063	IL4I1	0.00200558	-6.40553
CCL7	0.0349931	-3.53607	CHST8	0.0353442	-6.63884
HSPA12B	0.0131438	-3.59906	OR6N1	0.0141912	-7.02028
CH25H	0.00893032	-3.64039	G0S2	0.00103256	-7.60972
COL13A1	0.00136208	-3.72113	MMP1	0.00057377	-9.69951
ALDH1A3	0.0145858	-3.76022	HLA-DRB3	0.0408609	-12.2717

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Supplemental Table 9: Common mRNA expression changes in ASM cells from patients with non-severe and severe asthma following treatment with dexamethasone (10^{-7} M), before stimulation with FCS (2.5 %)

Gene Symbol	Gene Name	Non-Severe Asthma	Severe Asthma
		Microarray (FC)	Microarray (FC)
ASNSD1	Asparagine synthetase domain containing 1	-2.1 (< .01)	11.0 (< .01)
BEND6	BEN domain containing 6	-1.7 (< .01)	-1.8 (< .01)
C16orf74	Chromosome 16 open reading frame 74	-1.8 (< .01)	-1.6 (< .01)
C6orf108	2'-Deoxynucleoside 5'-Phosphate N-Hydrolase 1	-1.8 (< .01)	17.9 (< .01)
C9orf140	Suppressor APC Domain Containing 2	-1.8 (< .01)	-1.5 (< .01)
CAPNS2	Calpain, small subunit 2	-1.7 (< .01)	6.7 (< .01)
CD36	CD36 Molecule (Thrombospondin Receptor)	-2.3 (< .01)	-2.2 (< .01)
DCTN3	Dynactin 3 (p22)	-2.0 (< .01)	18.0 (< .01)
EFR3B	EFR3 homolog B	1.8 (< .01)	-1.8 (< .01)
GYG2	Glycogenin 2	-2.1 (< .01)	-2.6 (< .01)
OLFML1	Olfactomedin-like 1	2.0 (< .01)	-2.3 (< .01)
SDSL	Serine dehydratase-like	-1.5 (< .01)	8.7 (< .01)
SHC2	Src homology-2 domain containing transf protein 2	5.1 (< .01)	-1.8 (< .01)
SNRNP27	Small nuclear ribonucleoprotein 27kDa	-3.5 (< .01)	11.3 (< .01)
TRIP12	Thyroid hormone receptor interactor 12	-1.7 (< .01)	22.9 (< .01)
VLDLR	Very low density lipoprotein receptor	-1.9 (< .01)	-1.8 (< .01)
ZBTB16	Zinc finger and BTB domain containing 16	-1.7 (< .01)	16.2 (< .01)

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Supplemental Table 10: Baseline lncRNA expression changes in ASM cells from patients with non-severe asthma compared to healthy patients

Class of lncRNA	Ensemble gene ID	Transcript	FC	Flanking Loci	
				5 Prime	3 Prime
lincRNA	ENST00000514823	RP11-93L9.1	2.1 (< .05)	SPATA5	SPRY1
lincRNA	ENST00000434601	LINC00422	1.9 (< .05)	FGF9	BASP1P1
lincRNA	ENST00000450063	AC006159.3	1.9 (< .05)	MET	CAPZA2
lincRNA	ENST00000438897	AC068491.2	1.8 (< .05)	BCC2L11	LOC541471
lincRNA	ENST00000454968	LINC00963	1.8 (< .05)	NCS1	ASS1
lincRNA	ENST00000415714	RP1-60O19.1	1.8 (< .05)	ORSL1	NR_033557
lincRNA	ENST00000437696	RP11-359G22.2	1.8 (< .05)	LINC00261	SSTR4
lincRNA	ENST00000560760	RP11-38G5.2	1.7 (< .05)	MEX3B	EFTUD1
lincRNA	ENST00000413945	LINC00472	1.6 (< .05)	B3GAT2	RIM51
lincRNA	ENST00000443965	GS1-600G8.5	1.6 (< .05)	NR_045260	EGFL6
lincRNA	ENST00000456532	RP5-1158E12.3	1.6 (< .05)	CXORF36	ZNF673
lincRNA	ENST00000412685	HCG18	1.6 (< .05)	TRIM15	HLA-L

Processed Transcript	ENST00000447323	MSN	1.5 (< .05)	MSN	MSN
lincRNA	ENST00000503532	RP11-341G5.1	1.5 (< .05)	LOC152742	LOC441009
lincRNA	ENST00000418358	AC011747.3	1.5 (< .05)	LINC00299	IDZ
lincRNA	ENST00000524165	<i>PVT1</i>	-1.5 (< .05)	MYC	LOC728724
lincRNA	ENST00000446423	FKBP1A-SDCBP2	-1.6 (< .05)	SDCBP2	NSFLIC
Antisense	ENST00000501164	SDCBP2-AS1	-1.6 (< .05)	TP531NP1	C8ORF38
lincRNA	ENST00000443576	RP11-141M1	-1.8 (< .05)	RFC3	NBEA
lincRNA	ENST00000513480	CTD-2127H9.1	-1.8 (< .05)	LIFR	OSMR
lincRNA	ENST00000414790	H19	-3.0 (< .05)	DBX1	HTATIP2

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Supplemental Table 11: Baseline lincRNA expression changes in ASM cells from patients with severe asthma compared to healthy patients

Class of lincRNA	Ensemble gene ID	Name	FC	Flanking Loci	
				5 Prime	3 Prime
lincRNA	ENSG00000230590	FTX	1.8 (< .05)	ZCCHC13	SLC16A2
Antisense	ENST00000507244	STX18-AS1	1.8 (< .05)	D4S234E	NR_037888
lincRNA	ENST00000418006	LINC00940	1.7 (< .05)	CACNA1C	LOC283440
lincRNA	ENSG00000233237	LINC00472	1.7 (< .05)	B3GAT2	RIM51
Antisense	ENST00000433079	MKLN1-AS1	1.6 (< .05)	MKLN1	PODXL
lincRNA	ENSG00000237879	LINC00398	1.6 (< .05)	EEFIDP3	FRY
lincRNA	ENST00000521586	RP11-382A18.2	1.6 (< .05)	PCAT1	POU5F1B
lincRNA	ENST00000440496	LINC00630	1.5 (< .05)	NR_038988	BEX1
lincRNA	ENST00000456532	RP5-1158E12.3	1.5 (< .05)	CXORF36	ZNF673
lincRNA	ENST00000520431	RP11-527N22.2	1.5 (< .05)	KCNU1	ZNF703
lincRNA	ENSG00000249859	<i>PVT1</i>	1.5 (< .05)	MYC	LOC728724
lincRNA	ENST00000448786	AC007879.2	1.5 (< .05)	KLF7	CRABI
lincRNA	ENST00000433747	RP11-120D5.1	1.5 (< .05)	MID1	ARHGAP6
lincRNA	ENSG00000088832	FKBP1A-SDCBP2	-1.5 (< .05)	SDCBP2	NSFLIC
lincRNA	ENST00000420774	AC004540.5	-1.5 (< .05)	SNX10	LOC441204
lincRNA	ENST00000424283	RP1-261G23.5	-1.6 (< .05)	GTPBP2	MAD2L1BP

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Supplemental Table 12: lincRNA expression changes in ASM cells from patients with non-severe asthma after exposure with FCS (2.5 %)

Class of lincRNA	Ensemble gene ID	Name	FC	Flanking Loci	
				5 Prime	3 Prime
lincRNA	ENST00000552334	RP11-701H24.2	5.6 (< .05)	GABRA5	OCA2
Antisense	ENST00000439601	AC131097.3	4.1 (< .05)	CXXC11	AC093642
lincRNA	ENST00000415611	AC005682.5	3.5 (< .05)	<i>IL6</i>	KLHL7
lincRNA	ENST00000529893	RP1-80B9	3.2 (< .05)	FOXC1	C6orf195
Sense overlapping	ENST00000304425	MIR31 host gene	3.1 (< .05)	IFNA8	C9orf53
lincRNA	ENST00000443576	RP11-141M1	2.7 (< .05)	STARD13	RFC3
lincRNA	ENST00000508406	RP11-8L2.1	2.5 (< .05)	AGPAT9	NKX6-1
Processed transcript	ENST00000447430	AC016831.7	2.2 (< .05)	KLF14	MKLN1
lincRNA	ENST00000553465	MEG8-001	2.0 (< .05)	MIR136	MIR1197
lincRNA	ENST00000435643	AC007879.1	1.8 (< .05)	MIR2355	MIR1302
lincRNA	ENST00000433843	SNHG5	1.8 (< .05)	SYNCRIP	RN7SL643P
lincRNA	ENST00000561123	RP11-307C19.2	1.6 (< .05)	HMG20A	LINGO1
lincRNA	ENST00000435702	AP001046	1.6 (< .05)	CRYAA	SIK1
lincRNA	ENST00000505254	MIR143 host gene	1.6 (< .05)	GRPEL2	CSNK1A1

Sense overlapping	ENST00000314957	CTD-2201E18.3	1.5 (< .05)	CCDC152	NIM1
lincRNA	ENST00000417947	AC096574.5	-1.5 (< .05)	MLPH	RBM44
lincRNA	ENSG00000249859	<i>PVT1</i>	-1.6 (< .05)	MYC	LOC728724
lincRNA	ENST00000414120	LINC00887	-1.7 (< .05)	ATP13A4	CPN2
Antisense	ENST00000511571	RP11-453E17	-1.7 (< .05)	STAP1	TMPRSS11BNL
lincRNA	ENST00000423943	RP11-48O20.4	-1.8 (< .05)	DUSP23	PIGM
lincRNA	ENST00000418539	BCYRN1	-1.8 (< .05)	CALM2	AC138655
Antisense	ENST00000422059	RP5-1120P11.1	-1.8 (< .05)	VEGFA	MRPL14
lincRNA	ENST00000464767	LINC00341	-1.9 (< .05)	DICER1	TCL1A
lincRNA	ENST00000373171	LINC00951	-1.9 (< .05)	MOCS1	UNC5CL
lincRNA	ENST00000518765	RP11-527N22.1	-2.0 (< .05)	KCNU1	ERLIN2
lincRNA	ENST00000473636	LINC00882	-2.0 (< .05)	CBLB	BBX
lincRNA	ENST00000457340	RP11-503C24.1	-2.2 (< .05)	AL009178.1	DACT2
lincRNA	ENST00000514844	RP11-46C20.1	-2.3 (< .05)	CDH9	CDH6
lincRNA	ENST00000451230	AC108463.1	-2.5 (< .05)	BCL2L11	MIR4435
lincRNA	ENST00000455957	HCG17	-2.8 (< .05)	TRIM15	TRIM39
lincRNA	ENST00000506086	RP11-229C3.2	-3.2 (< .05)	GCNT4	ANKRD31

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Supplemental Table 13: lincRNAs in non-severe ASM changed in expression following treatment with dexamethasone (10^{-7} M), before stimulation with FCS (2.5 %)

Class of lincRNA	Ensemble gene ID	Name	FC	Flanking Loci	
				5 Prime	3 Prime
lincRNA	ENSG00000236605	ACO23115.4	3.9 (< .05)	MEIS1	ETAA1
Antisense	ENSG00000238273	ACO12360.6	3.6 (< .05)	MRPS9	NCK2
lincRNA	ENSG00000258123	RP11-314D7.2	3.5 (< .05)	TRHDE	ATXN7L3B
Antisense	ENSG00000270953	RP11-2E11.9	3.4 (< .05)	MEST	MIR29
lincRNA	ENSG00000259331	RP11-57P19.1	3.2 (< .05)	MCTP2	NR2F2
lincRNA	ENSG00000273615	RP11-1136G4.2	3.1 (< .05)	IRX3	IRX5
lincRNA	ENSG00000279440	CTA-992D9.11	3.0 (< .05)	CRYBA4	MN1
lincRNA	ENSG00000272798	CTA-390C10.9	3.0 (< .05)	LRP5L	ADREK2
lincRNA	ENSG00000254275	lincRNA00824	3.0 (< .05)	TMEM75	GSDMC
lincRNA	ENSG00000231082	RP11-514F8.2	3.0 (< .05)	SH2D4B	NRG3
lincRNA	ENSG00000256748	RP11-234B24.2	2.9 (< .05)	RAD51AP1	GALNT8
lincRNA	ENSG00000204603	lincRNA01257	2.8 (< .05)	GPR133	SFSWAP
lincRNA	ENSG00000229323	DLEU1-AS1	2.7 (< .05)	DLEU1	DLEU7
lincRNA	ENSG00000237756	RP11-77M5.1	2.7 (< .05)	NUF2	PBX1
lincRNA	ENSG00000260604	RP1-140K8.5	2.6 (< .05)	FAM50B	PRPF4B
lincRNA	ENSG00000266869	RP6-114E22.1	2.6 (< .05)	SIPA1L1	RGS6
lincRNA	ENSG00000271860	RP11-436D23.1	2.5 (< .05)	MMS22L	POU3F2
lincRNA	ENSG00000245149	RNF139-AS1	2.5 (< .05)	TRMT12	RNF139
lincRNA	ENSG00000244342	lincRNA00698	2.4 (< .05)	CADPS	SYNPR
lincRNA	ENSG00000267055	RP11-486P11.1	2.4 (< .05)	TMEM196	MACC1
lincRNA	ENSG00000230156	lincRNA00443	2.4 (< .05)	ARGLU1	FAM155A
lincRNA	ENSG00000231671	lincRNA01307	2.4 (< .05)	SIPR1	OLFM3
lincRNA	ENSG00000236983	lincRNA00614	2.4 (< .05)	ABI1	YME1L1
lincRNA	ENSG00000233365	RP4-655C5.4	2.3 (< .05)	T	PRR18
lincRNA	ENSG00000226673	lincRNA01108	2.2 (< .05)	CD83	JARID2
lincRNA	ENSG00000278630	RP11-78L16.1	2.2 (< .05)	OLFM4	PRR20A
Antisense	ENSG00000247381	PDX1-AS1	2.2 (< .05)	GSX1	PDX1
lincRNA	ENSG00000235152	RP5-865N13.2	2.2 (< .05)	DISC1	SIPA1L2
lincRNA	ENSG00000241475	RP4-781K5.5	2.1 (< .05)	IRF2BP2	TOMM20

lincRNA	ENSG00000270604	HCG17	2.1 (< .05)	TRIM26	HLA-L
Sense intronic	ENSG00000276672	RP11-142E9.1	2.0 (< .05)	RFC3	NBEA
lincRNA	ENSG00000272168	CASC15	2.0 (< .05)	SOX4	PRL
lincRNA	ENSG00000230587	AC093609.1	2.0 (< .05)	HAAO	ZFP36L2
lincRNA	ENSG00000233723	lincRNA01122	1.9 (< .05)	FANCL	BCL11A
lincRNA	ENSG00000228739	RP11-21817.2	1.9 (< .05)	MLANA	IL33
lincRNA	ENSG00000228798	AP000473.5	1.9 (< .05)	MIR125B2	CXADR
lincRNA	ENSG00000219445	RP11-3B12.3	1.9 (< .05)	POT1	GRM8
lincRNA	ENSG00000260986	RP11-854K16.3	1.9 (< .05)	POTEB2	POTEB3
lincRNA	ENSG00000246084	CTD-2506J14.1	1.9 (< .05)	VRK1	C14ORF177
lincRNA	ENSG00000223863	AC008074.4	1.8 (< .05)	LGALS1	AFTPH
lincRNA	ENSG00000226375	RP3-395P12.2	1.8 (< .05)	TNFSF18	TNFSF4
lincRNA	ENSG00000224717	RP11-576D8.4	1.8 (< .05)	LEMD1	CDK18
lincRNA	ENSG00000214870	AC004540.5	1.7 (< .05)	SNX10	KIAA0087
lincRNA	ENSG00000232413	RP11-343J18.2	1.7 (< .05)	PBX3	MVB12B
lincRNA	ENSG00000267586	lincRNA00970	1.7 (< .05)	PIK3C3	RIT2
lincRNA	ENSG00000272144	CTD-2035E11.5	1.7 (< .05)	ANXA2R	ZNF131
lincRNA	ENSG00000248300	RP11-74M11.2	1.7 (< .05)	HS3ST1	RAB28
lincRNA	ENSG00000257086	RP11-783K16.13	1.7 (< .05)	FERMT3	BAD
lincRNA	ENSG00000239482	RP11-90K6.1	1.6 (< .05)	SLC9C1	BTLA
lincRNA	ENSG00000259198	RP11-133K1.6	1.6 (< .05)	C15ORF52	DISP2
lincRNA	ENSG00000230812	lincRNA01358	1.5 (< .05)	JUN	FGGY
Antisense	ENSG00000258982	RP11-63812.4	1.5 (< .05)	DEGS2	YY1
lincRNA	ENSG00000248371	CTC-347C20.2	1.5 (< .05)	ZNF366	TNPO1
lincRNA	ENSG00000224228	RP1-15D23.2	1.5 (< .05)	FASLG	TNFSF18
lincRNA	ENSG00000263622	RP11-389J22.3	1.5 (< .05)	CDH7	CDH19
lincRNA	ENSG00000271788	CTD-2201E18.5	1.4 (< .05)	CCDC152	ANXA2R
Antisense	ENSG00000224743	TEX26-AS1	1.4 (< .05)	ALOX5AP	MEDAG
lincRNA	ENSG00000255839	RP11-338K17.8	1.3 (< .05)	TCTN2	ATP6VDA2
lincRNA	ENSG00000228636	RP5-1051H14.2	1.3 (< .05)	GATA3	CELF2
lincRNA	ENSG00000259725	CTD-3032H12.1	1.2 (< .05)	IRX3	IRX5
lincRNA	ENSG00000248605	CTD-2306M5.1	-1.1 (< .05)	CDH10	CDH9
lincRNA	ENSG00000268184	RP11-420K14.8	-1.3 (< .05)	ZNF100	ZNF43
lincRNA	ENSG00000273100	RP11-302L19.3	-1.6 (< .05)	ERMARD	DLL1
lincRNA	ENSG00000249631	RP11-281P23.2	-1.6 (< .05)	HS3ST1	RAB28
lincRNA	ENSG00000259504	RP11-352D13.5	-1.7 (< .05)	PAQR5	KIF23
lincRNA	ENSG00000225269	lincRNA00705	-1.8 (< .05)	KLF6	AKR1E2
lincRNA	ENSG00000235154	CTA-280A3_B.2	-1.8 (< .05)	FP325331.1	FAM19A5
lincRNA	ENSG00000249021	CTC-505O3.3	-1.9 (< .05)	TICAM2	CDO1
lincRNA	ENSG00000248515	RP11-608O21.1	-1.9 (< .05)	LCORL	SLIT2
lincRNA	ENSG00000236204	lincRNAO1376	-1.9 (< .05)	NT5C1B	OSR1
lincRNA	ENSG00000248588	CTC-458G6.4	-1.9 (< .05)	ARRDC3	NR2F1
lincRNA	ENSG00000254275	lincRNA00824	-2.1 (< .05)	TMEM75	GSDMC
lincRNA	ENSG00000257859	CASC18	-2.4 (< .05)	C12ORF75	NUAK1
lincRNA	ENSG00000251580	RP11-539L10.3	-2.4 (< .05)	MAN2B2	MRFAP1
lincRNA	ENSG00000249740	OSMR-AS1	-2.4 (< .05)	LIFR	OSMR
Antisense	ENSG00000233340	RP11-25C19.3	-2.7 (< .05)	VTI1A	TCFL2
lincRNA	ENSG00000239628	RP11-543D10.2	-2.7 (< .05)	SKIL	CLDN11
Antisense	ENSG00000224691	GS1-174L6.4	-3.4 (< .05)	HMCN1	PRG4
lincRNA	ENSG00000270020	RP11-463O9.9	-3.8 (< .05)	IRF8	FOXF1

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Supplemental Table 14: lincRNA expression changes in ASM cells from patients with severe asthma after exposure with FCS (2.5 %)

Class of lincRNA	Ensemble gene ID	Name	FC	Flanking Loci	
				5 Prime	3 Prime
lincRNA	ENST00000444958	DANCR	3.4 (< .05)	USP46	MIR4449
Processed transcript	ENST00000443587	DLEU2	3.2 (< .05)	MIR3613	DLEU7
Processed transcript	ENST00000451141	MIAT	2.9 (< .05)	CRYBB1	MN1
Antisense	ENST00000439601	AC131097.3	2.5 (< .05)	CXXC11	CICP10
lincRNA	ENST00000432823	RP1-80N2.2	2.4 (< .05)	LY86	RREB1
lincRNA	ENST00000438897	AC068491.2	2.4 (< .05)	BCL2L11	MIR4435
lincRNA	ENST00000478824	CTD-2377D24.6	2.1 (< .05)	HOXB4	MIR3185
lincRNA	ENST00000507058	CTC-276P9.2	1.9 (< .05)	PITX1	H2AFY
lincRNA	ENST00000512519	CTD-2127H9.1	1.9 (< .05)	LIFR	OSMR
Processed transcript	ENST00000447430	AC016831.7	1.8 (< .05)	KLF14	MKLN1
lincRNA	ENST00000366424	AC144450.2	1.7 (< .05)	TPO	PXDN
Antisense	ENST00000435800	RP11-31F15.1	1.7 (< .05)	SLC16A1	LRIG2
Antisense	ENST00000460833	ADAMTS9-AS2	1.7 (< .05)	ADAMTS9	MAGI1
lincRNA	ENST00000446884	RP1-30G7.2	1.7 (< .05)	MIR222	KRBOX4
lincRNA	ENST00000560760	RP11-38G5.2	1.5 (< .05)	KIAA1024	MTHFS
lincRNA	ENST00000416401	RP11-77M5.1	1.5 (< .05)	RGS5	NUF2
lincRNA	ENST00000433079	AC058791.2	-1.5 (< .05)	MIR29	MKLN1
lincRNA	ENST00000552334	RP11-701H24.2	-1.5 (< .05)	SNURF	UBE3A
Antisense	ENST00000519104	RP3-399L15.3	-1.5 (< .05)	HDAC2	FRK
lincRNA	ENST00000444265	LINC00340	-1.5 (< .05)	SOX4	PRL
lincRNA	ENST00000421322	XIST	-1.6 (< .05)	CHIC1	ZCCHC13
lincRNA	ENST00000464767	LINC00341	-1.6 (< .05)	CLMN	SYNE3
Antisense	ENST00000416630	DCTN1-AS1	-1.6 (< .05)	MTHFD2	MOGS
Sense intronic	ENST00000433544	RP11-488P3.1	-1.7 (< .05)	BCAR3	DNTTIP2
Processed transcript	ENST00000419628	AP001626.1	-1.8 (< .05)	SLC37A1	PDE9A
lincRNA	ENST00000437261	AC108066.1	-1.9 (< .05)	MIR548	IKZF2
Antisense	ENST00000434399	AC005154.6	-1.9 (< .05)	GGCT	GARS
lincRNA	ENST00000514791	RP11-434D9.2	-2.0 (< .05)	CD180	PIK3R1
lincRNA	ENST00000435643	AC007879.1	-2.2 (< .05)	KLF7	CREB1
lincRNA	ENST00000433747	RP11-120D5.1	-2.2 (< .05)	MID1	ARHGAP6
lincRNA	ENST00000418006	LINC00940	-2.3 (< .05)	LRTM2	DCP1B
lincRNA	ENST00000434601	RP11-101P17.9	-2.7 (< .05)	MRP63	ZDHHC20

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Supplemental Table 15: lincRNAs in severe ASM changed in expression following treatment with dexamethasone (10^{-7} M), before stimulation with FCS (2.5 %)

Class of lincRNA	Ensemble gene ID	Name	FC	Flanking Loci	
				5 Prime	3 Prime
lincRNA	ENST00000444958	DANCR	6.3 (< .05)	USP46	ERVMER34-1
lincRNA	ENST00000473636	LINC00882	3.4 (< .05)	CBLB	CCDC54
Processed transcript	ENST00000443587	DLEU2	3.1 (< .05)	TRIM13	DLEU7
lincRNA	ENST00000478824	CTD-2377D24.6	2.6 (< .05)	TTLL6	CALCOCO2
lincRNA	ENST00000412526	LINC00161	2.5 (< .05)	ADAMTS5	N6AMT1
lincRNA	ENST00000420594	AC073130.1	2.4 (< .05)	TES	CAV2
Processed transcript	ENST00000453698	SNHG11	2.4 (< .05)	LBP	RALGAPB
Antisense	ENST00000420563	AC053503.4	2.4 (< .05)	DNPEP	DES

lincRNA	ENST00000511497	RP11-420A23.1	2.3 (< .05)	PGRMC2	PHF17
Processed transcript	ENST00000413755	SNHG17	2.3 (< .05)	LBP	RALGAPB
lincRNA	ENST00000512322	RP11-792D21.2	2.2 (< .05)	ANXA3	BMP2K
Antisense	ENST00000519104	RP3-399L15.3	2.1 (< .05)	HDAC2	HS3ST5
lincRNA	ENST00000416534	AC007463.2	2.1 (< .05)	RNF144A	ID2
lincRNA	ENST00000427903	RP1-600I9.1	2.1 (< .05)	QRSL1	C6orf203
lincRNA	ENST00000442796	LINC00312	2.0 (< .05)	LMCD1	SSUH2
lincRNA	ENST00000437523	RP11-344P13.4	2.0 (< .05)	FCGR1B	PP1AL4G
lincRNA	ENST00000560760	RP11-38G5.2	2.0 (< .05)	KIAA1024	MTHFS
lincRNA	ENST00000454596	RP11-69I8.2	1.9 (< .05)	ENPP1	CTGF
lincRNA	ENST00000366424	AC144450.2	1.8 (< .05)	TPO	PXDN
lincRNA	ENST00000412606	AC096559.1	1.8 (< .05)	LPIN1	TRIB2
Antisense	ENST00000439075	RP11-510H23.1	1.8 (< .05)	NKAIN2	RNF217
lincRNA	ENST00000440888	RP11-315I14.2	1.8 (< .05)	DMRTA1	ELAVL2
lincRNA	ENST00000523242	CTB-43E15.1	1.7 (< .05)	BOD1	CPEB4
lincRNA	ENST00000366185	RP11-258C19.5	1.7 (< .05)	FAM156A	KDM5C
Processed transcript	ENST00000426282	CTA-217C2.1	1.7 (< .05)	PHF21B	KIAA0930
lincRNA	ENST00000436112	RP3-523C21.1	1.7 (< .05)	CTGF	MOXD1
lincRNA	ENST00000435967	RP4-594A5.1	1.6 (< .05)	ICA1	NXPH1
lincRNA	ENST00000488287	CT64	1.6 (< .05)	NMD3	SPTSSB
lincRNA	ENST00000446884	RP1-30G7.2	1.6 (< .05)	CXorf36	KRBOX4
lincRNA	ENST00000417112	RP11-554I8.2	1.5 (< .05)	PRKCQ	SFMBT2
lincRNA	ENST00000416401	RP11-77M5.1	1.5 (< .05)	RGS5	NUF2
lincRNA	ENST00000511840	CTD-2066L21.2	1.5 (< .05)	NPR3	TARS
Retained intron	ENST00000436578	AC005532.5	1.5 (< .05)	C1GALT1	COL28A1
lincRNA	ENST00000430244	RP11-166O4.5	1.5 (< .05)	TYW1	AUTS2
lincRNA	ENST00000471357	LINC00880	1.5 (< .05)	LEKR1	CCNL1
lincRNA	ENST00000508147	RP11-622A1.2	1.5 (< .05)	AFM	RASSF6
Sense overlapping	ENST00000530072	RP11-166D19.1	-1.5 (< .05)	SORL1	BLID
lincRNA	ENST00000455957	HCG17	-1.5 (< .05)	TRIM15	TRIM39
Retained intron	ENST00000521127	SNHG6	-1.5 (< .05)	MCMDC2	PPP1R42
lincRNA	ENST00000451230	AC108463.1	-1.6 (< .05)	BCL2L11	ZC3H8
lincRNA	ENST00000449259	AC007386.2	-1.6 (< .05)	SERTAD2	SLC1A4
lincRNA	ENST00000453722	LINC00511	-1.6 (< .05)	SOX9	SLC39A11
Processed transcript	ENST00000431616	LINC00630	-1.6 (< .05)	BHLHB9	RAB40AL
lincRNA	ENST00000443576	RP11-141M1.1	-1.7 (< .05)	STARD13	RFC3
Processed transcript	ENST00000430756	RP11-761E20.1	-1.7 (< .05)	PLS3	AGTR2
Processed transcript	ENST00000416650	RSBN1L-AS1	-1.7 (< .05)	PTPN12	RSBN1L
Sense intronic	ENST00000433544	RP11-488P3.1	-1.7 (< .05)	BCAR3	DNTTIP2
lincRNA	ENST00000415611	AC005682.5	-1.7 (< .05)	TOMM7	FAM126A
lincRNA	ENST00000505448	RP11-774O3.3	-1.7 (< .05)	HTRA3	ACOX3
Antisense	ENST00000496733	TMEM161B-AS1	-1.8 (< .05)	TMEM161B	MEF2C
lincRNA	ENST00000529893	RP1-80B9.2	-1.8 (< .05)	GMDS	C6orf195
lincRNA	ENST00000552334	RP11-701H24.2	-1.8 (< .05)	SNURF	UBE3A
lincRNA	ENST00000515871	CTC-325J23.3	-1.8 (< .05)	ANKRD34B	DHFR
lincRNA	ENST00000433747	RP11-120D5.1	-1.8 (< .05)	MID1	AMELX
lincRNA	ENST00000438762	AP000473.5	-1.8 (< .05)	USP25	CXADR

Antisense	ENST00000511571	RP11-453E17.1	-1.9 (< .05)	TMPRSS11A	TMPRSS11B
Antisense	ENST00000456602	RBM26-AS1	-1.9 (< .05)	RBM26	NDFIP2
lincRNA	ENST00000437261	AC108066.1	-1.9 (< .05)	ERBB4	IKZF2
lincRNA	ENST00000454635	LINC00963	-1.9 (< .05)	IER5L	NTMT1
lincRNA	ENST00000433079	AC058791.2	-1.9 (< .05)	KLF14	MKLN1
lincRNA	ENST00000444488	TPRG1-AS1	-1.9 (< .05)	LPP	TPRG1
lincRNA	ENST00000505155	RP11-584P21.2	-1.9 (< .05)	EPHA5	CENPC
lincRNA	ENST00000444265	LINC00340	-2.0 (< .05)	SOX4	PRL
lincRNA	ENST00000537192	RP11-1038A11.3	-2.0 (< .05)	KCNA5	NTF3
lincRNA	ENST00000514791	RP11-434D9.2	-2.0 (< .05)	CD180	PIK3R1
lincRNA	ENST00000508619	RP3-513G18.2	-2.0 (< .05)	LRPAP1	ADRA2C
Antisense	ENST00000437157	RP3-510D11.1	-2.0 (< .05)	GPR157	H6PD
lincRNA	ENST00000412722	LINC00427	-2.1 (< .05)	KATNAL1	HMGB1
lincRNA	ENST00000398518	MEG3	-2.1 (< .05)	DLK1	RTL1
lincRNA	ENST00000418006	LINC00940	-2.1 (< .05)	LRTM2	DCP1B
lincRNA	ENST00000534336	MALAT1	-2.2 (< .05)	FRMD8	SCYL1
Antisense	ENST00000434399	AC005154.6	-2.5 (< .05)	GGCT	GARS
lincRNA	ENST00000455395	FTX	-3.7 (< .05)	NAP1L2	ZCCHC13
Processed transcript	ENST00000451141	MIAT	-4.3 (< .05)	CRYBB1	MN1

134 **Supplementary Figure 1: Effect of dexamethasone and FCS upon asthmatic ASM cell**
135 **proliferation and IL-6 release.** ASM cells were incubated with dexamethasone (10^{-7} M) for 1
136 h before being stimulated with FCS (2.5 %) for 24 h. DNA synthesis (A), cell viability (B),
137 and IL-6 (C) release were measured by BrdU ELISA, MTT assay, or DuoSet ELISA
138 respectively. Bars represent mean \pm SEM from 9 ASM cell donors. ** $p < 0.01$; ***/### $p <$
139 0.001.

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141 **Supplementary Figure 2: Transfection efficiency in ASMCs from healthy subjects and**
142 **severe asthmatics at 8 days.**

143 IL-6 release (A&B), or cellular viability (C-F) were measured by DuoSet ELISA Assay (R&D
144 Systems), or MTT assay (Sigma) respectively at 8 days. Bars represent the means \pm SEMs of
145 9 ASM cell donors. ** $P < 0.01$; *** $P < 0.001$.

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References

- (1) Chung KF, Wenzel SE, Brozek JL, Bush A, Castro M, Sterk PJ et al. International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. *Eur Respir J* 2014; 43(2):343-73.
- (2) Perry MM, Durham AL, Austin PJ, Adcock IM, Chung KF. BET bromodomains regulate TGF-beta-induced proliferation and cytokine release in asthmatic airway smooth muscle. *J Biol Chem* 2015.
- (3) Perry M, Tsitsiou E, Austin P, Lindsay M, Gibeon D, Adcock I et al. Role of non-coding RNAs in maintaining primary airway smooth muscle cells. *Respiratory Research* 2014; 15(1):58.
- (4) Perry MM, Hui CK, Whiteman M, Wood ME, Adcock I, Kirkham P et al. Hydrogen Sulfide Inhibits Proliferation and Release of IL-8 from Human Airway Smooth Muscle Cells. *Am J Respir Cell Mol Biol* 2011; 45(4):746-52.
- (5) Perry MM, Baker JE, Gibeon DS, Adcock IM, Chung KF. Airway Smooth Muscle Hyperproliferation Is Regulated by MicroRNA-221 in Severe Asthma. *Am J Respir Cell Mol Biol* 2013; 50(1):7-17.
- (6) O'Leary L, Sevinc K, Papazoglou IM, Tildy B, Detillieux K, Halayko AJ et al. Airway Smooth Muscle Inflammation Is Regulated by MicroRNA-145 in COPD. *FEBS Lett* 2016.
- (7) Mosmann T. Rapid colorimetric assay for cellular growth and survival: application to proliferation and cytotoxicity assays. *J Immunol Methods* 1983; 65(1-2):55-63.
- (8) Perry MM, Moschos SA, Williams AE, Shepherd NJ, Larner-Svensson HM, Lindsay MA. Rapid Changes in MicroRNA-146a Expression Negatively Regulate the IL-1beta-Induced Inflammatory Response in Human Lung Alveolar Epithelial Cells. *The Journal of Immunology* 2008; 180(8):5689-98.
- (9) Perry MM, Baker JE, Gibeon DS, Adcock IM, Chung KF. Airway Smooth Muscle Hyperproliferation Is Regulated by MicroRNA-221 in Severe Asthma. *Am J Respir Cell Mol Biol* 2013; 50(1):7-17.
- (10) Larner-Svensson HM, Williams AE, Tsitsiou E, Perry MM, Jiang X, Chung KF et al. Pharmacological studies of the mechanism and function of interleukin-1beta-induced miRNA-146a expression in primary human airway smooth muscle. *Respir Res* 2010; 11:68.

