Revised manuscript ERJ-02298-2016

Transcriptomic gene signatures associated with persistent airflow limitation in patients with severe asthma

P.P. Hekking[1], M.J. Loza[2], S. Pavlidis[3], B. De Meulder[4], D. Lefaudeux[4], F. Baribaud[2], C. Auffray[4], A.H. Wagener[1], P. Brinkman[1], R. Lutter[1], A.T. Bansal[5], A.R. Sousa[6], S. Bates[6], Y. Pandis[3], L.J. Fleming[3], D.E. Shaw[7], S.J. Fowler[8], Y. Guo[3], A. Meiser[3], K. Sun[3], J. Corfield[9], P. Howarth[10], E.H. Bel[1], I.M. Adcock[11], K.F. Chung[11], R. Djukanovic[10], P.J. Sterk[1], and the U-BIOPRED Study Group*

1: Respiratory Medicine, Academic Medical Centre, Amsterdam, the Netherlands; 2: Janssen research and development; Johnsen & Johnsen, Springhouse, US; 3: Data Science Institute, Imperial College, London, UK; 4: European Institute for Systems Biology and Medicine, CIRI UMR5308, CNRS-ENS-UCBL-INSERM, Université de Lyon, France; 5: Acclarogen Ltd, Cambridge, UK; 6: Discovery Medicine, GlaxoSmithKline, Brentford, UK; 7: Respiratory Research Unit, University of Nottingham, UK; 8: Centre for Respiratory Medicine and Allergy, Institute of Inflammation and Repair, University of Manchester and University Hospital of South Manchester, Manchester Academic Health Sciences Centre, UK; 9: Areteva, Nottingham, UK; 10: NIHR Southampton Centre for Biomedical Research, University of Southampton, UK; 11: National Heart & Lung institute - Imperial College, London, UK;*A list of the U-BIOPRED study group can be found in the online supplement

Corresponding author:
Pieter-Paul Hekking,
Academic Medical Centre (AMC),
Department of Respiratory Medicine, F5-260
1105 AZ, Amsterdam, the Netherlands
Telephone: +31 (0) 20 566 1660
Fax: +31 (0) 20 566 9001
E-mail: p.w.hekking@amc.uva.nl

Take home message

Persistent airflow limitation in severe asthma is associated with a mechanism in which IL-13 and remodeling are involved.

Abstract (max 200 words)

Rationale: A proportion of severe asthma patients suffers from persistent airflow limitation, often associated with more symptoms and exacerbations. Little is known about the underlying mechanisms. Aiming for discovery of unexplored potential mechanisms, we used Gene Set Variation Analysis (GSVA), a sensitive technique that can detect underlying pathways in heterogeneous samples.

Methods: Severe asthma patients from the U-BIOPRED cohort with persistent airflow limitation (post-bronchodilator FEV_1/FVC ratio < lower limit of normal) were compared to those without persistent airflow limitation. Gene expression was assessed on the total RNA of sputum cells, nasal brushings and endobronchial brushings and biopsies. GSVA was applied to identify differentially-enriched pre-defined gene signatures based on all available gene expression publications and data on airways disease.

Results: Differentially-enriched gene signatures were identified in nasal brushings (1), sputum (9), bronchial brushings (1) and bronchial biopsies (4), that were associated with response to inhaled steroids, eosinophils, IL-13, IFN-alpha, specific CD4+ T-cells and airway remodeling.

Conclusion: Persistent airflow limitation in severe asthma has distinguishable underlying gene networks that are associated with treatment, inflammatory pathways and airway remodeling. These results point towards targets for the therapy of persistent airflow limitation in severe asthma.

Introduction

A small proportion of asthma patients suffers from uncontrolled disease despite treatment with high-dose inhaled or oral steroids, which is defined as severe asthma [1, 2]. These patients are in need of effective and steroid-sparing treatments. However, severe asthma is a heterogeneous disease, which complicates the development of these treatments [3, 4]. Emerging targeted treatments appear to be successful in selected subgroups of patients with specific characteristics, such as eosinophilic airway inflammation [5] and allergy [6] emphasizing the need for precision medicine in severe asthma [7].

Agusti *et al*. recently described a novel strategy for the treatment of chronic airways disease, focusing on treatable traits based on clinical, physiological and/or biological characteristics rather than solely on a diagnosis of asthma or COPD [8]. Persistent airflow limitation (PAL) was postulated as a treatable trait of airways disease, being characterized by reduced expiratory flow even after the administration of a short-acting bronchodilator. Notably, PAL is not only a determinant for the diagnosis of COPD, but regardless of a smoking history, has also long been implicated in patients with severe asthma [9].

PAL is clinically relevant in severe asthma as it may have prognostic implications. Even though PAL and exacerbations are different phenotypic characteristics, there is evidence of an association of PAL with more frequent exacerbations and more hospitalizations in subgroups of severe asthma patients [10, 11]. Clinical clustering studies showed that PAL is an important constituent for severe asthma phenotypes that are characterized by eosinophilic airway inflammation, poor quality of life and smoking history [11-14]. To understand this clinical trait, several studies have been conducted to identify risk factors for PAL in smoking and non-smoking severe asthmatics. Eosinophilic airway inflammation [9, 15], longer duration of disease [9, 15, 16], adult-onset of disease [9] and a history of smoking [16] appear to be the most important. However, management strategies for the prevention

or treatment of PAL in severe asthma are lacking, which is unsurprising given the lack of knowledge regarding its mechanism.

Airway remodeling, associated with chronic inflammation, may contribute to PAL in asthma. Thickening of the airway smooth muscle layer [15], changes in extracellular matrix e.g. subepithelial fibrosis [17] and infiltration of inflammatory cells in the bronchial airway wall [18] have been linked to increased lung function decline. Even though studies have been conducted to identify underlying pathways of airway remodeling [19, 20], little is known about the underlying mechanism of PAL in severe asthma. Notably, there are differences in airway remodeling between patients with severe and patients with non-severe asthma [21], demonstrating the need to examine the underlying pathways of PAL in patients with severe asthma themselves.

Gene Set Variation Analysis (GSVA) is a sensitive statistical technique that can be used for identifying underlying pathways in heterogeneous samples [22]. Instead of more conventional analysis of single gene expression, GSVA allows between-groups comparisons of the expression of gene sets that are known to be associated with biological networks of relevance. This identifies differences in underlying pathways in severe asthma patients with PAL in comparison to those without PAL.

We hypothesized that patients with severe asthma and PAL exhibit different gene expression profiles as compared to those without PAL. The aim of the present study was to identify transcriptomic pathways of PAL in severe asthma by applying GSVA in sputum, nasal brushings and endobronchial brushings and biopsies. This study was conducted in the severe asthma adult cohort of the U-BIOPRED study, which according to a recent cluster analysis based on clinical and physiological parameters includes subsets of patients with and without PAL [23].

45 **Methods**

46 The detailed methods section is provided in full in the Online Supplement.

47 Design and subjects

48 This was a cross-sectional, observational study using data from the adult severe asthma cohort of U-
49 BIOPRED. Details on the design of U-BIOPRED have been published previously [24]. Severe asthma
50 was defined according to the IMI consensus statement [25]. Patients were included who had a
51 confirmed diagnosis of asthma that was uncontrolled despite high intensity asthma treatment
52 (≥1000µg Fluticasone eq. plus a second controller) or could only be controlled with treatment by
53 systemic oral corticosteroids (OCS) or omalizumab, including current-smokers, ex-smokers and
54 never-smokers. The U-BIOPRED study was registered at ClinicalTrials.gov identifier NCT01976767 and
55 was approved by the Medical Ethics Boards of all participating centers. All patients provided written
56 informed consent.

57 Persistent Airflow Limitation

58 PAL was defined as post-bronchodilator FEV_1/FVC < lower limit of normal (LLN). The LLN was
59 calculated according to formulae provided by Quanjer *et al.* [26] (for male subjects: -0.18*AGE +
60 75.41; for female subjects: -0.19*AGE + 78.4), consistent to LLN defined by Global Lung Function
61 Initiative (GLI) [27]. In order to examine consistency with other criteria for PAL we additionally
62 performed an analysis based on PAL defined by post-bronchodilator FEV_1 < LLN.

63 Measurements

64 *mRNA samples*

65 Gene expression was assessed on the total RNA in unselected samples of severe asthma patients in
66 the following four airway compartments: (1) nasal brushing (n=37), (2) induced sputum (n=79), (3)

67 endobronchial brushings (n=62) and (4) endobronchial biopsies (n=50). There was no complete
68 overlap between the samples, mainly because of limited sputum induction success rate (Fig. 1). For
69 details on sample collection see online supplement.

70 Microarray analysis was performed with the Affymetrix HT HG-U133+ PM microarray platform
71 (Affymetrix, Santa Clara, Ca). For details see online supplement.

72 **Statistical analysis**

73 For details on the statistical analysis on clinical variables see online supplement.

74 Gene set variation analysis (GSVA) is a statistical technique that allows sensitive identification of
75 differences in expression of predefined sets of genes between heterogeneous groups and can be
76 used to explore underlying pathways [22]. Sets of genes used were based on all available gene
77 expression publications and data on airways disease, including human and murine models, from both
78 *in vivo* and *in vitro* studies, to assure sensitive pathway detection. These contained studies on the
79 gene expression associated with (1) airway disease treatment, (2) immunologic pathways and (3)
80 induced lung injury or inflammation. The latter included gene signatures that were identified at
81 several time points after the admission of either Poly(I:C) as a model for exacerbations [28] or
82 bleomycin, which is used as a model for mimicking the course of fibrotic processes in the lung [29].
83 For this discovery study 105 predefined gene sets were entered into the statistical models (Table E8).

84 *Enrichment scores and false discovery*

85 GSVA was used to calculate enrichment scores (ES) for each patient and for each of the gene
86 signatures based on the gene expression of genes in the sets. ES range from a value of -1 to 1 [22].
87 Subsequently, mean ES were calculated for patients with and without PAL and Generalized Linear
88 Models, including correction for smoking status, corticosteroid usage and duration of asthma, were
89 applied to statistically compare ES between the groups. To minimize the false discovery rate, only

90 gene signatures that had $p<0.05$ and a difference of ES (dES) between of the groups of ≥ 0.2 were
91 considered significantly different, following the Microarray Consortium for Quality Control (MACQC)
92 recommendations regarding the need for applying group-difference thresholds in order to stringently
93 limit false discovery [30].

94

95 **Results**

96 Of 421 severe asthma patients in the U-BIOPRED cohort 224 (58%) had PAL. These patients were
97 significantly older and had longer asthma duration than severe asthma patients without PAL (Table
98 1). In addition, they had significantly more eosinophilia in blood and sputum. Patients with and
99 without PAL did not significantly differ in smoking behavior, pack years and exacerbation rate. Some
100 distinct patient characteristics were found when patients were grouped according to site of mRNA
101 collection. Significantly fewer females and higher blood neutrophil counts were observed in patients
102 with PAL in the nasal and endobronchial brushing subsets. In addition, the number of pack years was
103 higher in patients with PAL in the endobronchial brushings and biopsies subsets (Table 2 and see
104 Tables E1-E4 for p-values).

105 <u>Identified Gene Signatures</u>

106 In total, GSVA identified 14 gene signatures that were significantly differentially enriched in patients
107 with PAL as compared to those without PAL: 1 in the nasal brushes, 9 in sputum, 1 in endobronchial
108 brushes and 4 in endobronchial biopsies (Table 3).

109 *Treatment gene signatures*

110 Two gene signatures that were expressed to a lesser extent in asthmatics and COPD patients after
111 treatment with fluticasone were significantly differentially enriched. The gene signature lowly
112 expressed in fluticasone-treated asthma (Table E7, #12) patients was significantly more enriched in
113 the bronchial brushes of patients with PAL (dES 0.22, p=0.0012). Similarly, the lowly expressed gene
114 signature after fluticasone treatment in COPD patients, containing a different set of genes (Table E7,
115 34), was also enriched to a greater extent in patients with PAL (dES 0.22; p=0.045) (Table 3 and Fig. 4
116 and Fig. 5).

117 *Immunologic gene signatures*

118 Four gene signatures that are associated with immunologic pathways were identified to be
119 significant differentially enriched between the groups. First, a gene signature that is upregulated in
120 the presence of eosinophils (Table E7, #55) was more enriched in the sputum of patients with PAL as
121 compared to without PAL (dES = 0.21, p=0.04) (Fig. 3). Second, a gene signature that is identified to
122 be associated with the presence of IL-13 (Table E7, #101) was more enriched in the nasal brushings
123 of PAL patients (dES=0.27; p=0.045) (Fig. 2). Third, the ES for the IFN-alpha gene signature (Table E7,
124 #36) was less enriched in the sputum of patients with PAL (dES=0.32; p<0.001) (Fig. 3). Finally, the ES
125 for CD4 T-cells of rheumatoid arthritis patients (Table E7, #27) was more enriched in patients with
126 PAL (dES = 0.21, p=0.029) (Fig. 3).

127 *Induced lung injury gene signatures*

128 In total eight gene signatures that are associated with induced airway inflammation or lung injury
129 were identified to be significantly differentially enriched. Five of them were discovered in a study in
130 which gene expression was assessed at different time points after the admission of Poly I:C (Table E7,
131 #57,58,62,64,65), mimicking viral replication. Patients with PAL had significant lower enrichment of
132 these signatures in sputum, ranging from dES -0.25 to -0.20 (Fig. 3). In addition, three gene
133 signatures associated with Bleomycin-induced lung injury (Table E7, #67,68,77) were significantly
134 differentially enriched, one associated with higher expression of genes during early development of
135 injury (Table E7, #67) demonstrating a significantly lower ES in sputum (dES = -0.24; p=0.012), and a
136 higher ES in endobronchial biopsy (dES = 0.22; p=0.045) in PAL patients. In addition, the gene
137 signatures identified to be higher expressed at later stages of bleomycin-induced injury (Table 5,
138 #67,77) had a lower ES in PAL patients (dES = -0.20; p=0.006) (dES = -0.41; p=0.026) (Table 3 and Fig.
139 5).

140

141 *Consistency when using different definition of PAL*

142 The data when using postbronchodilator-FEV_1 for defining PAL is given in the online supplement. This
143 showed that in general identified signatures between FEV_1/FVC < LLN and FEV_1 <LLN were similar,
144 including those associated with treatment with fluticasone, eosinophilic inflammation and
145 involvement of T_H2 helper cells and IFN-alpha. In addition, induced lung injury and inflammation
146 gene signatures were identified in both analyses as well (Table E6). However, specific involvement of
147 IL-13 and CD4 T-cells of rheumatoid arthritis was not consistent, and no significant gene signatures
148 were identified in the biopsies when applying FEV_1 < LLN.

149 Discussion

150 This study shows that severe asthma patients with PAL have differentially enriched gene sets as
151 compared to patients without PAL, suggesting that distinguishable underlying mechanisms are
152 involved. The identified gene signatures may indicate that these patients respond or have responded
153 differently to treatment with inhaled corticosteroids, and that particular immunologic pathways are
154 involved. These include the already recognized eosinophilic airway inflammation, but also specific
155 CD4+ T-cells and involvement of IL-13, possibly via T_H2-helper cells. In addition, a differentially
156 expressed gene network associated with remodeling was identified in the endobronchial airway wall,
157 whilst not being identified in other compartments, underlining local involvement of remodeling.
158 These results show that PAL is biologically distinguishable in severe asthma and point towards
159 possible targets for the prevention and treatment of PAL.

160 This study is the first to assess gene signatures underlying PAL for the discovery of its mechanisms in
161 severe asthma. Clinical characterization of the present patients with PAL showed no association with
162 exacerbation rate. Multiple studies in severe asthma have shown mixed results. Some found
163 associations between more frequent exacerbations and PAL, especially in certain phenotypes of
164 severe asthma [10, 11], whereas others observed no association [13] or even an inverse one
165 indicative of more frequent exacerbations in patients without PAL [9]. This suggests that certain
166 subgroups of severe asthma patients may suffer from both clinical traits. However, in a broad severe
167 asthma population, such as the present study, PAL and exacerbations may need to be seen as
168 separate clinical treats.

169 GSVA not only confirmed expected mechanisms but also identified novel pathways in PAL. First, the
170 results indicate that the airways of severe asthma patients with PAL respond differently to the
171 administration of inhaled corticosteroids. Even though a relation between severe asthma and
172 resistance to steroids has been recognized [31], a specific association with PAL has not previously

been reported. Second, not surprisingly, a gene set associated with eosinophilic airway inflammation was identified in the sputum of patients with PAL. Eosinophilic airway inflammation has been reported in patients with PAL by multiple studies in severe asthma and was present in this study population as well [9, 14, 15]. Third, IL-13 was identified to be involved in PAL in severe asthma, which was in concordance with a study by Kaminska *et al.* who identified IL-13 in bronchial biopsies of severe asthma patients with PAL [32].

Interestingly, in sputum samples we have identified a gene set associated with interferon-alpha (IFN-alpha) that was lower enriched in patients with PAL. Impaired or decreased IFN-alpha has been associated with severe asthma as compared to controls [33, 34] and, in a murine asthma model, where IFN-alpha inhibits eosinophilic airway inflammation and hyperresponsiveness [35]. However, a direct association with PAL in (severe) asthma has not been described before. In addition, patients with PAL appear to have lower enrichment of gene sets expressed after exposure to Poly(I:C), mimicking viral replication upon infection. The recognized link between Poly(I:C) and interferons strengthen these results [36]. Impaired lung function has been found after exposure to Poly(I:C) in mice [37], however it is unknown to what extent the ability to respond to viral infections influences lung function. Moreover, the present data indicate a role for CD4+ T-cells, which has been associated previously with reduced lung function in patients with asthma [18]. Finally, remodeling has been recognized to be associated with PAL in (severe) asthma [17, 18] and in concert with this, our data identified gene sets associated with bleomycin-induced lung injury and fibrotic processes in the endobronchial airway wall to be more enriched in severe asthma patients with PAL.

We believe the strengths of this study include the following. It was conducted in the severe asthma cohort of the pan-European U-BIOPRED study, which included a large number of well-selected and defined patients. The study included severe asthma patients with PAL and those without PAL with equally severe disease as an appropriate control group for analyzing the distinguishing gene

197 signatures of PAL amongst patients with severe asthma. The multi-centre design allowed
198 standardized collection of large numbers of samples from patients all over Europe. In addition,
199 collection of these samples was standardized and performed according to SOPs, whilst mRNA
200 expression in these samples was analyzed centrally to gain optimized data quality. Furthermore,
201 using GSVA as sensitive statistical technique enabled the identification of underlying pathways
202 involved in PAL even in heterogeneous samples, such as severe asthma. Finally, selection bias was
203 minimized by correction for smoking status, asthma duration and usage of oral corticosteroids as
204 such. However, correction for corticosteroid dose was not indicated as this was similar between the
205 groups. Similarly, no correction for cell counts was applied as this could partly obscure the disease
206 mechanism of PAL in severe asthma.

207 This study also has limitations. First, this was a cross-sectional study, whilst lung function may vary
208 over time. Stringent selection criteria for PAL were applied to minimize possible misdiagnosing of
209 patients, but we cannot exclude longitudinal variations in PAL. The definition of PAL was derived
210 from the LLN on two measures of PAL based on the Quanjer values. Applying the GLI reference
211 equations for the LLN to our dataset had very little influence on the distribution of patients with or
212 without PAL, since in total only 3 patients included in the GSVA analyses would switch groups.
213 Second, as shown in Figure 1, there is incomplete overlap of patients of whom various samples had
214 been collected, which was unintended but inevitable due to patient's consent, feasibility and quality
215 control (*e.g.* for bronchoscopies and induced sputum). This hampers comparison of the identified
216 gene sets between the different compartments. The sample size for nasal brushings for example was
217 modest. Nevertheless, concordance of identified gene signatures between the different
218 compartments (*e.g.* on gene sets for fluticasone treatment and Bleomycin-induced injury) and
219 concordance in identified gene signatures by applying two definitions for PAL lends validity to the
220 identified pathways in the different samples. Third, GSVA requires predefined gene sets to be put
221 into the analysis. These gene signatures are acquired from literature and are based on other studies

222 reported thus far. Inevitably, those studies had their own flaws as well, which were not taken into
223 account in this study. In addition, some of the gene signatures are derived from mouse model
224 studies. These data from mouse models was purposely included, because only by broad, non-
225 selective input of gene signatures into the analysis, novel mechanisms involving in PAL may be
226 discovered. However, it needs to be emphasized that murine models will certainly deviate from
227 human disease and it remains to be established whether the murine signatures can be used to
228 identify phenotypic differences in severe asthma. Furthermore, by applying predefined gene sets, we
229 may have gene interactions that are not annotated yet and thus not identified in this study. Finally,
230 this study did not include a separate validation set or internal validation. The sample sizes were not
231 large enough for splitting into a training and validation set. However, we have applied the most
232 stringent measures for the prevention of false discovery of gene signatures by only selecting gene
233 signatures with a low p-value and a minimum difference of enrichment score, following the
234 standardized Microarray Consortium for Quality Control (MACQC) recommendations for the
235 importance of applying group-difference thresholds for gaining best reproducible results [30]. In
236 addition, the results were largely consitent when defining PAL by using FEV_1 or FEV_1/FVC, which
237 contributes to the validity of the data.

238 Based on the present results a few well-defined mechanisms are revealed in relation to PAL in severe
239 asthma. First, involvement of IL-13 does not seem to be surprising. Not only because it has been
240 directly associated with PAL before [32], but also because it has been linked to the other identified
241 pathways in this study. IL-13 has been associated with resistance to steroids in asthma [31, 38], and
242 is recognized as promotor for local eosinophil recruitment in the lungs [39]. In addition, IL-13 has
243 been identified as a direct promotor for airway remodeling [40]. Thus, IL-13 may be an important hub
244 for the several pathways involved in PAL in severe asthma.

245 Second, IFN-alpha deficiency, which may impair anti-viral responses [41], has been associated with
246 persistent asthma as such [34]. In addition, a mouse model study indicates that IFN-alpha inhibits
247 eosinophilic inflammation [33]. The results of our study imply that only the subgroup of severe
248 asthma patients, suffering from PAL, exhibits IFN-alpha deficiency or impairment, which may well be
249 associated with lower expression of gene sets associated with Poly(I:C). One could speculate that
250 IFN-alpha deficiency could result in enhanced viral loads during an infection or exacerbation and in
251 augmented inflammation, which in turn could result in airway wall remodeling and eventually PAL.
252 Finally, different gene signatures appeared to be enriched in the four compartments. Gene
253 expression related to airway remodeling was found in the more profound layers of the airway wall
254 (biopsies), but not in the superficial layers and lumen. The opposite is true for gene signature related
255 to inflammatory involvement, such as eosinophilia and CD4+ T-cells. This seems to be highly relevant,
256 perhaps not unexpectedly implying differential pathways at different locations in the respiratory
257 tract.

258 PAL has been recognized as a treatable trait in chronic airways disease [8]. Especially severe asthma
259 patients with PAL have high disease burden and therefore are in need for more individualized
260 management, so-called precision medicine. The present results suggest that patients with PAL may
261 be less responsive to inhaled steroids. Taking into account that these patients have more symptoms
262 and higher rates of exacerbations and hospitalizations [10], they seem to be the ones in most need
263 for targeted medicines, such newly developed biologicals. For instance, the involvement of IL-13
264 pathways in these patients may make them primary candidates for treatment with anti-IL-13.

265 In conclusion, severe asthma patients with PAL express different gene mechanisms as compared to
266 those without, being suggestive of specific disease mechanisms, including IL-13-associated disease
267 pathways, such as eosinophilic airway inflammation and remodeling with involvement of impaired

268 IFN-alpha function. Therefore, these may be the patients to be selected for studies on emerging new
269 treatments.

270

Table 1: Patient characteristics of patients with persistent airflow limitation (PAL)

	no PAL	PAL	*P-value*
n	197	224	
Female (%)	131 (66.5)	130 (58.0)	0.087
Age (yrs)*	**49.6 ± 14.6**	**54.0 ± 12.0**	**0.001**
BMI (Kg/m2)*	29.8 ± 6.5	28.7 ± 6.0	0.081
Asthma Duration (yrs)†	**20.0 [10.0 - 31.0]**	**25.5 [13.0 - 41.0]**	**0.001**
Smoking history (%)			0.084
Never	133 (67.5)	131 (58.5)	
Ex-smoker	50 (25.4)	65 (29.0)	
Current smoker	14 (7.1)	28 (12.5)	
Packyears†	9.4 [3.9 - 20.0]	13.0 [4.5 - 22.5]	0.407
OCS dose†	10.0 [8.0 - 20.0]	10.0 [7.0 - 15.0]	0.288
ACQ*	2.6 ± 1.2	2.7 ± 1.2	0.143
Exacerbations per year †	2.0 [2.0 – 4.0]	2.0 [1.3 – 4.0]	0.750
pbFEV$_1$ (% pred)*	**89.0 ± 16.1**	**63.7 ± 18.0**	**<0.001**
Blood Eosinophils (x10^9/L)†	**0.2 [0.1 - 0.4]**	**0.3 [0.1 - 0.5]**	**0.009**
Blood Neutrophils (x10^9/L)†	4.7 [3.7 - 6.2]	5.0 [3.7 - 7.5]	0.119
Sputum Eosinophils (%)†	**1.2 [0.2 - 4.6]**	**4.8 [1.2 - 22.1]**	**0.001**
Sputum Neutrophils (%)*	51.2 ± 26.0	54.6 ± 26.2	0.412

* mean ± SD; † median [Interquartile Range]; PAL: persistent airflow limitation; OCS: Oral corticosteroids; ACQ: Asthma Control Questionnaire; FEV$_1$: Forced Expiratory Volume in the first second

271

272 **Table 2: Patient characteristics of patients with persistent airflow limitation (PAL) according to site of mRNA collection**

273

	Nasal Brush		Sputum		Endobronchial Brush		Endobronchial Biopsy	
	No PAL	**PAL**	**No PAL**	**PAL**	**No PAL**	**PAL**	**No PAL**	**PAL**
N	15	22	21	58	30	32	22	28
Gender = Female (%)	**11 (73.3%)***	**8 (36.4%)***	13 (61.9%)	35 (60.3%)	**19 (63.3)***	**10 (31.2)***	14 (63.6%)	12 (42.9%)
Age (yrs)	47.5 ± 16.2	53.2 ± 12.1	52.5 ± 13.9	54.2 ± 11.4	46.7 ± 14.0	53.0 ± 11.1	48.4 ± 12.6	52.7 ± 11.2
BMI (Kg/m^2)	34.1 ± 6.6	29.4 ± 5.7	28.2 ± 5.0	28.1 ± 5.3	31.3 ± 6.3	28.5 ± 6.1	30.2 ± 5.4	28.6 ± 6.4
Asthma Duration (yrs)	25.0 [14.0 - 38.0]	21.5 [17.0 - 40.5]	23.1 ± 14.5	26.8 ± 17.2	26.4 ± 16.8	26.7 ± 17.9	25.8 ± 15.5	30.5 ± 18.7
Smoking Status (%)								
Never Smokers	12 (80.0)	11 (50.0)	11 (52.4%)	35 (60.3%)	22 (73.3)	15 (46.9)	16 (72.7%)	16 (57.1%)
Ex-smokers	3 (20.0)	8 (36.4)	8 (38.1%)	18 (31.0%)	7 (23.3)	12 (37.5)	5 (22.7%)	6 (21.4%)
Current-smokers	0 (0.0)	3 (13.6)	2 (9.5%)	5 (8.6%)	1 (3.3)	5 (15.6)	1 (4.5%)	6 (21.4%)
Packyears†	5.0 [3.3 - 5.1]	20.0 [11.5 - 38.5]	13.8 [2.9 - 19.7]	10.0 [2.8 - 18.8]	**5.1 [1.4 - 8.1]***	**18.8 [7.0 - 24.0]***	**5.3 [2.0 - 13.4]***	**21.5 [18.0 - 27.5]***
OCS dose (mg)†	10.0 [8.0 - 25.0]	10.00 [8.12 - 13.75]	10.0 [8.8 - 12.5]	10.0 [6.9 - 13.1]	10.0 [10.0 - 21.3]	10.0 [6.5 - 16.3]	10.0 [7.9 - 10.0]	10.0 [6.0 - 15.0]
ACQ	1.9 ± 1.0	2.2 ± 1.2	2.6 ± 1.4	2.6 ± 1.3	2.1 ± 1.2	2.4 ± 1.0	2.3 (1.3)	2.4 (1.1)
Exacerbations per year†	2.5 [1.0 – 4.0]	3.0 [1.0 - 4.0]	2.0 [2.0 – 3.5]	2.0 [1.5 – 4.0]	2.0 [2.0 – 3.5]	3.0 [2.0 – 4.0]	2.0 [2.0 – 3.3]	3.0 [2.0 – 4.0]
pbFEV$_1$ (% predicted)	**99.4 ± 17.6***	**71.5 ± 14.9***	**90.2 ± 14.0***	**63.5 ± 19.9***	**91.9 ± 14.3***	**66.7 ± 15.5***	**89.6 ± 13.6***	**68.3 ± 15.2***
Blood Eosinophils (x10^3/L)†	0.2 [0.1 - 0.4]	0.2 [0.1 - 0.3]	0.2 [0.2 - 0.3]	0.4 [0.2 - 0.5]	0.2 [0.1 - 0.4]	0.2 [0.1 - 0.3]	0.2 [0.1 - 0.3]	0.2 [0.1 - 0.3]
Blood Neutrophils (x10^3/L)†	3.8 [3.6 - 5.1]	5.0 [4.2 - 7.8]	4.3 [3.3 - 6.3]	5.0 [3.9 - 7.5]	**4.0 [3.2 - 5.4]***	**5.8 [4.1 - 7.7]***	4.0 [3.5 - 5.3]	5.0 [4.3 - 7.3]
Sputum Eosinophils (%)†	1.4 [0.4 - 4.6]	2.6 [0.2 - 13.8]	**1.3 [0.2 - 3.8]***	**6.2 [1.3 - 28.5]***	1.4 [0.6 - 4.6]	4.5 [0.2 - 24.9]	2.0 [0.7 - 8.0]	2.6 [0.2 - 6.1]
Sputum Neutrophils (%)	46.6 ± 18.4	63.2 ± 18.8	61.5 ± 23.6	58.5 ± 27.1	48.5 ± 20.7	61.6 ± 23.3	50.4 ± 19.5	56.5 ± 27.0

* Significant different between the groups ($p<0.05$) within each sample; mean ± SD; † median [Interquartile Range]; PAL: persistent airflow limitation; OCS: Oral corticosteroids; ACQ: Asthma Control Questionnaire FEV$_1$: Forced Expiratory Volume in the first second

Table 3: Differentially enriched gene signatures in severe asthma patients with PAL as compared to severe asthma patients without PAL.

	Gene signatures associated with	Nasal brush		Sputum		Endobr. Brush		Endobr. Biopsy	
		dES	p-value	dES	p-value	dES	p-value	dES	p-value
Treatment gene signatures	Fluticasone treatment in COPD - DOWN[1]							0.22	0.048
	Fluticasone treatment in asthma – DOWN[1]					0.22	0.012		
Immunologic gene signatures	Eosinophils – UP[1]			0.21	0.040				
	IL13 (Type-2 High) – UP[1]	0.27	0.045						
	IFN-alpha – UP[1]			-0.32	<0.001				
	RA in CD4 T-cells – UP[2]							0.21	0.029
Induced lung injury gene signatures	Induced inflammation (Poly I:C - 2h) – UP[3]			-0.21	0.018				
	Induced inflammation (Poly I:C - 6h) – UP[3]			-0.23	<0.001				
	Induced inflammation (Poly I:C - 48h) – UP[3]			-0.23	<0.001				
	Induced inflammation (Poly I:C - 72h) – UP[3]			-0.25	0.001				
	Induced inflammation (Poly I:C - 96h) – UP[3]			-0.22	0.003				
	Induced injury (Bleomycin - Day 1) – UP[3]			-0.24	0.012			0.22	0.043
	Induced injury (Bleomycin - Day 2) – UP[3]			-0.20	0.006				
	Induced injury (Bleomycin - Day 28) – DOWN[3]							-0.41	0.026

Differences in mean gene signature enrichment scores between severe asthma patients with PAL as compared to those without PAL (in RED are higher and in BLUE are lower). [1]In vitro model in human sample; [2]In vivo model in human sample; [3]In vivo model in murine model

288 Figure 1: Venn diagram indicating the overlap between the samples.

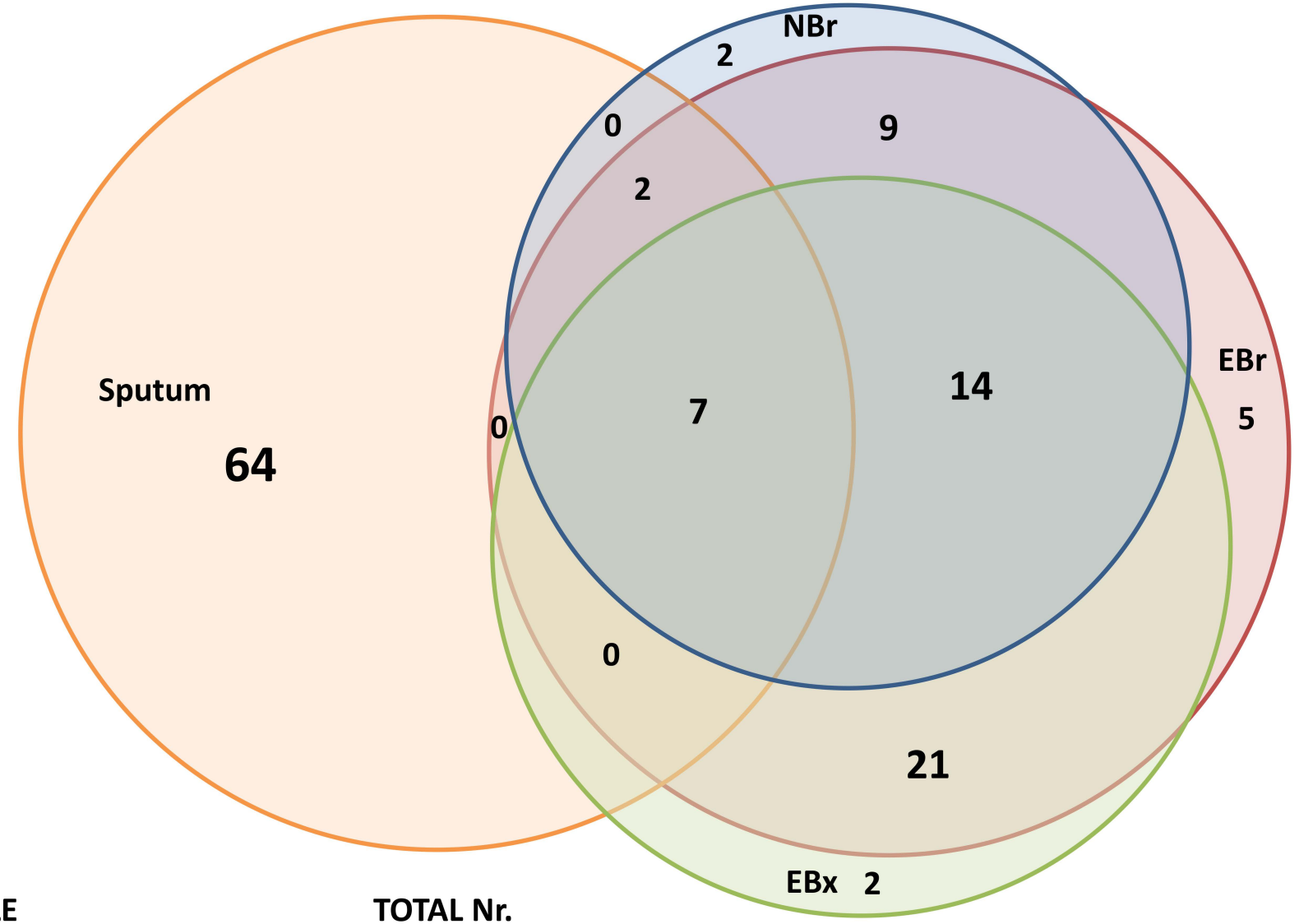
289 Figure 2: Significant gene signatures identified in nasal brushing samples. GSVA: Gene Set Variation
290 Analysis; PAL: Persistent airflow limitation

291 Figure 3: Significant gene signatures identified in sputum samples. GSVA: Gene Set Variation Analysis;
292 PAL: Persistent airflow limitation

293 Figure 4: Significant gene signatures identified in endobronchial brushing samples. GSVA: Gene Set
294 Variation Analysis; PAL: Persistent airflow limitation

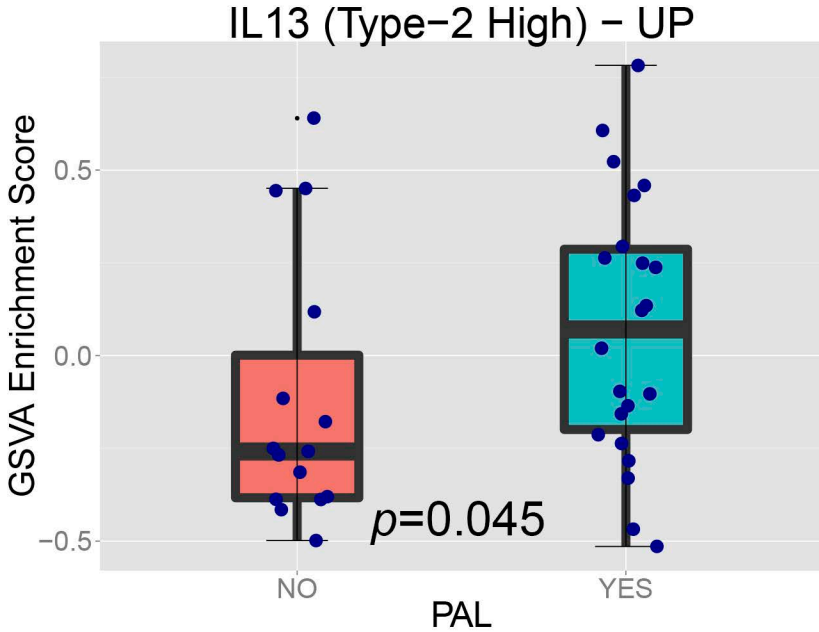
295 Figure 5: Significant gene signatures identified in endobronchial biopsy samples. GSVA: Gene Set
296 Variation Analysis; PAL: Persistent airflow limitation

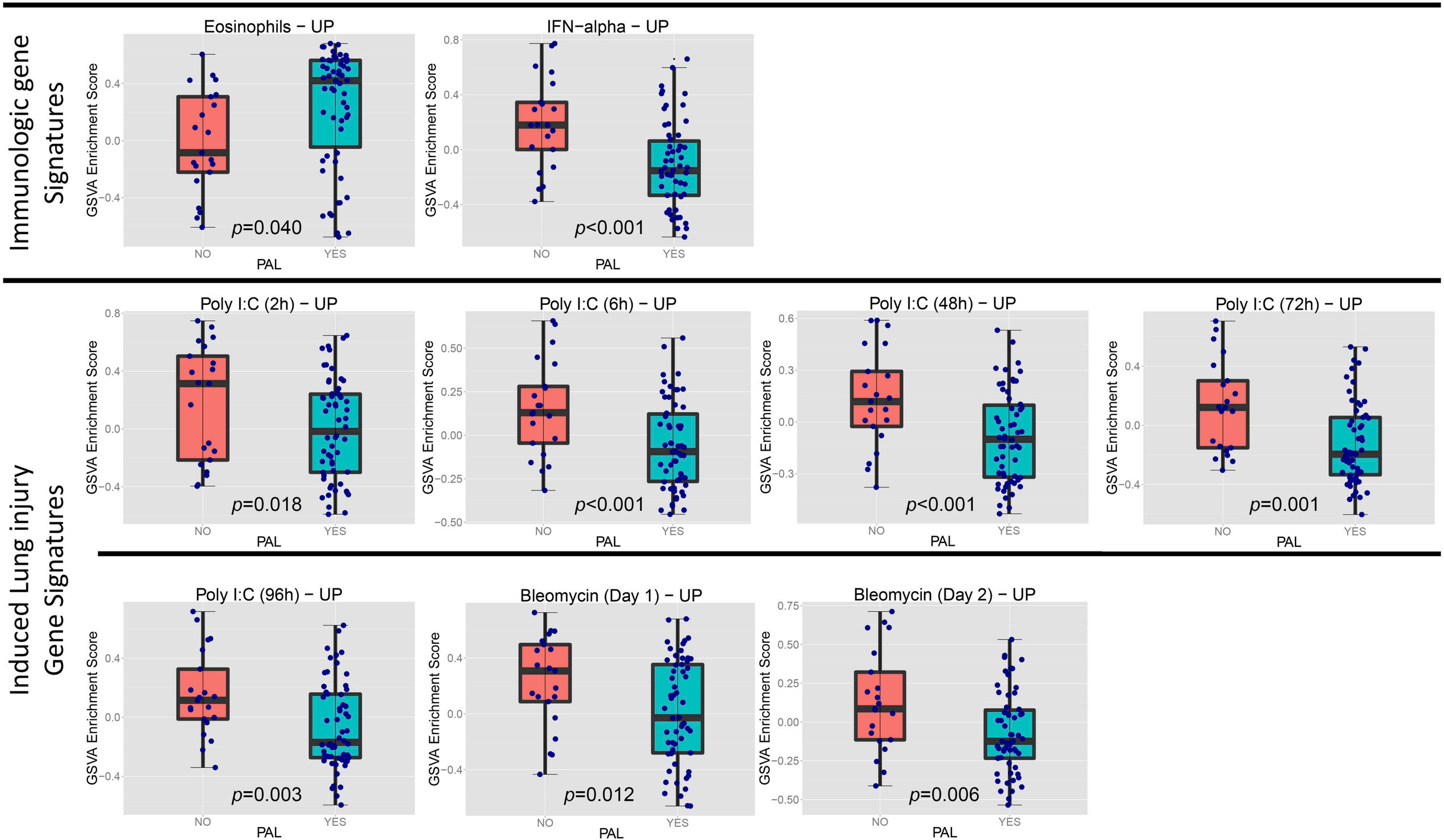
297



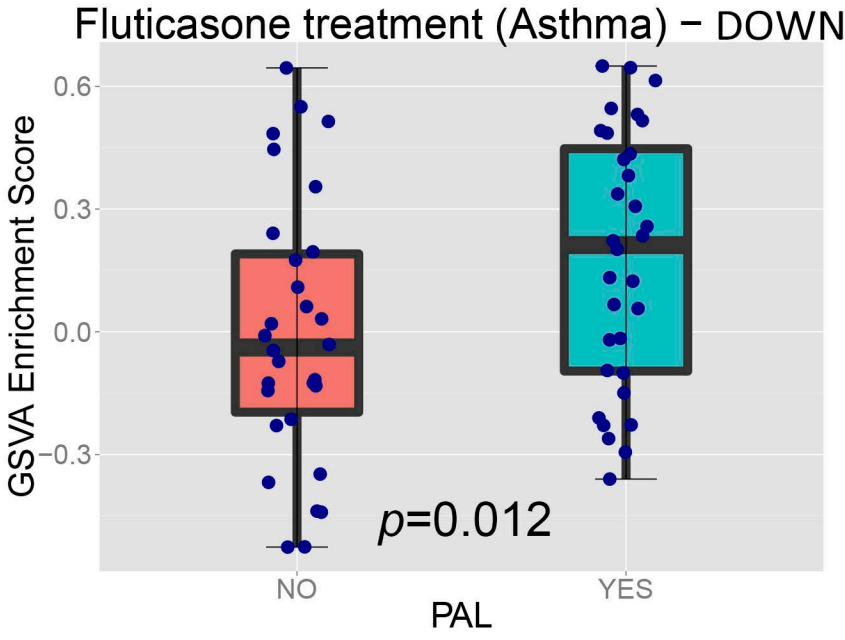
SAMPLE	TOTAL Nr.
Nasal Brush (NBr)	37
Sputum	79
Endobronchial Brush (EBr)	62
Endobronchial Biopsies (EBx)	50

Treatment gene signatures

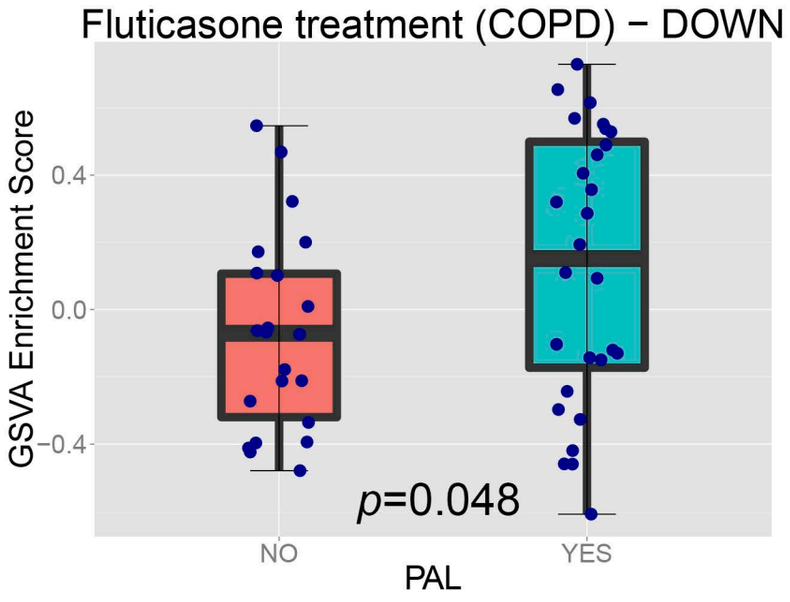



Immunologic gene Signatures
Eosinophils − UP
IFN−alpha − UP
Induced Lung injury Gene Signatures
Poly I:C (2h) − UP
Poly I:C (6h) − UP
Poly I:C (48h) − UP
Poly I:C (72h) − UP
Poly I:C (96h) − UP
Bleomycin (Day 1) − UP
Bleomycin (Day 2) − UP
GSVA Enrichment Score
PAL
NO
YES
p=0.040
p<0.001
p=0.018
p<0.001
p<0.001
p=0.001
p=0.003
p=0.012
p=0.006

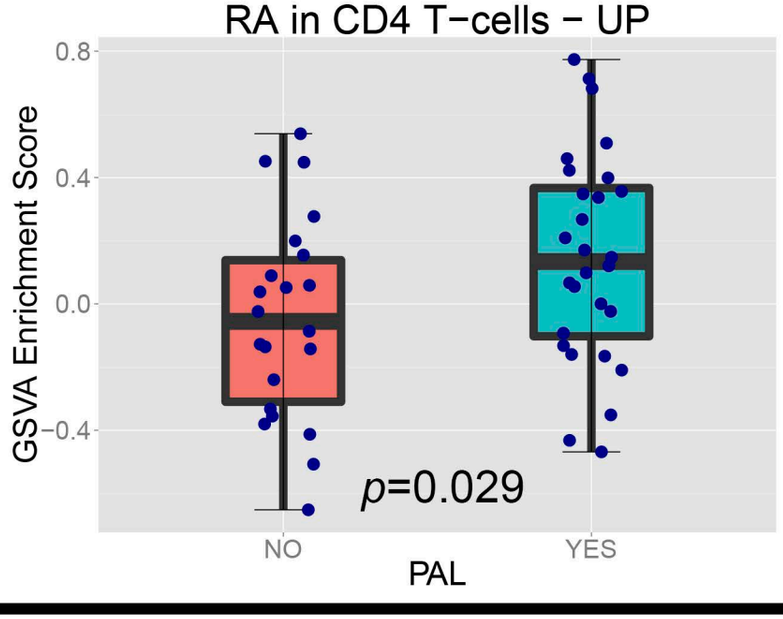
Treatment Gene Signatures



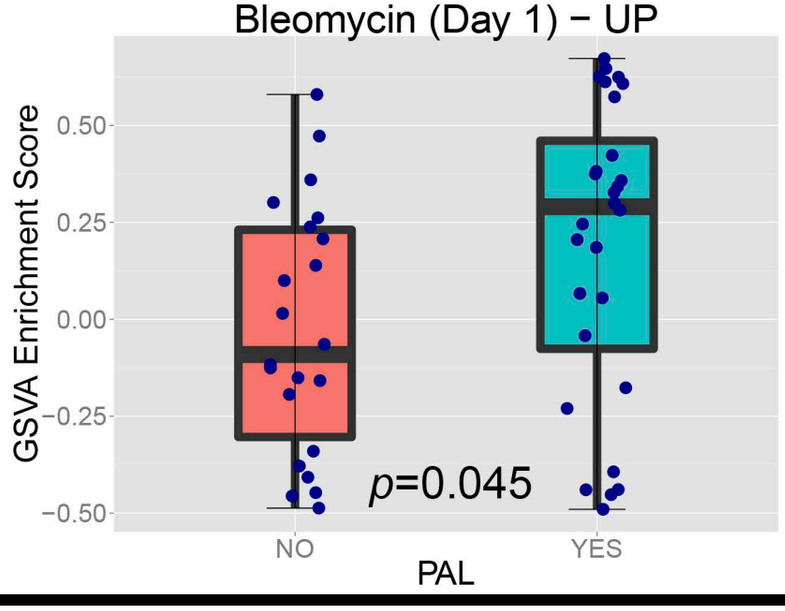
Treatment Gene Signatures

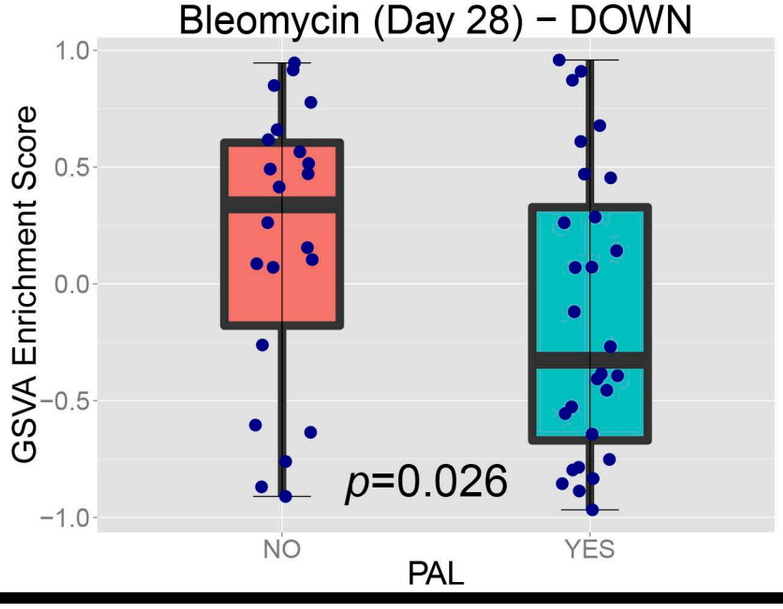


immunologic Gene Signatures



Induced Lung injury Gene Signatures





298 **References**

299 1. Chung KF, Wenzel SE, Brozek JL, Bush A, Castro M, Sterk PJ, Adcock IM, Bateman ED, Bel EH,
300 Bleecker ER, Boulet LP, Brightling C, Chanez P, Dahlen SE, Djukanovic R, Frey U, Gaga M, Gibson P,
301 Hamid Q, Jajour NN, Mauad T, Sorkness RL, Teague WG. International ERS/ATS guidelines on
302 definition, evaluation and treatment of severe asthma. *The European respiratory journal* 2014: 43(2):
303 343-373.
304 2. Hekking PP, Wener RR, Amelink M, Zwinderman AH, Bouvy ML, Bel EH. The prevalence of
305 severe refractory asthma. *The Journal of allergy and clinical immunology* 2015: 135(4): 896-902.
306 3. Hekking PP, Bel EH. Developing and emerging clinical asthma phenotypes. *The journal of*
307 *allergy and clinical immunology In practice* 2014: 2(6): 671-680.
308 4. Moore WC, Hastie AT, Li X, Li H, Busse WW, Jarjour NN, Wenzel SE, Peters SP, Meyers DA,
309 Bleecker ER. Sputum neutrophil counts are associated with more severe asthma phenotypes using
310 cluster analysis. *The Journal of allergy and clinical immunology* 2014: 133(6): 1557-1563.e1555.
311 5. Bel EH, Wenzel SE, Thompson PJ, Prazma CM, Keene ON, Yancey SW, Ortega HG, Pavord ID.
312 Oral Glucocorticoid-Sparing Effect of Mepolizumab in Eosinophilic Asthma. *The New England journal*
313 *of medicine* 2014.
314 6. Busse W, Corren J, Lanier BQ, McAlary M, Fowler-Taylor A, Cioppa GD, van As A, Gupta N.
315 Omalizumab, anti-IgE recombinant humanized monoclonal antibody, for the treatment of severe
316 allergic asthma. *The Journal of allergy and clinical immunology* 2001: 108(2): 184-190.
317 7. Chung KF. New treatments for severe treatment-resistant asthma: targeting the right patient.
318 *The Lancet Respiratory medicine* 2013: 1(8): 639-652.
319 8. Agusti A, Bel E, Thomas M, Vogelmeier C, Brusselle G, Holgate S, Humbert M, Jones P, Gibson
320 PG, Vestbo J, Beasley R, Pavord ID. Treatable traits: toward precision medicine of chronic airway
321 diseases. *The European respiratory journal* 2016: 47(2): 410-419.
322 9. ten Brinke A, Zwinderman AH, Sterk PJ, Rabe KF, Bel EH. Factors associated with persistent
323 airflow limitation in severe asthma. *American journal of respiratory and critical care medicine* 2001:
324 164(5): 744-748.
325 10. Ciebiada M, Domagala M, Gorska-Ciebiada M, Gorski P. Risk factors associated with
326 irreversible airway obstruction in nonsmoking adult patients with severe asthma. *Allergy and asthma*
327 *proceedings : the official journal of regional and state allergy societies* 2014: 35(5): 72-79.
328 11. Moore WC, Meyers DA, Wenzel SE, Teague WG, Li H, Li X, D'Agostino R, Jr., Castro M, Curran-
329 Everett D, Fitzpatrick AM, Gaston B, Jarjour NN, Sorkness R, Calhoun WJ, Chung KF, Comhair SA,
330 Dweik RA, Israel E, Peters SP, Busse WW, Erzurum SC, Bleecker ER. Identification of asthma
331 phenotypes using cluster analysis in the Severe Asthma Research Program. *AmJRespirCrit Care Med*
332 2010: 181(4): 315-323.
333 12. Amelink M, de Nijs SB, de Groot JC, van Tilburg PM, van Spiegel PI, Krouwels FH, Lutter R,
334 Zwinderman AH, Weersink EJ, ten Brinke A, Sterk PJ, Bel EH. Three phenotypes of adult-onset
335 asthma. *Allergy* 2013: 68(5): 674-680.
336 13. Schatz M, Hsu JW, Zeiger RS, Chen W, Dorenbaum A, Chipps BE, Haselkorn T. Phenotypes
337 determined by cluster analysis in severe or difficult-to-treat asthma. *The Journal of allergy and*
338 *clinical immunology* 2014: 133(6): 1549-1556.
339 14. Konno S, Taniguchi N, Makita H, Nakamaru Y, Shimizu K, Shijubo N, Fuke S, Takeyabu K, Oguri
340 M, Kimura H, Maeda Y, Suzuki M, Nagai K, Ito YM, Wenzel SE, Nishimura M. Distinct Phenotypes of
341 Cigarette Smokers Identified by Cluster Analysis of Patients with Severe Asthma. *Annals of the*
342 *American Thoracic Society* 2015: 12(12): 1771-1780.
343 15. Bumbacea D, Campbell D, Nguyen L, Carr D, Barnes PJ, Robinson D, Chung KF. Parameters
344 associated with persistent airflow obstruction in chronic severe asthma. *The European respiratory*
345 *journal* 2004: 24(1): 122-128.

16. Lee JH, Haselkorn T, Borish L, Rasouliyan L, Chipps BE, Wenzel SE. Risk factors associated with persistent airflow limitation in severe or difficult-to-treat asthma: insights from the TENOR study. *Chest* 2007: 132(6): 1882-1889.

17. Yamauchi K, Inoue H. Airway remodeling in asthma and irreversible airflow limitation-ECM deposition in airway and possible therapy for remodeling. *Allergology international : official journal of the Japanese Society of Allergology* 2007: 56(4): 321-329.

18. den Otter I, Willems LN, van Schadewijk A, van Wijngaarden S, Janssen K, de Jeu RC, Sont JK, Sterk PJ, Hiemstra PS. Lung function decline in asthma patients with elevated bronchial CD8, CD4 and CD3 cells. *The European respiratory journal* 2016: 48(2): 393-402.

19. Kwak HJ, Park DW, Seo JY, Moon JY, Kim TH, Sohn JW, Shin DH, Yoon HJ, Park SS, Kim SH. The Wnt/beta-catenin signaling pathway regulates the development of airway remodeling in patients with asthma. *Experimental & molecular medicine* 2015: 47: e198.

20. Perry MM, Durham AL, Austin PJ, Adcock IM, Chung KF. BET bromodomains regulate transforming growth factor-beta-induced proliferation and cytokine release in asthmatic airway smooth muscle. *The Journal of biological chemistry* 2015: 290(14): 9111-9121.

21. Pepe C, Foley S, Shannon J, Lemiere C, Olivenstein R, Ernst P, Ludwig MS, Martin JG, Hamid Q. Differences in airway remodeling between subjects with severe and moderate asthma. *The Journal of allergy and clinical immunology* 2005: 116(3): 544-549.

22. Hanzelmann S, Castelo R, Guinney J. GSVA: gene set variation analysis for microarray and RNA-seq data. *BMC bioinformatics* 2013: 14: 7.

23. Lefaudeux D, De Meulder B, Loza MJ, Peffer N, Rowe A, Baribaud F, Bansal AT, Lutter R, Sousa AR, Corfield J, Pandis I, Bakke PS, Caruso M, Chanez P, Dahlen SE, Fleming LJ, Fowler SJ, Horvath I, Krug N, Montuschi P, Sanak M, Sandstrom T, Shaw DE, Singer F, Sterk PJ, Roberts G, Adcock IM, Djukanovic R, Auffray C, Chung KF. U-BIOPRED clinical adult asthma clusters linked to a subset of sputum -omics. *The Journal of allergy and clinical immunology* 22016 Oct 20. doi: 10.1016/j.jaci.2016.08.048.

24. Shaw DE, Sousa AR, Fowler SJ, Fleming LJ, Roberts G, Corfield J, Pandis I, Bansal AT, Bel EH, Auffray C, Compton CH, Bisgaard H, Bucchioni E, Caruso M, Chanez P, Dahlen B, Dahlen SE, Dyson K, Frey U, Geiser T, Gerhardsson de Verdier M, Gibeon D, Guo YK, Hashimoto S, Hedlin G, Jeyasingham E, Hekking PW, Higenbottam T, Horvath I, Knox AJ, Krug N, Erpenbeck VJ, Larsson LX, Lazarinis N, Matthews JG, Middelveld R, Montuschi P, Musial J, Myles D, Pahus L, Sandstrom T, Seibold W, Singer F, Strandberg K, Vestbo J, Vissing N, von Garnier C, Adcock IM, Wagers S, Rowe A, Howarth P, Wagener AH, Djukanovic R, Sterk PJ, Chung KF. Clinical and inflammatory characteristics of the European U-BIOPRED adult severe asthma cohort. *The European respiratory journal* 2015.

25. Bel EH, Sousa A, Fleming L, Bush A, Chung KF, Versnel J, Wagener AH, Wagers SS, Sterk PJ, Compton CH. Diagnosis and definition of severe refractory asthma: an international consensus statement from the Innovative Medicine Initiative (IMI). *Thorax* 2011: 66(10): 910-917.

26. Quanjer PH, Tammeling GJ, Cotes JE, Pedersen OF, Peslin R, Yernault JC. Lung volumes and forced ventilatory flows. *The European respiratory journal* 1993: 6 Suppl 16: 5-40.

27. Quanjer PH, Stanojevic S, Cole TJ, Baur X, Hall GL, Culver BH, Enright PL, Hankinson JL, Ip MS, Zheng J, Stocks J. Multi-ethnic reference values for spirometry for the 3-95-yr age range: the global lung function 2012 equations. The European respiratory journal 2012: 40(6): 1324-1343.

28. Harris P, Sridhar S, Peng R, Phillips JE, Cohn RG, Burns L, Woods J, Ramanujam M, Loubeau M, Tyagi G, Allard J, Burczynski M, Ravindran P, Cheng D, Bitter H, Fine JS, Bauer CM, Stevenson CS. Double-stranded RNA induces molecular and inflammatory signatures that are directly relevant to COPD. *Mucosal immunology* 2013: 6(3): 474-484.

29. Peng R, Sridhar S, Tyagi G, Phillips JE, Garrido R, Harris P, Burns L, Renteria L, Woods J, Chen L, Allard J, Ravindran P, Bitter H, Liang Z, Hogaboam CM, Kitson C, Budd DC, Fine JS, Bauer CM,

394 Stevenson CS. Bleomycin induces molecular changes directly relevant to idiopathic pulmonary
395 fibrosis: a model for "active" disease. *PloS one* 2013: 8(4): e59348.
396 30. Shi L, Reid LH, Jones WD, Shippy R, Warrington JA, Baker SC, Collins PJ, de Longueville F,
397 Kawasaki ES, Lee KY, Luo Y, Sun YA, Willey JC, Setterquist RA, Fischer GM, Tong W, Dragan YP, Dix DJ,
398 Frueh FW, Goodsaid FM, Herman D, Jensen RV, Johnson CD, Lobenhofer EK, Puri RK, Schrf U, Thierry-
399 Mieg J, Wang C, Wilson M, Wolber PK, Zhang L, Amur S, Bao W, Barbacioru CC, Lucas AB, Bertholet V,
400 Boysen C, Bromley B, Brown D, Brunner A, Canales R, Cao XM, Cebula TA, Chen JJ, Cheng J, Chu TM,
401 Chudin E, Corson J, Corton JC, Croner LJ, Davies C, Davison TS, Delenstarr G, Deng X, Dorris D, Eklund
402 AC, Fan XH, Fang H, Fulmer-Smentek S, Fuscoe JC, Gallagher K, Ge W, Guo L, Guo X, Hager J, Haje PK,
403 Han J, Han T, Harbottle HC, Harris SC, Hatchwell E, Hauser CA, Hester S, Hong H, Hurban P, Jackson
404 SA, Ji H, Knight CR, Kuo WP, LeClerc JE, Levy S, Li QZ, Liu C, Liu Y, Lombardi MJ, Ma Y, Magnuson SR,
405 Maqsodi B, McDaniel T, Mei N, Myklebost O, Ning B, Novoradovskaya N, Orr MS, Osborn TW, Papallo
406 A, Patterson TA, Perkins RG, Peters EH, Peterson R, Philips KL, Pine PS, Pusztai L, Qian F, Ren H, Rosen
407 M, Rosenzweig BA, Samaha RR, Schena M, Schroth GP, Shchegrova S, Smith DD, Staedtler F, Su Z, Sun
408 H, Szallasi Z, Tezak Z, Thierry-Mieg D, Thompson KL, Tikhonova I, Turpaz Y, Vallanat B, Van C, Walker
409 SJ, Wang SJ, Wang Y, Wolfinger R, Wong A, Wu J, Xiao C, Xie Q, Xu J, Yang W, Zhang L, Zhong S, Zong
410 Y, Slikker W, Jr. The MicroArray Quality Control (MAQC) project shows inter- and intraplatform
411 reproducibility of gene expression measurements. *Nature biotechnology* 2006: 24(9): 1151-1161.
412 31. Barnes PJ. Corticosteroid resistance in patients with asthma and chronic obstructive
413 pulmonary disease. *The Journal of allergy and clinical immunology* 2013: 131(3): 636-645.
414 32. Kaminska M, Foley S, Maghni K, Storness-Bliss C, Coxson H, Ghezzo H, Lemiere C, Olivenstein
415 R, Ernst P, Hamid Q, Martin J. Airway remodeling in subjects with severe asthma with or without
416 chronic persistent airflow obstruction. *The Journal of allergy and clinical immunology* 2009: 124(1):
417 45-51.e41-44.
418 33. Wright AK, Mistry V, Richardson M, Shelley M, Thornton T, Terry S, Barker B, Bafadhel M,
419 Brightling C. Toll-like receptor 9 dependent interferon-alpha release is impaired in severe asthma but
420 is not associated with exacerbation frequency. *Immunobiology* 2015: 220(7): 859-864.
421 34. Rupani H, Martinez-Nunez RT, Dennison P, Lau LC, Jayasekera N, Havelock T, Francisco-Garcia
422 AS, Grainge C, Howarth PH, Sanchez-Elsner T. Toll-like Receptor 7 Is Reduced in Severe Asthma and
423 Linked to an Altered MicroRNA Profile. *American journal of respiratory and critical care medicine*
424 2016: 194(1): 26-37.
425 35. Kikkawa Y, Sugiyama K, Obara K, Hirata H, Fukushima Y, Toda M, Fukuda T. Interferon-alpha
426 inhibits airway eosinophilia and hyperresponsiveness in an animal asthma model [corrected]. *Asia*
427 *Pacific allergy* 2012: 2(4): 256-263.36. Sionov E, Mayer-Barber KD, Chang YC, Kauffman KD, Eckhaus
428 MA, Salazar AM, Barber DL, Kwon-Chung KJ. Type I IFN Induction via Poly-ICLC Protects Mice against
429 Cryptococcosis. *PLoS pathogens* 2015: 11(8): e1005040.
430 37. Stowell NC, Seideman J, Raymond HA, Smalley KA, Lamb RJ, Egenolf DD, Bugelski PJ, Murray
431 LA, Marsters PA, Bunting RA, Flavell RA, Alexopoulou L, San Mateo LR, Griswold DE, Sarisky RT, Mbow
432 ML, Das AM. Long-term activation of TLR3 by poly(I:C) induces inflammation and impairs lung
433 function in mice. *Respiratory research* 2009: 10: 43.
434 38. Saha SK, Berry MA, Parker D, Siddiqui S, Morgan A, May R, Monk P, Bradding P, Wardlaw AJ,
435 Pavord ID, Brightling CE. Increased sputum and bronchial biopsy IL-13 expression in severe asthma.
436 *The Journal of allergy and clinical immunology* 2008: 121(3): 685-691.

437 39. Pope SM, Brandt EB, Mishra A, Hogan SP, Zimmermann N, Matthaei KI, Foster PS,
438 Rothenberg ME. IL-13 induces eosinophil recruitment into the lung by an IL-5- and eotaxin-
439 dependent mechanism. *The Journal of allergy and clinical immunology* 2001: 108(4): 594-601.
440 40. Zhu Z, Homer RJ, Wang Z, Chen Q, Geba GP, Wang J, Zhang Y, Elias JA. Pulmonary expression
441 of interleukin-13 causes inflammation, mucus hypersecretion, subepithelial fibrosis, physiologic
442 abnormalities, and eotaxin production. *The Journal of clinical investigation* 1999: 103(6): 779-788.
443 41. Sykes A, Edwards MR, Macintyre J, del Rosario A, Bakhsoliani E, Trujillo-Torralbo MB, Kon
444 OM, Mallia P, McHale M, Johnston SL. Rhinovirus 16-induced IFN-alpha and IFN-beta are deficient in
445 bronchoalveolar lavage cells in asthmatic patients. *The Journal of allergy and clinical immunology*
446 2012: 129(6): 1506-1514.e1506.

447

1 Revised Online Supplement ERJ-02298-2016

2 Design and subjects

3 During the baseline visit data on demographics, medical history, physical examination and lung
4 function were collected to assess inclusion criteria and severity of asthma. Subsequently,
5 questionnaires were completed, atopy status was assessed and blood and sputum collected. Finally,
6 nasal brushings and endobronchial biopsies were collected in a separate visit.

7 Severe asthma was defined according to the IMI consensus statement [E1], and thereby, patients
8 were included who had a confirmed diagnosis of asthma that was uncontrolled despite high intensity
9 asthma treatment (≥1000µg Fluticasone eq. plus a second controller) or could only be controlled
10 with treatment by systemic oral corticosteroids (OCS) or omalizumab. Uncontrolled asthma was
11 diagnosed if ≥3 of the following features were present: 1) >2 weekly daytime symptoms, 2) any
12 limitations of activities, 3) ≥1 weekly nocturnal symptoms 4) >2 weekly need for reliever medication,
13 5) pre bronchodilator FEV1 <80% predicted or personal best, or if the patient encountered ≥2 yearly
14 severe exacerbations. Current-smokers, ex-smokers and never-smokers were included.

15 PAL was diagnosed in patients with a post-bronchodilator FEV1/FVC < lower limit of normal (LLN).
16 The LLN was calculated for each patient according to formulae stated by Quanjer *et al.* [E2] (for male
17 subjects: -0.18*AGE + 75.41; for female subjects: -0.19*AGE + 78.4) consistent to LLN defined by
18 Global Lung Function Initiative (GLI) [E3]. In order to examine consistency with other criteria for PAL
19 we additionally performed an analysis based on PAL defined by post-bronchodilator FEV_1 < LLN. The
20 U-BIOPRED study was registered at ClinicalTrials.gov identifier NCT01976767 and was approved by
21 the Medical Ethics Boards of all participating centers. All patients provided written informed consent.

22

23

24 Measurements

25 *Clinical data*

26 Clinical data were collected according to predefined standard operating procedures (SOPs) and
27 details on the methods of collection in U-BIOPRED have been published elsewhere [E4]. First, by
28 history taking data on age, gender, body mass index (BMI), age of onset of asthma, medication and
29 smoking history were assessed. Second, asthma symptoms were obtained by a questionnaire
30 (ACQ)[E5]. Third, lung function was measured pre- and post-bronchodilator and according to
31 standardized procedures [E6]. Fourth, eosinophil and neutrophil counts were assessed in blood and
32 induced sputum samples.

33 *mRNA samples*

34 Gene expression was assessed on the total RNA in unselected samples of severe asthma patients in
35 the following four different airway compartments: (1) nasal brushing (n=37), (2) induced sputum
36 (n=79), (3) endobronchial brushings (n=62) and (4) endobronchial biopsies (n=50). There was no
37 complete overlap between the samples, mainly because of limited sputum induction success rate
38 (Fig. 1).

39 *Sputum induction*

40 Sputum samples, induced by inhalation of hypertonic saline, were processed with 0.1%DTT by using
41 the selected sample technique, quality controlled according to ERS recommendations [E7]. Sputum
42 was processed within 2 hours after collection and processed suspension was preserved in RNAlater®
43 solution and then maintained at -80°C.

44 *Nasal brushing, endobronchial brushing and biopsy*

45 Nasal brushings were collected from one nostril (4mm plastic coated wire interdental brush
46 (DENT.O.CARE Limited, 7 Cygnus Business Centre, Dalmeyer Road, London, UK)). Samples were
47 embedded in phosphate buffer saline (PBS) directly after the procedure. Bronchoscopy procedures
48 were based on U-BIOPRED SOPs and performed according to safety standards [E8]. Patients had
49 refrained smoking ≥6 hours prior to the procedure, and subsequently received bronchodilator
50 medication and local anesthesia. A flexible scope (type of scope depending on preferences of
51 physician and clinical center) was introduced and, first, four endobronchial brushings were
52 performed in a large airway (bronchus intermedius) contacting the wall at least 4 times (with e.g.
53 Olympus REF: BC-202D-2010 (2mm brush size) or BC-202D-3010 (3mm brush size), KeyMed (Medical
54 & Industrial Equipment, Ltd OLYMPUS Group Company)). Subsequently, up to 8 endobronchial
55 biopsies were taken from the 2nd and 4th airway carinae of the right or left lower and middle lobes,
56 working upwards (with a disposable 1.8 mm cupped biopsy forceps). Nasal brushings and
57 endobronchial biopsies and brushings were immediately preserved in RNAlater® solution and then
58 maintained at -80°C. RNA was extracted using Qiagen miRNeasy kit (Qiagen; Germantown, MD) and
59 amplified with NuGen ovation pico WTA kit (NuGen Technologies; San Carlos, CA).

60 *mRNA microarray analysis*

61 Microarray analysis was performed with the Affymetrix HT HG-U133+ PM microarray platform
62 (Affymetrix, Santa Clara, Ca). Pre-processing and quality control were performed with multi-array
63 average normalization (Almac, Craiganvond, UK) and the obtained CEL files were normalized.
64 Technical outliers were excluded (chip image analysis, Affymetrix GeneChip QC, RNA degradation
65 analysis, distribution analysis, principal components analysis, and correlation analysis) and CEL files
66 re-normalized using the robust multi-array (RMA) method. Technical batch effects (e.g., from
67 microarray hybridization date/lot, RNA processing batch) were adjusted in the data matrices using
68 linear modeling of batch (as random factor).

69 **Statistical analysis**

70 Clinical variables were summarized as mean±standard deviation when normally distributed, as
71 median (interquartile range) when skewed and as their frequencies (proportion) when categorical.
72 Between group comparison was performed with independent t-tests, Mann-Whitney U test or chi-
73 square tests, as appropriate. Clinical variables with a $p<0.05$ were considered significantly different.

74 *GSVA*

75 Gene set variation analysis (GSVA) is a statistical technique that allows sensitive identification of
76 differences in expression of sets of genes between heterogeneous groups and can be used to explore
77 for underlying pathways [E9]. Sets of genes were predefined, and were based on the available gene
78 expression publications and data on airways disease, including human and murine models, both *in*
79 *vivo* and *in vitro* studies, to assure sensitive pathway detection. These included studies on the gene
80 expression associated with (1) airway disease treatment, (2) immunologic pathways and (3) induced
81 lung injury or inflammation. The latter included gene signatures that were identified at several time
82 points after the admission of either Poly(I:C) as a model for exacerbations [E10], or bleomycin, which
83 is used as a model for mimicking the course of fibrotic processes in the lung [E11]. For this discovery
84 study 105 predefined gene sets were entered into the statistical models (Table E7).

85 *Enrichment scores and false discovery*

86 Enrichment scores (ES) were calculated for each patient and for each of the gene signatures and
87 were based on the gene expression of genes in the sets. ES could range from a value of -1 to 1 [E9].
88 Subsequently, mean ES were calculated for patients with PAL and patients without PAL and
89 Generalized Linear Models, including correction for smoking status, corticosteroid usage and
90 duration of asthma, were applied to statistically compare ES between the groups. In order to
91 minimize false discovery, only gene signatures that had $p<0.05$ and a difference of ES (dES) between

of the groups of ≥0.2 were considered significantly different, following the Microarray Consortium for Quality Control (MACQC) recommendations regarding the need for applying group-difference thresholds in order to stringently limit false discovery [E12].

Consistency when using different definition of PAL

211 out of 421 patients (50.1%) were having PAL defined as FEV_1 < LLN. Patient characteristics were similar in both analyses, however patients with PAL defined as FEV_1 < LLN were also more frequent female and had a higher ACQ score (Table E5).

GSVA analysis showed that identified signatures between FEV_1/FVC < LLN and FEV_1 <LLN were also similar, including those associated with treatment with fluticasone, eosinophilic inflammation and involvement of T_H2 helper cells and IFN-alpha. In addition, induced lung injury and inflammation gene signatures were identified in both analyses as well (Table E6). However, involvement of CD4 T-cells of rheumatoid arthritis was not consistent, and no significant gene signatures were identified in the biopsies applying FEV_1 < LLN.

107

Table E1: Patient Characteristics of Nasal Brushings sample

	No PAL	PAL	*P*-Value
n	15	22	
Gender = Female (%)	**11 (73.3%)**	**8 (36.4%)**	**0.045**
Age (yrs)*	47.5 ± 16.2	53.2 ± 12.1	0.229
BMI (Kg/m^2)*	34.1 ± 6.6	29.4 ± 5.7	0.027
Asthma Duration (yrs)*	25.0 [14.0 - 38.0]	21.5 [17.0 - 40.5]	0.914
Smoking Status (%)			0.188
Never Smokers	12 (80.0)	11 (50.0)	
Ex-smokers	3 (20.0)	8 (36.4)	
Current-smokers	0 (0.0)	3 (13.6)	
Packyears†	5.0 [3.3 - 5.1]	20.0 [11.5 - 38.5]	0.052
OCS dose (mg)†	10.0 [8.0 - 25.0]	10.00 [8.12, 13.75]	0.616
ACQ*	1.9 ± 1.0	2.2 ± 1.2	0.414
Exacerbations per year†	2.0 [1.0 – 4.0]	3.0 [1.0 - 4.0]	0.982
pbFEV$_1$ (% predicted)*	**99.4 ± 17.6**	**71.5 ± 14.9**	**<0.001**
Blood Eosinophils (x10^3/L)†	0.2 [0.1 - 0.4]	0.2 [0.1 - 0.3]	0.817
Blood Neutrophils (x10^3/L)†	**3.8 [3.6 - 5.1]**	**5.0 [4.2 - 7.8]**	**0.033**
Sputum Eosinophils (%)†	1.4 [0.4 - 4.6]	2.6 [0.2 - 13.8]	0.614
Sputum Neutrophils (%)*	46.6 ± 18.4	63.2 ± 18.8	0.053

* mean ± SD; † median [Interquartile Range]; PAL: persistent airflow limitation; OCS: Oral corticosteroids; ACQ: Asthma Control Questionnaire FEV$_1$: Forced Expiratory Volume in the first second

108

109

110

Table E2: Patient Characteristics of sputum sample

	No PAL	PAL	*P*-Value
n	21	58	
Gender = Female (%)	13 (61.9%)	35 (60.3%)	1.000
Age (yrs)*	52.5 ± 13.9	54.2 ± 11.4	0.580
BMI (Kg/m^2)*	28.2 ± 5.0	28.1 ± 5.3	0.928
Asthma Duration (yrs)*	23.1 ± 14.5	26.8 ± 17.2	0.374
Smoking Status (%)			0.799
Never Smokers	11 (52.4%)	35 (60.3%)	
Ex-smokers	8 (38.1%)	18 (31.0%)	
Current-smokers	2 (9.5%)	5 (8.6%)	
Packyears†	13.8 [2.9 - 19.7]	10.0 [2.8 - 18.8]	0.922
OCS dose (mg)†	10.0 [8.8 - 12.5]	10.0 [6.9 - 13.1]	0.691
ACQ*	2.6 ± 1.4	2.6 ± 1.3	0.914
Exacerbations per year†	2.0 [2.0 – 3.5]	2.0 [1.5 – 4.0]	0.833
pbFEV$_1$ (% predicted)*	**90.2 ± 14.0**	**63.5 ± 19.9**	**<0.001**
Blood Eosinophils (x10^3/L)†	0.2 [0.2 - 0.3]	0.4 [0.2 - 0.5]	0.203
Blood Neutrophils (x10^3/L)†	4.3 [3.3 - 6.3]	5.0 [3.9 - 7.5]	0.051
Sputum Eosinophils (%)†	**1.3 [0.2 - 3.8]**	**6.2 [1.3 - 28.5]**	**<0.001**
Sputum Neutrophils (%)*	61.5 ± 23.6	58.5 ± 27.1	0.663

* mean ± SD; † median [Interquartile Range]; PAL: persistent airflow limitation; OCS: Oral corticosteroids; ACQ: Asthma Control Questionnaire FEV$_1$: Forced Expiratory Volume in the first second

111

112

113

Table E3: Patient Characteristics of endobronchial brushings sample

	No PAL	PAL	*P*-Value
n	30	32	
Gender = Female (%)	**19 (63.3)**	**10 (31.2)**	**0.021**
Age (yrs)*	46.7 ± 14.0	53.0 ± 11.1	0.052
BMI (Kg/m^2)*	31.3 ± 6.3	28.5 ± 6.1	0.081
Asthma Duration (yrs)*	26.4 ± 16.8	26.7 ± 17.9	0.940
Smoking Status (%)			0.077
Never Smokers	22 (73.3)	15 (46.9)	
Ex-smokers	7 (23.3)	12 (37.5)	
Current-smokers	1 (3.3)	5 (15.6)	
Packyears†	**5.1 [1.4 - 8.1]**	**18.8 [7.0 - 24.0]**	**0.031**
OCS dose (mg)†	10.0 [10.0 - 21.3]	10.0 [6.5 - 16.3]	0.246
ACQ*	2.1 ± 1.2	2.4 ± 1.0	0.314
Exacerbations per year†	2.0 [2.0 – 4.0]	3.0 [2.0 – 4.0]	0.768
pbFEV$_1$ (% predicted)*	**91.9 ± 14.3**	**66.7 ± 15.5**	**<0.001**
Blood Eosinophils (x10^3/L)†	0.2 [0.1 - 0.4]	0.2 [0.1 - 0.3]	0.319
Blood Neutrophils (x10^3/L)†	**4.0 [3.2 - 5.4]**	**5.8 [4.1 - 7.7]**	**0.005**
Sputum Eosinophils (%)†	1.4 [0.6 - 4.6]	4.5 [0.2 - 24.9]	0.520
Sputum Neutrophils (%)*	48.5 ± 20.7	61.6 ± 23.3	0.143

* mean ± SD; † median [Interquartile Range]; PAL: persistent airflow limitation; OCS: Oral corticosteroids; ACQ: Asthma Control Questionnaire FEV$_1$: Forced Expiratory Volume in the first second

114

115

116

117

Table E4: Patient Characteristics of endobronchial biopsies sample

	No PAL	PAL	*P*-Value
n	22	28	
Gender = Female (%)	14 (63.6%)	12 (42.9%)	0.166
Age (yrs)*	48.4 ± 12.6	52.7 ± 11.2	0.212
BMI (Kg/m^2)*	30.2 ± 5.4	28.6 ± 6.4	0.344
Asthma Duration (yrs)*	25.8 ± 15.5	30.5 ± 18.7	0.353
Smoking Status (%)			0.245
Never Smokers	16 (72.7%)	16 (57.1%)	
Ex-smokers	5 (22.7%)	6 (21.4%)	
Current-smokers	1 (4.5%)	6 (21.4%)	
Packyears†	**5.3 [2.0 - 13.4]**	**21.5 [18.0 - 27.5]**	**0.049**
OCS dose (mg)†	10.0 [7.9 - 10.0]	10.0 [6.0 - 15.0]	0.966
ACQ*	2.3 (1.3)	2.4 (1.1)	0.721
Exacerbations per year†	2.0 [2.0 – 3.3]	3.0 [2.0 – 4.0]	0.249
pbFEV$_1$ (% predicted)*	**89.6 ± 13.6**	**68.3 ± 15.2**	**<0.001**
Blood Eosinophils (x10^3/L)†	0.2 [0.1 - 0.3]	0.2 [0.1 - 0.3]	0.683
Blood Neutrophils (x10^3/L)†	4.0 [3.5 - 5.3]	5.0 [4.3 - 7.3]	0.050
Sputum Eosinophils (%)†	2.0 [0.7 - 8.0]	2.6 [0.2 - 6.1]	0.938
Sputum Neutrophils (%)*	50.4 ± 19.5	56.5 ± 27.0	0.518

* mean ± SD; † median [Interquartile Range]; PAL: persistent airflow limitation; OCS: Oral corticosteroids; ACQ: Asthma Control Questionnaire FEV$_1$: Forced Expiratory Volume in the first second

118

119

120

Table E5: Patient characteristics of patients with persistent airflow limitation (PAL) defined as post-bronchodilator FEV1 < LLN

	no PAL	PAL	*P*-value
n	**210**	**211**	
Female (%)	**118 (56.2)**	**143 (67.8)**	**0.016**
Age (yrs)*	**49.7 ± 14.8**	**54.1 ± 11.6**	**0.001**
BMI (Kg/m2)*	29.3 ± 6.3	29.2 ± 6.3	0.825
Asthma Duration (yrs)†	**20.0 [11.0 - 30.0]**	**26.0 [13.3 - 41.8]**	**<0.001**
Smoking history (%)			0.832
Never	133 (63.3)	131 (62.1)	
Ex-smoker	58 (27.6)	57 (27.0)	
Current smoker	19 (9.0)	23 (10.9)	
Packyears†	12.5 [4.5 - 20.0]	12.7 [3.8 - 21.4]	0.975
OCS dose†	12.8 ± 8.6	14.3 ± 10.6	0.345
ACQ*	**2.3 ± 1.3**	**3.0 ± 1.2**	**<0.001**
Exacerbations per year †	2.0 [1.0 - 4.0]	2.0 [2.0 - 3.0]	0.568
pbFEV1 (% pred)*	**91.5 ± 13.6**	**60.2 ± 15.1**	**<0.001**
Blood Eosinophils (x109/L)†	0.2 [0.1 - 0.4]	0.2 [0.1 - 0.4]	0.950
Blood Neutrophils (x109/L)†	4.9 [3.8 - 6.4]	4.8 [3.6 - 7.3]	0.969
Sputum Eosinophils (%)†	2.0 [0.4 - 9.6]	3.8 [1.0 - 20.7]	0.099
Sputum Neutrophils (%)*	51.7 [31.5 - 72.8]	56.5 [37.4 - 74.4]	0.298

* mean ± SD; † median [Interquartile Range]; PAL: persistent airflow limitation; OCS: Oral corticosteroids; ACQ: Asthma Control Questionnaire; FEV_1: Forced Expiratory Volume in the first second

121

Table E6: Differentially enriched gene signatures in severe asthma patients with FEV1 post-bronchodilator < LLN as compared to severe asthma patients without FEV1 post-bronchodilator < LLN

	Gene signatures associated with	Nasal brush		Sputum		Endobr. Brush		Endobr. Biopsy	
		dES	p-value	dES	p-value	dES	p-value	dES	p-value
Treatment gene signatures	Fluticasone treatment in asthma - DOWN[1]*					0.23	0.007		
	Fluticasone treatment in asthma - UP[1]*					0.23	0.009		
	Asthma (HDM induced model) - UP[3]					0.21	0.009		
Immunologic gene signatures	Eosinophils - UP[1]*			0.37	0.001	0.21	0.039		
	TH2 activated - DOWN[2]*	-0.21	0.033						
	IFN-alpha - UP[1]*			*-0.19*	0.011				
Induced lung injury gene signatures	Induced inflammation (Poly I:C - 72h) - UP[3]*			-0.21	0.002				
	Induced injury (Bleomycin - Day 2) - UP[3]*			*-0.19*	0.003				

Differences in mean gene signature enrichment scores between severe asthma patients with FEV1 post-bronchodilator < LLN as compared to severe asthma patients without FEV1 post-bronchodilator < LLN (in RED are higher and in BLUE are lower). * Comparable results as found in PAL defined as Fev1/FVC < LLN; [1]In vitro model in human sample; [2]In vivo model in human sample; [3]In vivo model in murine model

122 References
123
124 E1. Bel EH, Sousa A, Fleming L, Bush A, Chung KF, Versnel J, Wagener AH, Wagers SS, Sterk PJ,
125 Compton CH. Diagnosis and definition of severe refractory asthma: an international consensus
126 statement from the Innovative Medicine Initiative (IMI). *Thorax* 2011: 66(10): 910-917.
127 E2. Quanjer PH, Tammeling GJ, Cotes JE, Pedersen OF, Peslin R, Yernault JC. Lung volumes and
128 forced ventilatory flows. *The European respiratory journal* 1993: 6 Suppl 16: 5-40.
129 E3. Quanjer PH, Stanojevic S, Cole TJ, Baur X, Hall GL, Culver BH, Enright PL, Hankinson JL, Ip MS,
130 Zheng J, Stocks J. Multi-ethnic reference values for spirometry for the 3-95-yr age range: the global
131 lung function 2012 equations. *The European respiratory journal* 2012: 40(6): 1324-1343.
132 E4. Shaw DE, Sousa AR, Fowler SJ, Fleming LJ, Roberts G, Corfield J, Pandis I, Bansal AT, Bel EH,
133 Auffray C, Compton CH, Bisgaard H, Bucchioni E, Caruso M, Chanez P, Dahlen B, Dahlen SE, Dyson K,
134 Frey U, Geiser T, Gerhardsson de Verdier M, Gibeon D, Guo YK, Hashimoto S, Hedlin G, Jeyasingham
135 E, Hekking PW, Higenbottam T, Horvath I, Knox AJ, Krug N, Erpenbeck VJ, Larsson LX, Lazarinis N,
136 Matthews JG, Middelveld R, Montuschi P, Musial J, Myles D, Pahus L, Sandstrom T, Seibold W, Singer
137 F, Strandberg K, Vestbo J, Vissing N, von Garnier C, Adcock IM, Wagers S, Rowe A, Howarth P,
138 Wagener AH, Djukanovic R, Sterk PJ, Chung KF. Clinical and inflammatory characteristics of the
139 European U-BIOPRED adult severe asthma cohort. *The European respiratory journal* 2015.
140 E5. Juniper EF, Bousquet J, Abetz L, Bateman ED. Identifying 'well-controlled' and 'not well-
141 controlled' asthma using the Asthma Control Questionnaire. *RespirMed* 2006: 100(4): 616-621.
142 E6. Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, Crapo R, Enright P, van
143 der Grinten CP, Gustafsson P, Jensen R, Johnson DC, MacIntyre N, McKay R, Navajas D, Pedersen OF,
144 Pellegrino R, Viegi G, Wanger J. Standardisation of spirometry. *The European respiratory journal*
145 2005: 26(2): 319-338.
146 E7. Paggiaro PL, Chanez P, Holz O, Ind PW, Djukanovic R, Maestrelli P, Sterk PJ. Sputum
147 induction. *The European respiratory journal Supplement* 2002: 37: 3s-8s.
148 E8. Moore WC, Evans MD, Bleecker ER, Busse WW, Calhoun WJ, Castro M, Chung KF, Erzurum
149 SC, Curran-Everett D, Dweik RA, Gaston B, Hew M, Israel E, Mayse ML, Pascual RM, Peters SP, Silveira
150 L, Wenzel SE, Jarjour NN. Safety of investigative bronchoscopy in the Severe Asthma Research
151 Program. *The Journal of allergy and clinical immunology* 2011: 128(2): 328-336.e323.
152 E9. Hanzelmann S, Castelo R, Guinney J. GSVA: gene set variation analysis for microarray and
153 RNA-seq data. *BMC bioinformatics* 2013: 14: 7.
154 E10. Harris P, Sridhar S, Peng R, Phillips JE, Cohn RG, Burns L, Woods J, Ramanujam M, Loubeau M,
155 Tyagi G, Allard J, Burczynski M, Ravindran P, Cheng D, Bitter H, Fine JS, Bauer CM, Stevenson CS.
156 Double-stranded RNA induces molecular and inflammatory signatures that are directly relevant to
157 COPD. *Mucosal immunology* 2013: 6(3): 474-484.
158 E11. Peng R, Sridhar S, Tyagi G, Phillips JE, Garrido R, Harris P, Burns L, Renteria L, Woods J, Chen
159 L, Allard J, Ravindran P, Bitter H, Liang Z, Hogaboam CM, Kitson C, Budd DC, Fine JS, Bauer CM,
160 Stevenson CS. Bleomycin induces molecular changes directly relevant to idiopathic pulmonary
161 fibrosis: a model for "active" disease. *PloS one* 2013: 8(4): e59348.
162 E12. Shi L, Reid LH, Jones WD, Shippy R, Warrington JA, Baker SC, Collins PJ, de Longueville F,
163 Kawasaki ES, Lee KY, Luo Y, Sun YA, Willey JC, Setterquist RA, Fischer GM, Tong W, Dragan YP, Dix DJ,
164 Frueh FW, Goodsaid FM, Herman D, Jensen RV, Johnson CD, Lobenhofer EK, Puri RK, Schrf U, Thierry-
165 Mieg J, Wang C, Wilson M, Wolber PK, Zhang L, Amur S, Bao W, Barbacioru CC, Lucas AB, Bertholet V,
166 Boysen C, Bromley B, Brown D, Brunner A, Canales R, Cao XM, Cebula TA, Chen JJ, Cheng J, Chu TM,
167 Chudin E, Corson J, Corton JC, Croner LJ, Davies C, Davison TS, Delenstarr G, Deng X, Dorris D, Eklund
168 AC, Fan XH, Fang H, Fulmer-Smentek S, Fuscoe JC, Gallagher K, Ge W, Guo L, Guo X, Hager J, Haje PK,
169 Han J, Han T, Harbottle HC, Harris SC, Hatchwell E, Hauser CA, Hester S, Hong H, Hurban P, Jackson
170 SA, Ji H, Knight CR, Kuo WP, LeClerc JE, Levy S, Li QZ, Liu C, Liu Y, Lombardi MJ, Ma Y, Magnuson SR,

171 Maqsodi B, McDaniel T, Mei N, Myklebost O, Ning B, Novoradovskaya N, Orr MS, Osborn TW, Papallo
172 A, Patterson TA, Perkins RG, Peters EH, Peterson R, Philips KL, Pine PS, Pusztai L, Qian F, Ren H, Rosen
173 M, Rosenzweig BA, Samaha RR, Schena M, Schroth GP, Shchegrova S, Smith DD, Staedtler F, Su Z, Sun
174 H, Szallasi Z, Tezak Z, Thierry-Mieg D, Thompson KL, Tikhonova I, Turpaz Y, Vallanat B, Van C, Walker
175 SJ, Wang SJ, Wang Y, Wolfinger R, Wong A, Wu J, Xiao C, Xie Q, Xu J, Yang W, Zhang L, Zhong S, Zong
176 Y, Slikker W, Jr. The MicroArray Quality Control (MAQC) project shows inter- and intraplatform
177 reproducibility of gene expression measurements. *Nature biotechnology* 2006: 24(9): 1151-1161.

178

Table E7: Details on significantly different enriched gene signatures						
#	**Tissue**	**Species**	**Trigger**	**Direction**	**Gene Set**	**Source**
12	**Bronchial epithelia**	**HS**	Fluticasone in asthma	DOWN	TFCP2L1, HBB, MUC13, POSTN, SERPINB2	http://www.ncbi.nlm.nih.gov/pubmed/17898169
27	**Peripheral blood - CD4 Tcells**	**HS**	Rheumatoid Arthritis	UP	BCL3, SOCS3, PIM1, SBNO2, LDHA, CMAHP, PDCD1, IGFL1, LOC731186, MUC1, GPRIN3	http://www.ncbi.nlm.nih.gov/pubmed/22532634
34	**Lung biopsy**	**HS**	Fluticasone in COPD	DOWN	TMPRSS11D, SERPINB13, SPINK5, KRT4, TMPRSS11A, CSTA, GABRP, TYMS, GPR87, TMPRSS4, ATP10B, CH25H, SRPX2, IGKC, BNIPL, RAB38, CAPNS2, FANCD2, ABCC1, TENM2, BNC1, KLK10, PTAFR, CRABP2, TENM4, TRIM16, EYA2, GNA15, SMAGP, BICD2, EXOSC7, SCO1, BID, RHNO1, ITPA, TSPAN17	http://www.ncbi.nlm.nih.gov/pubmed/23925644
36	**Peripheral blood**	**HS**	Systemic lupus erythematosus (SLE) and PBMC	UP	IFI35, IRF7, MX1, MX2, XIAP, IFI44L, OAS2, LY6E, AGRN, IFIT1, RSAD2, ISG15, IFIT3, CCL2, TDRD7, PLSCR1, ACSL1, TNFSF10, OAS1, GBP1, SERPING1, FCGR1A, C2, TYMP, STAT1, LAMP3, LGALS3BP, IFITM3, TAP1, IFI6, APOBEC3F, APOBEC3C, APOBEC3B, APOBEC3A, APOBEC3D, APOBEC3G, G6PD	http://www.ncbi.nlm.nih.gov/pubmed/12642603
55	**Eosinophils (BAL)**	**HS**	Mild Asthma, Whole Lung	UP	ADAM28, CNR2, FFAR3, LGALS12, PRSS33, SPNS3, ADAM8, CORO1A, FHL3, LTC4S, RAB37, TESC, ARAP3, CYP4F12, GGT5, MCTP2, RAB3D, TNFSF14, ASB2, DACH1, GPR56, MMP25, RD3,	http://www.ncbi.nlm.nih.gov/pubmed/23844029

			Allergen Challenge		TREML2, ATP2A3, DAPK2, GPR97, NHSL2, RNASE2, TRPM6, CASS4, DGKD, ICAM3, P2RY2, RNASE3, TSPAN18, CD300LB, EMP4P, IFITM1, PADI2, SIGLEC10, VSTM1, CD69, FAM101B, IL1RL1, PADI4, SIGLEC8, CDA, FAM65B, IL5RA, PGLYRP1, SLC24A3, CHST15, FFAR2, KIF21B, PIK3R6, SORL1	
57	**Lung biopsy**	**MM**	Poly(I:C) - 2hr	UP	CXCL10, IFIT1B, MX1, MX1, OASL, IFIT2, CMPK2, HAS2, RSAD2, HAS1, RSAD2, CXCL11, CSF1, TNFAIP6, IFIT1B, GBP2, RSAD2, RTP4, IRGM, RND1, GBP4, RTP4, IFIH1, IRGM, CMPK2, HAS2, CXCL9, IRGM, IFNB1, CSF1, IL6, ADAMTS4, STAT1, PTX3, GEM, TNFAIP3, PARP14, GBP6, ADAMTS4, DDX58, PYHIN1, FAM26F, TNFAIP2, USP18, MMP13, CCL4, CCL8, CCL11, PYHIN1, MT1H, PLSCR2, TNFAIP3, VCAM1, ADM, CXCL11, C12orf75, ATF3, CP, CCL20, CXCL9, TIMP1, SLFN11, HPX, SAA1, IFI44L, CCL22, NTS, CH25H, IRG1, IFI44L, FGG, MT1A, RGS16, CXCL3, CXCL3, CXCL3, CXCL6, CXCL8, LEP,	http://www.ncbi.nlm.nih.gov/pubmed/22990623
58	**Lung biopsy**	**MM**	Poly(I:C) - 6hr	UP	NHLH1, CMPK2, IFIT2, CMPK2, GBP4, MX1, RSAD2, TOR3A, CD274, HERC6, DDX58, HERC6, HERC6, SAMD9L, STAT1, HERC6, GBP4, GBP2, GBP4, RNF213, MX1, ZNFX1, MITD1, PARP14, CXCL10, IRGM, GBP2, SETDB2, STAT1, IFIT1B, EIF2AK2, ENPP4, WARS, IRGM, IRGM, ATM, ASB13, WDR19, OASL, PML, PML, TLR3, IFIH1,	http://www.ncbi.nlm.nih.gov/pubmed/22990623

					RTP4, TOR3A, IFIT1B, SLFN11, ASB13, DDX60, STAT2, PARP11, TRIM5, STAT2, STAT1, TOR3A, TRIM6, RBL1, CXCL11, WDR19, DDX58, PARP9, TRIM21, USP18, WARS, DDX60, GBP2, DTX3L, IL15, GBP6, ENPP4, SLFN11, SECTM1, ADAR, MLKL, XAF1, RSAD2, INPP1, ZUFSP, WARS, MITD1, TRAFD1, RTP4, DHX58, UBE2L6, IDO1, LY6E, STAT1, IFI35, RSAD2, TRIM34, NAMPT, GNB4, CXCL9, NMI, IFI35, CXCL9, PLSCR2, PNPT1, HAS2, TRIM14, NLRC5, CXCL11, PYHIN1, DDX58, IRF9, HAP1, ZBP1, BATF2, IRF7, PYHIN1, DTX3L, DAXX, ZBP1, IFI44, KATNA1, SPATS2L, ADAR, Mar-05, PNP, NCOA7, SLFN5, FAM26F, SP100, IFI44L, RAB19, CX3CL1, ZNF836, PLEKHA4, SLFN11, ISG20, MISP, IFI44L, SERPINA3, CD40, SPPL2A, IFNB1, AIM1, MMP13, UBA7, ADAR, VCAM1, ZC3HAV1, SPATS2L, IFI44L, ATM, TOR1AIP2, TTC39B, DHX58, TMEM171, MOV10, CD40, PAPD7, TNFAIP6, SLFN12, PSMB8, LGALS9C, PARP14, ASAP3, TTC39B, HAS2, PSMB9, TAPBPL, ZSWIM5, CCRL2, CD40, CASP4, ATP10A, AREL1, DCP2, IL6, CCL5, UPP1, SLFN5, ECE2, APOL6, GCH1, CTRL, SP100, CX3CL1, CSF1, LAG3, IL18BP, TTC39B, TMEM106A, PNPT1, SPATS2L, TRIM25, RNF114, PLAC8, FCGR1A, SLC15A3, USP25, NAMPT, SLFN12, EPSTI1, GGT5, XAF1, CD69, CACNB4, SOCS1, MS4A4A, TLR2, ATF3, OAS3, SAMHD1, PYHIN1, GCH1, PPP1R14D, ASB13, TRIM5, LYPD8, NFKBIE,	

					ARHGAP8, CSF1, CASP1, ZC3HAV1, PLA1A, BRIP1, CD86, SOCS1, CCL8, LGALS3BP, OSMR, CCL4, ETNK1, OAS2, TIFA, EPSTI1, ARID5A, PPA1, XDH, TNFAIP3, CNR1, NFKBIE, MS4A4A, ERVFRD-1, CA13, PARP11, MARCKSL1, VCAM1, GLIPR2, LRRC4, SECTM1, GEM, RND1, PTX3, ARSI, AFTPH, NPC2, VCAN, GLIPR2, DNASE1L3, ABTB2, MS4A6A, SLC2A6, CA13, FRAS1, PAPSS2, MXD1, HSPBAP1, B2M, FAP, SLFN5, PCGF5, VCAM1, EPSTI1, MB21D1, ADAMTS4, PTPN2, IFNG, FCGR1A, GZMB, VCAN, POU3F1, CA13, TFPI2, TNFAIP3, VNN1, PML, IAPP, UBD, IRG1, ADAMTS6, IAPP, IAPP, RTN4RL2, DCK, TNFAIP2, RGS1, BCL3, CSRNP1, SLFN12, ADAMTS4, MT1H, KLRK1, VNN1, MSR1, IL12B, CH25H, NTS, CCL22, PYHIN1, IL1RN, TNF, CP, SOCS3, RAD54B, CCR2, TIMD4, TIMP1, XCL2, NAV3, IFITM1, HPX, DDX4, MS4A6A, GZMA, DCK, FCGR3B, CXorf21, NCR2, GPR84, MBD1, MSR1, IL1RN, SELP, IL1RN, MSR1, NCR1, SAA1, SLFN12, CCL3L1, MT1A, CXCL3, FGG, CXCL3, RGS16, CXCL3, ORM2, C15orf48, CXCL8	

62	**Lung biopsy**	**MM**	Poly(I:C) - 48hr	UP	IRF7, APOD, ZBP1, IFI44L, CXCL10, GBP4, PYHIN1, PYHIN1, ZBP1, IFI44, CXCL9, IFIT1B, CXCL11, LY6E, LGALS3BP, USP18, DDX60, SIGLEC1, GBP6, RTP4, LAIR2, MX1, IFI44L, BST2, MX1, RTP4, MS4A6A, XAF1, C3AR1, DDX60, SLAMF9, C3AR1, CMPK2, STAT1, CCR2, FCGR1A, OASL, IFIT2, MS4A4A, FCGR1A, OAS3, C3AR1, LAIR2, IL18BP, OAS2, AIF1, DHX58, LAIR2, CCR2, IRGM, HERC6, TM4SF5, APOC2, SLFN12, MS4A7, CNGB3, MS4A4A, MS4A6A, HERC6, IFI44L, APOBEC1, CCR2, FCGR2A, HERC6, RSAD2, PLA1A, MSR1, CXCL9, GDF3, TIMP1, IL12B, RSAD2, SLFN11, CLEC4A, CCR2, SIRPG, HERC6, B2M, SAA1, IFI27, NLRC5, CLEC4A, CCR2, FCGR2A, EPSTI1, CCL5, CLEC5A, BEX4, CCR2, CD72, SLFN12, MSR1, EPSTI1, TRIM5, MILR1, STAT1, XCL2, FCGR2A, FCGR2A, LPXN, DCK, GPR114, GPR65, MSR1, LST1, VNN1, DHX58, FAM26F, RSAD2, CCR1, MSR1, SAA4, CCL4, CCL8, NCR2, CXCL3, PYHIN1, CCR9, KLRK1, GZMK, IRG1, HAVCR1, PARP14, CCR2, MS4A7, RGS1, CXCL3, CXCL3, KLK1, CH25H, FYB, CXorf21, HPX, GPR35, CD180, FCGR3B, CXCL13, SLFN12, IL6, TLR1, KLK1, CXCL6, ORM2, TNFRSF9, CA13, KLK1, KLRB1, GZMB, C15orf48, EMR3, RGS16, CXCL13, ADAMTS4, CYBB, CXCL11, IL1RN, RFPL3, SLC26A4, CXCL8, UBD, CCL3L1, IFNG, IL1RN, ORM2	http://www.ncbi.nlm.nih.gov/pubmed/22990623

64	**Lung biopsy**	**MM**	Poly(I:C) - 72hr	UP	IRF7, APOD, CCNA1, PYHIN1, IFI44L, TOMM20L, PYHIN1, IFI44, IFI27, IFI44L, IFIT1B, MS4A7, OAS2, CXCL10, MX1, DDX60, ZBP1, CCR2, C3AR1, ZBP1, SPAG5, CXCL9, SAA1, CCDC67, CCR2, FCGR1A, KLK1, KLK1, OAS3, MX1, MS4A4A, SRSF11, NCAPG, CDK10, CEP55, MS4A4A, CCR2, ESCO2, CCR2, OASL, RGS1, SLFN12, IL12B, KLK1, ORM2, CXCL11, CXCL8, IRG1, CXCL3, CXCL3, CXCL3, SLC26A4, AGR2, CLCA1	http://www.ncbi.nlm.nih.gov/pubmed/22990623
65	**Lung biopsy**	**MM**	Poly(I:C) - 96hr	UP	APOD, IRF7, MS4A7, PYHIN1, C3AR1, C3AR1, CCL8, CCR2, MS4A7, PYHIN1, CCR2, C3AR1, CCNA1, IFI44L, SPAG5, TOMM20L, MX1, CDK10, CXCL9, IFI27, IL12B, SAA1, CEP55, OAS2, HAL, IFI44L, ESCO2, CXCL10, RGS1, HMMR, CH25H, CXCL11, ESCO2, C15orf48, ORM2, CXCL8, IRG1, AGR2	http://www.ncbi.nlm.nih.gov/pubmed/22990623
67	**Lung biopsy**	**MM**	Bleomycin - 1day	UP	GDF15, AEN, CCNG1, CDKN1A, EDA2R, CELF5, DDIAS, PSRC1, THEM5, PSAPL1, SAA1, CXCL3, CXCL10, RSAD2, ORM2, CCL20, CXCL6, TIMP1, CXCL8, CCL8, SLC26A4, IL6, ADAMTS4, CXCL9	http://www.ncbi.nlm.nih.gov/pubmed/23565148
68	**Lung biopsy**	**MM**	Bleomycin - 2days	UP	HERC6, VCAN, RSAD2, MX1, IFIT1B, DHX58, IFI44, IRF7, CXCL11, CXCL10, OAS3, FCGR1A, GDF15, MS4A6A, CXCL8, ZBP1, OASL, CYP7B1, DDIAS, SAA1, EDA2R, OAS2, APOD, SERPINA3, CELF5, CXCL3, TIMP1, PSRC1, CCL8, SECTM1, C15orf48, CCR2, CH25H, ORM2, MSR1, FOSL1, IRG1, CXCL6, SPINK1, LIF, SLFN12, IL6, CXCL9, IL1RN, EREG,	http://www.ncbi.nlm.nih.gov/pubmed/23565148

					MORC1, CXCL13, TNC, CHL1, CD177, BCAT1, ADAMTS4, SPRR1B,	
77	**Lung biopsy**	**MM**	Bleomycin - 28days	DOWN	BEX2, TMEM132D, SLC4A1, FABP1, TBX20, KCNJ3, TRDN	http://www.ncbi.nlm.nih.gov/pubmed/23565148
101	**Lung brushings**	**HS**	IL-13	UP	ADAMTS9, ALOX15, BCL2L15, C1QTNF1, CA2, CCBL1, CCL26, CD274, CD44, CDH26, CISH, CST1, CST2, CST4, CTSC, DPP4, FAM26E, FETUB, GGH, HS3ST1, LRRC31, NTRK1, NABP1, PCSK6, POSTN, SERPINB4, SH2D1B, SIDT1, SLC26A4, SLC39A8, SLC5A1, SOCS1, SUSD2, USP54	ADEPT cohort

HS: Human sample, IVV: In vitro sample; MM: Murine model

Table E8: All predefined gene sets entered into gene set variation analysis		
#	**Gene Set**	**Source**
1	LDLRAP1, ASPM, BCL11B, MIS18A, CAMK4, CCNA2, CCNB1, CCNB2, CD3D, CD3E, CD3G, CD5, CD6, CD8A, CD8BP, CD8B, CDK1, CPOX, CTLA4, CXCR6, DGKA, DNAJB1, DUSP2, EGLN3, PRR11, GPR15, GZMK, H2AFX, HDGFRP3, PIK3IP1, HMMR, ICOS, IL22, IL9, INPP4B, KIF14, LAG3, LEF1, LEPROTL1, LRRN3, MELK, TAF1D, MKI67, PAICS, PRC1, ATAD2, DUSP4, RRM1, DEPDC1, AURKA, TCF7, TRAC, TOP2A, TPX2, TRAT1, UBE2C, UBE2S, ZBED2, ZWINT, HAUS1, NUF2, CDCA2, CDCA5, DHX33, STAMBPL1, MTFR2, TRDV3, AC017002.1, GPATCH4, MTHFD1L, UBE2T, IL17F, OXNAD1, ZBED6CL, NDFIP2, NDNL2, TRAV12-1, TRIM59, ZNRF1	http://www.ncbi.nlm.nih.gov/pubmed/15789058
2	AMPD1, PPOX, BANK1, BCL11A, TNFRSF17, BLK, BLNK, BMP8B, STAP1, VCPKMT, C19orf10, EDEM2, CD19, MS4A1, CD79A, CD79B, KLF6, DDOST, EAF2, EIF2AK3, ELL2, PDIA4, FCRL2, FKBP11, FAM46C, TXNDC15, TMEM156, GNG7, GPRC5D, WHSC1L1, SPCS2, SEL1L3, LZTFL1, MAN1A1, MANEA, NXPE3, NGLY1, OSBPL10, MZB1, PAX5, SUB1, PNOC, POU2AF1, QRSL1, RPN1, SEC24A, KDM5D, SPATS2, SPIB, SSR1, HSPA13, TCF3, TCL1A, SEC62, HSP90B1, TRAM1, TRAM2, UBE2G1, UBE2J1, EZR, VPREB3, FAM129C, PRDM15, CPNE5, LINC00926, ERN1, FBXO18, FCRL1, EME1, DERL3, FCRLA, PPAPDC1B, FCRL5, KLHL14, TXNDC11, NLRP7, RALGPS2, TLR10, WNT10A	http://www.ncbi.nlm.nih.gov/pubmed/15789058
3	ATP13A3, AP1S2, BHLHE41, CASP1, CCL24, CCRL2, CD1D, CDK5RAP2, CLEC5A, VCAN, CTSD, CTSL, CXCL1, CXCL3, CXCL5, CYBB, DFNA5, HBEGF, DUSP6, EREG, THBS1, PID1, GNA15, HS3ST3B1, IER3, IL19, IL1A, IL1B, IL36G, IL1RN, IL24, IL3RA, IL6, MTF1, MMP1, MMP14, MMP19, MMP9, NPC1, NRIP3, PFKFB3, PLAUR, PLD3, PPBP, PPIF, PTX3, RNU2-1, PHACTR1, SERPINB2, SERPINB7, SLC28A3, SLC31A1, SLC3A2, SRC, TCIRG1, TFPI2, NEAT1, TNFSF15, ZFYVE16, POMZP3, LINC00158, LINC00936, RP11-384O8.1, GJB2, GPR84, PNPLA8, IRAK2, DNAJC5B, MPEG1, MS4A6A, GLIS3, PLD1, PRAM1, SGPP2, SNX9	http://www.ncbi.nlm.nih.gov/pubmed/15789058

4	CD244, CHST12, CLIC3, IVNS1ABP, IVNS1ABP, KIR3DL2, KIR3DL1, KIR2DL2, KIR2DL4, KIR2DS4, KIR2DS5, KIR2DS5, KIR3DS1, KLRF1, NS1-BP, PTGDR, TGFBR1, YPEL1	http://www.ncbi.nlm.nih.gov/pubmed/15789058
5	ABTB2, ADAM12, ALOX15, CBR3, CCL13, CCL17, CD1A, CD1B, CD1E, CD86, N4BP2L1, CHST7, CLEC10A, CLIC2, CRLF2, CXCL11, EHD4, TRAFD1, FSCN1, IFI6, GRSF1, H6PD, HLA-DQA1, HLA-DQB1, HMG20B, HMOX1, IFIT1, CD209, CERS6, IFIH1, POGLUT1, MFSD12, MMP12, MX1, NAGPA, NR4A3, OAS1, SLCO5A1, PDCD1LG2, RAB30, RAB9A, RASSF4, ARHGAP22, SLC27A3, SIGLEC1, SPRED2, TBC1D13, UBD, CNOT10, TIFAB, MAP3K13, WFDC21P, NAA25, GPR157, L3MBTL4, KDM2B, SRGAP2, NFXL1, ZNFX1, C17orf58, NEURL3, MOB1B, NT5C3AP1, AKT1S1, NUB1, BLOC1S6, PVRL2, TTYH2	http://www.ncbi.nlm.nih.gov/pubmed/15789058
6	ABTB1, AMPD2, FAM53C, CCR3, CDA, CMTM2, CLC, CREB5, CTBS, CTBS, DICER1, MSL1, FCGR2B, FCGR3B, FCGR3B, MANSC1, FPR2, FRAT2, GPR27, FFAR2, HSPA6, CXCR1, CXCR2, TMCC1, SLC45A4, KRT23, MBOAT7, TSEN34, MXD1, YPEL3, CEP19, R3HDM4, MPPE1, SLC25A37, NCF4, NRBF2, PHC2, PROK2, RALB, RNF141, SEC14L1, MSRB1, STX3, TSPAN16, VMP1, VNN2, XPO6	http://www.ncbi.nlm.nih.gov/pubmed/15789058
7	FCGR2A, FCGR2C, CXCR1, CXCR2, FPR1, MME	http://www.ncbi.nlm.nih.gov/pubmed/27677865
8	CCL26, LOXL4, NOS2, CD36, CDH13, JAM2, HIGD1B, CLCA1, FZD5, CST2, IGHE, ATP5J, ALOX15, FETUB, AADAC, TOX2, LYPD1, CYYR1, HS3ST4, CST1, KRT31, IL1R2, NKX1-2, TUBAL3, PRKD1	http://www.ncbi.nlm.nih.gov/pubmed/21819959
9	CLCA1, POSTN, PRR4, SERPINB2, CPA3, TPSB2, TPSAB1, C16orf54, STOM, ZMAT2, AHDC1, EVC2	http://www.ncbi.nlm.nih.gov/pubmed/17898169
10	GPR115, DMXL2, STEAP4, MUC5B, SCNN1G, TMEM45A, SCGB3A1	http://www.ncbi.nlm.nih.gov/pubmed/17898169
11	FKBP5, GAS1, PHACTR3, FAM107A, HIF3A, TSC22D3, KLF9, HCAR3, PER1, C6, SORD, LINC00964, FXYD1, AHNAK2, WIPI1, CST1, CLCA1	http://www.ncbi.nlm.nih.gov/pubmed/17898169

12	TFCP2L1, HBB, MUC13, POSTN, SERPINB2	http://www.ncbi.nlm.nih.gov/pubmed/17898169
13	CCL26, PTCHD4, CLCA1, CST1, TUBAL3, CST2, CDH13, JAM2, NOS2, NTRK1, TMEM132B, PTGDR2, ZNF436, IL1R2, IGHE, FETUB, HIGD1B, TOX2, GRM8, NAGS, KRT31, KRT34, ATP5J, FZD5, LOXL4, NKX1-2, AADAC, DOK1, HRH1, CYYR1, CTDSPL, NOVA2, WWC2-AS2, PRKD1, CEP72, SLCO2A1, CD36, DISP1, LYPD1, ADM5, ALOX15, FAM124B	http://www.ncbi.nlm.nih.gov/pubmed/21187436
14	IRS2, CXCL6, FOLR1, DUSP1, DUSP4, MUC5B, SAA4, GLRB, HS3ST4, PROS1, TMEM45A, NR1I2, CSF3, AKR1C1, ACHE, CLGN, GUSBP4, GJB7, HGD, PIP5K1B, NA, SLC13A3, ZNF331, PGLYRP4, C11orf63, KIAA0232, PTP4A1, NSUN7, TSPAN6, HNF1A-AS1, RHOV, LRRC37B, PCYT2, LRWD1, ODC1, GK5, OSBPL6, ACTA1, CES4A, TCTN1, CCDC30	http://www.ncbi.nlm.nih.gov/pubmed/21187436
15	HBG1, CAMKK2, CAV1, DUSP1, DUSP5, FLNC, TNFRSF17, ALPL, TRIB1, SGK1, MME, SOCS3, PTGS2, IL1RAP, IL1R2, LIFR, COL18A1, ITGB8, GPC1, SLIT1, POMZP3, KCNJ4, SELL, PABPC4, TRIM9, PDLIM4, IGKC, IGH, GYPC, CDKN2C, CCL11, CABP1, RAMP3, RRM2, RBFOX2, CXCL8, MMP9, CXCL2, CD38, FPR1, TOP2A, AKAP8L, TRIP6, BCL3, RB1, CDC45, CREBBP, EGR1, TFDP1, ADCY3, SAT1, CCL3, FOS, MXD1, NA	http://www.ncbi.nlm.nih.gov/pubmed/23190644
16	NCK1, FASLG, ABI1, PSTPIP1, ARNTL, CLTC, RPS6KB1, FEZ1, CD247, GNAI1, HLA-F, HLA-B, KLRD1, KLRC1, KLRC1, EIF3C, EIF3A, HTRA2, ITGAL, SMAD7, CUL4A, SF3B3, MLH1, CDC7, SNUPN, HNRNPAB, SYT11, PRF1, MAS1, IFNG, NUP210, CDK13, SLC4A4, KIAA1279, VPS4B, XCL1, C14orf1, NFE2L1, CTCF, BRD8, RAB9A, ID3, PRSS23, PSMA3, GZMA, TAF1A, ATF2, STAT4, CEBPG,	http://www.ncbi.nlm.nih.gov/pubmed/23190644
17	COPB2, S1PR4, GNB1, ARHGEF2, CAMKK2, RABAC1, KIF3B, MKNK1, FLOT2, GRAP, MINK1, MAP3K14, MAP2K4, FMNL1, PGAM1, GLS, MTOR, NEDD4L, PTPN6, CSK, STAT5B, PIK3CD, HCLS1, RPA1, PRDX1, RPA2, HADHB, PRDX4, FZD7, LIMK2, AP3D1, VAMP2, VAPB, CFL1, WIPF1, DDB1, STX12, GPSM3, S100A9, IFNGR2, DLGAP5, ARF3, TPD52L2, PHC2, MAP4K4, GPI, AIMP2, ENO1, AKAP8L, RXRA, MBD2, ACVR1, SPEN, ICAM3, TRIP12, S100A8, RBPJ, PPP4R1, TM9SF2, BAG1, USP4, MTA1, SMAD4, NUP98, MAML1, ANP32A, ARFIP2, PCMT1,	http://www.ncbi.nlm.nih.gov/pubmed/23190644

	RAC2, ALDOA, NFYC, TP53TG1, DNPEP, MAPK14	
18	CYCS, CALD1, SLC25A4, PNO1, METAP2, FASLG, PKN2, AKT2, FGF2, RNF216, SSX2IP, RHEB, PIK3R1, GNAI1, TFRC, SH2B3, NCR1, HSPA5, LIPC, GUCY1A2, DLG2, SMAD7, ARF6, IFNG, SLC4A4, TIMM17A, YES1, JUND, MED1, GTF2B, ARID4A, RORA, CDKN1B, ENC1, ID2, MATK, ID3, ID1, KRR1, TNPO1, ANXA1, SKI, SRSF7, CHD1, SRSF3, MXD4, HIST1H1B	http://www.ncbi.nlm.nih.gov/pubmed/23190644
19	GNA12, MINK1, MAP3K14, RIPK1, GRB14, BCL10, SNTA1, HMOX1, SDC4, NEDD4L, PRG2, TGFBR2, CD5, PTGS2, LIFR, TLR6, IGF2, FURIN, ITGB8, CCL7, SORT1, LCT, FZD7, PABPC4, BMP6, GYPC, CDKN2C, CXCL9, CXCR3, MCM6, Mar-02, RAMP3, DLGAP5, RBFOX2, REPS2, CXCL3, CXCL2, HAPLN1, LCN2, CTSL, GEMIN4, TRIP6, BMP2, TRIP12, PHLDA1, TAB2, HMGA1, MSC, NUP98, EGR1, ADCY3, PRDM1, DNPEP, MAX, CCL3, ZFP36L1,	http://www.ncbi.nlm.nih.gov/pubmed/23190644
20	CYCS, SOS1, PSTPIP1, CRELD1, TARS, SSX2IP, ACD, P2RX7, MAP2K5, SYK, BLNK, PLCG2, HLA-B, NCR1, SEBOX, ATP2B4, IL2RG, ZRSR2, ARF6, TESK1, SF3B3, FANCA, VPS4B, ITGB1BP1, ITGA4, IRF8, NFE2L1, IRF1, HDAC3, STX8, MNAT1, GTF2H4, ANXA1, ARFRP1, HIST1H1B	http://www.ncbi.nlm.nih.gov/pubmed/23190644
21	YWHAE, SNCA, GPRIN2, APLP2, GRK5, CNN1, GNA12, KLK6, COPB2, CYB5R3, HBG1, NRGN, RGS2, S1PR4, GNAQ, TBXA2R, TOR1A, TUBA1A, GNB1, ARHGEF2, CTNNAL1, ADRBK2, GNG10, BDKRB2, SFN, NTRK2, MAPK3, CAV1, RIN2, RABAC1, DUSP1, RAB4A, SYN1, NOS1AP, PAK2, MKNK1, NCK2, WASF1, DUSP5, NTRK3, TNFRSF1B, MINK1, BST1, SOD2, SNCG, LTA, DUSP6, BUB1B, LSM1, GRB14, MAP2K4, CLIC1, FLNC, TRAF3, PCBP1, CSF2RA, ALPL, LDHA, BCL10, EIF6, TRIB1, LSM5, TNIP1, ACTN1, PDLIM1, FBP1, ADORA2A, PICALM, POR, TOM1, SNTA1, PGAM1, HMOX1, SVIL, TGFB1I1, SGK1, RAP1A, PTPN12, TNFRSF10C, SDCBP, BRAF, SDC4, FKBP1A, NEDD4L, BSG, SLC16A3, PRG2, PSEN1, PDLIM7, GAB2, ADM, MME, CSK, TLR2, PIK3CB, CSF2RB, LILRB2, FCAR, FCGR1A, CSF3R, SOCS3, STAT5B, FCER1G, WASF3, NDN, PTGS2, PECAM1, GAST, IL1RAP, MYD88, SLA, IL1R2, SSTR2, NUCB1, LILRB1, LY96, FCGR2A, GABARAP, TLR6, CD14, HCLS1, IGF2, NOV, GSN, LRP1, LRPAP1, APP, CR1, C4A, DMC1, RPA1, FURIN, GAPDH, TG, NOTCH2, ITGB8, HADHB,	http://www.ncbi.nlm.nih.gov/pubmed/23190644

	MMP14, TIMP2, CASP4, PGK1, CST3, BGN, CCL7, C4A, GPC4, CTSD, DSG3, SERPINA3, CHM, SORT1, NUMB, ITGB5, ADAM9, FLOT1, PRDX4, F5, LCT, RAB11A, GPC1, SLIT1, ITM2B, POMZP3, F8, C3AR1, ANXA5, PSAP, ICAM1, KCNJ4, LIN7A, CHP1, KIF1B, KCNJ2, S100P, SDC2, CAPNS1, LIMK2, ACTC1, ABLIM3, AP3D1, VAPB, VASP, STXBP2, DMTN, PIP5K1C, SSH1, CDC42BPA, LASP1, XPO6, VAMP7, ZYX, SRSF9, WIPF1, WDR1, TRIM9, TESK2, HIST1H2BD, PDLIM4, SF3B4, BMP6, UBOX5, EXO1, FCGR3A, TLR1, NAPA, STX12, MPP1, CDKN2A, UBE2C, ENSA, SMARCD3, CXCL9, CCL11, MCM6, STX6, Mar-02, BID, CD101, CD80, CD86, TYR, TYRP1, PITPNA, F2RL1, ST14, IL1RN, ABI2, ACVR2B, PDHA2, TPM4, GPSM3, ADRA2A, CABP1, CHST15, RRAGD, RAMP3, LAMP2, CTSA, IRAK3, IFNGR2, CP, DLGAP5, GYPA, RHAG, ARF3, CENPB, RNASE2, APOBEC1, RBFOX2, CA4, GP1BA, CDC42EP2, REPS2, ANXA3, TPD52L2, PLP2, HP, CD163, DPEP1, CHMP1A, C2, AQP1, PHC2, AFG3L2, S100A2, TPM1, ITGB1, MAP4K4, CXCL3, CXCR2, AMFR, GPI, COL4A4, TGFBI, CD36, CD93, CXCL8, CXCR1, MMP9, TIMP1, CXCL2, AIMP2, HAPLN1, CXCL1, CCL2, VCAN, CD63, EPS8, CD9, LCN2, COL1A1, SAA1, TLN1, ENO1, FPR1, UBE2E3, IRF2, GATA2, AKAP8L, MAPK7, THRB, CRMP1, CTSL, SPRY2, BCL6, RXRA, BMP7, PLSCR1, CUX1, NCOR2, TRIP6, ARNT, SERPINB3, MBD2, ACVR1, BMP2, SPEN, TRIP12, PHLDA1, SLPI, ANXA11, S100A8, RBPJ, FHL2, PPP4R1, KLHL35, RNF11, TAB2, CDK14, TM9SF2, RB1, RNF40, CREG1, BAG1, HMGA1, FRK, POU3F1, CAT, LILRA3, RBPMS, ZDHHC3, PRUNE2, MVK, CALM1, KCNMB1, SALL2, TPGS2, TFE3, ALDH2, NUP214, MAML1, ANP32A, H3F3A, TGM2, SMAD2, FTL, HIST2H2BE, MCF2L, RHOG, EGR1, HIST1H4A, S100A11, PCMT1, ZEB2, ALDOA, SPR, TFDP1, PRDM1, HDGF, NFYC, RAB13, AGT, SAT1, GBP2, TP53TG1, B4GALT3, NFATC4, ELK3, MAPK14, MAPKAPK3, ELK1, MAPK11, MAX, CEBPB, RBM42, MAPK10, KCNK1, CCR4, TRIM29, HOMER3, FOS, CCR1, SPAG9, USF2, MXD1, CASP5, ZBED1, CDC25C	

22	CALM1, SIAH1, PIK3CA, AKAP13, TTN, MRAS, FDX1, SLC25A4, PNO1, NCK1, METAP2, BIN1, CYFIP2, ABI1, AKAP1, EIF4A2, EIF4G2, EXOSC8, FBL, HSP90AB1, RPS6, TNFRSF10B, CDC37, HSP90AA1, HNRNPD, CAPN3, CHUK, AKT2, HARS, RPL5, RPSA, AIP, DDX39A, EXOSC9, CRELD1, OFD1, RPL6, ARNTL, SNRPN, RPL4, XRCC6, GSE1, UTRN, ACD, NCALD, RHEB, SOX4, RPS6KB1, RASGRP2, YWHAQ, MAGOH, KIF5B, TRAF4, P2RX7, PRKCZ, MAP2K5, FEZ1, DAPK3, YME1L1, CD247, PIK3R1, HNRNPU, BLNK, HLA-F, TRAC, CD72, FOLR1, IL6ST, KLRD1, INPP4A, KLRC1, SH2B3, NPM1, KLRB1, NCR1, EIF3G, EIF3H, EIF3E, EIF1AX, EIF3A, EIF3K, EIF5B, HSPA5, RECQL, XPA, RABGGTB, LRP8, PTP4A2, HMOX2, ITGAL, DLG1, EZR, ATP2B4, IL2RG, PIAS4, PRPF40A, RIF1, CLK1, SRSF6, U2AF2, ZRSR2, PPIG, SYNE1, SNRPD2, DYNC1LI2, NOL3, VAMP1, TRA2B, TWF1, SKP2, CUL4A, BRAP, CAND1, ZMYND11, BMPR1A, SF3B2, SF3B3, SF3B1, MLH1, SNRNP200, NONO, SFPQ, HSPA9, MVD, MPHOSPH10, IMP4, CD40LG, ZNF337, ATP5C1, ORC4, PSMC3, CDC7, ENO2, SNUPN, RPL17, SYNCRIP, SYT11, CSE1L, KPNA6, DPP4, STX16, GZMB, PRF1, SRSF5, SRRM1, IL12RB2, PI4KA, FBLN5, MAS1, PDHB, KPNA5, RPS19, ITPR3, ACIN1, AKR1C3, SRSF10, TRA2A, RRM1, AK1, CD48, IFNG, PARP2, NUP210, ABCE1, CELF2, CDK13, SLC4A4, OSGEP, 39326, TIMM17A, TIMM44, KIF22, REPS1, EMG1, SMARCC2, SMARCE1, TPD52, CCT4, RPL14, RPL7, TNNT2, ITGB1BP1, YES1, IGFBP3, EEF1B2, KARS, ITGA4, RPL10, XCL1, DFFB, NACA, TBP, C14orf1, ZNF24, ZBTB16, IRF8, COPS2, LAMTOR5, JUND, HMGB1, MED1, GTF2B, DHX9, ILF3, CTCF, TAF5, DPM1, POLR3F, PSMC2, STX8, SEPHS1, TRRAP, NDUFV2, KLF6, ARID4A, BRD8, HNRNPH3, CBFA2T2, RAB9A, EEF1D, DLST, DLG5, GATA3, CIR1, ILF2, SRRT, PMAIP1, RORA, ATM, TMPO, REL, PURA, CDKN1B, CCNE1, POLA1, DDX18, RAD17, GTF2H4, ELF1, CCNT2, NKRF, ENC1, MDM4, HBP1, CCND2, THOC1, PRDM2, AKAP8, TCOF1, UBTF, ERCC5, NOP56, RBBP5, PHB, EEF1E1, EWSR1, TRIM37, ID2, TCF4, MATK, ID3, ID1, PRSS23, RPS15A, ZMIZ2, KRR1, DDX5, PSMA3, GZMA, SET, NUP88, TNPO1, HSPD1, MAP3K12, RAN, ARF1, ANXA1, AES, PTMA, CAMK2G, MCF2, NXF1, MED6, SS18L1, E2F5, SRSF7, HIRIP3, TLE2, PPP2R1B, SMARCA5, TAF1A, RAE1, RPS7, HMGN1, ATF2, HNRNPK, MAPKAPK5, RAD52, UBE2I, CHD1, SRSF3, MKNK2, NOLC1, RPS6KA5, AIMP1, HOMER1, MXD4, STAT4, HSF2, CEBPG, MATR3	http://www.ncbi.nlm.nih.gov/pubmed/23190644

23	YWHAE, SNCA, GPRIN2, APLP2, GRK5, CNN1, GNA12, KLK6, CYB5R3, NRGN, GNAQ, TBXA2R, TOR1A, TUBA1A, GNB1, CTNNAL1, ADRBK2, GNG10, BDKRB2, SFN, NTRK2, MAPK3, RIN2, RABAC1, DUSP1, RAB4A, SYN1, NOS1AP, PAK2, MKNK1, NCK2, WASF1, FLOT2, NTRK3, TNFRSF1B, MINK1, BST1, SOD2, SNCG, LTA, DUSP6, BUB1B, LSM1, GRB14, MAP2K4, CLIC1, TNFRSF17, TRAF3, PCBP1, CSF2RA, ALPL, LDHA, EIF6, TRIB1, LSM5, TNIP1, ACTN1, PDLIM1, FBP1, ADORA2A, PICALM, POR, FMNL1, TOM1, PGAM1, HMOX1, SVIL, TGFB1I1, SGK1, RAP1A, PTPN12, TNFRSF10C, SDCBP, BRAF, SDC4, FKBP1A, MTOR, NEDD4L, BSG, SLC16A3, PDLIM7, GAB2, ADM, MME, CD5, TLR2, PIK3CB, CSF2RB, LILRB2, FCAR, FCGR1A, CSF3R, SOCS3, FCER1G, WASF3, NDN, PTGS2, PECAM1, GAST, IL1RAP, MYD88, IL1R2, SSTR2, NUCB1, LILRB1, LY96, FCGR2A, GABARAP, TLR6, CD14, HCLS1, IGF2, NOV, GSN, LRP1, LRPAP1, APP, CR1, C4A, DMC1, FURIN, GAPDH, PRDX1, TG, NOTCH2, ITGB8, MMP14, TIMP2, CASP4, PGK1, CST3, BGN, CCL7, GPC4, CTSD, DSG3, SERPINA3, SORT1, NUMB, ITGB5, ADAM9, PRDX4, F5, RAB11A, ITM2B, F8, C3AR1, ANXA5, PSAP, ICAM1, LIN7A, CHP1, KIF1B, KCNJ2, S100P, SDC2, CAPNS1, SELL, LIMK2, ACTC1, ABLIM3, VAMP2, VASP, STXBP2, DMTN, PIP5K1C, SSH1, CDC42BPA, LASP1, XPO6, VAMP7, ZYX, SRSF9, WIPF1, WDR1, TESK2, HIST1H2BD, SF3B4, BMP6, UBOX5, EXO1, IGK, FCGR3A, IGH, TLR1, NAPA, MPP1, CDKN2A, UBE2C, ENSA, SMARCD3, CXCL9, MCM6, STX6, Mar-02, BID, CD101, CD80, CD86, TYRP1, PITPNA, IL1RN, ABI2, ACVR2B, PDHA2, TPM4, GPSM3, ADRA2A, RRAGD, RAMP3, S100A9, LAMP2, CTSA, IRAK3, RRM2, IFNGR2, CP, DLGAP5, GYPA, RHAG, ARF3, CENPB, RNASE2, APOBEC1, CA4, GP1BA, CDC42EP2, REPS2, ANXA3, TPD52L2, PLP2, HP, CD163, DPEP1, CHMP1A, C2, AQP1, PHC2, AFG3L2, S100A2, TPM1, ITGB1, CXCR2, AMFR, GPI, TGFBI, CD36, CD93, CXCL8, CXCR1, MMP9, TIMP1, CXCL2, CXCL1, VCAN, CD63, EPS8, CD9, LCN2, COL1A1, CD38, SAA1, TLN1, ENO1, FPR1, UBE2E3, TOP2A, IRF2, GATA2, AKAP8L, MAPK7, THRB, CRMP1, CTSL, SPRY2, BCL6, RXRA, BMP7, PLSCR1, CUX1, NCOR2, ARNT, SERPINB3, MBD2, ACVR1, PHLDA1, BCL3, SLPI, ANXA11, S100A8, FHL2, PPP4R1, KLHL35, RNF11, TM9SF2, RNF40, CREG1, HMGA1, FRK, CDC45, MTA1, POU3F1, CAT, MSC, LILRA3, RBPMS, ZDHHC3, PRUNE2, MVK, CALM1, KCNMB1, SALL2, TPGS2, CREBBP, SMAD4, TFE3, ALDH2, NUP214, MAML1, ANP32A, H3F3A, TGM2, SMAD2, FTL, HIST2H2BE, MCF2L, RHOG, EGR1, HIST1H4A, S100A11, ZEB2, ALDOA, SPR,	http://www.ncbi.nlm.nih.gov/pubmed/23190644

	TFDP1, HDGF, NFYC, RAB13, AGT, SAT1, GBP2, NFATC4, ELK3, MAPK14, MAPKAPK3, ELK1, MAPK11, CEBPB, RBM42, MAPK10, KCNK1, ZFP36L1, CCR4, TRIM29, HOMER3, FOS, CCR1, SPAG9, USF2, MXD1, CASP5, ZBED1,	
24	CALM1, PIK3CA, PRKCE, AKAP13, TTN, MRAS, CALD1, FDX1, NCK1, SOS1, METAP2, BIN1, CYFIP2, PKN2, AKAP1, EIF4A2, EXOSC8, FBL, HSP90AB1, RPS6, TNFRSF10B, CDC37, HSP90AA1, CAPN3, CHUK, AKT2, HARS, RPL5, RPSA, MAP2K7, AIP, FGF2, DDX39A, EXOSC9, OFD1, RPL6, TARS, SNRPN, RNF216, RPL4, CLTC, XRCC6, UTRN, ACD, NCALD, SOX4, RPS6KB1, RASGRP2, MAGOH, KIF5B, TRAF4, P2RX7, PRKCZ, DAPK3, YME1L1, CD247, HNRNPU, BLNK, HLA-F, TRAC, CD72, FOLR1, PLCG2, IL6ST, KLRD1, INPP4A, TFRC, KLRC1, SH2B3, NPM1, KLRB1, EIF3G, EIF3H, EIF3J, EIF3E, EIF1AX, EIF3K, EIF5B, RECQL, HTRA2, RABGGTB, LIPC, LRP8, PSEN2, HMOX2, DLG1, EZR, MYO6, PIAS4, PRPF40A, RIF1, CLK1, SRSF6, U2AF2, ZRSR2, PPIG, SYNE1, SNRPD2, DYNC1LI2, NOL3, VAMP1, TESK1, SKP2, BRAP, CAND1, ZMYND11, BMPR1A, SF3B2, SF3B1, SNRNP200, NONO, SFPQ, HSPA9, MVD, MPHOSPH10, IMP4, CD40LG, ZNF337, ORC4, PSMC3, ENO2, SNUPN, RPL17, SYNCRIP, HNRNPAB, CSE1L, KPNA6, DPP4, PSMA1, STX16, GZMB, SRSF5, PI4KA, FBLN5, PDHB, KPNA5, RPS19, ITPR3, ACIN1, AKR1C3, SRSF10, TRA2A, AK1, CD48, PARP2, NUP210, ABCE1, CELF2, OSGEP, 39326, TIMM44, KIF22, REPS1, EMG1, SMARCC2, TPD52, KIAA1279, CCT4, RPL14, RPL7, TNNT2, IGFBP3, EEF1B2, KARS, RPL10, XCL1, DFFB, TBP, ZNF24, ZBTB16, IRF8, COPS2, LAMTOR5, HMGB1, IRF1, HDAC3, MED1, GTF2B, DHX9, ILF3, TAF5, DPM1, POLR3F, PSMC2, SEPHS1, TRRAP, RPS27A, NDUFV2, KLF6, ARID4A, BRD8, HNRNPH3, CBFA2T2, EEF1D, DLST, DLG5, GATA3, CIR1, ILF2, SRRT, PMAIP1, ATM, TMPO, REL, PURA, MNAT1, POLA1, DDX18, RAD17, GTF2H4, ELF1, CCNT2, NKRF, MDM4, HBP1, CCND2, THOC1, PRDM2, AKAP8, TCOF1, UBTF, ERCC5, NOP56, RBBP5, PHB, EEF1E1, EWSR1, TRIM37, ID2, TCF4, MATK, TCF12, RPS15A, ZMIZ2, KRR1, DDX5, PSMA3, SET, NUP88, TNPO1, HSPD1, MAP3K12, RAN, ARF1, ARFRP1, AES, PTMA, CAMK2G, NXF1, MED6, SS18L1, E2F5, SRSF7, HIRIP3, DDX19A, PPP2R1B, SMARCA5, TAF1A, RAE1, RPS7, HMGN1, HNRNPK, RAD52, SRSF3, MKNK2, NOLC1, RPS6KA5, AIMP1, HOMER1, MXD4,	http://www.ncbi.nlm.nih.gov/pubmed/23190644

	STAT4, HSF2, CEBPG, MATR3,	
25	RGS2, S1PR4, RABAC1, DUSP1, KIF3B, FLOT2, GRAP, SOD2, DUSP6, RIPK1, TNFRSF17, TRAF3, ALPL, TRIB1, ADORA2A, GLS, SVIL, SGK1, TNFRSF10C, SLC16A3, PRG2, PSEN1, TGFBR2, MME, PTPN6, FCAR, CSF3R, SOCS3, STAT5B, PTGS2, PIK3CD, SLA, IL1R2, TLR6, CD14, HCLS1, NOV, RPA2, COL18A1, CHM, FLOT1, C3AR1, S100P, SELL, LIMK2, CFL1, XPO6, DDB1, IGK, IGH, TLR1, CXCR3, STX6, CD80, TYR, F2RL1, ST14, CHST15, IFNGR2, PLP2, PHC2, CXCL3, CXCR2, COL4A4, CXCL8, CXCR1, MMP9, CXCL2, CXCL1, CCL2, FPR1, IRF2, BCL6, GEMIN4, ARNT, ICAM3, SLPI, S100A8, CDK14, USP4, NUP214, ARFIP2, EGR1, S100A11, RAC2, PRDM1, B4GALT3, CCL3, CCR4, FOS, CCR1, MXD1	http://www.ncbi.nlm.nih.gov/pubmed/23190644

26	SIAH1, PRKCE, EIF4G2, HNRNPD, MAP2K7, OFD1, RPL4, SSX2IP, XRCC6, GSE1, YWHAQ, P2RX7, YME1L1, SYK, KLRD1, KLRB1, EIF3H, EIF3J, EIF3E, EIF3C, EIF3K, SEBOX, XPA, LRP8, PSEN2, PTP4A2, GUCY1A2, DLG2, MYO6, SYNE1, DYNC1LI2, NOL3, TRA2B, TWF1, CUL4A, ATP5C1, RPL17, FANCA, PSMA1, GZMB, SRRM1, IL12RB2, ITPR3, AKR1C3, SRSF10, TRA2A, RRM1, IFNG, 39326, REPS1, SMARCE1, TNNT2, KARS, NACA, ZBTB16, HMGB1, POLR3F, PSMC2, STX8, RPS27A, HNRNPH3, CBFA2T2, RAB9A, CIR1, CCNE1, MDM4, HBP1, TCF12, RPS15A, KRR1, TNPO1, SKI, MCF2, TLE2, DDX19A, RPS7, MAPKAPK5, UBE2I, HOMER1	http://www.ncbi.nlm.nih.gov/pubmed/23190644
27	BCL3, SOCS3, PIM1, SBNO2, LDHA, CMAHP, PDCD1, IGFL1, LOC731186, MUC1, GPRIN3	http://www.ncbi.nlm.nih.gov/pubmed/22532634
28	CFH, CFLAR, PLXND1, CYB561, TYMP, ANK1, RORA, TRIB2, TXK, PLD1, MCAM, IL12RB2, P2RX5, MAP3K4, ABCB1, TBC1D2, IL12RB1, TNFSF13B, CTSH, CA2, TRPS1, KCNN4, IMPDH1, SPOCK2, HLF, IL26, KLRB1, IL17A, IL17F, CCL20, ITGA4, IL1R1, EPAS1, ELOVL4, CCR2, APOL3, PALLD, ARNTL, SCRN1, FURIN, ITGAX, TOB1, RORC, SLC4A10, ADAM12, DST, GBP5, AUTS2, ACE, ZFYVE28, CCR5, IL23R, B3GALT2, ANTXR2, PTPN13, ANXA5, HPGD, CTSB, AQP3, KIF5C, LIMS1, CXCR6, DAB1, PTPRM, LONRF3, GREM2, FES, ZNRF1, GIMAP5, DPP4, LINGO4, TNFRSF25, LINC00299, LGALS3, ALPK1, PFKFB3, RNASET2, PDCD4, MAGED4, MAST4, ITGA6, CITED2, OSBP2, CERK, VDR, AK3, CDH4, S100A6, LRP12, MAPK10, RUNX1, MXD1, EMP1, SMOX, DTX1, AGPAT4, MYC, PCBP4, SPG20, PDE4D, NR1D2, NPDC1, CEBPD, ATP6V0A1, RCL1, LATS2, RAB11FIP5, RARG, GRAMD1B, SLC35G1, IL6R, GABBR1, ENTPD6, IL7R, SSBP3, GNA15, YBX3, TTC39C, FHL1, MLLT4, FLOT1, CCDC65, PERP, ADAM15, RPS6KA3, TGFBR2, STOM, NEO1, IL4I1, IL18RAP, TDRKH, AGO4, PHLDA1, PPP4R1, LIMS3, GAB3, CLIC3, ADTRP, EVA1C, SEC31B, ME1, FLT3LG, NMRK1, MVP, EPG5, MAN2A2, C3AR1, ZNF652, PLEKHF1, DSE, CD274, CASK, FKBP11, OBFC1, ELOVL6, PXK, PPP2R2B, GALNT10, CYP27B1, PPT1, MAPK3, METRNL, SETD7, THBS1, NR1D1, C14orf182, LTBP4, SLAMF1, SRD5A3, ADCY3, ACKR3, ABCD1, CLOCK, MCF2L2, JUN, RNF144B, SFXN3, VSIG1, AMPD2, IFI44, ZDHHC9, KCNA2, LMO4, ECE1, FEZ1, TMEM184B, NCF4, TRADD, UNC93B1, MB21D2, PPAP2C, LST1, MYO5A, C4orf26, CYFIP1, PLAUR, MAST1, METTL21B, NUAK2, FAM159A, CRYBG3, SH2B2, MDM2, CSNK1E, ADA, SLC38A5, CFHR1, MAML3,	http://www.ncbi.nlm.nih.gov/pubmed/22715389

	SOX5, SMAD3, RIPK2, NPHP4, GLA, MAP3K7CL, PAG1, CFP, LAPTM4B, PITPNC1, MPI, SFXN2, ZFP36L1, CDC42EP3, TSHZ3, ROPN1L, SIAE, NPC1, LPCAT4, MINA, NT5E, ARL3, TANC2, USP30, ITGA3, THOC3, B3GALNT2, MAP3K3, GIMAP1, BOP1, PGS1, C10orf2, DHX32, TNFRSF10B, TCEAL3, IRF1, KCNA3, PLSCR3, PLXNC1, ADPRH, PRKCD, ANKRD28, DHX58, NDRG1, EXT1, PHF11, CHN1, RANBP9, WDR59, RNF19A, CORO2A, CACNB3, OSTF1, MKNK2, ENPP2	

29	MCM8, CDKN2AIPNL, MMP25, CD74, CFLAR, FOXK1, CSNK1G2, ZNF250, DMC1, MAGT1, ZNF14, HLA-E, FAM115A, SSTR2, SPTLC1, NA, METTL21A, NLRP8, NCF1C, NA, ZFYVE20, ZNF321P, YRDC, ITGA2, NA, IL10, OCIAD1, STAT1, C5orf28, ALPP, RNF24, IL17RD, GABPB2, DDX51, C8orf37, KCNH6, ITPK1-AS1, GPR1, CASP4, NA, EID2B, ZNF682, TNFSF13B, HSD17B7, N4BP2, CDAN1, FKBP14, TUBA3FP, BLZF1, HYPK, SPI1, XPNPEP3, DTWD2, ADAR, SDHAP1, AK1, PDE4C, GJC1, FKTN, GGA1, RBCK1, ZNF549, SLC16A12, MCMDC2, DHFR, MBOAT7, INIP, MSRB3, SHISA5, MSH3, SLC35E1, MIF, ZNF430, MTMR12, CFAP74, NA, AUNIP, EIF2AK2, XRCC2, FAM73A, ZNF814, PNPT1, VCAN, VIM, ZNF69, RASGRP2, NUBPL, PARP14, SLC44A2, SORL1, AFF3, ZNF530, NA, ORC6, FBXO40, USP49, IFI35, AKNA, ZMAT3, NPIPB3, PPA2, FCGR1A, MLKL, ARL16, SLC44A4, GPSM3, LILRB1, PSME2, ZYX, TAPBP, PLIN3, NA, ARHGDIA, SEMA3E, CORO1A, CEP19, IRF9, ZNF652, SERPING1, MAP3K11, GNAI2, EXO5, SERPINA1, ACAP1, SLC25A44, CYB5RL, VHL, MVP, IL4R, PSMB8, ZNF394, TDP1, RHBDF2, LRRC47, ERAP2, IRF7, HLA-G, PARP10, ZNF683, TNFSF14, MBD4, AHR, CREB1, PLEKHO2, CATSPER2, ZNFX1, ZNF786, SNRNP70, RPL7L1, AKT1, LPAR2, SLC16A3, INTS7, CMTM7, ATHL1, PDCD7, SYAP1, CCR6, CTDSP1, TIAF1, MYO1F, C17orf62, LAP3, STAT5A, ADRM1, IL18, BCYRN1, KIAA0101, ARF3, FAM177A1, CSF2RA, CTSW, CAPZB, C15orf39, PDPR, PPP2R1A, TCIRG1, MAST3, SP110, AKR1D1, ISG15, IL17RA, UNC93B1, CFD, HNRNPU, JUP, NOP56, DAPP1, RN7SL1, ANKRD22, PTPN6, CD27, MBD6, TRPC4AP, CD97, MKNK2, MYO1G, TRANK1, ATG16L2, NDE1, LAPTM5, CPT2, AHCYL1, CD37, SLC25A28, PLCB2, NCOR2, MICAL1, ZNF483, NBEAL2, PIGR, GAPDH, ITIH5, PGS1, ACADVL, IRF2BPL, RBM23, TMEM17, RNF167, VPS9D1, MED22, SBNO2, PRKD2, LAT2, LILRB3, SDF2L1, CNDP2, GRIPAP1	http://www.ncbi.nlm.nih.gov/pubmed/21357945

30	GPR183, CD300LF, UBE2A, CRLF3, 37500, PRDX5, RSBN1, TPM1, C5orf15, DNAJB6, SMOX, ADSS, ZMAT2, HMBS, INSIG1, TRIM33, TMEM183B, H2AFY, CEPT1, DNAJA4, TOR1AIP1, ANP32B, SCAMP1, GPX4, RGS10, KIAA0430, KIAA1551, LBR, XPO7, CCNI, TM6SF1, HNRNPK, RPL6, SLC44A1, TLE4, SLC40A1, VEZF1, SRP14, MS4A7, PNRC2, EFR3A, ARRDC3, HPS1, CDKN1B, TMBIM4, SNX3, TMEM87A, OGT, BCL2L1, ATP6V0C, MBP, XK, CD47, ANXA5, TFDP1, PRDX6, NPRL3, SIAH1, CHMP3, FGL2, IGF2BP2, OPTN, BAZ2B, CD302, ARPC3, GLO1, SNRK, PRKRIR, UBE2D3, PGRMC1, ATP6V1A, PAPD4, PRNP, FAM60A, TMED5, EVI2B, PELI1, KLHDC8B, PRDX3, PTEN, DAZAP2, OR2W3, SUZ12, VMP1, EEF1A1, BPGM, LST1, GUCD1, JTB, UBXN4, NDUFB5, TNS1, F2RL1, SRP9, MAP3K7CL, YPEL5, OLR1, ACP1, FBXO33, FTL, YOD1, ETS1, ATP5L, Mar-08, MPP1, CMTM6, AP1S2, BTF3, PRDX2, C2orf88, SH3BGRL, DPM2, CAB39, GYPB, RIOK3, RAB10, GOLGA7, RAB31, ITGB1, CLK1, EEF1A1P12, EIF3E, YBX1, ACTR2, SLC6A10P, CCNDBP1, CXCR4, ATP5E, DCAF6, PTBP3, HAGH, TMSB4X, POLR1D, C9orf78, CD46, CHPT1, YWHAH, ATP5EP2, LYZ, PTGS2, YBX3, TMEM71, PIP4K2A, OXR1, GNG11, ARL6IP1, IFIT1B, CAPZA2, GRINA, RGCC, TMEM123, MMD, NPTN, TMOD1, SDPR, SGK1, IFNGR1, HIST1H2AC, RPL30, RNF11, SERF2, CXCL8, TRAM1, GYPC, PCNP, PRKAR1A, RAB11A, PAIP2, PSMF1, SESN3, ZFAND5, FBXO7, SRGN, CHURC1, FAM104A, UBXN6, GABARAPL2, Mar-07, TPGS2, PPM1A, HBA2, MS4A3, OAZ1, HBB, UBB, ASCC2, ADIPOR1, SELENBP1, NINJ2, VNN2, CA2, ODC1, TSPAN5, SLC25A39, E2F2, TPT1, TRIM58, DCAF12, NCOA4, MBNL3, CEACAM8, RAB2B, GSPT1, OLFM4, RAP1GAP, SNCA, EPB42, MKRN1, RGS18, GYPE, ELANE, SLC4A1, GLRX5, PITHD1, VWCE, BNIP3L, AHSP, STRADB, HBD, ALAS2, YBX3P1, CAMP, FAM46C, DEFA4, DEFA1B	http://www.ncbi.nlm.nih.gov/pubmed/21357945
31	BCL11A, CCR7, KIAA0125, RBP5, CD22, FAIM3, DHRS9, ATP2C2, FCRLA, KBTBD12, CES3, C8orf34, GPR110, CR2, C5orf20, LOC130576, ZFYVE19, IGDCC4, DERL3, OSBPL3, MZB1, UNQ6228, SIGLEC6, CXCL13, MAN1C1, UGT8, CD79A, DMRT2, TMEM200A, GPR110, LRRC75A, TMEM9, SLC4A8, CALB2, RALGPS2, FAM129C, FOLH1, KLHL6, PDGFRL, TMEM182, ANKS1B, PRDM15, PRRX1, SLC45A3, IRF4, PNMAL1, CD79B, AMPD1	http://www.ncbi.nlm.nih.gov/pubmed/23925644

32	PAPSS2, WFDC1, NOSTRIN, NDEL1, NEDD9, STARD13, ASRGL1, EDNRB, KLF13, STOM, GPR4, MT1JP, SYN2, TMEM2, STX12, COL4A2, PAG1, RTN4, ABTB2, FCN3, ACVRL1, NES, PLXNA2, PODXL, PECAM1, RGCC, S100A8, TACC1, ENG, TPST2, KRT7, SYCP2L, MYH9, CYP4Z1, PHLDB1, WNT2B, BTNL3, SMAD6, RCOR1, LUZP1, PRKCE, ARHGEF10, HPCAL1, QKI, HERC3, COL4A1, GABARAPL1, CTTNBP2NL, KL, RIC1, CELF2, FOXF1, TMBIM1, BRINP1, CSPG4, SH3BP5, STXBP6, ATOH8, TAL1, CRMP1, RAI2, S1PR1, LPHN2, MAP2, CMTM8, SDE2, VIPR1, PKN1, ECHDC3, ADRB1, GREB1L, GPR133, ZNF358, PTPN12, LRRC8A, MAOA, TGFBR2, EPAS1	http://www.ncbi.nlm.nih.gov/pubmed/23925644
33	FKBP5, PDK4, RHOBTB3, ART3, PPM1K, HIF3A, KLF9, SLC39A8, PDE4DIP, JADE1, KLF15, KCNAB1, PRPH, TMX4	http://www.ncbi.nlm.nih.gov/pubmed/23925644
34	TMPRSS11D, SERPINB13, SPINK5, KRT4, TMPRSS11A, CSTA, GABRP, TYMS, GPR87, TMPRSS4, ATP10B, CH25H, SRPX2, IGKC, BNIPL, RAB38, CAPNS2, FANCD2, ABCC1, TENM2, BNC1, KLK10, PTAFR, CRABP2, TENM4, TRIM16, EYA2, GNA15, SMAGP, BICD2, EXOSC7, SCO1, BID, RHNO1, ITPA, TSPAN17	http://www.ncbi.nlm.nih.gov/pubmed/23925644
35	PPP2R1B, SCUBE3, ADAM22, GCC2, ACTA2, KIAA0319, FAM129A, MYOCD, NTN1, SYNPO2, CCDC30	http://www.ncbi.nlm.nih.gov/pubmed/23491407
36	IFI35, IRF7, MX1, MX2, XIAP, IFI44L, OAS2, LY6E, AGRN, IFIT1, RSAD2, ISG15, IFIT3, CCL2, TDRD7, PLSCR1, ACSL1, TNFSF10, OAS1, GBP1, SERPING1, FCGR1A, C2, TYMP, STAT1, LAMP3, LGALS3BP, IFITM3, TAP1, IFI6, APOBEC3F, APOBEC3C, APOBEC3B, APOBEC3A, APOBEC3D, APOBEC3G, G6PD	http://www.ncbi.nlm.nih.gov/pubmed/12642603
37	CD3D, DLEU1, COX11, HNRNPDL, DAP3, SORL1, PRNP, SLC25A6, EIF4B, PABPC4, RAB4A, CD3G	http://www.ncbi.nlm.nih.gov/pubmed/12642603
38	CCL5, GZMA, GZMK, PDCD1, IFNG, PACSIN1, CLIC3, TIGIT, CD70, TBX21, LYAR, ST8SIA1, CFH, IRF5, CTSH, OSM, LMO4, CCR4	http://www.ncbi.nlm.nih.gov/pubmed/23870669

39	SEMA5A, LOC729041, GATA3-AS1, NEFL, GAB2, KLRB1, NRIP3, ZP1, METRNL, TPPP, CAPG, ITPRIPL1, GATA3, ZDHHC11B, TNFRSF18, CADM1, ZDHHC11, NOD2, FANK1, LOC100131176, ABCA2, SUSD4, BEGAIN, HOMER3, MRC2, ZBTB16, DUSP23, SNED1, C16orf45, BAI2, PPP1R9B, GALT, SNTN, ASPH, PRMT9, LMCD1, BEST4, RORC, NOS3, SLC25A33, PPAPDC1B, ARHGAP42, SEMA5A, LOC729041, GATA3-AS1, NEFL, GAB2, KLRB1, NRIP3, ZP1, METRNL, TPPP, CAPG, ITPRIPL1, GATA3, ZDHHC11B, TNFRSF18, CADM1, ZDHHC11, NOD2, FANK1, LOC100131176, ABCA2, SUSD4, BEGAIN, HOMER3, MRC2, ZBTB16, DUSP23, SNED1, C16orf45, BAI2, PPP1R9B, GALT, SNTN, ASPH, PRMT9, LMCD1, BEST4, RORC, NOS3, SLC25A33, PPAPDC1B, ARHGAP42,	http://www.ncbi.nlm.nih.gov/pubmed/23870669
40	BCL2L11, FLJ46446, NECAB3, TULP4, NXPE3, E2F3, TMEM2, CD27, LOC100128031, MBD5, GBP5, SLC12A6, PELI2, KBTBD11, CCR7, NRIP1, SNN, GPA33, PRAGMIN, TXK, ACTN1, IGF1R, BTBD11, ADTRP, TMIGD2,	http://www.ncbi.nlm.nih.gov/pubmed/23870669
41	KLRB1, RORC, PLXND1, CTSH, ALOX5, PTPN13, IL4I1, SMCO4, NEFL, HLF, JAKMIP2, DSE, LIMS1, HLA-DRB1, LTK, HLA-DRB4, USP10, NR1D1	http://www.ncbi.nlm.nih.gov/pubmed/23870669

42	MYO1F, MIAT, ADAM19, LINC00152, E2F2, FAM129A, RP3-527F8.2, TESC, PDCD1, ANXA2, PRDM1, FAM46C, HLA-DRB1, LOC541471, ITGB1, NPDC1, ANXA2P1, HLA-DRB4, LOC338620, NCF4, TNFRSF4, LGALS1, TIGIT, MPST, SAP30, OASL, CPNE7, CALHM2, CD70, SRXN1, PMAIP1, GPR68, C12orf75, PLA2G16, PTGER2, PTTG1, PERP, HNRNPLL, FAS, IER5, MAF, ACTN4, RPL39L, SYT11, ANXA4, CDKN2C, AHNAK, LRFN4, RP11-374F3.4, APOBEC3C, IRF5, CHST7, DNAI2, PREX1, RNF214, S100A11, ATXN1, TNFRSF1B, SMCO4, S100A4, TUBB4B, TP53INP1, CYSTM1, CCR10, ANXA5, LOC284475, NDC80, TBK1, CREM, GALM, NBEAL2, PPP1R15A, ODF3B, ZC3H12A, CLIC5, TST, CD82, PRDM8, IL10RA, DLG3, PIEZO1, AIM2, YWHAH, HN1, CAPG, CTSH, PHACTR2, CD58, ACOT9, AAED1, CD99, GGTLC1, CLDND1, ATP2B4, PDIA6, SLC35B2, PI16, NABP2, SAMSN1, MYO1G, CLIC1, EZR, SLAMF1, CHST11, FAM53B, OSBPL3, LMNA, RILPL2, RALGDS, ARPC1B, GLIPR1, TRIM59, CRIP1, GATA3, SRGAP2, IL32, CDKN2A, BTG3, CCDC167, RUNX2, SRGN, ANTXR2, NLRP3, ADAM8, TPM4, GLIPR2, TXN, SSBP4, NABP1, CD63, OPTN, ASNA1, MTHFD2, RGS2, SURF4, CREB3L2, CD84, IDS, ZFYVE28, FLNA, COTL1, RAB11FIP1, COMMD5, SQRDL, PDP1, PANX1, RNF135, AQP3, FAM45A, SMC4, BNIP1, HERPUD1, GLB1, CAPN1, SHKBP1, SLC9A9, HSPA1A, SCO2, GDE1, TUBB2A, RABGAP1L, EAF1, SLC25A24, PRKCD, TRIM47, CAPN2, CCR4, SLCO3A1, PFKP, S1PR2, REEP5, SNAI3, PMVK, S100A10, GGTLC2, CTSA, AHR	http://www.ncbi.nlm.nih.gov/pubmed/23870669
43	TPCN1, ZSCAN18, DBH-AS1, CDCA7L, ZNF204P, CITED4, TCTN1, NAA16, GHRLOS, MYH3, LRRC24, ACVR1C, hCG_1990547, SLC12A7, LOC100128670, MYL5, CAPN5, GPRASP1, LAMB2P1, SMIM1, PCED1B, PPP1R3E, TXK, ROBO3, NUCB2, MEIS3P1, TLE2, MPZL1, CHI3L2, IL6ST, ACSS2, MPP1, ZNF573, PPT2, CCR7, FAM117B, SNN, EPHX2, AMIGO1, PLAG1, NET1, CHKA, MAN1C1, FBP1, SATB1, MDS2, GSAP, LOC100132345, LOC100131662, NLGN2, ITGA6, TRABD2A, TSPAN3, SCARNA16, B4GALT4, ACTN1, CERS6, NUAK2, GPC2, FBXO15, FLJ41649, BCAS4, TNFRSF10D, PDE9A, GNG7, GSTM2, CCDC106, FAM153A, PRAGMIN, AK5, PTPRS, LOC650392, APBA2, SOX8, IGF1R, BACH2, EPHB4, MYO15B, RIN1, FAM153B, AEBP1, PCSK5, AIF1, FAM213A, FHIT, LOC100129534, COL18A1, TMIGD2, CELA1, HSPG2, CLEC11A, NOG, LRRN3,	http://www.ncbi.nlm.nih.gov/pubmed/23870669

44	TRIB1, FANK1, HLA-DRB1, HLA-DRB4, LOC541471, DUSP4, CD70, TIGIT, IL2RA, FOXP3, PMAIP1, CKS2, IKZF2, ICA1, SMPD3, CPNE2, RORC, PTPLA, BFSP2, MGST2, RPL39L, CTLA4, TNFRSF1B, NUSAP1, VAV3, DUSP10, SLC2A8, TOX, KLRB1, SPATS2L, CTNNAL1, LOC284475, F5, IKZF4, PCTP, BASP1, LMCD1, RHOXF1, SETD7, TRIM16L, SHMT2, CXCR5, RP3-527F8.2, HLA-DMB, GBP5, HLA-DOA, FLJ46446, SMC6, HLA-DMA, IRF4, LOC730631, HS3ST3B1	http://www.ncbi.nlm.nih.gov/pubmed/23870669
45	AP3M2, TSPAN18, ZFP36L2, GPR35, LOC100131646, DPP4, SOS2, NLRP3, ASPH, MSX2P1, WNT10B, TMEM71, IL7R, WNT7A, STAT4, NOSIP, NR3C2, NOG, PDIA5, RBMS1, RECK, ACSL6, LOC643988, APP, CD40LG, VIPR1, WNT7B, CACNA1I, THEMIS, ID2, C1orf228, SCML4, LOC100132345, SOX8, DENND5A, AXIN2, ANK3, LOC650392, SLC40A1, NELL2	http://www.ncbi.nlm.nih.gov/pubmed/23870669
46	ALOX5, ANXA4, BIVM, BPI, BRD7, CAMP, CASK, CD63, CEACAM6, CEACAM8, CFLAR, DEFA4, GCA, LCN2, LOC23117, LOC728358, LTF, MBOAT1, MMP8, MNDA, PDE4D, POLR2J2, PPP1R16B, PRKCB, RETN, RNASE3, RUNX2, S100A12, S100A8, S100A9, S100P, SLC38A2, SPATA13, SRGN, SRGN, STOM, TNIP1, TTYH2, UGCG, ZNF749	http://www.ncbi.nlm.nih.gov/pubmed/21917308
47	AGPS, AKIRIN1, ANAPC5, ANKRD12, ANKRD17, ANXA3, ARFGEF2, ARG1, ARIH1, AZU1, BAG2, BPI, CASD1, CASP2, CASP6, CD24, CEACAM1, CEACAM6, CEACAM6, CEACAM8, CFLAR, CHI3L1, CHI3L1, CPEB4, CSNK1A1, CYCS, DOCK9, EHBP1L1, ELANE, FAM20B, FAS, FLJ10038, FLJ38717, GCA, GGA1, GNAQ, HERPUD2, HP, HP1BP3, KDM4B, KLF9, LCN2, LOC23117, LOC728358, LRRC8C, LTF, MINA, KMT2A, MPO, MS4A3, MSI2, NBPF11, NIPSNAP1, NMT2, NUP160, OXR1, MTPAP, PGLYRP1, PLP2, PLRG1, POGK, POLR2J2, POLR2J2, PRKX, PTER, PTPLAD1, RBM6, RECQL, RNASE3, RNPC3, RPL37A, RPS10, RSL1D1, S100P, SAMHD1, 38961, SF1, SMARCC2, SNRPN, SPEN, SRP72, TAF15, TCN1, TMEM106B, TMEM63A, TMF1, TNRC6B, UBE2H, UGCG, UGCG, YTHDC2, ZFP90, ZNF131, ZNF195, ZNF749	http://www.ncbi.nlm.nih.gov/pubmed/21917308

48	ABCC3, ABCC8, ABLIM2, ACTL6B, ADAM19, ADAMTS7, ADO, ALPPL2, APOBEC3F, APOBEC3G, APOC3, APOE, AQP2, ARTN, ARTN, ASCL2, BIRC7, BOC, CD1C, CD74, CDKN1C, CHRNA2, CLDN9, CLEC10A, CLEC2L, CLEC7A, COL11A2, COX6A1, CSF1R, CSPG5, CST3, DKFZp761P0212, DNALI1, EIF3B, ENPP7, C2CD4B, FAM71A, FCER1G, FGD2, FGFR1, FGL2, FLJ20021, RTP5, GALNT9, GDF9, GNPTAB, GP1BB, GPR114, GPR20, GPR39, GPRC5B, HAB1, HBA1, HBA2, HBA2, hCG_2007354, HES4, HLA-DQB1, HMOX1, IFI30, IGHA1, IGHA1, IL18RAP, IRF8, NMRK2, KDM8, KCNC4, KIAA1598, KIAA1648, PLIN4, KIF26B, KLF4, KLK13, KLRB1, KRT8, LGALS1, LILRA4, LMNA, GPAT2, LOC283177, FBXL19-AS1, SSC5D, LOC284837, LOC349114, LPAR3, LRRC16B, LRRC25, LRRN4, LRTM2, LST1, LST1, LST1, LST1, LST1, MAFB, MNT, Mar-02, MPEG1, MPEG1, MS4A6A, MUC4, MUC5AC, NF1, NFIX, NPPB, NUPR1, NYX, OXCT2, PALLD, PAPLN, PARD6G, PIK3AP1, PILRA, PRDM12, PRDM8, PRKD2, PSG5, RAB40B, RAPGEF3, RASGRF1, RHOV, RIF1, RUNX1T1, SAT1, SIGLEC10, SLC22A7, SLC7A7, SMARCB1, SMTNL1, SNCA, SNCA, SNCG, SNX22, SPON2, TBC1D9, TBX1, TBXA2R, TGFBI, TLE6, TMEM132A, TMEM151B, TMEM176B, TMEM198, TNFSF13B, TPCN1, TRAJ17, TRIM29, TTBK2, TYROBP, USP2, VASH1, VENTX, WIZ, WNK2, WNT6, ZFP36L2, ZNF20, ZNF703	http://www.ncbi.nlm.nih.gov/pubmed/21917308
49	NFKBIZ, ZC3H12A, RELB, BIRC3, CXCL1, ZC3H12C, TNFAIP3, MAP3K8, CXCL2, CASZ1, IER3, LENG1, SOD2, RRAD, NFKB2, ID2, TATDN1, CBR3, CCL3, ICAM1, PIK3R6, GADD45B, ADAM21, ZBTB25	http://www.ncbi.nlm.nih.gov/pubmed/24393021
50	MAP3K8, OPLAH, OR13C2, IER3, TMA16, KRTAP8-1, ZC3H12A, RIMBP3, OR2T10, GPIHBP1, HNRNPCL1, NFKBIZ, PTTG1, BDKRB1, CXCL1, F13A1, IL6, LTF, CXCL10, LRMP, TLR5, NFKBIA, CXCL2, GDPGP1	http://www.ncbi.nlm.nih.gov/pubmed/24393021

51	IL1B, IL6, CSF1, IL1R1, IL27RA, TNFRSF9, TNFRSF12A, IL1RN, CCL4, CXCL1, CCL7, CXCL3, CCL5, CCRL2, CXCL8, RGS1, LIF, CD69, LAT, CD83, ADORA2A, CRIP1, HLA-DQB1, PFDN6, TRAF1, NKG7, PTX3, FCGR2B, TNFAIP6, PTGER2, CLEC5A, GPR183, TREM1, BIRC3, FCAR, TLR2, HIVEP1, FOSB, FOS, EGR3, PHLDA2, SERPINB2, FGFR1, EGR2, INSIG1, PDGFA, IER3, PDGFB, BTG2, KLF10, PLK3, NAMPT, TNFAIP3, TNFAIP8, MARCKSL1, CRABP2, IRF2, RASAL1, FLRT2, SMARCD3, RND3, KAL1, FLNB, CD151, ARF6, ALCAM, MAFF, MSC, NFKB1, BCL6, NFATC1, ATF3, NFKBIA, NFKBIE, MYC, EMP1, ELL2, TOP2A, GTF2H2, DUSP2, THBD, NR4A2, GEM, OLR1, GCH1, SPHK1, NDUFA7, HBEGF, JAG1, LDLR, SMAD7, MALT1, SPRY2, DUSP6, MAP2K3, CREM, DUSP1, MAP3K14, FUT4, JUN, CYTIP, FYN, PGGT1B, VRK2, AKAP13, TTK, ENC1, SLC16A6, HIST2H2AA3, CYP3A4, HIST1H1C, NDC80, STK17A, PELI1, KCNAB1, B4GALT4	http://www.ncbi.nlm.nih.gov/pubmed/16911805
52	MS4A2, TPSAB1, TPSAB2, CPA3, RGS13, C1orf186	http://www.ncbi.nlm.nih.gov/pubmed/27677865
53	CLC, CPA3, DNASE1L3, IL1B, ALPL, CXCR2	http://www.ncbi.nlm.nih.gov/pubmed/24582314
54	CD83, JMJD6, STAT4, TRAF1, SLC7A5, TBCD, NFKB1, CD44, DESI1, NELFE, XCL2, IL4R, DUSP2, DUSP4, NUP188	http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1253826/
55	ADAM28, CNR2, FFAR3, LGALS12, PRSS33, SPNS3, ADAM8, CORO1A, FHL3, LTC4S, RAB37, TESC, ARAP3, CYP4F12, GGT5, MCTP2, RAB3D, TNFSF14, ASB2, DACH1, GPR56, MMP25, RD3, TREML2, ATP2A3, DAPK2, GPR97, NHSL2, RNASE2, TRPM6, CASS4, DGKD, ICAM3, P2RY2, RNASE3, TSPAN18, CD300LB, EMP4P, IFITM1, PADI2, SIGLEC10, VSTM1, CD69, FAM101B, IL1RL1, PADI4, SIGLEC8, CDA, FAM65B, IL5RA, PGLYRP1, SLC24A3, CHST15, FFAR2, KIF21B, PIK3R6, SORL1	http://www.ncbi.nlm.nih.gov/pubmed/23844029
56	CLC, SIGLEC8, EMR1, EMR4P, LGAL312, HRH4, CEBPE, DACH1, VSTM1	http://www.ncbi.nlm.nih.gov/pubmed/27677865

57	CXCL10, IFIT1B, MX1, MX1, OASL, IFIT2, CMPK2, HAS2, RSAD2, HAS1, RSAD2, CXCL11, CSF1, TNFAIP6, IFIT1B, GBP2, RSAD2, RTP4, IRGM, RND1, GBP4, RTP4, IFIH1, IRGM, CMPK2, HAS2, CXCL9, IRGM, IFNB1, CSF1, IL6, ADAMTS4, STAT1, PTX3, GEM, TNFAIP3, PARP14, GBP6, ADAMTS4, DDX58, PYHIN1, FAM26F, TNFAIP2, USP18, MMP13, CCL4, CCL8, CCL11, PYHIN1, MT1H, PLSCR2, TNFAIP3, VCAM1, ADM, CXCL11, C12orf75, ATF3, CP, CCL20, CXCL9, TIMP1, SLFN11, HPX, SAA1, IFI44L, CCL22, NTS, CH25H, IRG1, IFI44L, FGG, MT1A, RGS16, CXCL3, CXCL3, CXCL3, CXCL6, CXCL8, LEP	http://www.ncbi.nlm.nih.gov/pubmed/22990623
58	NHLH1, CMPK2, IFIT2, CMPK2, GBP4, MX1, RSAD2, TOR3A, CD274, HERC6, DDX58, HERC6, HERC6, SAMD9L, STAT1, HERC6, GBP4, GBP2, GBP4, RNF213, MX1, ZNFX1, MITD1, PARP14, CXCL10, IRGM, GBP2, SETDB2, STAT1, IFIT1B, EIF2AK2, ENPP4, WARS, IRGM, IRGM, ATM, ASB13, WDR19, OASL, PML, PML, TLR3, IFIH1, RTP4, TOR3A, IFIT1B, SLFN11, ASB13, DDX60, STAT2, PARP11, TRIM5, STAT2, STAT1, TOR3A, TRIM6, RBL1, CXCL11, WDR19, DDX58, PARP9, TRIM21, USP18, WARS, DDX60, GBP2, DTX3L, IL15, GBP6, ENPP4, SLFN11, SECTM1, ADAR, MLKL, XAF1, RSAD2, INPP1, ZUFSP, WARS, MITD1, TRAFD1, RTP4, DHX58, UBE2L6, IDO1, LY6E, STAT1, IFI35, RSAD2, TRIM34, NAMPT, GNB4, CXCL9, NMI, IFI35, CXCL9, PLSCR2, PNPT1, HAS2, TRIM14, NLRC5, CXCL11, PYHIN1, DDX58, IRF9, HAP1, ZBP1, BATF2, IRF7, PYHIN1, DTX3L, DAXX, ZBP1, IFI44, KATNA1, SPATS2L, ADAR, Mar-05, PNP, NCOA7, SLFN5, FAM26F, SP100, IFI44L, RAB19, CX3CL1, ZNF836, PLEKHA4, SLFN11, ISG20, MISP, IFI44L, SERPINA3, CD40, SPPL2A, IFNB1, AIM1, MMP13, UBA7, ADAR, VCAM1, ZC3HAV1, SPATS2L, IFI44L, ATM, TOR1AIP2, TTC39B, DHX58, TMEM171, MOV10, CD40, PAPD7, TNFAIP6, SLFN12, PSMB8, LGALS9C, PARP14, ASAP3, TTC39B, HAS2, PSMB9, TAPBPL, ZSWIM5, CCRL2, CD40, CASP4, ATP10A, AREL1, DCP2, IL6, CCL5, UPP1, SLFN5, ECE2, APOL6, GCH1, CTRL, SP100, CX3CL1, CSF1, LAG3, IL18BP, TTC39B, TMEM106A, PNPT1, SPATS2L, TRIM25, RNF114, PLAC8, FCGR1A, SLC15A3, USP25, NAMPT, SLFN12, EPSTI1, GGT5, XAF1, CD69, CACNB4, SOCS1, MS4A4A, TLR2, ATF3, OAS3, SAMHD1, PYHIN1, GCH1, PPP1R14D, ASB13, TRIM5, LYPD8, NFKBIE, ARHGAP8, CSF1, CASP1, ZC3HAV1, PLA1A, BRIP1, CD86, SOCS1, CCL8, LGALS3BP, OSMR, CCL4, ETNK1, OAS2, TIFA, EPSTI1, ARID5A, PPA1, XDH, TNFAIP3, CNR1, NFKBIE, MS4A4A,	http://www.ncbi.nlm.nih.gov/pubmed/22990623

	ERVFRD-1, CA13, PARP11, MARCKSL1, VCAM1, GLIPR2, LRRC4, SECTM1, GEM, RND1, PTX3, ARSI, AFTPH, NPC2, VCAN, GLIPR2, DNASE1L3, ABTB2, MS4A6A, SLC2A6, CA13, FRAS1, PAPSS2, MXD1, HSPBAP1, B2M, FAP, SLFN5, PCGF5, VCAM1, EPSTI1, MB21D1, ADAMTS4, PTPN2, IFNG, FCGR1A, GZMB, VCAN, POU3F1, CA13, TFPI2, TNFAIP3, VNN1, PML, IAPP, UBD, IRG1, ADAMTS6, IAPP, IAPP, RTN4RL2, DCK, TNFAIP2, RGS1, BCL3, CSRNP1, SLFN12, ADAMTS4, MT1H, KLRK1, VNN1, MSR1, IL12B, CH25H, NTS, CCL22, PYHIN1, IL1RN, TNF, CP, SOCS3, RAD54B, CCR2, TIMD4, TIMP1, XCL2, NAV3, IFITM1, HPX, DDX4, MS4A6A, GZMA, DCK, FCGR3B, CXorf21, NCR2, GPR84, MBD1, MSR1, IL1RN, SELP, IL1RN, MSR1, NCR1, SAA1, SLFN12, CCL3L1, MT1A, CXCL3, FGG, CXCL3, RGS16, CXCL3, ORM2, C15orf48, CXCL8	
59	KIF26B, CXXC4, DCDK1, FMO3, SPTSSB, 37865, HMGCS2, ADH7, RAB17, ASGR1, HEPACAM2, CCDC176, CLDN8, SYT17, PCLO, TMEM232, GDF10, ATP6V1B1, C11orf87, CDH26	http://www.ncbi.nlm.nih.gov/pubmed/22990623
60	IFIT2, CMPK2, CXCL9, IL18BP, CXCL10, STAT1, CXCL11, CD274, GBP4, HERC6, HERC6, MX1, HERC6, ZBP1, RNF213, RSAD2, TRIM5, BST2, IRF7, GBP2, LAG3, IRGM, IRGM, TOR3A, SAMD9L, OASL, MX1, XAF1, IFI44L, STAT2, IDO1, SPPL2A, ZNFX1, HERC6, STAT2, IRGM, CXCL9, GBP4, IFIT1B, PARP11, UBE2L6, ZBP1, PYHIN1, IFI27, IFI35, TOR3A, CMPK2, PYHIN1, USP18, LGALS3BP, DDX60, RTP4, RSAD2, MLKL, GBP2, STAT1, COL11A2, MS4A6A, UBA7, ISG20, GBP2, ADAR, DTX3L, IFIT1B, DHX58, GBP6, DHX58, TRIM34, RTP4, MS4A4A, OAS3, RSAD2, DDX58, IFI44L, MTHFD2, IFI44, IFI44L, TRIM6, DDX60, IRF9, PML, IFIH1, FCGR1A, PLA1A, PSMB8, CXCL11, CNGB3, EIF2AK2, PARP9, FCGR1A, NMI, MS4A4A, LYPD8, SECTM1, GZMB, NLRC5, APOD, MS4A6A, TRIM5, PLEKHA4, CLEC4A, CCR2, PSMB9, APOL6, DNASE1L3, MTHFD2, SLFN11, EPSTI1, PLAC8, ACP2, LAIR2, LGALS9C, TMEM106A, SIGLEC1, PML, FAM26F, IL1RN, GPR84, TAPBP, C2, LY6E, TMEM106A, HAP1, LAIR2, XCL2, SPATS2L, IL1RN, AIM1, OAS2, HCK, BATF2, EPSTI1, TRIM14, SLFN12, STAT1, IL1RN, CCL5, SLAMF9, UBD, MSR1, HPSE, OCSTAMP, FCER1G, AIF1, PYHIN1, DNASE1L3, LAIR2, MSR1, EVI2A, SCT, NAIP, ZC3HAV1, KLRK1, CST7, DCK, CCL8, MSR1, DAXX, SLC39A2, TLR3, CASP4,	http://www.ncbi.nlm.nih.gov/pubmed/22990623

	TGFBI, SLFN12, PYCARD, ADAR, TREML4, SLC2A6, SETDB2, THEMIS2, MSR1, SERPINA3, TIMP1, IL6, GNGT2, SLC15A3, VCAN, FCGR2A, NCR2, CCL4, CCR2, TRIM21, CYBB, SIRPG, IKBKG, BEX4, CA13, CYBB, FGR, VCAM1, CASP1, CCR2, SLFN11, SLC7A5, IRG1, CLEC5A, DDX58, SLFN5, FCGR3B, DCK, KLK1, CA13, RUNX3, TIFAB, APOBEC1, PARP14, MYO1F, AFTPH, MISP, EMR3, TLR7, XDH, SLAMF7, SEMA4D, PLEK, PRF1, AFTPH, DCP2, CYBB, TNFRSF1B, CD86, SLAMF8, HAVCR2, GLIPR2, KLK1, FPR2, IGSF6, NAMPT, CD180, SPI1, VCAN, TGFBI, SLFN11, TRIM25, HPX, LST1, CXorf21, SLFN12, XAF1, GLIPR2, BID, VCAN, PTPN6, NFKBIE, NFKBIE, C3AR1, MILR1, CD69, IFI27, PLD4, PPA1, ORM2, UPP1, PLEK, C3AR1, Mar-01, TLR2, GCH1, FASLG, VCAM1, SPIC, FASLG, CXCL13, P2RY13, GPR35, IL12B, CD48, DDX4, GZMB, SPIC, CA13, IL2RB, SFRP1, CD68, CLEC4A, PARP11, CTSW, SERPINA3, ABCB1, PILRB, CD80, CD40, KLRB1, TIFAB, GPR65, LCP2, FCGR2A, RGS1, VNN1, EPSTI1, C15orf48, EMR3, LILRB2, CCR9, GPR114, FOSL1, CD300A, SAA1, MS4A4A, CH25H, VAV1, FCGR2A, DCLK1, CD33, B2M, GZMA, MS4A7, CCR9, NKG7, IL12B, CCR2, CXCL13, SAMSN1, HAVCR1, KLRB1, RASA4, COCH, PTPRO, GPR171, C3AR1, FGR, NCR1, NCF4, CCL8, POU3F1, PLA2G7, CLEC4E, F10, FCGR2A, IFITM1, SLFN12, CD8A, LCP2, CLEC6A, CD8A, CXCL3, TLR1, GZMK, LPXN, ITIH1, DUSP2, TBX21, SELP, CD72, CD8A, SELL, FYB, ADM, UPB1, CLEC4E, RNASE6, KLK1, TNFRSF9, LAT2, OOEP, VNN1, PTPN2, CXCL3, CLEC6A, IL2RB, PIWIL2, CXCL3, TNF, CCR2, TNFRSF9, MAB21L3, TNFAIP2, ATF3, LCN2, ERVFRD-1, IL18RAP, AOAH, SECTM1, CCR2, ZC3H12A, IFNG, IFNB1, CXCL6, CD244, TLR7, CCR1, IL10RA, CSF3, CCL3L1, CD53, GIMAP7, TNFAIP6, FST, NOXO1, RGS16, CCR1, RFPL3, CXCL8, EOMES, CCL15, ADAMTS4, KLRC2, SLA2, GPR176	
61	GLS, HEPACAM2, RELN, GRIA1, GPC6, ACAA1, GRIA1, DIRAS2, GSTA1, LRRC17, HTRA3, FCRL2, GDF10, GPC6, ASGR1, DNAH6, SLC7A10, PON1, RYR3, DNER, NOTUM, KIF26B, GNG4, RBFOX3, FAT3, CD207, BCAN, CD163, SYT17, PER1, SHISA9, CES2, DCDK1, NTM, ATP6V1B1, SCARA5, DNER, KLF15, FMO3, CNTN4, GLB1L3, CYP1A1, ANGPTL7, OLFM2, CD209, C11orf87, FABP1, FABP1, HPCAL4, NTRK2, DHRS7C, TTN, TMEM182, TTN, TTN, MB,	http://www.ncbi.nlm.nih.gov/pubmed/22990623

62	IRF7, APOD, ZBP1, IFI44L, CXCL10, GBP4, PYHIN1, PYHIN1, ZBP1, IFI44, CXCL9, IFIT1B, CXCL11, LY6E, LGALS3BP, USP18, DDX60, SIGLEC1, GBP6, RTP4, LAIR2, MX1, IFI44L, BST2, MX1, RTP4, MS4A6A, XAF1, C3AR1, DDX60, SLAMF9, C3AR1, CMPK2, STAT1, CCR2, FCGR1A, OASL, IFIT2, MS4A4A, FCGR1A, OAS3, C3AR1, LAIR2, IL18BP, OAS2, AIF1, DHX58, LAIR2, CCR2, IRGM, HERC6, TM4SF5, APOC2, SLFN12, MS4A7, CNGB3, MS4A4A, MS4A6A, HERC6, IFI44L, APOBEC1, CCR2, FCGR2A, HERC6, RSAD2, PLA1A, MSR1, CXCL9, GDF3, TIMP1, IL12B, RSAD2, SLFN11, CLEC4A, CCR2, SIRPG, HERC6, B2M, SAA1, IFI27, NLRC5, CLEC4A, CCR2, FCGR2A, EPSTI1, CCL5, CLEC5A, BEX4, CCR2, CD72, SLFN12, MSR1, EPSTI1, TRIM5, MILR1, STAT1, XCL2, FCGR2A, FCGR2A, LPXN, DCK, GPR114, GPR65, MSR1, LST1, VNN1, DHX58, FAM26F, RSAD2, CCR1, MSR1, SAA4, CCL4, CCL8, NCR2, CXCL3, PYHIN1, CCR9, KLRK1, GZMK, IRG1, HAVCR1, PARP14, CCR2, MS4A7, RGS1, CXCL3, CXCL3, KLK1, CH25H, FYB, CXorf21, HPX, GPR35, CD180, FCGR3B, CXCL13, SLFN12, IL6, TLR1, KLK1, CXCL6, ORM2, TNFRSF9, CA13, KLK1, KLRB1, GZMB, C15orf48, EMR3, RGS16, CXCL13, ADAMTS4, CYBB, CXCL11, IL1RN, RFPL3, SLC26A4, CXCL8, UBD, CCL3L1, IFNG, IL1RN, ORM2	http://www.ncbi.nlm.nih.gov/pubmed/22990623
63	GRIA1, GRIA1, HEPACAM2, ACAA1, CNTN1, ASGR1, CD207, CD209, SCARA5, FABP1, FABP1, ITGB1BP2, SLC47A1, MYL3, MYL3, MYL3, MB, MYL7, TNNC1, MYL4, SMPX, RYR2, TTN, TTN, CASQ2, PGAM2, CKMT2, SRL, TTN, DHRS7C, CA3, TRDN, TCAP, TTN, TNNT2, LDB3, CFD, MYOZ2, TNNI3, TNNT2, MYBPHL, CSRP3, TXLNB	http://www.ncbi.nlm.nih.gov/pubmed/22990623
64	IRF7, APOD, CCNA1, PYHIN1, IFI44L, TOMM20L, PYHIN1, IFI44, IFI27, IFI44L, IFIT1B, MS4A7, OAS2, CXCL10, MX1, DDX60, ZBP1, CCR2, C3AR1, ZBP1, SPAG5, CXCL9, SAA1, CCDC67, CCR2, FCGR1A, KLK1, KLK1, OAS3, MX1, MS4A4A, SRSF11, NCAPG, CDK10, CEP55, MS4A4A, CCR2, ESCO2, CCR2, OASL, RGS1, SLFN12, IL12B, KLK1, ORM2, CXCL11, CXCL8, IRG1, CXCL3, CXCL3, CXCL3, SLC26A4, AGR2, CLCA1	http://www.ncbi.nlm.nih.gov/pubmed/22990623
65	APOD, IRF7, MS4A7, PYHIN1, C3AR1, C3AR1, CCL8, CCR2, MS4A7, PYHIN1, CCR2, C3AR1, CCNA1, IFI44L, SPAG5, TOMM20L, MX1, CDK10, CXCL9, IFI27, IL12B, SAA1, CEP55, OAS2, HAL, IFI44L, ESCO2, CXCL10, RGS1, HMMR, CH25H, CXCL11, ESCO2, C15orf48, ORM2,	http://www.ncbi.nlm.nih.gov/pubmed/22990623

	CXCL8, IRG1, AGR2	
66	CNTN1, CD209, FABP1, FOSB, ZBTB16,	http://www.ncbi.nlm.nih.gov/pubmed/22990623
67	GDF15, AEN, CCNG1, CDKN1A, EDA2R, CELF5, DDIAS, PSRC1, THEM5, PSAPL1, SAA1, CXCL3, CXCL10, RSAD2, ORM2, CCL20, CXCL6, TIMP1, CXCL8, CCL8, SLC26A4, IL6, ADAMTS4, CXCL9	http://www.ncbi.nlm.nih.gov/pubmed/23565148
68	HERC6, VCAN, RSAD2, MX1, IFIT1B, DHX58, IFI44, IRF7, CXCL11, CXCL10, OAS3, FCGR1A, GDF15, MS4A6A, CXCL8, ZBP1, OASL, CYP7B1, DDIAS, SAA1, EDA2R, OAS2, APOD, SERPINA3, CELF5, CXCL3, TIMP1, PSRC1, CCL8, SECTM1, C15orf48, CCR2, CH25H, ORM2, MSR1, FOSL1, IRG1, CXCL6, SPINK1, LIF, SLFN12, IL6, CXCL9, IL1RN, EREG, MORC1, CXCL13, TNC, CHL1, CD177, BCAT1, ADAMTS4, SPRR1B,	http://www.ncbi.nlm.nih.gov/pubmed/23565148
69	BEX2, ATP6V1B1, ASGR1, ACVR1C, PCK1, ADIPOQ, CA3, TMEM45B, CFD	http://www.ncbi.nlm.nih.gov/pubmed/23565148
70	CWH43, NTM, SFRP1, IL23A, SPRR1B, FCGR2A, PSRC1, CLDN4, GPNMB, CLEC5A, CDCA8, ATG9B, C3AR1, DCSTAMP, CCNG1, TREM2, CENPH, EXO1, TPX2, DDIAS, CPA4, CHODL, C1QA, NRIP3, AURKB, PIF1, C1QB, TFPI2, PLA1A, FST, PKHD1, GAS2L3, MSR1, SPP1, SHCBP1, C1QC, CCNB2, WFDC12, CLDN6, CCNA2, LRR1, FIGNL1, CHL1, FCRL2, NRCAM, CDCA3, BRINP1, SPC25, CLSPN, STIL, KIAA0101, TRIP13, CEP55, CD200R1L, CDCA5, SKA1, PTGER4, KIF11, VCAN, MMP10, CLEC4A, KIF2C, CCR2, SERPINB2, KIAA1524, CYP7B1, HTR7, C15orf48, GTSE1, VSIG4, PARPBP, CLEC6A, EDA2R, SERPINA3, NCAPG, MIS18BP1, CERS3, KIF18B, SPAG5, RAD51, COL24A1, MS4A6A, CGREF1, CDKN3, TK1, S100A14, NUSAP1, CDK1, GPR85, ELN, CCL17, TNC, FN1, CCL8, TIMP1, DTL, CENPE, P4HA3, CHSY3, E2F8, DEPDC1, ASPM, CENPP, CDK10, TTK, GPR176, GJB4, GATM, DMP1, EREG, THBS4, IQGAP3, CHEK1, FAM3B, RGS16, ESCO2, GJB5, CA13, CASC5, RTN4RL2, UBE2C, FCGR1A, HTR4, HMMR, KLHDC8A, RAD51AP1, MS4A7, TGM1, CCL15, AADAC, PBK, FBN1, DDIT4L, WISP1, LIF, PRSS22, E2F7, HAS2, GDF15, FXYD4, GLOD5, ADAMTS12, GCNT3, LAMA1, CSMD1, HNF4A, FKBP5, CDKN1A, MMP13, CENPF, CXCL10, FOSL1, ACKR1, ALDH1A3,	http://www.ncbi.nlm.nih.gov/pubmed/23565148

	SLC26A4, CCR1, SAA1, SECTM1, CEMIP, TUBB3, CILP, RHBDL2, BCL2L15, BCAT1, PTX3, CALCA, CELF5, CXCL9, ADAMTS4, IL1RL1, SPINK1, CLDN2, CH25H, IL1RN, CXCL13, TFAP2A, MORC1, ORM2, CD177, IL6	
71	IGFBP3, ECM2, ASGR1, SLC7A10, CYP1A1, KIAA0408, FABP1, BCAN, CST8, SNCA, ALAS2	http://www.ncbi.nlm.nih.gov/pubmed/23565148
72	THBS4, ANKRD34B, PSRC1, FN1, ELN, SFRP1, TREM2, COL24A1, NRCAM, EXO1, KIF11, PIF1, CDCA8, CD200R1L, COL5A2, FXYD4, CDCA2, PKHD1, THBS2, CHODL, AURKB, CCNA2, P4HA3, KIAA0101, STIL, ZRANB3, C3AR1, C1QB, AADAC, LHFPL2, GAS2L3, GLOD5, ADAMTS12, ILDR2, CTHRC1, C1QA, TPX2, TNC, CLEC6A, FBN2, C1QC, CCNB2, CEP55, CDK10, TTK, LRR1, CENPF, CFI, CDCA3, ADAM12, SPP1, SYT13, DEPDC1, CTSK, CCR2, CDK1, CASC5, SKA1, KIF18B, PTX3, CSMD1, FMOD, LAMA1, MIS18BP1, NCAPG, ASPM, CLSPN, CILP, DCSTAMP, GPNMB, SPAG5, CLEC5A, RAD51, FRZB, MS4A7, BRINP1, EDA2R, DDIAS, KIF2C, ATG9B, CHSY3, DTL, FST, E2F8, SHCBP1, IQGAP3, CERS3, GPR176, SPRR1B, PARPBP, UBE2C, CDCA5, CEMIP, CENPP, CDKN1A, MMP10, DMP1, HAS2, TMEM26, PBK, FBN1, CDKN3, E2F7, MSR1, CENPE, PLA1A, NUSAP1, CHL1, COL5A3, ESCO2, CLDN4, RAD51AP1, TUBB3, IGF1, IL1RL1, HMMR, MS4A6A, MEGF10, EREG, TIMP1, WFDC12, PDCD1, MMP13, CTLA4, FCGR1A, C15orf48, TFAP2A, CELF5, ADAMTS4, ACKR1, CCL8, IBSP, RGS16, LIF, PRND, IL1RN, GREM1, BCAT1, FOSL1, CXCL10, SAA1, SLC26A4, CXCL9, IGJ, IL6	http://www.ncbi.nlm.nih.gov/pubmed/23565148
73	IGFBP3, ASGR1, BEX2, TMEM132D, SLC7A10, CYP1A1, NRN1, KCNA2, FABP12, FABP1, CST8, GRIA1, ANKRD63, KRT79, CIDEC, CYP2E1, CA3, RETN, ADIPOQ, PCK1, CFD, TMEM45B, SMPX, NPPA,	http://www.ncbi.nlm.nih.gov/pubmed/23565148
74	CD200R1L, CLEC6A, ATP6V0D2, LHFPL2, PSRC1, ANKRD34B, FXYD4, ZRANB3, AADAC, CTSK, OLR1, TREM2, F7, GPNMB, MS4A6A, SLC26A4, CCR2, MSR1, EDA2R, MMP13, EREG, COL24A1, MS4A7, CDKN1A, CCL3L1, TNC, SPRR1B, IL1RL1, CEP55, PTX3, C3AR1, IL1RN, ESCO2, DMP1, CCL8, RGS16, CHODL, SAA1, CHL1, IGJ, ADAMTS4, ORM2, GP2, IL6	http://www.ncbi.nlm.nih.gov/pubmed/23565148
75	CNN1, BEX2, GRIA1, ANKRD63, NR4A1, TNNT3	http://www.ncbi.nlm.nih.gov/pubmed/23565148

76	TREM2, ZRANB3, ANKRD34B, CLEC6A, PSRC1, GPNMB, FXYD4, COL24A1, THBS4, MS4A7, MSR1, DMP1, SERPINB5, CLEC4D, IL1RN, SPRR1B, CHODL, IGJ, TNC, EREG, PKP1, CHL1, SAA1	http://www.ncbi.nlm.nih.gov/pubmed/23565148
77	BEX2, TMEM132D, SLC4A1, FABP1, TBX20, KCNJ3, TRDN	http://www.ncbi.nlm.nih.gov/pubmed/23565148
78	PSRC1, TREM2, ZRANB3, CLEC6A, SLC26A4, FXYD4, CDKN1A, TNC, MS4A7, MS4A6A, GPR176, EREG, COL24A1, NTRK2, GPNMB, C3AR1, IGJ, CCL8, SPRR1B, RGS16, TFAP2A, DMP1, CHL1, CHODL, SAA1, IGHM, ADAMTS4, CXCL9	http://www.ncbi.nlm.nih.gov/pubmed/23565148
79	ABLIM3, ADAMDEC1, ADM, ADORA3, ALOX15B, ANGPTL4, ARID5B, BIN1, C1QB, CAMP, CCL7, CCL8, CD163, CES1, CES1P1, CYFIP2, DAAM2, DDIT4, DHRS9, DPYSL3, FBLN5, FKBP1A, FKBP5, FLVCR2, GADD45B, GLDN, HIPK2, HPGD, HS3ST2, HTRA1, IL1R2, IRS2, KCNMA1, KLF9, MERTK, METTL7A, METTL7B, MFGE8, MMP19, MS4A6E, MT1A, MT2A, MTMR11, MTSS1, NAPSB, OLFML2B, PAPSS2, PCOLCE2, PDK4, PHLDA1, PLIN2, PMP22, PPARGC1A, PTGER2, RBP7, RCAN1, RNASE1, SDC4, SERPINE1, SERPINF1, SESN1, SH3PXD2B, SLA, SLC16A10, SLC16A6, SLC1A3, SLC29A1, SPRY1, SRPX, TBC1D16, TCN2, TFCP2L1, TFPI, THBS1, TIAM2, TMEM236, TPST1, TSC22D3, VSIG4, ZCCHC6	http://www.ncbi.nlm.nih.gov/pubmed/24395918
80	ABCG1, ACAT2, ATP8B4, BCL11A, CCL22, CD4, CD74, CD93, CDH23, CHI3L1, CHST13, CIR1, CLEC4A, CYB561A3, CYP27B1, ENTPD1, EPSTI1, FAIM, FCN1, FSCN1, GAL, GBP5, GIMAP4, GJB2, GM2A, GREM1, GSTM1, GSTM2, H2AFY2, HAMP, HCP5, HK3, HLA-DOA, HLA-DPA1, HLA-DPB1, HLA-DQA1, HLA-DRA, HLA-DRB3, HLA-DRB4, HLA-DRB6, HLA-F, HMG20B, HPSE, HSD11B1, HTRA4, IFI27, IFIT1, IL18BP, KIAA0101, LILRA3, LILRA5, LST1, LXN, MMP7, MMP9, MX1, NBEAL2, OAS2, PGD, PLAU, PTGS1, PTTG1, PTTG3P, RARRES1, RARRES3, RASSF4, RGS12, RHBDF1, SCG5, SLC2A5, ST6GAL1, STAT1, TAP1, TDRD9, TGFBI, TGM2, TIMP3, TMEM138, TNFSF13B, TNNI2, TSC22D1, TSPAN32, TXNRD1, VWF, WARS	http://www.ncbi.nlm.nih.gov/pubmed/24395918

81	DUSP1, NFKBIA, TFCP2L1, SRGN, TNFAIP3, AGPAT2, SH2D4A, METTL7A, RHOU, PRDM1, ISG20, ITGB1, CITED2, RABAC1, TXNIP, ABHD5, ERMAP, KLF9, CEBPD, FKBP5, MAL, PDK4, ERRFI1, DDIT4, PERP, AHNAK, ADHFE1, TMEM56, CYSTM1, LYPD6B, ADORA2B, ALOX5AP, KLF5, TSPO, CAPG, CD9, COL4A3, FCER1G, GLRX, LMO7, LOX, RGS1, S100A6, SDC1, RASSF7, VAMP8, MAP3K6, CYTIP, SPRY1, TIPARP, HILPDA, FXYD5, PNPLA2, NCEH1, TMEM243, HOPX, PARD6B, BIRC3, GLUL, SOCS1, TBC1D2, EMILIN2, PRDX6, ANG, ERN1, OLR1, MMRN1, CGN, CCND3, LTB4R, IL6ST, MT1X, MT2A, PER1, PYGB, IL1R2, HOMER2, CCHCR1, CHPT1, DEPTOR, SFXN5, CYP4V2, SEC14L1, SOD2, HRASLS2, TMEM62, ZC3H12A, SLC41A2, TMEM116, RHOB, ATP6V0A1, C5AR1, KLF6, GADD45A, FCGR2A, GCNT1, GCLC, HAGH, FOXN2, KCNK1, MYH6, POU5F1, MAPK13, PXN, MARCO, IL18RAP, PER2, P4HA2, LPIN2, HERPUD1, SPRY2, FSTL3, SERINC3, ELL2, ZNF281, PIK3R5, MKRN1, RASD1, SLC37A1, EPB41L4B, TRIB3, TMEM8A, PLEKHF2, SLC16A10, SLC25A29, RNF149,	http://www.ncbi.nlm.nih.gov/pubmed/25192440
82	HLA-DRB1, MDK, PASK, CDKN2C, E2F7, TNFSF10, AURKA, ADAM19, CKAP4, SPDL1, CDK1, VCAN, DBN1, IGFBP4, KIF20B, DEPDC1, CENPK, BORA, HLA-DMA, ST8SIA4, C12orf75, CAMK4, CYP1A1, DDIT3, DNMT3A, GEM, GUCY1A3, ITGA1, LCK, PDE4B, PDGFRB, PLK1, SOX4, SPIB, ZEB1, ZNF207, FZD3, ENC1, BHLHE40, IER3, NREP, GDF15, IER2, ZEB2, PLK2, FNBP4, ANGPTL2, SLC39A6, PARM1, RND1, UBE2T, DACT1, ARRDC3, MARCKSL1, C1orf54, VASH2, NETO2, CDCA3, AFAP1L2, SGOL1, TUBB2B, TCF7, BCL2, HES1, PHIP, PKIA, TIA1, GIT2, CCDC88A, ABLIM1, SLC5A3, WIPI1, MAP3K8, SMARCC1, MAP3K14, INTS6, EPHB1, HOXB2, ID3, ITGA4, MEF2D, NAB2, CDK17, POLB, ST3GAL2, TNFSF9, SUCLA2, TRAF4, CLCF1, PPP1R15A, RASGRP3, MOXD1, SERTAD3, EVL, DPH5, ZFR, BCL11A, ACKR3, PELI1, PLEKHG1, TGIF2, DOCK7, L3HYPDH, MB21D1, RHOV, ARL5B,	http://www.ncbi.nlm.nih.gov/pubmed/25192440
83	DUSP1, NFKBIA, TFCP2L1, SRGN, TNFAIP3, AGPAT2, SH2D4A, METTL7A, RHOU, PRDM1, ISG20, ITGB1, CITED2, RABAC1, TXNIP, ABHD5, ERMAP, KLF9, CEBPD, FKBP5, MAL, PDK4, ERRFI1, DDIT4, PERP, AHNAK, ADHFE1, TMEM56, CYSTM1, LYPD6B, ADORA2B, ALOX5AP, KLF5, TSPO, CAPG, CD9, COL4A3, FCER1G, GLRX, LMO7, LOX, RGS1, S100A6, SDC1, RASSF7, VAMP8, MAP3K6, CYTIP, SPRY1, TIPARP, HILPDA, FXYD5, PNPLA2, NCEH1,	http://www.ncbi.nlm.nih.gov/pubmed/25192440

	TMEM243, HOPX, PARD6B,	
84	HLA-DRB1, MDK, PASK, CDKN2C, E2F7, TNFSF10, AURKA, ADAM19, CKAP4, SPDL1, CDK1, VCAN, DBN1, IGFBP4, KIF20B, DEPDC1, CENPK, BORA, HLA-DMA, ST8SIA4, C12orf75, CAMK4, CYP1A1, DDIT3, DNMT3A, GEM, GUCY1A3, ITGA1, LCK, PDE4B, PDGFRB, PLK1, SOX4, SPIB, ZEB1, ZNF207, FZD3, ENC1, BHLHE40, IER3, NREP, GDF15, IER2, ZEB2, PLK2, FNBP4, ANGPTL2, SLC39A6, PARM1, RND1, UBE2T, DACT1, ARRDC3, MARCKSL1, C1orf54, VASH2, NETO2, CDCA3, AFAP1L2, SGOL1, TUBB2B	http://www.ncbi.nlm.nih.gov/pubmed/25192440
85	MLLT4, ELL2, NMT2, SLC43A3, IL4I1, MCOLN2, MAOA, ZFP36L1, APOBEC3A, TXN, FTH1, CCL7, ACSL1, CCL23, VWA8, RBM47, RPLP1, HSP90B3P, RHBDF2, RPN2, HNRNPC, HMGN2P46, SDF4, FABP5, ANXA2P1, TNIP1, TNIP3, LILRB1, TIMP1, PSTPIP2, MARCKSL1, ADAMDEC1, SLC3A2, SRC, NMI, CYP27B1, KYNU, WSB2, SLC41A2, IL3RA, S100A12, VRK2, YWHAG, CXCL5, ATP2C1, NFS1, BID, MTF1, PPBP, PPP2CB, PDE4DIP, CCL5, SLC2A6, CXCL6, CD40, FABP5P3, IFIH1, LAD1, SDC2, GPR84, C1orf122, LILRA3, CFLAR, CAPZA1, LGALS3, GCH1, EIF1AX, P2RX4, NFE2L3, SLBP, CLIC4, MMP12, ACP2, MYC, ARL6IP1, ATP11B, ZSWIM4, VPS37A, SRGN, FTH1P3, TDP2, OAS3, C6orf211, SMAD7, SMARCA5, HSPA13, GPBP1, PARP10, BOLA2, NUP62, IL7R, G3BP1, LARP4, LILRB4, ILK, SLC16A3, GRINA, C1QTNF1, SOD2, FAM129B, RPS29, TPI1, LOC440704, HSPB1, MT1H, EXOG, CD68, PTMA, MT1X, KIAA1147, PDIA3P1, MT1IP, MT1E, GYPC, TPT1, SLC29A1	http://www.ncbi.nlm.nih.gov/pubmed/24530056
86	DCK, CAT, EIF4B, P2RY13, SLC2A9, CPED1, ATP2B4, HENMT1, FGL2, EEF1B2, SRSF6, QPRT, PTEN, ACAT2, RNF7, RAB11A, CUTA, RAB7A, AGTPBP1, TSPAN32, ETFA, HADH, C14orf159, GSTK1, FLOT2, PRKAR1A, GNS, C5, ALAD, TMEM131, AP1S2, BHLHE40, GPN1, CPNE3, MPPE1, NDUFA1, ATP6V0E2, DOCK2, MGST2, ARHGEF6, HCP5, LRMP, HEXB, NDUFB5, LY86, PBX3, PQLC3, RNF125, ESYT2, RGS18, RPS4X, VAMP8, TMEM256, ARHGAP15, ERP29, NUDT1, ACACA, ATP5A1, NAA20, ACTR2, CHN2, FBXO33, SLC25A3, PLEK, ALG13, SNCA	http://www.ncbi.nlm.nih.gov/pubmed/24530056

87	CD69, HAPLN3, C15orf48, DUSP5, LGALS3BP, ISG20, LILRA3, AARS, C1orf228, IRF8, TMEM38B, SERPING1, MTHFD2, HCAR3, APOBEC3A, AIM2, PTPN1, JAK2, LAP3, B4GALT5, MT2A, NCOA7, CCND1, STAT1, BATF2, STAT2, MT1A, RHBDF2, PARP14, PSAT1, NCF1, MAP3K7CL, GBP1, RARRES3, SCO2, IFIT3, CD274, CPD, FEM1C, TGM2, LONRF1, BTG3, SLC1A5, IRF1, EXOG, C2, SLAMF7, CD86, ADAMDEC1, SIK1, C18orf8, SLC7A5, STX11, ARID5B, ASCL2, IL15, LYSMD2, GK, BHLHE41, SLCO4A1, WARS, PARP9, HIST2H2BE, TMEM140, KYNU, IFIT2, TAGAP, CXCL9, TSC22D3, TAP1, GREM1, APOL3, PTRF, RIPK2, P2RX7, HPS3, HLA-F, BPI, HIST2H2AC, UBE2L6, SLAMF1, GBP4, CCL8, GBP2, CFB, SSPN, IL1B, LRRK2, SCML1, ITGB7, TAP2, KLF9, FAM126B, SLC6A12, IFIH1, PDE4B, LILRB3, GPR84, TNFAIP6, PSME2, HELZ2, TSC22D1, GPC4, CRISPLD2, CXCL10, DDX60, PLEK, ASNS, IRF7, SAMD9L, ANKRD22, TNFSF10, BTN3A1, RHBDF1, XRN1, VAMP5, MYOF, FAM129A, C12orf57, GCH1, NINJ1, SCG5, FAM26F, CCL5, NCF1C, GBP5, HLA-H, MT1IP, AKIRIN2, SNX10, MT1E, HLA-A, PPARGC1B, CD38, AK4, LILRB4, ATF3, PSMB9, PSMB8, DUSP10, LAT, SOD2	http://www.ncbi.nlm.nih.gov/pubmed/24530056
88	CAT, FHOD1, ZNF428, STAB1, PLAU, RBP1, STMN1, TGFBI, ITGB5, NUDT14, SLC18B1, DCAF6, SVIL, FAM198B, CTSD, APMAP, LINC00857, EPDR1, RGS19, GSTP1, NREP, CPVL, PDGFC, TNFSF12, TOP2A, CCL23, S100A4, COLEC12, SNX2, GPR34, EPAS1, FCGRT, NRGN, CLEC4A, SUSD1, CYBRD1, PCED1B, PFN1, CORO1A, PON2, AGRP, F13A1, PEPD, TSPAN4, HADH, MS4A6A, CD163, TLR5, NUSAP1, LDHB, YWHAH, ID3, MMD, CHST13, APOE, RAB3IL1, FOLR2, PCOLCE2, TCEAL4, FUCA1, PLA2G15, SORL1, SLCO2B1, ADAMTSL4, MFNG, PPBP, RAB7B, PLTP, TMEM236, CFD, ATP8B4, CD36, SEPP1, APOC1, MFSD1, DDIAS, RNASE1, ALOX5AP, PNPLA6, NME4, NAIP, MGST2, MYL6, POTEKP, ACTG1, RGS18, TMEM173, ACTB, CXCL5, CYTL1, PPIA, HNMT, DBI, TSPO, NGFRAP1, MS4A4A, AKR1A1, CTSH, CTDSPL	http://www.ncbi.nlm.nih.gov/pubmed/24530056

89	CBR3, CLEC10A, FZD2, CD1C, SIGLEC10, PARM1, CCL26, FCER2, MAOA, MAP4K1, FOXQ1, HOMER2, PDXK, GALNT18, NAGPA, CD209, INSIG2, RTKN, SUCNR1, NFXL1, FAM60A, FCER1A, DUOX1, ASAP1, CXCR2P1, FGL2, GPD1L, PALLD, QPRT, C17orf58, C1orf54, CMTM8, CARD9, ADAM19, LIPA, SLC27A3, CTNNAL1, ASCL2, CD1A, RAB33A, DHRS2, RASGRP3, GATM, DTNA, RASSF7, ZNF366, BLOC1S6, PTPRE, ACOT7, STARD7, CCDC6, RASL10A, INTS3, ST6GAL1, DHRS11, ADAM15, PTRF, SGK223, PPP1R14A, BATF3, RAMP1, CERK, MMP12, SLAMF1, IL1R2, KIAA1671, SOCS1, RAP1GAP, ALOX15, CD1E, CDKN1A, SOX8, DENND1B, VCL, SPINT2, PFKP, RHBDF1, FSCN1, RRP1B, SNX8, LOC283070, PPM1F, GOLGA8B, ESPNL, CDR2L, NMNAT3, CCL22, TTC9C, CLEC4G, AUH, PTPRO, CLEC4A, CHN2	http://www.ncbi.nlm.nih.gov/pubmed/24530056
90	RBP1, LRPAP1, NUP214, CXCL8, ANKRD33, MLKL, FCN1, DRAM1, VSIG4, DFNA5, TCF7L2, CTSD, GAPT, NCEH1, CPED1, DUSP6, CTSG, CYBB, CXCL2, PGAM4, TOP2A, C5AR1, LTA4H, RHBDF2, CEBPB, GCHFR, JAKMIP2, CYP27A1, AKR1C3, AGRP, AQP9, ADAMDEC1, NFKBIZ, CCL2, STX11, CD163, OLR1, NUSAP1, S100A8, BOK, FOLR3, GLRX, CD14, APOE, SLC11A1, PLSCR1, ITGAL, S100A9, CXCL5, HDDC2, FAM213A, ENG, MCEMP1, PPBP, SCPEP1, TBC1D2, LAPTM5, PLTP, PNKD, IL1B, CLEC5A, ENPP4, CEBPD, CD37, APOC1, SNTB1, PGD, DNASE2, SPARC, ALOX5AP, PLIN2, GPNMB, S100P, FKBP15, IFI30, SLC7A7, NUPR1, SCARB2, PIM1, LYZ, ALDH1A1, CD300LF, HBEGF, FCER1G, DAB2, TMEM173, CYTL1, CD68, WLS, FAM89A, NCF4, SERPINA1, IL7R, NGFRAP1, CTSL, PLAUR, FCGR1B	http://www.ncbi.nlm.nih.gov/pubmed/24530056

91	SELM, EHD1, IL10RA, NAMPT, MCTP1, C15orf48, SLC7A11, SIGLEC10, CDK5RAP2, EREG, TERF2IP, IL1A, ISG20, MYH11, MCOLN2, CLCF1, DDIT4, ANKRD12, AARS, SQSTM1, FLNB, NUB1, DCUN1D3, CXCL8, RILPL2, DRAM1, ATOX1, PTGS2, MAP3K4, UPB1, ADARB1, CREG1, PTPN1, RNF19B, IER3, NKG7, FAM60A, IL2RA, SLC7A1, MT1H, SAMSN1, ASCC1, FYN, MT2A, ETS1, PPP3CC, MT1A, LAT, RHBDF2, G0S2, CEP135, PANX2, C5orf15, HMGN2P46, ORM1, TRAF1, C17orf58, MB21D2, LPAR1, TRAF3IP2, TNFAIP3, SEMA4A, ARHGEF2, LMO4, TNIP1, TBC1D9, ACSL5, CYP2S1, BTG3, TNIP3, EXOG, NLRP3, SEMA6B, PSTPIP2, PTGES, MARCKSL1, CD86, NFKB1, LSS, AQP9, TANK, CCR7, MT1G, LAMB3, SLC25A37, RUNX2, ADAMDEC1, NFKBIE, SYT11, PVRL2, MLLT6, MT1F, ETS2, SLC7A5, CA12, MRPS6, GK, SLC3A2, BHLHE41, WARS, TNFAIP2, CXCL16, PILRA, CCDC115, TMEM205, HIST2H2BE, SIK3, ITGB8, PPP1R18, PTPRE, NBN, HIVEP1, GRAMD1A, KYNU, SLC1A3, NFE2L1, PCNX, CD14, CYP27B1, APBB3, FPR2, CEP350, CTTN, IRAK2, DDX59, CCM2L, PIM2, TSPAN33, ACO1, TAP1, RNF144B, CXCL5, IKBKE, EMR3, APOL3, H1F0, NADK, ZMIZ2, NFS1, HLA-F, BATF3, HIF1A, MTF1, YARS, STOM, RASGRP1, HIST2H2AC, GJB2, SLAMF1, CLEC4E, CCL5, KIAA0226L, GNA15, CFB, AMPD3, PNKD, MT1X, SMOX, IL1B, BIRC3, MAP1LC3A, ZMYND15, SLC2A6, SPECC1L, OSM, PRKCH, C1S, LAD1, PDE4B, STAT4, GPR84, TNFAIP6, C1orf122, PLAGL2, SLC43A2, HELZ2, TSC22D1, SLC5A3, CXCL1, HEY1, ABHD17C, CRISPLD2, DNAJB6, PGD, NDP, MMP9, ASNS, IRF7, ACKR3, RCN1, SLC9A1, RFTN1, EBI3, TGFA, PPA1, ADORA2A, CLEC4D, MUCL1, GPR132, RELB, FAM20A, GCH1, CTSL, NINJ1, ST3GAL1, SMAP2, MYO1B, TYMP, TNFRSF4, NCF1C, GBP5, HBEGF, CYB561A3, MT1IP, ZSWIM4, IL36G, LAMP3, MT1E, ZHX2, PFKFB3, N4BP1, MXD1, GNA12, CD38, PARP10, DTX2, LILRB2, TMEM132A, EMR2, SPHK1, SIRPA, PLAUR, VEGFA, PTPRF, C1QTNF1, STEAP3, MPZL1, CD82, CLEC4A, DUSP10, GLIS3, SOD2, ISCU	http://www.ncbi.nlm.nih.gov/pubmed/24530056

92	CD69, SPP1, CAT, LSP1, NUCB2, CRIP1, ATP1B1, DUSP23, RPSAP52, LAMP2, PAQR4, BTK, GCNT1, SULF2, ANKRD33, FCN1, H2AFY, CTSD, COL8A2, LINC00857, ADCY3, CTSG, NREP, PGAM4, PDGFC, S100A4, ITGAM, TOP2A, COLEC12, DPEP2, SCD, FGL2, CD300A, GCHFR, CD9, PYGL, FABP5, VAT1, SAP30, TREM2, ATP5C1, GPR34, JAKMIP2, ADORA2B, NRGN, PLBD1, RBPJ, NFE2, CYBRD1, PCED1B, PON2, AGRP, CEBPA, F13A1, LIPA, TSPAN32, HADH, PTPRO, MS4A6A, TLR5, GRAMD4, CD1B, NUSAP1, VEGFB, MPC2, EVL, DHRS9, CHST13, ME1, MNDA, CHCHD10, APOE, SLFN11, FUCA1, PLXDC2, MGAT4A, PLA2G15, CSTB, HHEX, MFNG, HSPD1, SCPEP1, IQGAP2, RAB7B, HLA-DPA1, PHYH, PLTP, NDUFS5, TMEM236, CFD, FABP5P3, CD36, SEPP1, CD37, LPL, APOC1, DDIAS, SIDT2, RNASE1, MGMT, C1QB, S100A10, TUBA1B, CST3, PLIN2, GPNMB, S100P, APBB1IP, CCDC109B, NTAN1, MGST2, NNT, RPL7A, NUPR1, CORO2A, CKS2, ACP5, SERINC2, AP1S2, KLF4, CAMK1, RCBTB2, CHPT1, CD52, CD68, UBE2C, GPBAR1, SLC29A1, NGFRAP1, MS4A4A, FCGR2B,	http://www.ncbi.nlm.nih.gov/pubmed/24530056
93	ZFYVE16, HNRNPDL, MCTP1, SLC7A11, Mar-03, IL1A, MCOLN2, NEK6, DDIT4, MAOA, NUB1, PHLDB1, TNS3, DRAM1, COX10, SLC20A1, VNN1, INSIG2, OCSTAMP, PTPN1, FAM60A, IL2RA, SLC7A1, ETS1, RHBDF2, G0S2, TSC22D1, EEF1B2, IDH3A, C17orf58, TRAF3IP2, PACSIN2, LMO4, TNIP1, MPO, ACSL5, CS, KLHL5, BTG3, OTUD4, PLGRKT, F5, SIAH1, NFKB1, AQP9, LAMB3, RPL32, ADAMDEC1, PFDN1, SYT11, MT1F, TNC, SLC7A5, CA12, METTL21B, MRPS6, GK, BHLHE41, WARS, EFTUD1, SRC, CCDC115, FILIP1L, ARFGAP3, ATP1A1, PTPRE, NBN, HIVEP1, GRAMD1A, KYNU, SLC1A3, NFE2L1, PCNX, CYP27B1, ANXA5, QPCT, SH3PXD2A, SERPINE1, CTTN, CLINT1, TTC13, IRAK2, SLC41A2, TSPAN33, ACO1, RNF144B, HNRNPA0, FAM213A, NFS1, MTF1, BCAT1, UCK2, SLAMF1, STRN3, GPR124, CCL5, IL1B, BIRC3, SLC50A1, SLC2A6, CLEC5A, LINC00938, PRKCH, LAD1, SLC25A3, GPR84, DENND5A, TNFAIP6, SLC35F2, CRISPLD2, PRKCDBP, DNAJB6, NDP, PLEK, MMP9, SPARC, F3, ANKRD22, SLC9A1, RFTN1, TSKU, EBI3, PPA1, ADORA2A, RGS16, MYOF, ATP5L, METTL1, TNPO1, AK4, ESYT2, SCG5, COA1, FNBP4, TNFRSF4, HBEGF, MT1H, TMEM194A, ZSWIM4, IL36G, RPS4X, ACVR1B, BCL2, FYN, DTX2, HOPX, TMEM132A, PTGES2, EMR2, SPHK1, SFXN4, BID, VEGFA, PTPRF, C1QTNF1, HSD11B1, C6orf48, CD82,	http://www.ncbi.nlm.nih.gov/pubmed/24530056

	FMNL3, MTHFD2, SOD2	
94	LSP1, NUCB2, STAB1, METTL7A, GFRA2, RBP1, LAMP2, BTK, SOD1, TGFBI, ANKRD33, FCN1, FOS, LOC440704, CTSD, LINC00857, GAPT, RGS19, TLR7, NREP, CXCL2, CPVL, PDGFC, CCNL1, TNFSF12, S100A4, COLEC12, DPEP2, HSP90B3P, CD300A, FES, GCHFR, KLHDC8B, PYGL, FABP5, ANKRD36B, LGMN, ANXA2P1, C1orf85, TREM2, GPR34, JAKMIP2, B3GNT5, CYP27A1, NRGN, TLR4, EIF2AK2, GMFG, NFE2, PCED1B, AGRP, CD68, F13A1, HLA-DRB3, LIPA, GADD45B, MAF, ZFP36, MS4A6A, TLR5, MAP3K1, NUSAP1, RNF130, S100A8, BOK, ARHGDIA, KLF6, KLF2, IFI27L2, RAB3IL1, FOLR2, PCOLCE2, ITPRIPL2, OTUD1, FUCA1, MPZL2, C1orf162, HEBP2, CLTC, PLA2G15, SLCO2B1, MAFB, SCPEP1, RAB7B, PHYH, TMEM236, CFD, FABP5P3, CEBPD, NPL, CCL13, CD36, SEPP1, CD37, FAM102B, AIF1, RNASE1, PTGER4, C1QB, BLVRB, STK17B, CST3, HMOX1, GPNMB, S100P, NAIP, CCDC109B, NTAN1, CAPZA1, LGALS3, IFI30, HMGB1, NUPR1, GRN, CORO2A, ADD3, POTEKP, HLA-DRB6, HIST1H4C, ACP5, ALDH1A1, SERINC2, KLF4, SHISA5, MAN2A1, RCBTB2, CAT, NBPF10, SLFN11, ECHDC1, HLA-A, CHPT1, CD52, SRP14, TUBA3D, LYL1, HMGB2, PRMT2, FAM89A, ITGB5, GPBAR1, RTN3, LILRB5, PON2, ILK, NGFRAP1, MS4A4A, LTB, DHRS9, TGFBR2, ARRB2, HNRNPUL1, OSBPL1A	http://www.ncbi.nlm.nih.gov/pubmed/24530056

95	SELM, CYP26A1, EHD1, IL10RA, HNRNPDL, NAMPT, SAP25, MCTP1, C15orf48, PRDM1, SLC7A11, SIGLEC10, ELL2, DUSP5, EREG, IL1A, ISG20, MCOLN2, PFKFB3, CSF2RA, DDIT4, LILRA3, IRAK3, TFDP1, SQSTM1, TFPI, BANP, VAMP4, NUB1, RAB27A, CXCL8, FCGR2A, PID1, ZC3H12A, TMEM71, VNN1, YPEL2, PTGS2, MAP3K4, RILPL2, UPB1, VNN2, ADARB1, MAMLD1, HIF1A, PTPN1, FOXO3, IER3, NKG7, ZNF281, ST3GAL1, FAM60A, IL2RA, SAMSN1, THBS1, FYN, ETS1, UIMC1, LAT, RHBDF2, G0S2, SPRY1, CEP135, GADD45A, CYTH1, PANX2, TNFRSF10B, TNFRSF21, C17orf58, SLC44A1, MB21D2, TRAF3IP2, AKR1B1, TNFAIP3, SEMA4A, CPD, ETV3, TNIP1, PTGER2, CD93, ULK1, ACSL5, CYP2S1, DMXL2, BTG3, TNIP3, LILRB1, ADAM8, IRF1, RNF145, NLRP3, SEMA6B, PTGES, MARCKSL1, CD86, NFKB1, AQP9, TANK, CCR7, MET, LAMB3, SLC25A37, ADAMDEC1, SYT11, LOR, MLLT6, MT1F, ETS2, SLC7A5, CA12, ARID5B, RYBP, MRPS6, SESTD1, GK, MS4A14, BHLHE41, CXCL16, SLC16A6, TMEM205, GPR162, CHST7, PTPRE, NBN, A4GALT, TBC1D8, HIVEP1, VMO1, GRAMD1A, KYNU, SLC1A3, TBK1, PCNX, CD14, APBB3, FPR2, CEP350, DLL1, PLSCR1, IRAK2, FJX1, BMP6, PIM2, S100A12, TSPAN33, RNF144B, CXCL5, EMR3, APOL3, ST8SIA4, RIPK2, THBD, STX1A, SRGN, ZMIZ2, MEF2D, MTF1, BCAT1, IL13RA1, HIST2H2AC, GJB2, RAPGEF1, TM4SF1, SLAMF1, CLEC4E, NFKBIA, CCL5, DNAJB9, GNA15, IL24, SMOX, IL1B, BTG1, BIRC3, MAP1LC3A, CREBRF, ZMYND15, SLC2A6, CXCL6, PELI2, OSM, PRKCH, LAD1, PDE4B, SLC16A10, RFX8, STAT4, GPR84, DENND5A, TNFAIP6, SLC43A2, RUNX3, SLC5A3, CXCL1, HEY1, ABHD17C, CRISPLD2, PDE4D, SOD2, DNAJB6, CRLF2, HIST1H2BK, SMPDL3A, PTPRF, ACKR3, RFTN1, CXCR4, PRDM8, EBI3, VEGFA, VNN3, TGFA, ADORA2A, XBP1, LAMC1, CYP3A5, GCH1, ANKDD1A, CEMIP, NINJ1, AK4, TXN, PGS1, SMAP2, IRS2, MYO1B, NUAK2, FNBP4, EPB41L3, TNFRSF4, GBP5, HBEGF, ZSWIM4, IL36G, ITGAV, LAMP3, ZHX2, ARRDC3, NSUN7, MXD1, TMCO3, PILRA, DTX2, WTAP, C9orf72, LILRB2, HOPX, TGIF1, IL7R, GPR64, KL, BTN2A1, FCAR, PLAUR	http://www.ncbi.nlm.nih.gov/pubmed/24530056

96	CD69, SPP1, ATP5D, BCL2L1, CD1C, LSP1, STAB1, METTL7A, GFRA2, MDH1, CRIP1, STMN1, DUSP23, RPSAP52, RNH1, APEX1, AP2S1, CLEC12A, UQCRQ, GCNT1, RBX1, PLD3, ANKRD33, PPT1, VSIG4, NUDT14, HK3, ALCAM, GALM, ATP5F1, QDPR, ATIC, H2AFY, CTSD, COL8A2, HSPB1, ADCY3, CTSG, NREP, PGAM4, FKBP1A, LAP3, S100A4, ITGAM, TOP2A, IFI6, LST1, CDK4, DPEP2, SCD, ITGB1BP1, HSP90AA1, SNX2, FGL2, EIF3K, PCNA, GCHFR, LY6E, CD9, PYGL, FABP5, IDH1, SLC38A6, ANXA2P1, C1orf85, PYCARD, HCST, VAT1, TREM2, ATP5C1, GPR34, JAKMIP2, AIF1, TUBB, NRGN, PLBD1, RBPJ, IFI16, GMFG, NFE2, ANXA2, PCED1B, CARD9, HSPH1, PFN1, CORO1A, PON2, AGRP, AHNAK, CEBPA, F13A1, LIPA, TSPAN32, HADH, CCL2, PTPRO, TECR, MSMO1, MS4A6A, C14orf159, CD163, SLC29A1, LGALS1, GRN, CD1B, NUSAP1, LDHB, FBP1, BOK, ATP1B1, EVL, MARCO, ID3, RGS10, DHRS9, CHST13, ARHGDIA, ME1, CALR, SH3BGRL3, PSMD14, C1QA, MNDA, CHCHD10, ACOT7, IFI27L2, APOE, NME1, RAB3IL1, TUBA1A, EGR2, A2M, CORO1C, FOLR2, S100A11, IDH2, CECR1, DHRS3, FUCA1, PLXDC2, NDUFS3, PLA2G15, ADAM15, HCFC1R1, IFI44, SEPN1, ESYT1, CSTB, HHEX, HSPD1, SCPEP1, IQGAP2, RAB7B, HLA-DPA1, PHYH, PLTP, TMEM236, CFD, ITGB7, BSG, FABP5P3, IMMT, CCL13, CD36, SEPP1, C1QC, CD37, LPL, 40787, APOC1, MFSD1, DDIAS, UQCC2, SIDT2, DCSTAMP, RNASE1, PTGER4, DNASE2, C1QB, S100A10, MCM6, ACAT1, TUBA1B, CST3, NME4, GPNMB, S100P, EMP1, APBB1IP, CCDC109B, NTAN1, MGST2, HIBADH, IFI30, SLC7A8, NUPR1, POTEKP, ACTB, ACTG1, CKS2, ACP5, GGCT, MRPL15, PGAM1, CISD1, YBX1, LRP3, CTNNAL1, KLF4, CAMK1, TMEM173, SLFN11, NDUFAB1, BANF1, COX7B, CYTL1, PPIA, CD52, LYL1, MRPL18, TSPO, KCNMA1, ITGB5, HMGA1, GPBAR1, CD1E, YIF1B, CD276, ALG8, NGFRAP1, MS4A4A, ZYX, CD74, FCGR1B, CTDSPL, OSBPL1A, LGALS9,	http://www.ncbi.nlm.nih.gov/pubmed/24530056
97	ZBTB34, SLC7A11, OAS2, IFNGR1, FAM60A, STAT2, CENPBD1, VMP1, LPAR1, TLR8, CD86, ADAMDEC1, CXCL16, PARP9, VMO1, PRKAR1A, PCNX, MKLN1, MAPK13, CFB, TRIM22, HELZ2, BCDIN3D, MOB3C, ZNF22, HCP5, CCDC117, SAMD9, ISG15, SMAP2, FNBP4, BCL2L13, MX2, PTPRE	http://www.ncbi.nlm.nih.gov/pubmed/24530056

98	ANKRD33, CTSD, CCNL1, PPIA, FABP5, ANXA2P1, SAP30, JAKMIP2, UBE2C, NFKBIZ, NUSAP1, LDHB, BOK, KLF2, DBI, CLTC, PLTP, TMEM236, CFD, FABP5P3, IMMT, 40787, MGMT, PTGER4, STK17B, HMGB1, NUPR1, POTEKP, HLA-DRB6, CKS2, RPL5, YBX1, SKAP2, KLF4, NBPF10, KANSL1, SRP14, MYADM, ILK, MS4A4A, UGP2	http://www.ncbi.nlm.nih.gov/pubmed/24530056
99	KCTD12, SOX4, NOV, LRRC17, TBX18, SCD, BDKRB2, WNT2, SLC7A14, FER1L6, CLDN11, VCAM1, ADAMTS14, CCKAR, CREB5, TNFAIP6, CRABP2, IGDCC4, TMEM35, GDF15, TSLP, ADAM12, AQP3, FST, PER3, PRSS35, PIEZO2, TNFRSF11B, RND2, CDH6, LIF, ITGA11, ADCY1, SIPA1L2, PHGDH, AMOT, HMOX1, PGBD5, CDON, MXRA5, PLA2G4A, FAM171B, CPA4, AIF1L, GPR68, HSD17B6, LHFPL2, SLC6A9, C4orf46, OLFML2A, EPHB2, GXYLT2, SLC14A1, LRRC15, ODZ4, BDKRB1, BMPER, FAM46C, MARCKS, WARS, ARHGAP28, RCAN2, TMEM119, RAP2B, CDKN2B, MEST, IFIT1, SLC39A10, EPHB3, TUBB, RPS6KA5, LDB2, TUBA1A, C14orf132, TMEM200A, NCKAP5, TUBB3, NEK10, PHLDA1, LOC148145, NYNRIN, RN5-8S1, SLC6A6, RHOJ, FLRT3, TRIM45, CIT, PDE5A, RTKN2, ARSI, G0S2, VEGFA, FAM46A, SEMA3A, JUN, SAMD12, CLIC2, SOX9, GRAMD4,	http://www.ncbi.nlm.nih.gov/pubmed/24926665
100	C7, CCDC69, DUSP1, FKBP5, GPX3, KLF15, MAOA, SAMHD1, SERPINA3, SPARCL1, RGCC, TSC22D3, CRISPLD2, PER1, ERRFI1, STEAP4, MT2A, METTL7A, IRS2, RASL11A, FGD4, INHBB, NNMT, KCNK6, GLUL, KLF9, NA, ITGA10, CORO6, ADRA1B, IMPA2, ZBTB16, FOXO1, ADAMTS5, PDK4, ENDOD1, SORT1, CACNB2, ADARB1, NEXN, NAV3, DCXR, STC1, TRNP1, IGFBP2, MAMDC2, SUN2, FSTL3, PTX3, GPRC5B, HSPA2, FAM107A, TJP2, PPP1R14A, MTSS1, CYR61, USP53, GPM6B, ADAMTS1, TRPC6, RASL11B, LMCD1, MMD, ACSL1, PKDCC, STEAP1, ACSS1, TIMP4, COL11A1, PLXNA4, MT1X, APCDD1, DNAJB4, ACTG2, GGT5, LEP, CD302, MT1E, AOX1, CEBPD, DAAM2, TEX2, TCEAL4, SAT1, PHC2, SPON1, KLF5, AFAP1L1, NKD1, PIK3R1, CDC42EP3, CTPS1, INPP5A, PRODH, FBN2, PXDC1, NID1, ALPK3, NR4A3, HPS5, PDPN, EPHB6, ATF3, OXTR, RAB11FIP1, CITED2, RAPGEF5, COL4A1, NEGR1, PRKAG2, SLC16A12, SMARCD2, NEDD9, GALNT15, MYADM, FZD8, CILP, GFPT2, AHCTF1, EOGT, SSH2, SMIM3, DLL4, C10orf10, CHST7, GCNT4, SCARA5, STON1, SLC7A6, ABLIM1, NCOA3, TGFBR2, MOB3B, COL4A4, RNF144B, FOXO3, GCLM, DAPK2,	http://www.ncbi.nlm.nih.gov/pubmed/24926665

	MAP1LC3C, COL7A1, CYTH3, FIBIN, DIO2, HIGD1A, CPM, NFIL3, RHOB, HSPB3, CD82, STARD7, WFDC1, ZCCHC5, ANXA4, RAI2, KANK1, SCN7A, ABHD5, STOM, SYNPO2, LBH, RASD1, CALCOCO2, POTEE, C1QTNF1, CADPS2, LAMA3, ZHX3, LGI3, ZCCHC6, TSPAN8, CORIN, ENPP1, GADD45B, SAMD4A, LRRC16A, DHRS3, PREB, HMGB2, MAFF, NAMPT, JADE1, ARMC8, NUAK1, ARHGAP29, DDAH1, MICAL2, ANPEP, PNPLA2, KLF6, AASS, CBS, WASF3, LMOD1, RSPO1, AP1M1, FAM43A, FAM46B, SQRDL, LINC00312, FZD5, SAP30, VGLL3, ING2, TM4SF1, DUSP5, FADS3, CTGF, RWDD4, KLHL42, STK17B, REV3L, EBF1, APBB2, HSD11B1, AXIN2, TXNRD1, ABCA6	
101	ADAMTS9, ALOX15, BCL2L15, C1QTNF1, CA2, CCBL1, CCL26, CD274, CD44, CDH26, CISH, CST1, CST2, CST4, CTSC, DPP4, FAM26E, FETUB, GGH, HS3ST1, LRRC31, NTRK1, NABP1, PCSK6, POSTN, SERPINB4, SH2D1B, SIDT1, SLC26A4, SLC39A8, SLC5A1, SOCS1, SUSD2, USP54	ADEPT cohort
102	KLRC4, CCL3L3, IL12RB2, CCL5, KLRD1, GZMA, KLRC4, GZMB, CCL4, CCR2, PLEK, SULF2, ENTPD1, ITGAX, MS4A4A, GPR55, IL21R, GRAMD3, DENND4A, PRF1, IRG1, TIGIT, CD2, SYTL2, MMP9, UGCG, CST7, CPNE7, CD28, C1orf21, SH2D2A, KLRB1, PMEPA1, CHSY1, SAMD3, SEPN1, GAS7, NCF1, HOPX, CDH1, MCTP2, SULT2B1, BCL2L11, GPR18, TRAT1, GPR174, ICAM1, PIK3R5, ADAMTS14, ZDHHC15, PADI2, GPC1, SEMA6D, SATB1, ITM2A, KDM2B, LYST, GLP1R, LRRC8D, EOMES, SELL, BAIAP3, BAIAP2	http://www.ncbi.nlm.nih.gov/pubmed/25621825
103	CCR8, CCR4, IL5, KLRG1, IL17RB, HS3ST1, IL1RL1, IL13, SLC7A8, CD27, NEB, RXRG, CALCA, IL6, IL4, PTPN13, PDCD1, NPNT, HLA-DOA, HES1, LPCAT2, IL9R, PPARG, TPH1, STXBP6, CYBB, BMP7, INPP4B, CCL1, BMP2, AR, MC5R, ATP8A2, PPP2R3A, KCNN4, DGAT2, NMUR1, KCNQ5, RAB27B, LRRC52, ALOX5, PTGIR, ZC3H12C, TGM2, IL10RA, ACER2, HBA2, GATA3, CHDH, NCK2, BZW2, NAIP, MRAS, C19orf38, HBA2, TSPAN13, AREG, EBI3, KLF5, PLAUR, ADAM19, IRF4, EEPD1, PDLIM1, NCKAP5, TANC2, SERPINE1, FBXL21, UBE2E2, RNF128, IPMK, CA13, MED12L, CXorf57, PARD3, CHD7, PDE7B, PCSK1, MAP4K3, LGMN, TAF1D, RPS19, CACNA1D, SPCS3, ST6GALNAC5, RPLP1, NFKB1, GALNT3, CXCL1, NAIP, SNORA45A, LPHN2, DHX40, STAB2, PLK2, GLB1, PTPN9, RAB4A, NFIX, BAMBI, UBE2L6,	http://www.ncbi.nlm.nih.gov/pubmed/25621825

	NAV2, ACBD7, SNORD8, FAM71F2, APBB2, MBOAT1, C9orf72, ARL5C, RUNX1T1, HLF, CSF2, EMP3, HOMER2, CYP51A1, SPRY1, GRIN2D, CYP2D7, FOXP3, UNC5B, SPECC1, DUSP10, C21orf62, KRT80, KLF4,	
104	GSTM3, UPP1, EPS8L3, IL1R2, CXorf23, F2RL2, CAPG, FAH, DUSP4, GDA, NMBR, CCNE2, GJB2, RYK, TMTC2, DPEP2, B3GALT2	http://www.ncbi.nlm.nih.gov/pubmed/25621825
105	CXCR5, IL1R1, STOM, PTGES, CNTN1, NRP1, VIPR2, HMGN3, CTSH, CCR6, APOBEC1, CD2AP, MAPK10, P2RY1, GUCY1A3, IGFBP4, LINGO4, DLL1, TIFA, PTGER2, SDC4, HS6ST2, IGF1R, CX3CL1, IL17RE, GRIA3, GALM, NPL, SDC2, KIAA1598, ATRNL1, PPAP2B, SNORD14C, SLC6A13, CACNA1G, DNAJC6, ERMP1, RNASE6, OR4C12, PDE6D, PDGFRB, DDC, NAPEPLD, EEF2K, TUBA8, ADK, FAM184B, TRAPPC2, TOX2, HELLS, SLC41A3, KHDRBS3, BATF3, ALG14, MSRB3, FLRT2, TTYH2, SDC1, LTB, DSG2, TMEM60, CITED4, LDHB, SLC6A7, ACTR6, ACAT1, HLA-DQA1, ABCA3, SRR, IRGM, HK3, DNAJB1, GOLPH3L, HTRA2, PARVB, TM9SF2, FERMT2, PLB1, CDC14A, ABHD15, DENND3, MED21, TMEM70, RHOB, FANCL, PMPCB, GDPD5, DSCAM, TMEM229B, P2RX1, APOA1, EID1, LSM10, ZNF43, TMEM126B, ABCA1,	http://www.ncbi.nlm.nih.gov/pubmed/25621825

179 Appendix: **The members of the U-BIOPRED Study Group are as follows:**

Adcock Ian, National Heart and Lung Institute, Imperial College, London, UK;
Adriaens Nora, Academic Medical Centre, University of Amsterdam, The Netherlands;
Ahmed Hassan, European Institute for Systems Biology and Medicine, CNRS-ENS-UCBL-INSERM, Lyon, France;
Aliprantis Antonios, Merck Research Laboratories, Boston, USA;
Alving Kjell, Dept Women's & Children's Health, Uppsala University, Sweden
Auffray Charles, European Institute for Systems Biology and Medicine, CNRS-ENS-UCBL-INSERM, Lyon, France;
Badorrek Philipp, Fraunhofer ITEM; Cornelia Faulenbach, Fraunhofer ITEM;
Bakke Per, Department of Clinical Science, University of Bergen, Bergen, Norway;
Balgoma David, Centre for Allergy Research, Karolinska Institutet, Stockholm, Sweden
Bansal Aruna T., Acclarogen Ltd, St. John's Innovation Centre, Cambrigde, UK;
Barber Clair, NIHR Southampton Respiratory Biomedical Research Unit and Clinical and Experimental Sciences, Southampton, UK;
Baribaud Frédéric, Janssen R&D, USA;
Bates Steward, Respiratory Therapeutic Unit, GSK, UK;
Bautmans An, MSD, Brussels, BE
Behndig Annelie F., Dept of Public Health and Clinical Medicine, Umeå University, Umeå, Sweden;
Bel Elisabeth, Academic Medical Centre, University of Amsterdam, The Netherlands;
Beleta Jorge, Almirall S.A., Barcelona, Spain;
Berglind Ann, Dept. Women's and Children's Health & Centre for Allergy Research, Karolinska Institutet, Stockholm, Sweden

Berton Alix, AstraZeneca, Mölndal, Sweden
Bigler Jeannette, Previously at: Amgen Inc.;
Bisgaard Hans, COPSAC, Copenhagen Prospective Studies on Asthma in Childhood, Herlev and Gentofte Hospital, University of Copenhagen, Copenhagen, Denmark
Bochenek Grazyna, II Department of Internal Medicine, Jagiellonian University Medical College, Krakow, Poland;
Boedigheimer Michel J., Amgen Inc.;
Bøonnelykke Klaus, COPSAC, Copenhagen Prospective Studies on Asthma in Childhood, Herlev and Gentofte Hospital, University of Copenhagen, Copenhagen, Denmark;
Brandsma Joost, University of Southampton, UK
Braun Armin, Fraunhofer Institute for Toxicology and Experimental Medicine, Hannover, Germany;
Brinkman Paul, Academic Medical Centre, University of Amsterdam, The Netherlands;
Burg Dominic, Centre for Proteomic Research, Institute for Life Sciences, University of Southampton, UK
Campagna Davide, Department of Clinical and Experimental Medicine, University of Catania, Italy;
Carayannopoulos Leon, MSD, USA;
Caruso Massimo, Dept. Clinical and Experimental Medicine, University of Catania, Italy;
Carvalho da Purificação Rocha João Pedro, Royal Brompton and Harefield NHS Foundation Trust, UK;
Chaiboonchoe Amphun, European Institute for Systems Biology and Medicine, CNRS-ENS-UCBL-INSERM, CIRI-UMR5308, Lyon, France;
Chaleckis Romanas, Centre of Allergy Research, Karolinska Institutet, Stockholm, Sweden
Chanez Pascal, Assistance publique des Hôpitaux de Marseille - Clinique des bronches, allergies et

sommeil, Aix Marseille Université, Marseille France
Chung Kian F., National Heart and Lung Institute, Imperial College, London, UK;
Coleman Courtney, Asthma UK, London, UK;
Compton Chris, Respiratory Therapeutic Unit, GSK, UK
Corfield Julie, Areteva R&D, Nottingham, UK;
D'Amico Arnaldo, University of Rome 'Tor Vergata', Rome Italy;
Dahlen Barbro, Karolinska University Hospital & Centre for Allergy Research, Karolinska Institutet, Stockholm, Sweden
Dahlén Sven-Erik, Centre for Allergy Research, Karolinska Institutet, Stockholm, Sweden
De Alba Jorge, Almirall S.A., Barcelona, Spain;
de Boer Pim, Longfonds, Amersfoort, The Netherlands;
De Lepeleire Inge, MSD, Brussels, BE
De Meulder Betrand, European Institute for Systems Biology and Medicine, CNRS-ENS-UCBL-INSERM, Lyon, France;
Dekker Tamara, Academic Medical Centre, University of Amsterdam, The Netherlands;
Delin Ingrid, Centre for Allergy Research, Karolinska Institutet, Stockholm, Sweden
Dennison Patrick, NIHR Southampton Respiratory Biomedical Research Unit, Clinical and Experimental Sciences, NIHR-Wellcome Trust Clinical Research Facility, Faculty of Medicine, University of Southampton, UK;
Dijkhuis Annemiek, Academic Medical Centre, University of Amsterdam, The Netherlands;
Djukanovic Ratko, NIHR Southampton Respiratory Biomedical Research Unit and Clinical and Experimental Sciences, Southampton, UK;
Draper Aleksandra, BioSci Consulting, Maasmechelen, Belgium;

Edwards Jessica, Asthma UK, London, UK;
Emma Rosalia, Department of Clinical and Experimental Medicine, University of Catania, Italy;
Ericsson Magnus, Karolinska University Hospital, Stockholm, Sweden
Erpenbeck Veit, Translational Medicine, Respiratory Profiling, Novartis Institutes for Biomedical Research, Basel, Switzerland;
Erzen Damijan, Boehringer Ingelheim Pharma GmbH & Co. KG; Biberach, Germany
Fichtner Klaus, Boehringer Ingelheim Pharma GmbH & Co. KG; Biberach, Germany
Fitch Neil, BioSci Consulting, Maasmechelen, Belgium;
Fleming Louis J., National Heart and Lung Institute, Imperial College, London, UK;
Flood Breda, Asthma UK, UK;
Fowler Stephen J., Centre for Respiratory Medicine and Allergy, Institute of Inflammation and Repair, University of Manchester and University Hospital of South Manchester, Manchester Academic Health Sciences Centre, Manchester, United Kingdom
Frey Urs, University Children's Hospital, Basel, Switzerland;
Gahlemann Martina, Boehringer Ingelheim (Schweiz) GmbH, Switzerland;
Galffy Gabriella, Semmelweis University, Budapest, Hungary;
Gallart Hector, Centre for Allergy Research, Karolinska Institutet, Stockholm, Sweden
Garrett Trevor, BioSci Consulting, Maasmechelen, Belgium;
Geiser Thomas, Department of Respiratory Medicine, University Hospital Bern, Switzerland;
Gent Julaiha, Royal Brompton and Harefield NHS Foundation Trust, UK;
Gerhardsson de Verdier Maria, AstraZeneca; Molndal, Sweden;
Gibeon David, National Heart and Lung Institute, Imperial College, UK;

Gomez Cristina, Centre for Allergy Research, Karolinska Institutet, Stockholm, Sweden
Gove Kerry, NIHR Southampton Respiratory Biomedical Research Unit and Clinical and Experimental Sciences, Southampton, UK;
Gozzard Neil, UCB, UK;
Guo Yi-ke, Data Science Institute, Imperial College, UK;
Hashimoto Simone, Academic Medical Centre, University of Amsterdam, The Netherlands;
Haughney John, International Primary Care Respiratory Group, Aberdeen, Scotland;
Hedlin Gunilla, Dept. Women's and Children's Health & Centre for Allergy Research, Karolinska Institutet, Stockholm, Sweden;
Hekking Pieter-Paul, Academic Medical Centre, University of Amsterdam, The Netherlands;
Henriksson Elisabeth, Karolinska University Hospital & Karolinska Institutet, Stockholm, Sweden
Hewitt Lorraine, NIHR Southampton Respiratory Biomedical Research Unit, Southampton, UK
Higgenbottam Tim, Allergy Therapeutics, West Sussex, UK;
Hoda Uruj, Imperial College, UK;
Hohlfeld Jens, Fraunhofer Institute for Toxicology and Experimental Medicine, Hannover, Germany;
Holweg Cecile, Respiratory and Allergy Diseases, Genentech, San Francisco CA;
Horvath Ildiko, Semmelweis University, Budapest, Hungary;
Howarth Peter, NIHR Southampton Respiratory Biomedical Research Unit, Clinical and Experimental Sciences and Human Development and Health, Southampton, UK;
Hu Richard, Amgen Inc.;
Hu Sile, National Heart and Lung Institute, Imperial College, UK;
Hu Xugang, Amgen Inc.;

Hudson Val, Asthma UK, London, UK;
James Anna J., Centre for Allergy Research, Karolinska Institutet, Stockholm, Sweden;
Kamphuis Juliette, Longfonds, Amersfoort, The Netherlands;
Kennington Erika J., Asthma UK, London, UK;
Kerry Dyson, CromSource, Stirling UK;
Klüglich Matthias, Boehringer Ingelheim Pharma GmbH & Co. KG; Biberach, Germany
Knobel Hugo, Philips Research Laboratories, Eindhoven, The Netherlands;
Knowles Richard, Knowles Consulting, UK
Knox Alan, Respiratory Research Unit, University of Nottingham, UK;
Kolmert Johan, Centre for Allergy Research, Karolinska Institutet, Stockholm, Sweden
Konradsen Jon, Dept. Women’s and Children’s Health & Centre for Allergy Research, Karolinska Institutet, Stockholm, Sweden
Kots Maxim, Chiesi Pharmaceuticals, SPA, Parma, Italy;
Krueger Linn, University Children's Hospital Bern, Switzerland
Krug Norbert, Fraunhofer Institute for Toxicology and Experimental Medicine, Hannover, Germany;
Kuo Scott, National Heart and Lung Institute, Imperial College, UK;
Kupczyk Maciej, Centre for Allergy Research, Karolinska Institutet, Stockholm, Sweden
Lambrecht Bart, University of Gent, Gent, Belgium;
Lantz Ann-Sofie, Karolinska University Hospital & Centre for Allergy Research, Karolinska Institutet, Stockholm, Sweden;
Larsson Lars, AstraZeneca, Mohlndal, Sweden;
Lazarinis Nikos, Karolinska University Hospital & Karolinska Institutet, Stockholm, Sweden

Lefaudeux Diane, European Institute for Systems Biology and Medicine, CNRS-ENS-UCBL-INSERM, Lyon, France;
Lone-Latif Saeeda, Academic Medical Centre, University of Amsterdam, The Netherlands;
Loza Matthew J., Janssen R&D, USA;
Lutter Rene, Academic Medical Centre, University of Amsterdam, The Netherlands;
Marouzet Lisa, NIHR Southampton Respiratory Biomedical Research Unit, Southampton, UK
Martin Jane, NIHR Southampton Respiratory Biomedical Research Unit, Southampton, UK
Masefield Sarah, European Lung Foundation, Sheffield, UK;
Mathon Caroline, Centre of Allergy Research, Karolinska Institutet, Stockholm, Sweden
Matthews John G., Respiratory and Allergy Diseases, Genentech, San Francisco CA, USA;
Mazein Alexander, European Institute for Systems Biology and Medicine, CNRS-ENS-UCBL-INSERM, CIRI-UMR5308, Lyon, France;
Meah Sally, National Heart and Lung Institute, Imperial College, UK;
Meiser Andrea, National Heart and Lung Institute, Imperial College, UK;
Menzies-Gow Andrew, Royal Brompton and Harefield NHS Foundation Trust, UK;
Metcalf Leanne, Previously at: Asthma UK, London, UK;
Middelveld Roelinde, Centre for Allergy Research, Karolinska Institutet, Stockholm, Sweden
Mikus Maria, Science for Life Laboratory & The Royal Institute of Technology, Stockholm, Sweden;
Miralpeix Montse, Almirall, Barcelona, Spain;
Monk Philip, Synairgen Research Ltd, Southampton, UK;
Montuschi Paolo, Università Cattolica del Sacro Cuore, Italy;
Mores Nadia, Università Cattolica del Sacro Cuore, Italy;

Murray Clare S., Centre for Respiratory Medicine and Allergy, Institute of Inflammation and Repair, University of Manchester and University Hospital of South Manchester, Manchester Academic Health Sciences Centre, Manchester, United Kingdom
Musial Jacek, II Department of Internal Medicine, Jagiellonian University Medical College, Krakow, Poland;
Myles David, Respiratory Therapeutic Unit, GSK, UK;
Naz Shama, Centre for Allergy Research, Karolinska Institutet, Stockholm, Sweden
Nething Katja, Boehringer Ingelheim Pharma GmbH & Co. KG; Biberach, Germany
Nicholas Ben, University of Southampton, UK
Nihlen Ulf, AstraZeneca; Molndal, Sweden;
Nilsson Peter, Science for Life Laboratory & The Royal Institute of Technology, Stockholm, Sweden;
Nordlund Björn, Dept. Women's and Children's Health & Centre for Allergy Research, Karolinska Institutet, Stockholm, Sweden
Östling Jörgen, AstraZeneca, Mölndal, Sweden;
Pacino Antonio, Lega Italiano Anti Fumo, Catania, Italy;
Pahus Laurie, Assistance publique des Hôpitaux de Marseille, Clinique des bronches, allergies et sommeil Espace Éthique Méditerranéen, Aix-Marseille Université, Marseille, France;
Palkonen Susanna, European Federation of Allergy and Airways Diseases Patient's Associations, Brussels, Belgium.
Pandis Ioannis, Data Science Institute, Imperial College, London, UK;
Pavlidis Stelios, National Heart and Lung Institute, Imperial College, UK
Pennazza Giorgio, University of Rome 'Tor Vergata', Rome Italy;
Petrén Anne, Centre for Allergy Research, Karolinska Institutet, Stockholm, Sweden

Pink Sandy, NIHR Southampton Respiratory Biomedical Research Unit, Southampton, UK
Postle Anthony, University of Southampton, UK
Powel Pippa, European Lung Foundation, Sheffield, UK;
Rahman-Amin Malayka, Previously at: Asthma UK, London, UK;
Rao Navin, Janssen R&D, USA;
Ravanetti Lara, Academic Medical Centre, University of Amsterdam, The Netherlands;
Ray Emma, NIHR Southampton Respiratory Biomedical Research Unit, Southampton, UK
Reinke Stacey, Centre for Allergy Research, Karolinska Institutet, Stockholm, Sweden
Reynolds Leanne, Previously at: Asthma UK, London, UK;
Riemann Kathrin, Boehringer Ingelheim Pharma GmbH & Co. KG; Biberach, Germany
Riley John, Respiratory Therapeutic Unit, GSK, UK;
Robberechts Martine, MSD, Brussels, BE
Roberts Amanda, Asthma UK, UK;
Roberts Graham, NIHR Southampton Respiratory Biomedical Research Unit, Clinical and Experimental Sciences and Human Development and Health, Southampton, UK;
Rossios Christos, National Heart and Lung Institute, Imperial College, UK;
Rowe Anthony, Janssen R&D, UK;
Russell Kirsty, National Heart and Lung Institute, Imperial College, UK;
Rutgers Michael, Longfonds, Amersfoort, The Netherlands;
Sandström Thomas, Dept of Public Health and Clinical Medicine, Umeå University, Umeå, Sweden;
Santini Giuseppe, Università Cattolica del Sacro Cuore, Italy;

Santoninco Marco, University of Rome 'Tor Vergata', Rome Italy;
Schoelch Corinna, Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach, Germany
Schofield James P. R., Centre for Proteomic Research, Institute for Life Sciences, University of Southampton, UK
Seibold Wolfgang, Boehringer Ingelheim Pharma GmbH, Biberach, Germany
Shaw Dominick E., Respiratory Research Unit, University of Nottingham, UK;
Sigmund Ralf, Boehringer Ingelheim Pharma GmbH & Co. KG; Biberach, Germany
Singer Florian, University Children's Hospital, Zurich, Switzerland;
Sjödin Marcus, Centre for Allergy Research, Karolinska Institutet, Stockholm, Sweden
Skipp Paul J., Centre for Proteomic Research, Institute for Life Sciences, University of Southampton, UK
Smids Barbara, Academic Medical Centre, University of Amsterdam, The Netherlands;
Smith Caroline, NIHR Southampton Respiratory Biomedical Research Unit, Southampton, UK
Smith Jessica, Asthma UK, London, UK;
Smith Katherine M., University of Nottingham, UK;
Söderman Päivi, Dept. Women's and Children's Health, Karolinska Institutet, Stockholm, Sweden
Sogbesan Adesimbo, Royal Brompton and Harefield NHS Foundation Trust, UK;
Sousa Ana R., Respiratory Therapeutic Unit, GSK, UK;
Staykova Doroteya, University of Southampton, UK
Sterk Peter J., Academic Medical Centre, University of Amsterdam, The Netherlands;
Strandberg Karin, Karolinska University Hospital & Karolinska Institutet, Stockholm, Sweden
Sun Kai, National Heart and Lung Institute, Imperial College, UK;

Supple David, Asthma UK, UK;
Szentkereszty Marton, Semmelweis University, Budapest, Hungary;
Tamasi Lilla, Semmelweis University, Budapest, Hungary;
Tariq Kamran, NIHR Southampton Respiratory Biomedical Research Unit, Clinical and Experimental Sciences, NIHR-Wellcome Trust Clinical Research Facility, Faculty of Medicine, University of Southampton, UK;
Thörngren John-Olof, Karolinska University Hospital, Sweden
Thornton Bob, MSD, USA;
Thorsen Jonathan, COPSAC, Copenhagen Prospective Studies on Asthma in Childhood, Herlev and Gentofte Hospital, University of Copenhagen, Copenhagen, Denmark;
Valente Salvatore, Università Cattolica del Sacro Cuore, Italy;
van Aalderen Wim, Academic Medical Centre, University of Amsterdam, The Netherlands;
van de Pol Marianne, Academic Medical Centre, University of Amsterdam, The Netherlands;
van Drunen Kees, Academic Medical Centre, University of Amsterdam, The Netherlands;
van Geest Marleen, AstraZeneca, Mölndal, Sweden;
Versnel Jenny, Previously at: Asthma UK, London, UK;
Vestbo Jorgen, Centre for Respiratory Medicine and Allergy, Institute of Inflammation and Repair, University of Manchester and University Hospital of South Manchester, Manchester Academic Health Sciences Centre, Manchester, United Kingdom
Vink Anton, Philips Research Laboratories, Eindhoven, The Netherlands;
Vissing Nadja, COPSAC, Copenhagen Prospective Studies on Asthma in Childhood, Herlev and Gentofte Hospital, University of Copenhagen, Copenhagen, Denmark;

von Garnier Christophe, University Hospital Bern, Switzerland;
Wagener Ariane, Academic Medical Centre, University of Amsterdam, The Netherlands;
Wagers Scott, BioSci Consulting, Maasmechelen, Belgium;
Wald Frans, Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach, Germany
Walker Samantha, Asthma UK, London, UK;
Ward Jonathan, Histochemistry Research Unit, Faculty of Medicine, University of Southampton, Southampton, UK;
Weiszhart Zsoka, Semmelweis University, Budapest, Hungary;
Wetzel Kristiane, Boehringer Ingelheim Pharma GmbH, Biberach, Germany
Wheelock Craig E., Centre for Allergy Research, Karolinska Institutet, Stockholm, Sweden;
Wiegman Coen, National Heart and Lung Institute, Imperial College, UK;
Williams Siân, International Primary Care Respiratory Group, Aberdeen, Scotland;
Wilson Susan J., Histochemistry Research Unit, Faculty of Medicine, University of Southampton, Southampton, UK;
Woodcock Ashley, Centre for Respiratory Medicine and Allergy, Institute of Inflammation and Repair, University of Manchester and University Hospital of South Manchester, Manchester Academic Health Sciences Centre, Manchester, United Kingdom
Yang Xian, National Heart and Lung Institute, Imperial College, UK;
Yeyasingham Elizabeth, UK Clinical Operations, GSK, Stockley Park, UK;
Yu Wen, Amgen Inc.;
Zetterquist Wilhelm, Dept. Women's and Children's Health & Centre for Allergy Research, Karolinska Institutet, Stockholm, Sweden
Zwinderman Koos, Academic Medical Centre, University of Amsterdam, The Netherlands;