

Interferon response factor-3 promotes the pro-Th2 activity of mouse lung CD11b⁺ conventional dendritic cells in response to house dust mite allergens

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16	APC	Antigen presenting-cell
17	cDC	Conventional dendritic cell
18	DC	Dendritic cell
19	FACS	Fluorescence-activated cell sorting
20	GO	Gene ontology
21	HDM	House dust mite
22	Ifn	Interferon
23	IL	interleukin
24	Irf	Interferon response factor
25	Isgf3	Interferon stimulated gene factor 3
26	MACS	Magnetism activated cell sorting
27	OVA	Ovalbumin
28	TCR	T cell receptor
29	Th	T helper
30	WT	Wild type

31 Abstract

32 Very few transcription factors have been identified that are required by antigen-presenting cells
33 (APCs) to induce T helper type 2 (Th2) responses. Because lung CD11b⁺ conventional dendritic cells
34 (CD11b⁺ cDCs) are responsible for priming Th2 responses in house-dust mite (HDM)-induced airway
35 allergy, we used them as a model to identify transcriptional events regulating the pro-Th2 activity of
36 cDCs. Transcriptomic profiling of lung CD11b⁺ cDCs exposed to HDM in vivo revealed first that

HDM triggers an antiviral defence-like response, and second that the majority of HDM-induced transcriptional changes depend on the transcription factor Interferon Response Factor-3 (Irf3). Validating the functional relevance of these observations, Irf3-deficient CD11b⁺ cDCs displayed reduced pro-allergic activity. Indeed, Irf3-deficient CD11b⁺ cDCs induced less Th2, more regulatory T-cell, and similar Th1 differentiation in naïve CD4⁺ T cells compared to their wild-type counterparts. The altered APC activity of Irf3 CD11b⁺ cDCs was associated with reduced expression of CD86 and was phenocopied by blocking CD86 activity in wild-type CD11b⁺ cDCs. Altogether, these results establish Irf3, known mostly for its role in antiviral responses, as a transcription factor involved in the induction of Th2 responses through the promotion of pro-Th2 costimulation in CD11b⁺ DCs.

Introduction

T helper type 2 (Th2) cells play key roles in anti-helminthic immunity but also in allergic diseases such as atopic dermatitis and airway allergy [1]. It is now generally well accepted that Th2 cell differentiation in vivo depends mainly, in most if not all pathophysiological contexts, on the instruction of naïve T cells by dendritic cells (DCs), the professional antigen-presenting cells [2-5]. Recent years have seen tremendous progress in our understanding of DC diversity and ontogeny [6, 7]. Conventional dendritic cells (cDCs) mainly derive from a bone marrow-derived common dendritic cell precursor and can be subdivided into 2 major subsets based on the respective transcription factors required for their terminal differentiation [6]. These 2 subsets consist of cDC1 DCs, which include tissue resident CD103⁺ DCs and CD8α⁺ spleen DCs and require the transcription factor Batf3 [8, 9], and cDC2 DCs, which include tissue resident CD11b⁺ CD103⁻ DCs and CD4⁺ spleen DCs and depend on Irf4 [10-13]. Accumulating data support the notion that distinct DC subsets preferentially trigger different types of Th cell responses [14]. Regarding type 2 responses, a consensus is emerging on the

fact that tissue resident CD11b⁺ cDC2s are the DC subset most capable of triggering Th2 cell differentiation in vivo [2]. This notion is documented by studies in mouse models comparing the pro-Th2 activity of different tissue-resident DC subsets through approaches involving adoptive transfer [15], conditional ablation [16], or genetic deficiencies impairing cDC2 development or function [11, 17-19].

A longstanding and not yet fully resolved question regards the mechanisms through which cDCs instruct naïve Th cells to become Th2 cells. Indeed, cDCs do not produce interleukin (IL)-4, the key pro-Th2 cytokine. Instead of DCs, it has been proposed that bystander cells such as basophils or Th cells themselves produce the IL-4 required for Th2 cell differentiation [20]. This however leaves open the question of whether DCs play an active role in Th2 cell polarization. One model indeed postulates that Th2 responses are "default" responses, instructed by DCs when they are not activated to upregulate their expression of costimulatory signals and to produce cytokinic polarizing signals such as IL-12 [21, 22]. On the other hand, costimulatory molecules and cytokines expressed by DCs have been proposed to actively promote Th2 cell differentiation. DCs indeed may express costimulatory molecules such as CD86 and OX40L, which favor Th2 polarization in vivo [23, 24]. They may also express the cytokines IL-6, IL-10 and IL-33, which have been proposed to favor Th2 cell responses [25-27].

Our understanding of the pro-Th2 activity of cDC2s could benefit from a deeper knowledge of the transcription factors that orchestrate its underlying gene expression program. To date, only a handful of transcription factors involved in the induction of Th2 responses by DCs have been identified, usually based on candidate gene approaches without high throughput assessment of their underlying gene expression program. Activation of STAT5 downstream of GM-CSF and TSLP

81 signalling is required for optimal allergic responses in models of atopic dermatitis and airway allergy
82 through the promotion of CD11b⁺ cDC2 migration and expression of pro-Th2 costimulatory
83 molecules [17]. C-Fos stabilization following TLR2 activation, or activation of the non-canonical NF-
84 κ B subunit Bcl3 downstream of DC-SIGN, were also shown to inhibit IL-12, while promoting IL-10
85 expression by DCs, which could tilt the Th1/Th2 balance in favor of Th2 cell differentiation [28, 29].
86 Mice deficient for Irf4 in CD11c⁺ cells are also protected from various types of allergic responses [11,
87 18, 30]. This protection likely derives in part from impaired terminal differentiation and antigen
88 presentation of tissue-resident CD11b⁺ cDC2 cells [12, 13, 18], and in part from the control of IL-10
89 and IL-33 expression by Irf4 in these cells [30]. Finally and more recently, it was shown that Klf4
90 deficiency in CD11c⁺ cells impairs Th2 cell development in mouse models of helminth infection and
91 house dust mite-induced airway allergy, but the mechanisms of this impairment have not been
92 investigated to date [19].

93 Here, we aimed to identify transcription factors involved in establishing a pro-Th2 phenotype in
94 DCs by studying as a model the changes induced by extracts of house dust mite (HDM), the major
95 respiratory allergen in humans, on the gene expression program of mouse lung CD11b⁺ cDC2s.

96 Results

97 Lung CD11b⁺ cDC2s mount an "antiviral" Irf3-dependent transcriptional response to house 98 dust mite

99 Evidence from independent laboratories indicates that, among lung DC subsets, CD11b⁺ cDC2s are
100 the main inducers of Th2 responses to inhaled dust mite allergens [15, 16, 18]. Previous studies
101 further showed that CD11b⁺ cDC2s isolated from the lung of mice 24h after a single intranasal

exposure to HDM can efficiently prime HDM-specific Th2 responses after intratracheal adoptive transfer to naïve congenic recipient animals [15]. In order to characterize the transcriptional events taking place in cDC2s in this allergenic context, we performed microarray analyses on lung CD11b⁺ cDC2s sorted to high purity (>95%) from the lung of C57BL/6 mice 12h after a single exposure to either HDM or saline excipient (Figure 1A). Analysis for differentially expressed probesets (fold change ≥ 2 , $p \leq 0.05$) identified 643 upregulated probesets and 236 downregulated probesets in lung CD11b⁺ cDC2s following exposure to HDM (Figure 1B), referred to herein as the "HDM signature" (Supporting Information Table 1). Genes in the HDM signature were significantly enriched in 8 biological processes in statistical enrichment tests in Gene Ontology (Figure 1C), all but one related to immunity. The 2 most significantly enriched processes were "defense response to virus (GO:0051607)" and "response to virus (GO:0009615)". Indeed, many genes involved in antiviral responses were upregulated in the HDM signature, including type I interferons (Ifna1, Ifna2, Ifna6, Ifnb1), Mx proteins (Mx1, Mx2) and 2'-5'-oligoadenylate synthases (Oas1b, Oas2, Oas3, Oas11, Oas12), as well as the transcription factor Interferon Response Factor 7 (Irf7) (Figure 1B).

We further carried a TRANSFAC analysis to identify the transcription factors potentially orchestrating the "antiviral-like" response in the HDM signature. As may have been expected, among 113 potentially enriched transcription factor binding motifs ($p < 0.05$, fold enrichment > 3 , Supporting Information Table 2), putative binding sites for the 3 key antiviral transcription factors Isgf3 (Interferon stimulated gene factor 3, a complex of Stat1, Stat2 and Irf9), Irf3 and Irf7 were significantly enriched in the proximal promoter region of the HDM signature geneset (Figure 1D).

Previous studies indicate that, whereas Irf7 and type I IFNs are dispensable, Irf3 is required for optimal development of HDM-induced airway allergy in mice [31]. In these studies, DCs were not

distinguished according to their different subpopulations and the role of lung cDC2s as preferential inducers of Th2 responses was not yet documented. This however suggested that *Irf3*, but not *Isgf3* or *Irf7*, could play a role in the pro-Th2 activity of lung CD11b⁺ cDC2s. We hence compared the transcriptome of lung CD11b⁺ cDC2s from HDM-exposed wild-type (WT) and *Irf3*-deficient (*Irf3*^{-/-}) mice. 808 probesets were found to be significantly upregulated and 578 downregulated ($p \leq 0.05$) in *Irf3*^{-/-} cDC2s compared to their WT counterparts (Figure 2A). Out of the 643 upregulated probesets of the HDM signature, 365 (56.8 %) were significantly less expressed ($p \leq 0.05$) in *Irf3*^{-/-} compared to WT cDC2s (Supporting Information Table 3), an overlap unlikely to have occurred by chance ($p < 2.2e^{-16}$ of finding an overlap of 366 or more genes by chance sampling, hypergeometric test). Furthermore, we observed a significant anticorrelation (Pearson's correlation, $R^2 = -0.60$, $p < 2.2e^{-16}$) of the fold changes in expression of the genes significantly upregulated in the HDM signature and significantly regulated when comparing cDC2s from HDM-exposed WT and *Irf3*^{-/-} mice (Figure 2B). These analyses reveal that, in order to be optimal, a majority of the transactivation events taking place in lung CD11b⁺ cDC2s following HDM exposure require intact *Irf3* signalling. In line with these observations, statistical enrichment tests in GO identified "defense response to virus (GO:0051607)" and "response to virus (GO:0009615)" as the biological processes with the most significant underrepresentation in *Irf3*^{-/-} compared to WT cDC2s (Figure 2A, C). Furthermore, as expected, genes differentially expressed between cDC2s from HDM-treated WT and *Irf3*^{-/-} mice had their proximal promoters most significantly enriched in putative *Irf3* binding sites (Figure 2D). Real-time RT-PCR analysis of the expression of key antiviral genes identified as being regulated in the above transcriptomic analyses, namely *Ifnb1*, *Mx1* and *Irf7*, confirmed that these genes are induced in lung CD11b⁺ cDC2s following HDM exposure, and that this induction is significantly reduced in *Irf3*-deficient cDC2s (Figure 2E). Altogether, the above data identify an "antiviral response-like"

transcriptional response of lung CD11b⁺ cDC2s following HDM exposure, and establish the master regulator of antiviral responses Irf3 as a transcription factor playing a predominant role in this response.

Irf3-deficient DCs display reduced pro-Th2 APC function and ability to prime airway allergy

We next assessed the potential functional significance of the Irf3-dependent transcriptional program in driving the pro-Th2 activity of lung cDC2s. To do so, we compared the pro-allergic activity of WT and Irf3-deficient cDC2s in adoptive transfer experiments (Figure 3A). Lung cDC2s were sorted to high purity from the lung of WT or *Irf3*^{-/-} mice 24h after intranasal exposure to HDM and transferred directly into the trachea of naïve syngeneic recipient mice, as was done previously [15]. Ten days later, we exposed the recipient animals to low doses of HDM intranasally and assessed lung eosinophilic inflammation. Following exposure to HDM, mice that had received Irf3-deficient cDC2s developed lower eosinophilia in their bronchoalveolar lavage fluid than mice that had received WT cDC2s (Figure 3B). Perivascular and peribronchial infiltration of inflammatory cells was also significantly lower in mice that had received Irf3-deficient cDC2s compared to mice that had received WT cDC2s (-1 shift in median score, p=0.02 and -1 shift in median score, p=0.002, respectively, Wilcoxon rank-sum tests with Bonferonni correction) (Figure 3C). These experiments hence indicated that Irf3 activity was required for the full development of the pro-allergic activity of lung cDC2s in response to HDM.

Previous studies reported on reduced migration of DCs in HDM-treated *Irf3*^{-/-} mice [31]. Yet, this study considered DCs as CD11c⁺ F4/80⁻ autofluorescence-negative cells, which we now know includes cDC1s, cDC2s, macrophages and classical monocyte-derived DCs (mo-DCs). We hence compared numbers of cDC1s, cDC2s and mo-DCs in the lung and bronchial lymph node of excipient- or HDM-treated WT and *Irf3*^{-/-} mice. Whereas WT and *Irf3*^{-/-} mice had comparable numbers of lung and bronchial lymph node cDC2s in excipient- and HDM-treated conditions (Figure 4A), numbers of mo-DCs and cDC1s were significantly reduced (Supporting Information Figure 1A-C). Hence, when considering cDC1s, cDC2s and mo-DCs as a whole, HDM-induced recruitment of DCs indeed is reduced in the absence of *Irf3* (Supporting Information Figure 1D). Given that neither cDC1s nor mo-DCs are thought to be essential for HDM-specific Th2 cell priming [15,16], we reasoned that defective DC migration likely is not a major driver of defective Th2 cell priming in *Irf3*^{-/-} mice. We next sought to determine which specific aspect of the activity of lung cDC2s besides migration could be impacted by *Irf3* deficiency. We observed no significant differences in the numbers of neither lung Sirpα⁺ CD24⁺ cDC2s, which should represent Klf4-dependent cDC2s [19], nor lung Sirpα⁺ CD24⁻ cDC2s in WT and *Irf3*^{-/-} mice following treatment with saline or HDM (Supporting Information Figure 2A, B), arguing against a different composition of the lung cDC2 pool of *Irf3*^{-/-} mice. Uptake of fluorescently labelled HDM by lung cDC2s was comparable in WT and *Irf3*-deficient mice (Figure 4B). Likewise, the numbers of total CD11b⁺ cDC2s and HDM-loaded cDC2s in the bronchial lymph nodes were not significantly different following HDM treatment between WT and *Irf3*-deficient mice (Figure 4C, D). Hence, *Irf3* deficiency does not appear to affect antigen uptake and migration of cDC2s.

The above results suggested that *Irf3*-deficient cDC2s could instead have decreased APC activity toward naïve T cells. To test this hypothesis, we isolated lung cDC2s from WT or *Irf3*-deficient mice exposed to a mixture of endotoxin-free ovalbumin (OVA) as an antigen, and HDM as a pro-Th2 adjuvant and co-cultured them with naïve OT-II CD4⁺ T cells, which express a transgenic TCR recognizing a major epitope of OVA (Figure 5A). At the end of the coculture, we assessed the resulting profiles of cytokine secretion and transcription factor expression in antigen-specific T cells. The secretion of the Th2 cytokines IL-4 and IL-13 was significantly lower in the supernatant of OT-II CD4⁺ T cells cultured with *Irf3*^{-/-} cDC2s (by 27.5 %: 12.23 [10.3, 14.6] pg/ml vs 8.9 [7.3, 10.8] pg/ml, mean [95% C.I.], p=0.006 and by 56.2 %: 215.9 [183.0, 254.6] pg/ml vs 94.5 [73.7, 121.2] pg/ml, mean [95% C.I.], p=0.004, respectively, in linear mixed effect models). In contrast, the production of Ifn-γ was significantly increased (by 58.5 %: 291.9 [156.3, 545.4] pg/ml vs 470.1 [269.2, 820.8] pg/ml, mean [95% C.I.], p=0.02 in a linear mixed effect model) (Figure 5B). Intracellular flow cytometry indicated that the percentage of Gata3⁺ OT-II CD4⁺ T cells was slightly, although significantly decreased after coculture with *Irf3*-deficient cDC2s (by 9.5 %: 84.6 [75.6, 93.6] vs 76.6 [65.8, 87.4], mean [95% C.I.], p=0.0005 in a linear mixed effect model), whereas the percentage of Tbet positive OT-II CD4⁺ T cells was not significantly different (Figure 5C, D). Of note, co-culture with *Irf3*-deficient cDC2s also induced on average twice as much differentiation of OT-II cells into Foxp3⁺ cells (0.8 [0.2, 1.4] % vs 1.6 [1.1, 2.1] %, mean [95% C.I.], p=0.0003 in a linear mixed effect model), although these cells remained a minor population in these cultures (Figure 5C, D). Altogether, these results indicate that *Irf3*-deficient cDC2s have lower ability to induce Th2 cell responses from naïve T cells, while they also may display increased ability to promote Th1 cytokine secretion and regulatory T cell differentiation.

211 **Irf3 promotes the expression of genes encoding pro-Th2 costimulatory molecules**

212

213 We next sought to determine which aspects of the pro-Th2 APC function of cDC2s were impacted by
214 Irf3 deficiency. We analyzed the transcriptome of HDM-exposed WT and *Irf3*^{-/-} cDC2s to identify
215 differentially expressed cytokines/chemokines and costimulatory molecules within the HDM
216 signature (Figure 6A). None of the differentially expressed cytokines/chemokines appeared as likely
217 pro-Th2 candidates (Figure 6A). Out of the 13 differentially expressed genes encoding known
218 costimulatory molecules, 12 were less expressed in cDC2s from *Irf3*^{-/-} mice (Figure 6A). This
219 supports the notion that Irf3 contributes to the maturation program of cDC2s in response to HDM.
220 Most of these genes encoded either "generalist" costimulatory molecules not known to be associated
221 with particular orientation of Th cell responses (e.g. Tnfsf15, Fas), or molecules known to favor Th1
222 or Treg responses (CD70), reported to costimulate cell types other than Th cells (Klrl1, Btl1), or
223 reported to be expressed mainly by T cells themselves (Ox40). These molecules were deemed as
224 unlikely to contribute to a specific pro-Th2 activity of cDC2s. In contrast, *Irf3*^{-/-} cDC2s also expressed
225 lower levels of transcripts encoding proposed pro-Th2 costimulatory molecules, namely CD86, Ox40
226 ligand (Ox40l) and Pdl1. We assessed the surface expression of these costimulatory molecules by
227 flow cytometry (Figure 6B, C). Following HDM treatment, surface expression levels of CD86 on lung
228 cDC2s from *Irf3*^{-/-} mice were significantly lower than that of their WT counterparts (22055 [15641,
229 31099] vs 8646 [5828, 12826], mean [95% C.I.], $p < 0.0001$ in a linear mixed effect model followed by
230 Tukey's tests). In contrast, HDM treatment had no effect on the surface expression levels of Pdl1, and
231 led to decreased mean surface expression of Ox40l on cDC2s of both WT and *Irf3*^{-/-} mice (Figure 6C).

We hence reasoned that expression levels of Pdl1 and Ox40l were unlikely to cause the differences observed between WT and *Irf3*^{-/-} cDC2s.

CD86 is an important co-stimulatory molecule that has been associated with the preferential induction of Th2 responses, including in models of airway allergy [23, 32, 33]. We therefore tested its functional importance on the APC activity of lung cDC2s. We isolated lung cDCs from WT mice treated with an intranasal dose of a mixture of HDM and OVA and cocultured them in the presence of neutralizing anti-CD86 antibodies or isotype control and naïve OT-II CD4⁺ T cells. Neutralization of CD86 led to a significant decrease in the secretion of IL-4 (16.2 [11.3, 23.2] pg/ml vs 7.7 [5.3, 11.0] pg/ml, mean [95% C.I.], p=0.0005 in a linear mixed effect model) and IL-13 (178.5 [100.5, 317.1] pg/ml vs 63.5 [35.7, 112.8] pg/ml, mean [95% C.I.], p=0.0006 in a linear mixed effect model) but did not significantly change Ifn- γ production (205.0 [160.0, 250.0] pg/ml vs 174.5 [51.9, 297.1], mean [95% C.I.], p=0.4 in a linear mixed effect model) (Figure 6D). Hence, decreasing CD86 signalling from cDC2s phenocopies *Irf3* deficiency regarding the pro-Th2 APC activity of these cells.

Discussion

Limited high throughput data is currently available on the transcriptional changes taking place in tissue-resident cDCs in pro-Th2 pathophysiological contexts. To our best knowledge, our study provides the first in depth characterization of the transcriptome of lung cDC2s in an allergenic context, i.e. following exposure to HDM, the major respiratory allergen in human. As may have been expected, exposure of cDC2s to HDM leads to the upregulation of genes encoding proteins associated with DC maturation (e.g. CD70, CD86, CD40, OX40L, Pdl1 and Tnfsf15), migration (e.g. Ccr2 and

Cxcr5) and antigen processing and presentation (e.g. CD1d, Psme1, Psmb9, Psmb10, Psmb8, Psmg4, Tap1). More surprisingly, unbiased analysis for enriched gene sets associated with defined biological processes identified a prominent "antiviral-like" response in lung cDC2s following HDM exposure. It is unlikely that genes with known direct antiviral functions such as Mx genes would play a direct role in the APC activity of cDCs. In contrast, cDC-derived type I IFNs play important roles in the promotion of Th1 and CD8⁺ T cells responses [34, 35]. Yet, type I IFN signalling does not seem to impact on Th2 cell responses in mice [31, 36], and may inhibit Th2 cell responses in human [36]. Hence, it is likely that the upregulation of most "antiviral response" genes following allergen exposure is a bystander event that does not contribute to the pro-Th2 APC activity of lung cDC2s. Nevertheless, evidence from mouse models suggests that respiratory viral infections may favor Th2 responses to inhaled allergens, although the cellular mechanisms at hand have not been fully elucidated [37, 38]. It was hence tempting to speculate in our study that exposure of lung cDC2s to HDM could activate a genetic program driven by "antiviral" transcription factors that could promote Th2 cell responses.

Three transcription factors are classically considered as the master controllers of type I IFN-driven antiviral responses, namely Isgf3, Irf3 and Irf7 [39]. Previous studies showed that mice deficient for type I IFN signalling or Irf7 developed normal Th2 responses toward inhaled HDM, whereas Irf3-deficient mice were protected from airway allergy in the same model [31]. We hence focused our attention on the potential role of Irf3 in the response to HDM and the pro-Th2 activity of lung cDC2s. The comparison of the transcriptome of lung cDC2s from HDM-exposed WT and *Irf3*^{-/-} mice unambiguously indicated that Irf3 was implicated in a majority of HDM-triggered transcriptional events. We did not address in this study the nature or origin of the signals responsible

for the activation of Irf3 but can speculate on a few likely scenarios. First, Irf3 may be activated downstream of Toll-like receptor-4 (Tlr4) signalling [40], which was shown to be required for optimal development of airway allergy toward HDM [41]. Yet, Tlr4 expression mainly by airway epithelial cells, not hematopoietic cells, is required in this context [42]. In addition, mice deficient for the Tlr4 adaptor molecule TRIF develop normal responses toward inhaled HDM [31], making it unlikely that Tlr4 signalling drives pro-Th2 Irf3 activation in this context. Alternatively, many other signalling pathways may also lead to Irf3 activation in cDCs, notably the detection of nucleic acids (exogenous or endogenous) in the extracellular space [40, 43]. In this regard, HDM extracts contain DNA (Janss & Desmet, personal observation), which could be directly responsible for Irf3 activation. The identification of the activation pathway of Irf3 in response to HDM will hence require further investigation.

Irf3^{-/-} mice displayed reduced numbers of lung cDC1s following exposure to excipient or HDM, and reduced numbers of mo-DCs in the lung and bronchial lymph node following HDM treatment. This opens the perspective that Irf3 could be involved in the development, recruitment to the lung or survival of specific DC subsets, which will be investigated in future studies. Importantly, mo-DCs have been suggested to act as lung-resident activators of memory Th2 cells [16], suggesting that the protection of *Irf3*^{-/-} mice from HDM-induced allergy [31] could also in part be due to reduced mo-DC populations in the lung. Yet, Irf3 deficiency had no significant impact on the antigen-uptake or migratory activity of lung cDC2s in response to HDM. This is in contrast with what has been observed in mice deficient for STAT5 [17] or Irf4 [12, 13, 18], in which antigen presentation and/or migration of cDCs were reduced. Unlike was observed in the case of c-Fos, Bcl3 or Irf4 deficiency [28-30], our high-throughput analyses also did not detect significant differences in the gene

expression of key pro-Th2 or pro-Th1 cytokines. It would however be of interest to test compare protein expression of key polarizing cytokines between *Irf3*-deficient and WT cDC2s, as regulation by *Irf3* may be missed by our single time point transcriptomic analyses. The major defect of *Irf3*-deficient cDC2s that we detected at the transcriptomic level lied in the lower gene expression of costimulatory/coinhibitory molecules, reminiscent in this regard of part of the phenotype of *STAT5*-deficient DCs [17]. Since *STAT5* and *Irf3* signalling are not directly interconnected, it is likely that multiple signalling pathways need to be simultaneously activated to lead to optimal pro-Th2 maturation of cDC2s.

Microarray analyses detected lower gene expression of CD86, Ox40l and Pdl1 in lung cDCs from *Irf3*-deficient mice exposed to HDM compared to their WT counterparts. Yet, cell surface protein expression levels as assessed by flow cytometry only correlated with microarray data for CD86. We detected no change in surface expression of Pdl1 on cDC2s after exposure to HDM, whereas Ox40l surface expression was reduced to a comparable extent in both WT and *Irf3*^{-/-} mice. One possibility could be that the dynamics of Pdl1 or Ox40l turnover are altered following DC activation, so that surface expression does not reflect global protein levels in the entire cell. Another possibility is that there could be extensive post-transcriptional regulation of Pdl1 and Ox40l protein expression in cDCs. Accumulating evidence in this regard indicates that translational and post-translational regulation accounts for a large part of the expression levels of proteins [44]. In other words, changes in transcript expression often poorly correlate with changes in protein expression [44, 45]. Upregulation of Ox40l gene expression is often presented as a marker and cause of the pro-Th2 activity of DCs, while direct assessment of OX40l protein expression is seldom reported. We argue that Ox40l gene activation likely is a good marker of the activation of pro-Th2 gene expression

programs in DCs, but that caution should be taken before concluding that this single event drives the pro-Th2 activity of the studied DCs.

Irf3 deficiency led to lower upregulation of CD86 in response to HDM in lung cDC2s. Yet, the proximal promoter of the *CD86* gene does not contain predicted Irf3 binding sites. This does not preclude the possibility that Irf3 could promote CD86 expression directly through binding to more distal cis-regulatory elements. Alternatively, Irf3 could indirectly promote CD86 expression through the regulation of the expression of other transcription factors. Because of the current absence of anti-Irf3 antibodies suitable for reliable chromatin immunoprecipitation, this question remains difficult to address. CD86 has long been recognized as a key costimulatory molecule favoring Th2 cell responses [46], and its role in promoting Th2 responses toward inhaled allergens has been well established [23, 32, 33]. In agreement with this notion, we observed in coculture experiments between naïve CD4⁺ T cells and cDC2s that neutralization of CD86 impaired Th2 cell responses, but had no inhibitory impact on Th1 responses. Based on these observations, we propose that downregulation of CD86 expression likely is a major contributor to the decreased pro-Th2 activity of Irf3-deficient lung cDC2s. We however do not argue that altered expression of CD86 is the sole explanation for the reduced pro-Th2 activity of Irf3-deficient lung cDC2s. Other molecules not investigated here, such as other costimulatory/coinhibitory molecules or cytokines, could also contribute. One likely possibility is that in order to optimally induce Th2 responses, cDC2s need a fine-tuning of their co-stimulatory/co-inhibitory activity, which is perturbed in the absence of Irf3 signalling. Furthermore, the coculture experiments that were used here are only a model allowing assessment of the general APC activity of lung cDC2s. Other processes that are not amenable for study in this system, like DC

340 survival, localization in the lymph nodes or recruitment of T cells and accessory cells might also be
341 perturbed in the absence of Irf3.

342 We used lung cDC2s exposed to HDM as a model for pro-Th2 cDCs. It yet remains to be
343 determined whether Irf3 is required in other pro-Th2 contexts. Furthermore, given its importance as
344 an antiviral transcription factor and controller of type I IFN expression, it is likely that the function of
345 Irf3 in lung cDC2s is not limited to the induction of type 2 responses, even though we observed no
346 impact of Irf3 deficiency on the induction of Th1 responses in our in vitro models of coculture with
347 naïve T cells. As evoked earlier, it is tempting to speculate that some sort of molecular mimicry could
348 exist between viral infections and allergen exposure that could trigger common pro-Th2 gene
349 expression programs in lung cDC2s. Further investigation into this hypothesis could provide leads for
350 a better understanding of the observed association between respiratory viral infections and allergic
351 airway sensitization and exacerbations [47]. Altogether, our results support the notion that Irf3
352 signalling is required for optimal pro-Th2 activity of lung cDC2s.

353 **Materials and methods**

354 *Mice*

355 *Irf3*^{-/-} mice [48] were from purchased from the RIKEN Bioresource Center. WT and OTII C57BL/6
356 mice were from The Jackson Laboratory. All transgenic mice were backcrossed in total for at least 16
357 generations onto a C57BL/6 background and housed and bred in our specific pathogen free facility.
358 Age- and sex-matched groups of mice were used at 8-12 weeks of age. All experiments were
359 conducted with approval of the Institutional Animal Care and Use Committee of the University of
360 Liège. We also followed the "Guide for the Care and Use of Laboratory Animals" prepared by the

Institute of Laboratory Animal Resources, National Research Council, and published by the National Academy Press (revised 1996).

Antibodies and reagents

Lyophilized HDM (*Dermatophagoides farinae*) extracts were from Greer Laboratories (Lenoir USA). Fluorescent HDM was produced by labelling with the Alexa fluor 647 Protein Labelling kit (Molecular Probes, Eugene USA). 2.4G2 Fc receptor antibodies were produced in house. A list of the antibodies used is provided in Supporting Information Table 4.

Isolation and phenotyping of lung dendritic cells

To obtain single-lung-cell suspensions, lungs were perfused with 5 ml of HBSS through the right ventricle, cut into small pieces, and digested for 1 h at 37°C in HBSS (Lonza, Bale Switzerland) containing 1 mg/ml collagenase A (Roche, Bale Suisse) and 0.05 mg/ml DNase I (Roche, Bale Suisse). For cell sorting, lung cells were first enriched in CD11c-expressing cells by MACS using CD11c microbeads (Miltenyi Biotec, Bergisch Gladbach, Germany). Staining reactions were performed at 4°C after incubation with 2.4G2 Fc receptor antibodies to reduce non-specific binding. Flow cytometric analyses and FACS sorting were performed on a FACSARIA III (BD Biosciences, San Jose USA). Results were analyzed using FlowJo (Tree Star, Ashland USA).

RNA isolation, microarray and real-time RT-PCR

Groups of 10 WT mice were treated intranasally with PBS or 100 µg HDM, and groups of 10 *Irf3*^{-/-} mice were treated intranasally with 100 µg HDM. Biological triplicates were prepared independently for each of the 3 conditions. Twelve hours after treatment, lung CD11b⁺ cDC2s were directly sorted in Trizol (Thermo Scientific, Waltham USA). For microarray analyses, mRNA was isolated according to the Immgen protocol (www.immgen.org). Quality-tests and microarrays were performed following a standard Affymetrix protocol (Mouse Gene 1.0 ST arrays). Microarray raw data was analyzed using Bioconductor in R (version 3.2.4) [49] and is available under reference GSE80809 on Gene Expression Omnibus (<http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE80809>). Data was normalised by RMA using the oligo package from biocLite and differentially expressed genes between groups were identified using linear models from the limma package [50, 51] with Benjamini-Hochberg correction. Samples were then clustered by principal component analysis using the pcaMethods package [52]. One sample of lung cDC2s from PBS-treated WT mice and one sample of lung cDC2s from HDM-treated WT mice failed to cluster with the other 2 replicates of the same conditions. These samples were hence discarded and the remaining biological duplicates were analyzed. The 3 samples of lung cDC2s from HDM-treated *Irf3*^{-/-} mice clustered together as expected. For real-time RT-PCR, mRNA was purified using a Direct-zol kit (Zymo Research, Irvine USA) followed by DNase digestion and clean-up using an RNeasy micro kit (Qiagen, Hilden Germany). mRNA was amplified with a Quantitect Whole transcriptome kit (Qiagen, Hilden Germany) and real-time PCR analyses were performed on 7900HT taqman with ABsolute Blue qPCR SYBR Green ROX mix (Thermo Scientific, Waltham USA). *18S*, *B2m* and *Hprt* were used as reference genes in qPCR. The sequences of the primers used were as follows: *18S* 5'-AGTTAGCATGCCAGAGTCTCG-3' and 3'-TGCATGGCCGTTCTTAGTTG-5', *B2m* 5'-CATGGCTCGCTCGGTGACC-3' and 3'-AATGTGAGGCGGGTGGAACTG-5', *Hprt* 5'-AGCTACTGTAATGATCAGTCAACG-3' and 5'-

AGAGGTCCTTTTCACCAGCA-3'; *Irf7* 5'-ACAGGGCGTTTATCTTGCG-3' and 3'-
CTGAGGCTCACTTCTTCCCT-5' ; *Mxl* 5'-TAGTCCCCAGCAATGTGGAC-3' and 3'-
CGAAGGCAGTTTGGACCATC-5' ; *Ifnb* 5'-AGCACTGGGTGGAATGAGAC-3' and 3'-
TCCCACGTCAATCTTTCCTC-5'.

Bioinformatic analyses

Statistical enrichment tests for GO biological processes were performed using PANTHER [53].
Significantly regulated genes in microarray analyses were ranked based on their fold change and
default parameters were used. TRANSFAC analyses (Biobase Biological Databases) were performed
using the "vertebrates" database on the proximal promoter region (-500 to +100 from transcription
start site) of the genesets of interest.

Adoptive transfer model

1.10⁵ cDC2s from WT and *Irf3*^{-/-} mice injected i.n. 24 h earlier with 100 µg HDM were transferred
into the trachea of anesthetized naive recipients mice. Ten and 11 days later, recipient mice were
challenged with 5 µg HDM i.n. Airway allergy was evaluated 3 days later. To perform broncho-
alveolar lavage, the trachea was catheterized and the lung were perfused with 2 mL of ice cold PBS
(Lonza, Bale Switzerland). Cell concentration in bronchoalveolar lavage fluid was assessed with a
Thoma cell. Differential cell counts were performed on cytospin preparations stained with Diff-Quick
(Dade Behring, Glasgow USA). Lungs were fixed in 10% formalin, paraffin embedded, and cut in 5-
µm sections. The extent of peribronchial and perivascular inflammation was estimated by a score

calculated by means of quantification of inflammatory cells in lung sections stained with hematoxylin and eosin, as described previously [54]. Briefly, score 0 was assigned to bronchi/vessels with no surrounding mononuclear cell infiltration; score 1 corresponded to few mononuclear cells infiltrating; and score 2 was assigned if there were from 1 to 5 layer(s) of inflammatory cells surrounding the bronchus/vessel. Five bronchi and vessels were counted per mice and the bronchus/vessel with the highest score determined the overall score of each mouse.

Coculture experiments

Lung cDC2s were isolated from WT and *Irf3*^{-/-} mice as described above and naïve CD4⁺ T cells were isolated from the spleen and lymph nodes of OT-II mice using a Naïve CD4⁺ T Cell Isolation Kit (Miltenyi Biotec, Bergisch Gladbach Germany). 1.10⁴ lung cDC2s were cocultured with 2.10⁵ naïve CD4⁺ T cells for 3 days in RPMI 1640 medium (Lonza, Bale Switzerland) supplemented with 10% of foetal bovine serum (GIBCO BRL, Life Technologies LTD., Paisley, Ecosse), 0,1 mM of non-essential amino acid (GIBCO BRL, Life Technologies LTD., Paisley, Ecosse), 50 UI/mL of penicillin G, et 5 µg/mL de streptomycin (GIBCO BRL, Life Technologies LTD., Paisley, Ecosse), sodium pyruvate 1 mM (GIBCO BRL, Life Technologies LTD., Paisley, Ecosse) and 10 µg/mL of β-mercaptoethanol (GIBCO BRL, Life Technologies LTD., Paisley, Ecosse). Culture supernatants were assayed for cytokines production by ELISA (eBioscience, San Diego USA) and the expression of T-bet, Gata3, Foxp3 and RorγT in T cells was measured by intracellular flow cytometry. Cells were stained according to the protocol of the Transcription Factor Buffer Set kit (BD biosciences, San Jose USA). For functional assays, an anti-CD86 neutralizing antibody (Clone G1-1, Sony Biotechnology,

Weybridge United Kingdom) or a control isotype antibody was added at a concentration of 10µg/mL to the culture medium.

DC antigen uptake and migration

WT and *Irf3*^{-/-} C57BL/6 mice were injected i.n. with 100µg of HDM labelled with alexa fluor-647 or PBS. 24 hours later the mice were sacrificed and single lung cell suspensions were obtained from the lung and bronchial lymph nodes as described above. The number of total and HDM⁺ cDC2s were determined in both organs by flow cytometry.

Statistical analyses

Statistical analyses were performed using R (version 3.2.4) [55]. Unless specified otherwise, data from 3 independent experiments were pooled for analysis in each data panel. Raw data was transformed when needed and was back-transformed for graphical presentation. Respect of the assumptions of normal distribution of residuals and homoscedasticity was verified using diagnostic plots. For linear mixed effect models, we used the lme4 package [56]. In these models, the genotype and/or treatment were taken as fixed variables, and the date of the experiment was taken as a random variable to account for interexperimental variation between the 3 independent experiments. The models were encoded as ([cytokine] ~ genotype + (genotype|date)) in Figure 5C, (MFI ~ genotype + (genotype|date)) in Figure 5D, (MFI ~ genotype * treatment + (genotype|date) + (treatment|date)) in Figure 6C and ([cytokine] ~ treatment + (treatment|date)) in Figure 6D. We considered a p-value lower than 0.05 as significant.

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Conflict of interest disclosure

The authors declare no commercial or financial conflict of interest

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Figure legends

Figure 1. Sorting strategy and comparison of the transcriptome of lung cDC2s from wild-type C57BL/6 mice exposed to HDM or saline excipient. (A) Gating strategy for the FACS sorting of cDC2s from the lung of mice exposed 12 h earlier to a single dose of HDM or PBS excipient. Cells were gated based on morphology and cell doublets were excluded. A "dump" staining (DUMP) containing antibodies against CD3e, NK1.1, Siglec-F, CD19, Ly6g and CD64 was used to exclude non-DC cells. DUMP⁻ CD11c⁺ MHCII⁺ cells were considered as DCs, and cDC2s were selected based on their CD11b⁺ Ly6C⁻ phenotype [15]. Post-sort purity (right) was always >95%. (B) Heat map (left) of differentially expressed genes (fold change > 2, p < 0.05 by microarray) in lung cDC2s isolated as in (A) from the lung of mice exposed to PBS or HDM, constituting the "HDM signature". Each column represents an analysis of cells pooled from 10 mice. The names and fold-change of

658 differentially expressed genes belonging to the GO category "Response to virus (GO:009615)" are
659 also provided (right). (C) PANTHER GO statistical enrichment tests on the genes of the HDM
660 signature. Number of genes (black histograms) and $-\log(P\text{-value})$ (grey dots) of the enriched
661 biological processes are plotted. (D) TRANSFAC analysis of the enrichment of the proximal
662 promoter of the genes of the HDM signature for putative transcription factor binding sites. Only the
663 results for Isgf3, Irf7 and Irf3 are shown here. The full results are provided in Supporting Information
664 Table 2. The table provides from left to right the name of the binding site matrix, the name of the
665 transcription factor, the core sequence similarity (CSS), the matrix sequence similarity (MSS), the
666 enrichment P-value and the fold enrichment compared to a randomly selected set of genes of the size
667 of the HDM signature.

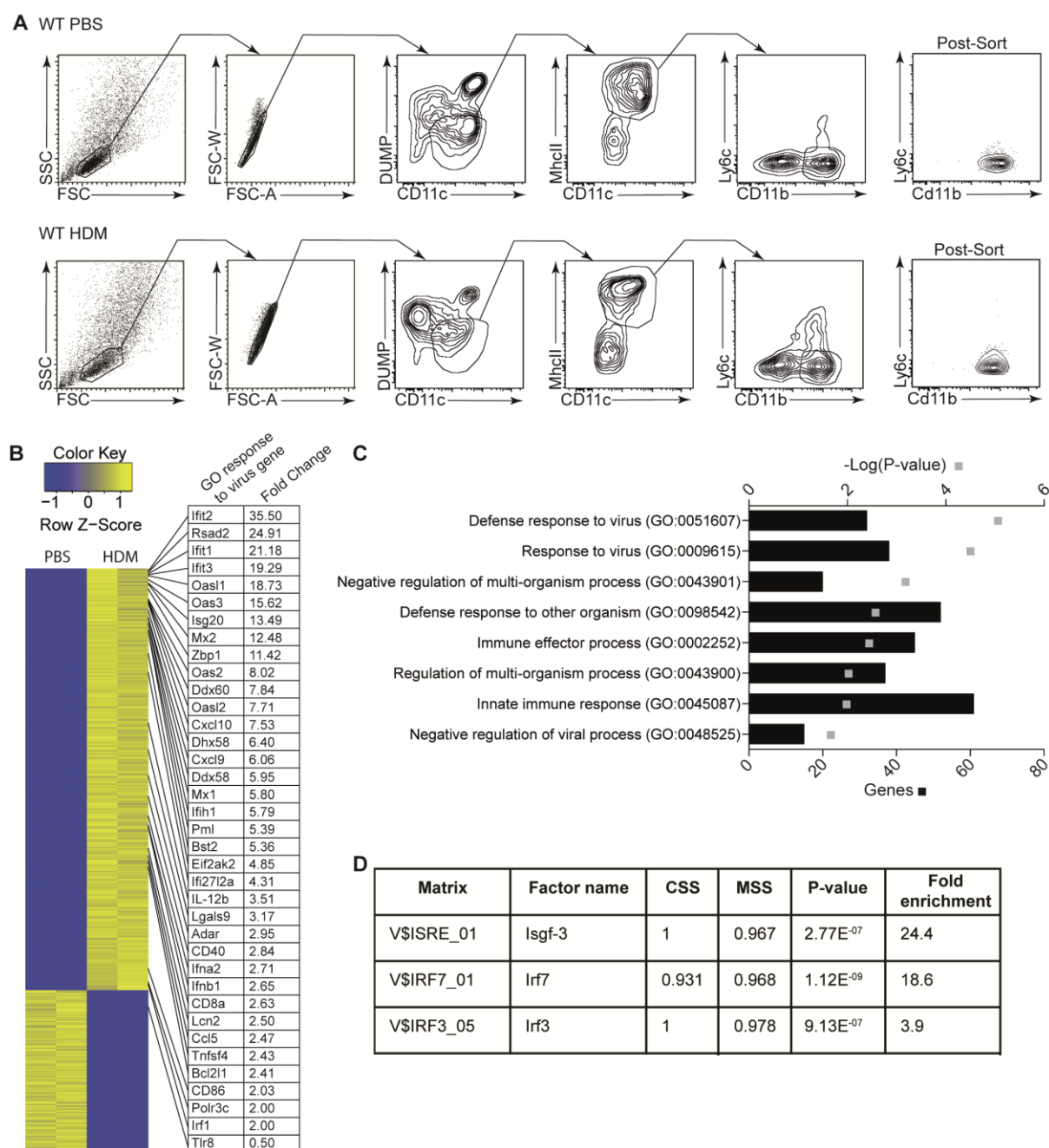


Figure 2. Impact of *Irf3* deficiency on the expression of HDM signature genes in lung cDC2s. (A) Heat map (left) of differentially expressed genes ($p < 0.05$ in microarray analysis) in lung cDC2s FACS sorted from the lung of WT or *Irf3*^{-/-} mice exposed to HDM as in Figure 1A. Each column represents an analysis of cells pooled from 10 mice. The names and fold-change of differentially expressed genes belonging to the GO category "Response to virus (GO:009615)" are also provided (right). (B) Correlation plot of the log2 fold changes (logFC) of the expression of the genes upregulated in the HDM signature (y axis) and significantly regulated when comparing cDC2s from HDM-exposed WT and *Irf3*^{-/-} mice (x axis) (Pearson's correlation, $R^2 = -0.60$, $p < 2.2 \times 10^{-16}$). (C) PANTHER GO statistical enrichment tests on the genes of the HDM signature whose expression is significantly impacted ($p < 0.05$) by *Irf3* deficiency in mice exposed to HDM. Number of genes (black histograms) and $-\log(P\text{-value})$ (grey dots) of the enriched biological processes are plotted. (D) TRANSFAC analysis of the enrichment for putative transcription factor binding sites of the proximal promoter of the genes of the HDM signature differentially expressed in cDC2s from HDM-treated *Irf3*^{-/-} mice. Only the results for *Isgf3*, *Irf7* and *Irf3* are shown here, as in Figure 1D. (E) Real-time RT-PCR analysis of the expression of *Ifnb1*, *Irf7* and *Mx1* in lung cDC2s from wild-type (WT) and *Irf3*^{-/-} mice exposed to PBS or HDM ($n = 3$ independent pools of lung cDC2s from 10 mice, data presented as mean $\pm$ SEM, $*p < 0.05$ in an ANOVA followed by Tukey's tests, CNRQ: calibrated normalized relative quantities).

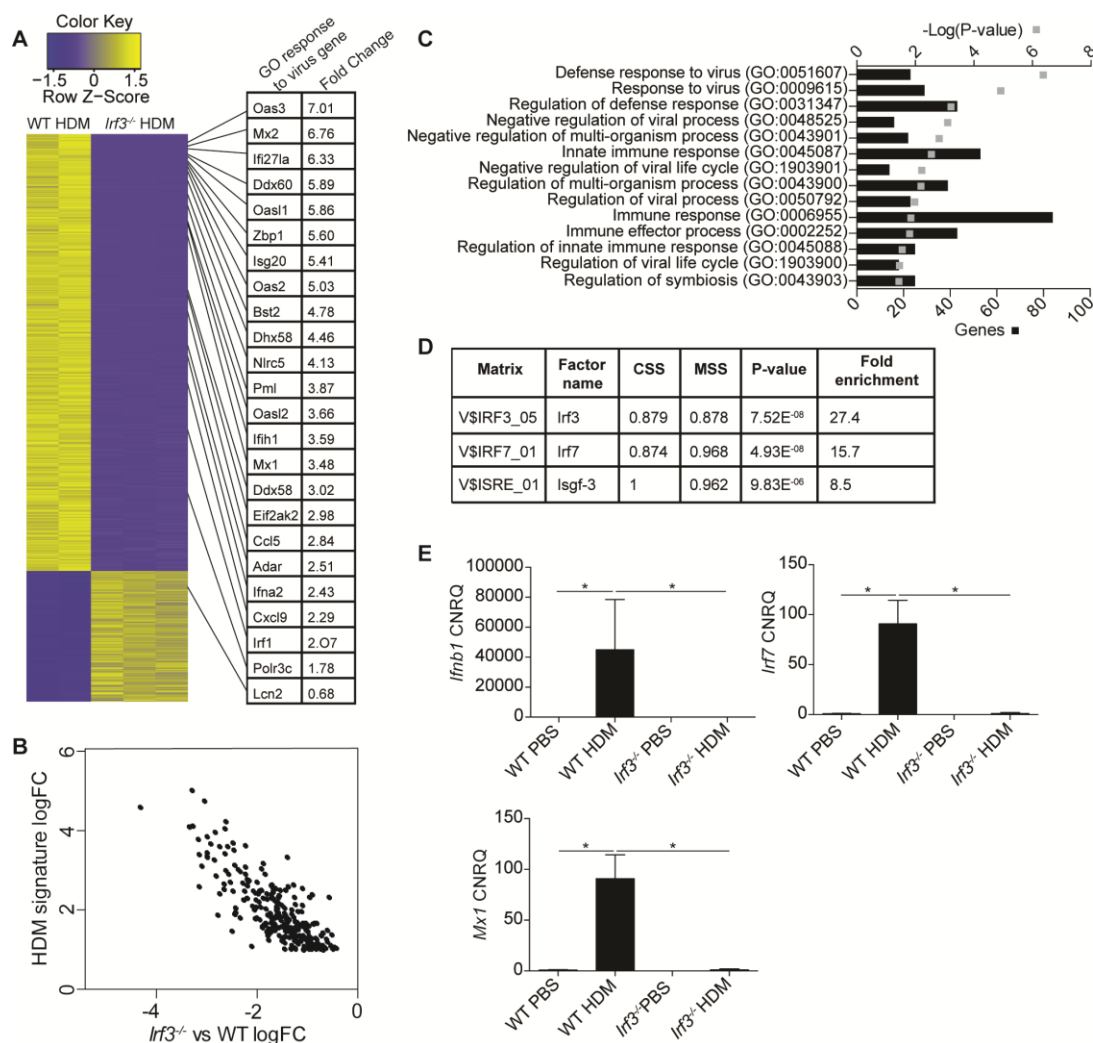


Figure 3. Comparison of the pro-allergic activity of WT and *Irf3*-deficient lung cDC2s. (A) Experimental outline. 24 h after intranasal exposure to a single dose HDM, donor WT or *Irf3*^{-/-} mice were sacrificed and their lung cDC2s were FACS sorted to high purity as in Figure 1A and transferred directly into the trachea of syngeneic recipient WT mice (WT cDC2s and *Irf3*^{-/-} cDC2s groups). Negative control recipient mice received PBS only (PBS group). Recipient mice were subsequently exposed to 2 low doses of intranasal HDM and parameters of allergic airway inflammation were

evaluated 3 days after the last exposure (i.n. : intranasal, i.t. : intratracheal). (B) Concentration of eosinophils in the bronchoalveolar lavage fluid of mice treated as in (A). Data pooled from 3 independent experiments (n= 5 mice/group per experiment, ****p < 0.0001 in an ANOVA followed by Tukey's tests, data presented as mean $\pm$ SEM). (C) Quantification of the peribronchial and perivascular inflammation (left) in the lung of mice treated as in (A) and representative haematoxylin-eosin staining of lung sections used for quantification (right, scale bar = 100 μ m). Data pooled from 3 independent experiments (n=5 mice/group per experiment, *p < 0.05, ***p < 0.001 in Wilcoxon rank sum tests for the indicated comparisons followed by Bonferonni correction).

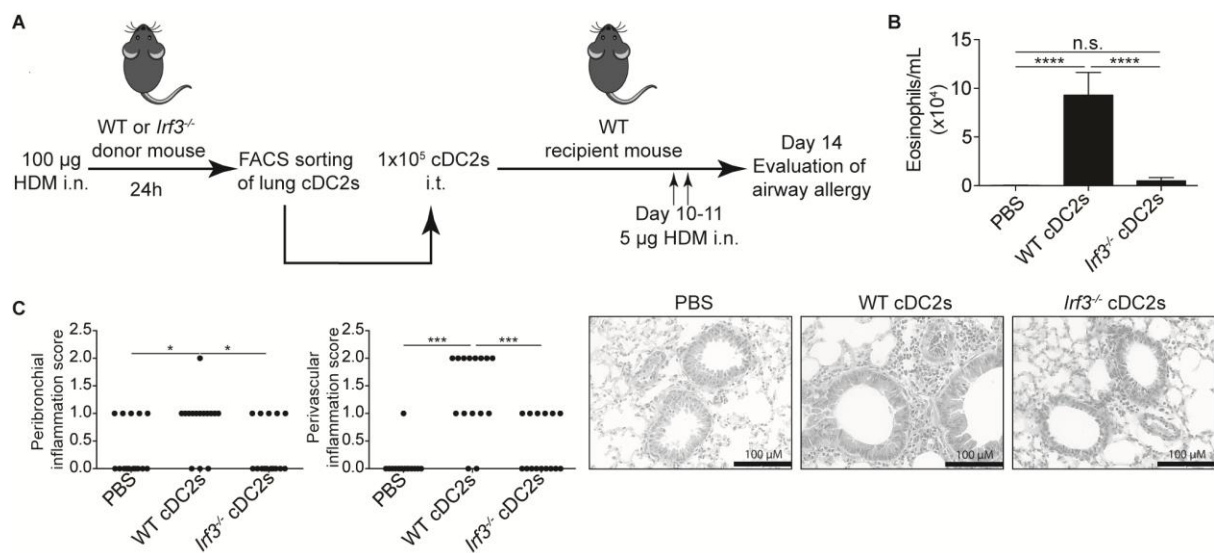


Figure 4. Comparison of the antigen uptake and migratory activity of lung cDC2s in WT and *Ir3*^{-/-} mice. (A, B) Lung cDC2s were gated as described in Figure 1A. (A) Number of cDC2s in the lung of WT or *Ir3*^{-/-} mice treated 24 h earlier with intranasal fluorescently labelled HDM or PBS excipient (**p < 0.01 in an ANOVA followed by Tukey's tests, data presented as mean $\pm$ SEM). (B) Number of HDM⁺ cDC2s in the lung of WT or *Ir3*^{-/-} mice treated with intranasal fluorescently labelled HDM

(left) and representative flow cytometry plots (right) (n.s. in a Student's t test, data presented as mean $\pm$ SEM). (C) Gating strategy for the identification of total and HDM⁺ cDC2s in the bronchial lymph node of WT and *Irf3*^{-/-} mice (DUMP = staining for CD3e, NK1.1, Siglec-F, CD19, Ly6g and CD64). (D) Number of cDC2s in the bronchial lymph node of WT or *Irf3*^{-/-} mice treated 24 h earlier with intranasal fluorescently labelled HDM or PBS excipient (****p < 0.0001 in an ANOVA followed by Tukey's tests, data presented as mean $\pm$ SEM). (E) Number of HDM⁺ cDC2s in the bronchial lymph node of WT or *Irf3*^{-/-} mice treated with intranasal fluorescently labelled HDM (n.s. in a Student's t test, data presented as mean $\pm$ SEM). In all panels, data are pooled from 3 independent experiments (n=6 mice/group per experiment).

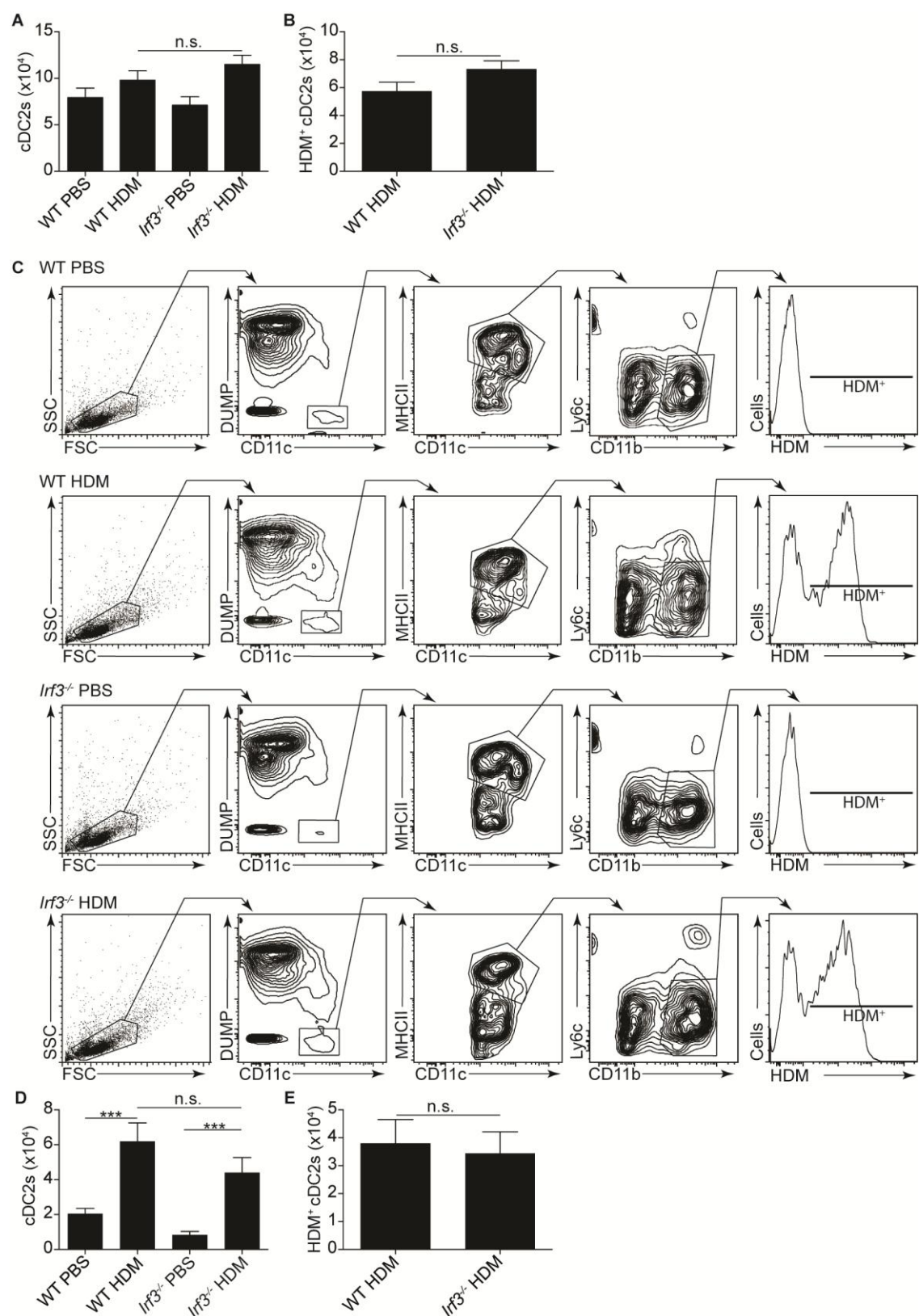


Figure 5. Comparison of the pro-Th2 activity of lung cDC2s from WT and *Irf3*^{-/-} mice. (A) Experimental outline. Lung cDC2s were FACS sorted from the lung of WT or *Irf3*^{-/-} mice treated 24 h earlier intranasally with a mixture of HDM and ovalbumin (OVA). In parallel, naïve CD4⁺ T cells from lymphoid organs of OT-II mice were sorted by magnetism-activated cell sorting (MACS). Lung cDC2s and naïve OT-II T cells were then cocultured for 3 days before ELISA assessment of cytokine secretion and intracellular flow cytometric analyses. (B) ELISA assessment of the secretion of IFN- γ , IL-4 and IL-13 at the end of the coculture. (C) Intracellular flow cytometric assessment of the expression of T-bet, Gata3 and Foxp3 in OT-II cells at the end of the coculture. (D) Gating strategy used in (C). (C, D) Data are pooled from 3 independent experiments (n = 4/group per experiment) and analyzed in linear mixed effect models (**p < 0.01, ***p < 0.001). Data of one representative experiment are presented as mean $\pm$ SEM and summary statistics of the models are provided in the main text.

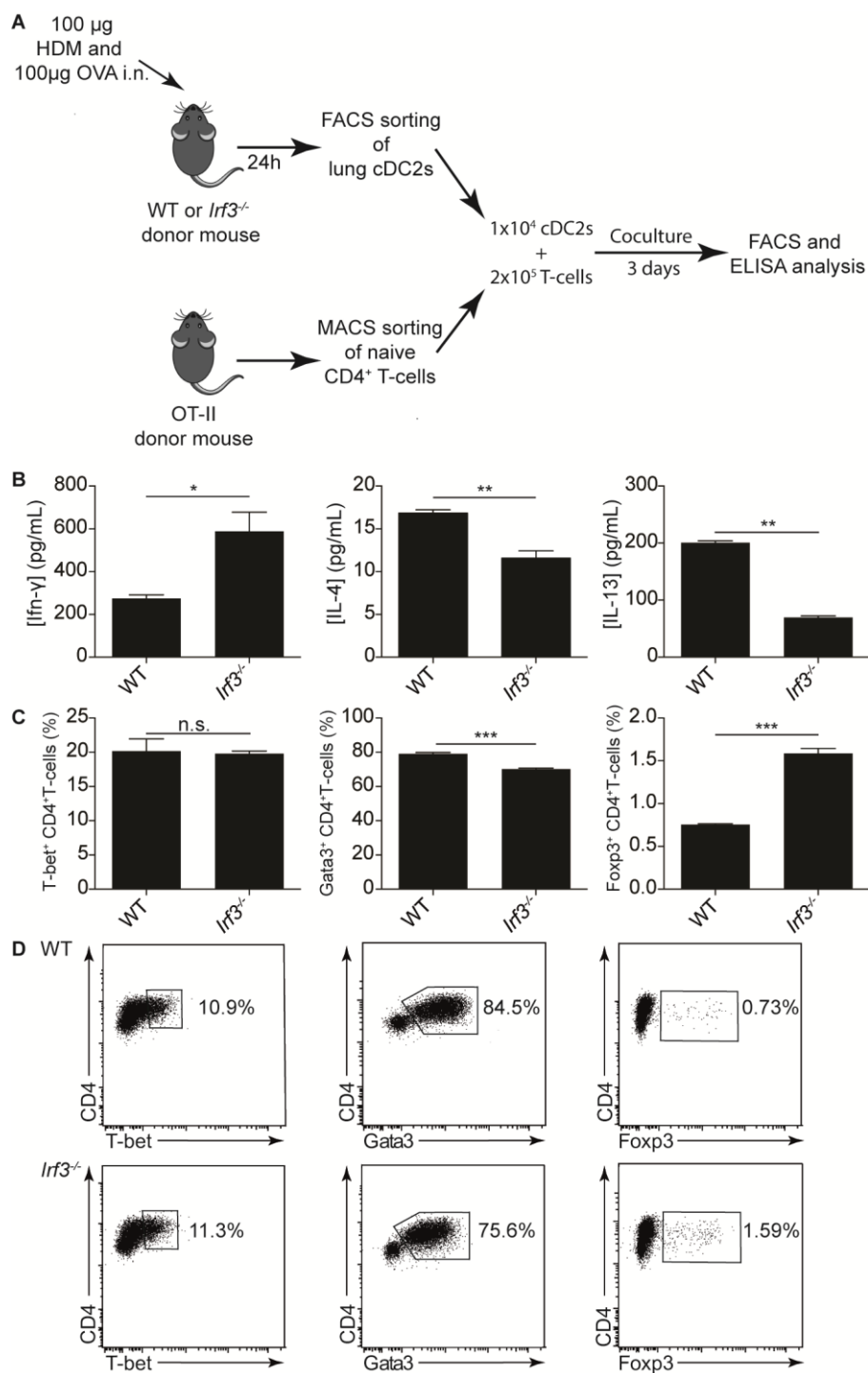
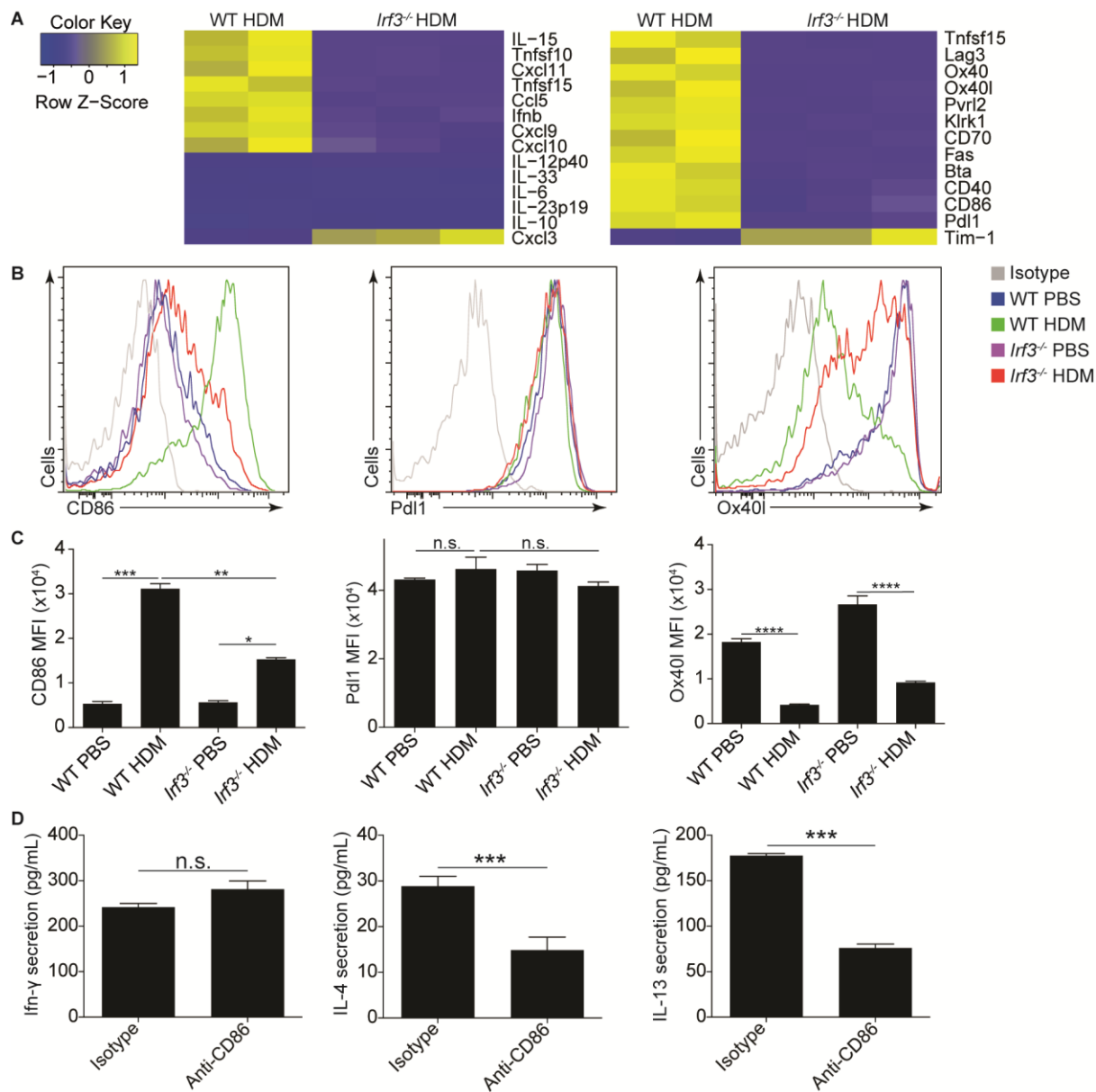
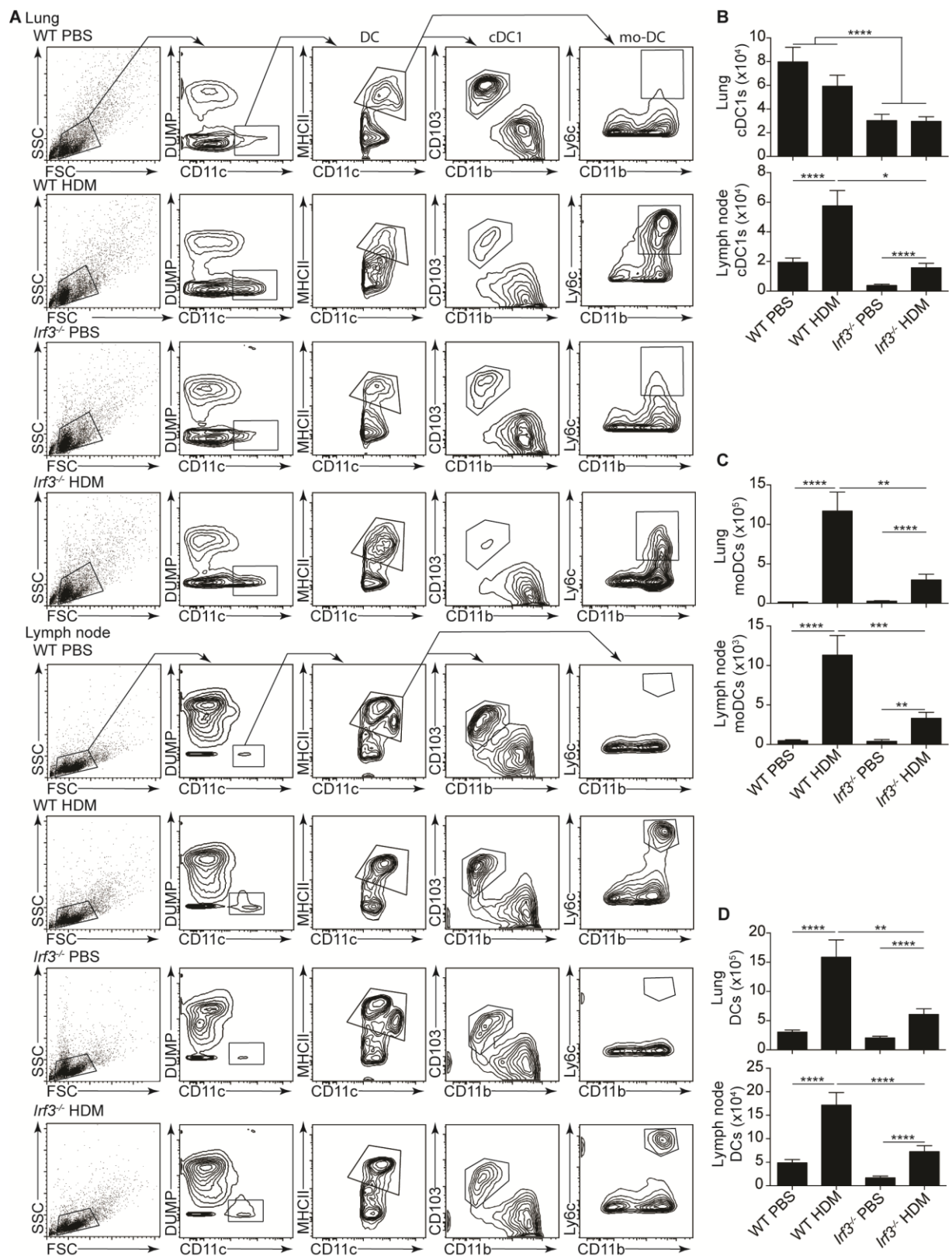


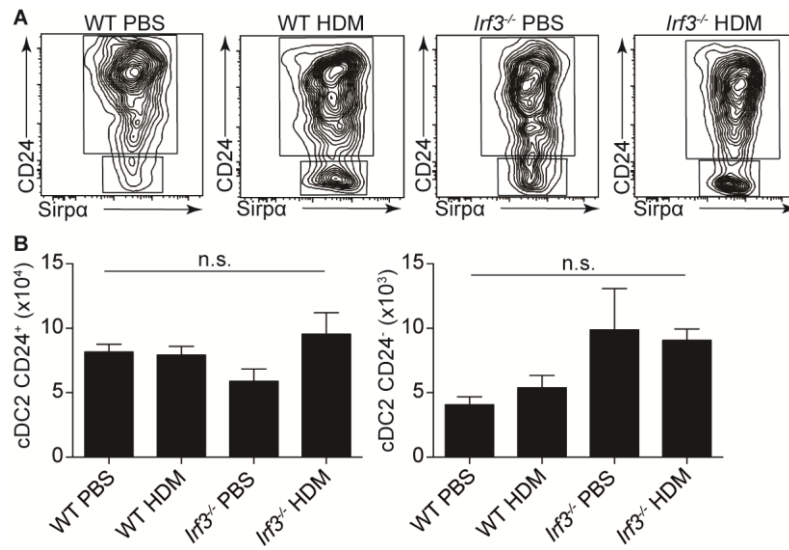
Figure 6. Comparison of the expression profile of cytokines and costimulatory/coinhibitory molecules of lung cDC2s from WT and *Irf3*^{-/-} mice and implication of CD86 in the pro-Th2 activity of lung cDC2s. (A) Heatmaps of differentially expressed genes encoding cytokines (left) or costimulatory/coinhibitory molecules (right) in lung cDC2s of WT versus *Irf3*^{-/-} mice exposed to HDM. The proposed pro-Th2 cytokines IL-6, IL-33 and IL-10, as well as IL12p35 and IL23-p19 are also included. Data extracted from the microarrays described in Figure 2A. (B) Representative plots of the flow cytometric assessment of the surface expression of CD86, Pdl1 and Ox40l in lung cDC2s from WT and *Irf3*^{-/-} mice exposed to PBS or HDM. Lung cDC2s were gated as in Figure 1A. (C) Quantification of the surface expression of CD86, Pdl1 and Ox40l in lung cDC2s from WT and *Irf3*^{-/-} mice exposed to PBS or HDM, assessed as in (C) (MFI: mean fluorescence intensity). Data are pooled from 3 independent experiments (n = 3/group per experiment) and analyzed in linear mixed effect models followed by Tukey's tests (*p<0.05, **p<0.01, ***p < 0.001, ****p < 0.0001). Data of one representative experiment is presented as mean ± SEM and summary statistics of the models are provided in the main text. (D) ELISA assessment of the secretion of Ifn-γ, IL-4 and IL-13 at the end of the coculture of naïve OT-II CD4⁺ T cells with lung cDC2s isolated from the lung of WT mice exposed intranasally to HDM and OVA as in Figure 5A. The cocultures were treated with either isotype control or neutralizing monoclonal anti-CD86 antibodies. Data are pooled from 3 independent experiments (n = 3 or 4/group per experiment) and analyzed in linear mixed effect models (***p < 0.001). Data of one representative experiment are presented as mean ± SEM and summary statistics of the models are provided in the main text.





Supporting Information Figure 1. Comparison of the numbers of total DCs, cDC1s and monocyte-derived DCs (mo-DCs) in the lung and bronchial lymph node of WT and *Irf3*^{-/-}

mice. (A) Gating strategy for the identification of DCs, cDC1s and mo-DCs in the lung and bronchial lymph node of WT and *Irf3*^{-/-} mice. Compared to the gating strategy shown in the rest of the article, the DUMP here did not include anti-CD64 antibody so as not to exclude mo-DCs. (B) Number of cDC1s, (C) mo-DCs and (D) total DCs in the lung (upper panels) and bronchial lymph node (lower panels) of WT or *Irf3*^{-/-} mice treated 24h earlier with intranasal HDM or PBS excipient (*p<0.05, **p < 0.01, ***p<0.001 and ****p<0.0001 in ANOVA followed by Tukey's tests, data presented as mean ± SEM). In all panels, data are pooled from 3 independent experiments (n=6 mice/group per experiment).



Supporting Information Figure 2. Comparison of the numbers of Sirp α ⁺ CD24⁻ and Sirp α ⁺ CD24⁺ cDC2s in the lung of WT and *Irf3*^{-/-} mice. Lung cDC2s were gated as described in Figure 1A, and subsequently subdivided based on their expression of Sirp α and CD24. (A) Representative flow cytometric profile and (B) number of Sirp α ⁺ CD24⁻ and Sirp α ⁺ CD24⁺ cDC2s in the lung of WT or *Irf3*^{-/-} mice treated 24h earlier with HDM or PBS excipient (n.s. in an ANOVA, data presented as mean $\pm$ SEM). Data are pooled from 2 independent experiments (n=3 mice/group per experiment).

Supporting information Table 1. List of differentially expressed probesets in lung cDC2s from wild-type mice exposed to intranasal house dust mite or PBS as determined by microarray analysis.

Probe ID	Fold change	P value	ENTREZ ID	MGI symbol	Description
10379633	32.30368589	0.001406661	20555	Slfn1	schlafen 1
10462621	26.91392776	0.001070116	667370	I830012O16Rik	RIKEN cDNA I830012O16 gene
10462613	25.27107703	0.000606561	15958	Ifit2	interferon-induced protein with tetratricopeptide repeats 2
10399710	24.4700369	0.000606561	58185	Rsad2	radical S-adenosyl methionine domain containing 2
10379636	24.00511918	0.000606561	20558	Slfn4	schlafen 4
10462623	21.87147032	0.000606561	15957	Ifit1	interferon-induced protein with tetratricopeptide repeats 1
10524631	18.61992824	0.000606561	231655	Oas1	2'-5' oligoadenylate synthetase-like 1
10360373	17.26492571	0.000869035	623121	Pydc4	pyrin domain containing 4
10462618	17.10091268	0.000606561	15959	Ifit3	interferon-induced protein with tetratricopeptide repeats 3
10451287	17.04498554	0.001070116	677168	Gm9706	predicted gene 9706
10395039	16.56673194	0.000606561	22169	Cmpk2	cytidine monophosphate (UMP-CMP) kinase 2, mitochondrial
10569102	15.62326624	0.000606561	54123	Irf7	interferon regulatory factor 7
10360367	15.58312298	0.001889188	NA	NA	NA
10533213	14.26993145	0.000802248	246727	Oas3	2'-5' oligoadenylate synthetase 3
10502791	13.91944637	0.001691006	99899	Ifi44	interferon-induced protein 44
10439009	13.6946494	0.001076007	11815	Apod	apolipoprotein D
10554240	12.88377005	0.000606561	57444	Isg20	interferon-stimulated protein
10429560	12.66844384	0.000606561	57248	Ly6i	lymphocyte antigen 6 complex, locus I
10455970	12.45393036	0.022812171	NA	NA	NA
10531420	12.21137813	0.002379478	56066	Cxcl11	chemokine (C-X-C motif) ligand 11
10437224	12.19084379	0.000606561	17858	Mx2	MX dynamin-like GTPase 2
10496539	12.09605955	0.000606561	229898	Gbp5	guanylate binding protein 5
10351880	11.97095625	0.001768381	NA	NA	NA
10490150	11.40932997	0.000606561	58203	Zbp1	Z-DNA binding protein 1
10420497	10.82452432	0.001734551	628705	Phf11c	PHD finger protein 11C
10376324	10.62104629	0.000685255	631323	Gm12250	predicted gene 12250
10360370	10.5949625	0.000759202	545384	BC094916	cDNA sequence BC094916
10544982	10.25830911	0.001406661	107569	Nt5c3	5'-nucleotidase, cytosolic III
10490903	10.06375732	0.000634536	71934	Car13	carbonic anhydrase 13
10599598	9.99538093	0.004365243	100504594	A630012P03Rik	RIKEN cDNA A630012P03 gene
10466314	9.687852919	0.002614397	NA	NA	NA
10531987	9.675738414	0.001191975	NA	NA	NA
10434778	9.604245092	0.000606561	67775	Rtp4	receptor transporter protein 4
10580752	9.602062859	0.00687446	320377	9330175E14Rik	RIKEN cDNA 9330175E14 gene
10385518	9.553555966	0.000869035	NA	NA	NA
10450325	9.262423381	0.000606561	NA	NA	NA
10490632	9.027057153	0.000606561	229003	Helz2	helicase with zinc finger 2, transcriptional coactivator
10571984	8.738741577	0.001070116	234311	Ddx60	DEAD (Asp-Glu-Ala-Asp) box polypeptide 60
10455954	8.662600339	0.002115596	240327	Gm4951	predicted gene 4951
10385533	8.544926349	0.001070116	NA	NA	NA
10378068	8.450572543	0.000685255	327959	Xaf1	XIAP associated factor 1
10455961	8.217903621	0.002289775	NA	NA	NA
10538590	8.149333868	0.001070116	67138	Herc6	hect domain and RLD 6
10375515	8.080305002	0.002585338	NA	NA	NA
10533198	8.028864675	0.000781347	246728	Oas2	2'-5' oligoadenylate synthetase 2
10450675	7.9667018	0.000781347	15042	H2-T24	histocompatibility 2, T region locus 24
10400299	7.834283703	0.002747018	14762	Gpr33	G protein-coupled receptor 33
10385507	7.513566959	0.013095727	620913	Gm12185	predicted gene 12185
10524621	7.499126058	0.000869035	23962	Oas2	2'-5' oligoadenylate synthetase-like 2
10420488	7.440779524	0.001070116	219132	Phf11d	PHD finger protein 11D
10389190	7.423194716	0.000869035	629303	Heat9	HEAT repeat containing 9
10531724	7.268350206	0.01063193	231507	Plac8	placenta-specific 8
10389143	6.79625176	0.001459533	276950	Slfn8	schlafen 8
10360382	6.787685875	0.001352589	NA	NA	NA
10541307	6.740559725	0.001070116	24110	Usp18	ubiquitin specific peptidase 18
10376326	6.708296615	0.001070116	NA	NA	NA

10582862	6.697066701	0.001406661	NA	NA	NA
10531994	6.635611706	0.001070116	NA	NA	NA
10531415	6.612923017	0.001489965	15945	Cxcl10	chemokine (C-X-C motif) ligand 10
10391207	6.587645772	0.000869035	80861	Dhx58	DEXH (Asp-Glu-X-His) box polypeptide 58
10466932	6.535661007	0.001070116	27356	InsI6	insulin-like 6
10537426	6.480601771	0.000887825	75379	4930599N23Rik	RIKEN cDNA 4930599N23 gene
10584458	6.394981035	0.002487495	258783	Olfir920	olfactory receptor 920
10530692	6.260308532	0.001406661	16542	Kdr	kinase insert domain protein receptor
10592888	6.233919388	0.001076007	12145	Cxcr5	chemokine (C-X-C motif) receptor 5
10441233	6.195850065	0.001070116	17857	Mx1	MX dynamin-like GTPase 1
10525158	6.138845932	0.001191975	NA	NA	NA
10385500	6.118736892	0.001070116	15944	Irgm1	immunity-related GTPase family M member 1
10608681	6.117357992	0.03657386	225594	Gm4841	predicted gene 4841
10444056	6.10082253	0.004015715	13163	Daxx	Fas death domain-associated protein
10379708	6.045683812	0.000887825	NA	NA	NA
10466127	6.001897464	0.001691006	107350	AW112010	expressed sequence AW112010
10473356	5.984793145	0.001070116	56791	Ube2I6	ubiquitin-conjugating enzyme E2L 6
10496975	5.979656939	0.001070116	242259	Slc44a5	solute carrier family 44, member 5
10383208	5.857988018	0.001191975	672511	Rnf213	ring finger protein 213
10496592	5.849712025	0.001070116	14469	Gbp2	guanylate binding protein 2
10531407	5.819565165	0.001070116	17329	Cxcl9	chemokine (C-X-C motif) ligand 9
10512067	5.794083821	0.001076007	230073	Ddx58	DEAD (Asp-Glu-Ala-Asp) box polypeptide 58
10416837	5.77253394	0.003967809	16365	Irg1	immunoresponsive gene 1
10420483	5.74865494	0.007029423	219131	Phf11a	PHD finger protein 11A
10483110	5.677673279	0.002379478	71586	Ifih1	interferon induced with helicase C domain 1
10434291	5.632928715	0.001191975	108105	B3gnt5	UDP-GlcNAc:betaGal beta-1,3-N-acetylglucosaminyltransferase 5
10533246	5.621170566	0.001489965	23960	Oas1g	2'-5' oligoadenylate synthetase 1G
10533256	5.5841972	0.001070116	246730	Oas1a	2'-5' oligoadenylate synthetase 1A
10383210	5.573955522	0.001070116	672511	Rnf213	ring finger protein 213
10579532	5.544998568	0.001710547	69550	Bst2	bone marrow stromal cell antigen 2
10389134	5.536501717	0.00245221	237886	Slfn9	schlafen 9
10398039	5.534738342	0.002204659	NA	NA	NA
10417526	5.528563175	0.001986809	13421	Dnase1I3	deoxyribonuclease 1-like 3
10581813	5.518125549	0.003863885	74568	Mlkl	mixed lineage kinase domain-like
10469289	5.494607911	0.001070116	16169	Il15ra	interleukin 15 receptor, alpha chain
10582860	5.41911381	0.003250833	NA	NA	NA
10582877	5.41911381	0.003250833	NA	NA	NA
10594053	5.404374127	0.001070116	18854	Pml	promyelocytic leukemia
10345527	5.385287928	0.036818177	NA	NA	NA
10347919	5.361067961	0.002712038	NA	NA	NA
10356291	5.361067961	0.002712038	NA	NA	NA
10513722	5.330276671	0.001406661	326623	Tnfsf15	tumor necrosis factor (ligand) superfamily, member 15
10383206	5.322475737	0.001070116	672511	Rnf213	ring finger protein 213
10579958	5.310383596	0.003069664	16168	Il15	interleukin 15
10500911	5.303033909	0.001070116	17454	Mov10	Moloney leukemia virus 10
10339171	5.301266067	0.002146606	NA	NA	NA
10506714	5.255083217	0.001070116	16975	Lrp8	low density lipoprotein receptor-related protein 8, apolipoprotein e receptor
10383200	5.245599688	0.001070116	672511	Rnf213	ring finger protein 213
10439651	5.242218444	0.001070116	17470	Cd200	CD200 antigen
10429564	5.172555186	0.001125923	110454	Ly6a	lymphocyte antigen 6 complex, locus A
10383192	5.035554479	0.001214385	672511	Rnf213	ring finger protein 213
10472350	5.030905827	0.002669387	227960	Gca	grancalcin
10566366	5.021989721	0.001070116	209387	Trim30d	tripartite motif-containing 30D
10469278	4.979956986	0.001352589	16184	Il2ra	interleukin 2 receptor, alpha chain
10497689	4.965553567	0.001076007	14696	Gnb4	guanine nucleotide binding protein (G protein), beta 4
10452980	4.963079662	0.003392094	19106	Eif2ak2	eukaryotic translation initiation factor 2-alpha kinase 2
10367224	4.944398011	0.001070116	20847	Stat2	signal transducer and activator of transcription 2
10542287	4.929957956	0.001489965	66813	Bcl2l14	BCL2-like 14 (apoptosis facilitator)
10574145	4.918277439	0.001459533	434341	Nlrc5	NLR family, CARD domain containing 5
10389151	4.901933305	0.001889188	NA	NA	NA
10368616	4.89863521	0.002204659	72580	Zufsp	zinc finger with UFM1-specific peptidase domain
10458028	4.87112763	0.001070116	71683	Gypc	glycophorin C

10383196	4.856467547	0.001070116	672511	Rnf213	ring finger protein 213
10574135	4.844080397	0.002632952	434341	Nlrc5	NLR family, CARD domain containing 5
10383212	4.839713869	0.001076007	672511	Rnf213	ring finger protein 213
10383204	4.76870472	0.001150617	672511	Rnf213	ring finger protein 213
10395273	4.754869616	0.002422501	100504486	Gdap10	ganglioside-induced differentiation-associated-protein 10
10419578	4.751715153	0.010684631	29811	Ndrp2	N-myc downstream regulated gene 2
10375341	4.710129463	0.002445448	NA	NA	NA
10379615	4.702892393	0.003554753	327978	Slfn5	schlafen 5
10492556	4.67990207	0.001070116	68725	1110032F04Rik	RIKEN cDNA 1110032F04 gene
10406852	4.679543838	0.003967809	NA	NA	NA
10346191	4.64936483	0.001788881	20846	Stat1	signal transducer and activator of transcription 1
10360406	4.638963846	0.002841911	226695	Ifi205	interferon activated gene 205
10435514	4.615368679	0.001352589	106347	Ildr1	immunoglobulin-like domain containing receptor 1
10383194	4.605652877	0.001070116	672511	Rnf213	ring finger protein 213
10563597	4.566934781	0.04543112	20210	Saa3	serum amyloid A 3
10347933	4.533135489	0.001150617	NA	NA	NA
10356269	4.530949308	0.001125923	381287	A530032D15Rik	RIKEN cDNA A530032D15Rik gene
10379646	4.518738699	0.001734551	20557	Slfn3	schlafen 3
10385504	4.486979141	0.003863885	432555	Gm5431	predicted gene 5431
10439249	4.48052992	0.001710547	547253	Parp14	poly (ADP-ribose) polymerase family, member 14
10383198	4.446159426	0.001282074	672511	Rnf213	ring finger protein 213
10574139	4.431131939	0.001734551	434341	Nlrc5	NLR family, CARD domain containing 5
10587659	4.420492016	0.002451309	NA	NA	NA
10474181	4.397634116	0.002422501	99382	Abtb2	ankyrin repeat and BTB (POZ) domain containing 2
10383233	4.373951436	0.001556066	672511	Rnf213	ring finger protein 213
10383152	4.371624302	0.001150617	672511	Rnf213	ring finger protein 213
10429140	4.350550452	0.00334505	17988	Ndrp1	N-myc downstream regulated gene 1
10545135	4.322547706	0.001989563	16162	Il12rb2	interleukin 12 receptor, beta 2
10519482	4.313058484	0.013327789	667705	Gm8773	predicted gene 8773
10383202	4.295674111	0.001191975	672511	Rnf213	ring finger protein 213
10496580	4.241246919	0.008738242	55932	Gbp3	guanylate binding protein 3
10574157	4.234604866	0.002735366	434341	Nlrc5	NLR family, CARD domain containing 5
10491091	4.222133035	0.002379478	22035	Tnfrsf10	tumor necrosis factor (ligand) superfamily, member 10
10595371	4.193107338	0.007204029	94353	Hmgn3	high mobility group nucleosomal binding domain 3
10500710	4.192706574	0.001352589	242125	Mab2113	mab-21-like 3 (C. elegans)
10435457	4.185100382	0.001489965	80285	Parp9	poly (ADP-ribose) polymerase family, member 9
10482517	4.177400289	0.001851186	64685	Nmi	N-myc (and STAT) interactor
10483381	4.168978783	0.002163126	53416	Stk39	serine/threonine kinase 39
10462683	4.154878884	0.004987651	76073	Pcgf5	polycomb group ring finger 5
10347925	4.149132848	0.002423268	NA	NA	NA
10461093	4.145865381	0.019855197	225845	Pla2g16	phospholipase A2, group XVI
10495659	4.119298989	0.004741793	71994	Cnn3	calponin 3, acidic
10574163	4.103628449	0.00245221	434341	Nlrc5	NLR family, CARD domain containing 5
10566050	4.101267039	0.007029423	16068	Il18bp	interleukin 18 binding protein
10403229	4.070959033	0.005242984	320910	Itgb8	integrin beta 8
10531980	4.069886721	0.005317021	236573	Gbp9	guanylate-binding protein 9
10347915	4.069510332	0.002394448	100503923	LOC100503923	uncharacterized LOC100503923
10437205	4.025962955	0.004661133	NA	NA	NA
10359181	3.995818583	0.002311838	30935	Tor3a	torsin family 3, member A
10544133	3.994826017	0.001691006	243771	Parp12	poly (ADP-ribose) polymerase family, member 12
10574104	3.983607934	0.001489965	434341	Nlrc5	NLR family, CARD domain containing 5
10383214	3.964881396	0.002268952	672511	Rnf213	ring finger protein 213
10356248	3.95630021	0.001691006	NA	NA	NA
10383168	3.955767839	0.001734551	672511	Rnf213	ring finger protein 213
10411459	3.94635148	0.002721248	380863	Tmem171	transmembrane protein 171
10582879	3.94466228	0.002735366	NA	NA	NA
10439442	3.935680828	0.007611914	85031	Pla1a	phospholipase A1 member A
10350800	3.901821576	0.001734551	240832	Tor1aip2	torsin A interacting protein 2
10363195	3.890477182	0.003849533	15500	Hsf2	heat shock factor 2
10560608	3.859097053	0.004554071	11813	Apoc2	apolipoprotein C-II
10346168	3.84405686	0.002320223	20849	Stat4	signal transducer and activator of transcription 4
10368644	3.837479795	0.013828424	215900	Fam26f	family with sequence similarity 26, member F

10519270	3.817594914	0.001710547	11603	Agri	agrin
10547976	3.792859932	0.001691006	213233	Tapbpl	TAP binding protein-like
10566350	3.755201355	0.002379478	244183	Trim30b	tripartite motif-containing 30B
10351873	3.749121612	0.001889188	236312	Pyhin1	pyrin and HIN domain family, member 1
10452301	3.745245527	0.005347624	21948	Cd70	CD70 antigen
10410931	3.744237888	0.02495198	13003	Vcan	versican
10346960	3.740597221	0.002601433	227210	Ccnyl1	cyclin Y-like 1
10510270	3.719397087	0.004661133	17769	Mthfr	5,10-methylenetetrahydrofolate reductase
10550627	3.711873736	0.003460976	319197	Gpr4	G protein-coupled receptor 4
10574137	3.70711745	0.002146606	434341	Nlrc5	NLR family, CARD domain containing 5
10404439	3.692074727	0.002422501	20706	Serpinb9b	serine (or cysteine) peptidase inhibitor, clade B, member 9b
10574133	3.691502976	0.003324094	434341	Nlrc5	NLR family, CARD domain containing 5
10351197	3.686249892	0.014512553	20343	Sell	selectin, lymphocyte
10420503	3.678487972	0.012177093	239122	Setdb2	SET domain, bifurcated 2
10574143	3.675991772	0.002379478	434341	Nlrc5	NLR family, CARD domain containing 5
10356271	3.673574282	0.001710547	381287	A530032D15Rik	RIKEN cDNA A530032D15Rik gene
10574159	3.671515152	0.002632952	434341	Nlrc5	NLR family, CARD domain containing 5
10377010	3.649375742	0.00585028	52892	Sco1	SCO cytochrome oxidase deficient homolog 1 (yeast)
10574098	3.648562383	0.003523902	434341	Nlrc5	NLR family, CARD domain containing 5
10402347	3.646589092	0.011307051	76933	Ifi2712a	interferon, alpha-inducible protein 27 like 2A
10405125	3.644432014	0.004937269	109082	Fbxw17	F-box and WD-40 domain protein 17
10595836	3.636664388	0.005242984	NA	NA	NA
10347968	3.614727958	0.001994407	20684	Sp100	nuclear antigen Sp100
10608719	3.603637745	0.001734551	231002	Plekhn1	pleckstrin homology domain containing, family N member 1
10356274	3.60284212	0.004437039	NA	NA	NA
10404429	3.595298093	0.001807494	20723	Serpinb9	serine (or cysteine) peptidase inhibitor, clade B, member 9
10360410	3.586687712	0.002163126	404222	Olfrc231	olfactory receptor 231
10574102	3.584106007	0.002130807	434341	Nlrc5	NLR family, CARD domain containing 5
10482929	3.576942617	0.003535142	17076	Ly75	lymphocyte antigen 75
10356267	3.567188836	0.002422501	381287	A530032D15Rik	RIKEN cDNA A530032D15Rik gene
10499160	3.562450861	0.002138463	12479	Cd1d1	CD1d1 antigen
10395259	3.561677748	0.001710547	59027	Nampt	nicotinamide phosphoribosyltransferase
10420362	3.56045298	0.002487495	14619	Gjb2	gap junction protein, beta 2
10452613	3.558194473	0.002614397	268970	Arhgap28	Rho GTPase activating protein 28
10455957	3.54213934	0.028556634	NA	NA	NA
10574151	3.521947914	0.00242761	434341	Nlrc5	NLR family, CARD domain containing 5
10381408	3.516796519	0.00242761	70110	Ifi35	interferon-induced protein 35
10479833	3.51579932	0.004741793	71648	Optn	optineurin
10341175	3.511382538	0.035407122	NA	NA	NA
10364722	3.503959923	0.003533684	13637	Efna2	ephrin A2
10461622	3.502363777	0.008311382	69774	Ms4a6b	membrane-spanning 4-domains, subfamily A, member 6B
10535174	3.496779123	0.037768659	231832	Tmem184a	transmembrane protein 184a
10574149	3.496574565	0.002735366	434341	Nlrc5	NLR family, CARD domain containing 5
10359375	3.494661755	0.013088068	620246	Gpr52	G protein-coupled receptor 52
10429843	3.489910836	0.002146606	NA	NA	NA
10572772	3.481651985	0.002311838	209488	Hsh2d	hematopoietic SH2 domain containing
10574161	3.480342325	0.00209843	434341	Nlrc5	NLR family, CARD domain containing 5
10532019	3.480290308	0.002320223	NA	NA	NA
10453049	3.4716421	0.010529111	260409	Cdc42ep3	CDC42 effector protein (Rho GTPase binding) 3
10500335	3.461714713	0.015229292	14129	Fcgr1	Fc receptor, IgG, high affinity I
10439268	3.457544666	0.002601433	NA	NA	NA
10423593	3.440783102	0.002379478	114128	Laptm4b	lysosomal-associated protein transmembrane 4B
10461605	3.426654688	0.003069664	60361	Ms4a4b	membrane-spanning 4-domains, subfamily A, member 4B
10569168	3.408835124	0.00310807	68267	Slc25a22	solute carrier family 25 (mitochondrial carrier, glutamate), member 22
10574141	3.408121626	0.002268952	434341	Nlrc5	NLR family, CARD domain containing 5
10347921	3.406638493	0.004686384	621875	A530040E14Rik	RIKEN cDNA A530040E14 gene
10566144	3.397984954	0.002445448	20821	Trim21	tripartite motif-containing 21
10534909	3.373842246	0.002204659	624083	Gm15753	predicted gene 15753
10429568	3.363442336	0.019550716	NA	NA	NA
10608646	3.359480366	0.010904597	435565	Iigp1b	interferon inducible GTPase 1B
10347928	3.350419154	0.002059091	NA	NA	NA
10582874	3.350419154	0.002059091	NA	NA	NA

10582868	3.333193281	0.002204659	664787	LOC664787	Sp110 nuclear body protein-like
10574155	3.322691196	0.002747018	434341	Nlrc5	NLR family, CARD domain containing 5
10585778	3.315116184	0.002955045	20361	Sema7a	sema domain, immunoglobulin domain (Ig), and GPI membrane anchor, (semaphorin) 7A
10545921	3.2973263	0.004554071	17119	Mxd1	MAX dimerization protein 1
10356278	3.290134614	0.002146606	NA	NA	NA
10436662	3.280058337	0.004054633	NA	NA	NA
10545154	3.25569707	0.018950042	209590	Il23r	interleukin 23 receptor
10576034	3.252426367	0.002735366	15900	Irf8	interferon regulatory factor 8
10350792	3.235107952	0.002311838	240832	Tor1aip2	torsin A interacting protein 2
10504672	3.233208257	0.002268952	100121	Tdrd7	tudor domain containing 7
10531972	3.231876133	0.002422501	76074	Gbp8	guanylate-binding protein 8
10496569	3.215607385	0.003562641	229900	Gbp7	guanylate binding protein 7
10499811	3.190975778	0.008858383	18160	Npr1	natriuretic peptide receptor 1
10582008	3.190544355	0.003537065	66531	Cmc2	COX assembly mitochondrial protein 2
10341446	3.182148966	0.009748851	NA	NA	NA
10489850	3.17600705	0.004661133	98999	Znfx1	zinc finger, NFX1-type containing 1
10535065	3.174423518	0.002735366	231821	Adap1	ArfGAP with dual PH domains 1
10560644	3.169756247	0.003849533	19294	Pvrl2	poliovirus receptor-related 2
10542040	3.163406928	0.002268952	101187	Parp11	poly (ADP-ribose) polymerase family, member 11
10522368	3.162926916	0.002735366	70701	Nipal1	NIPA-like domain containing 1
10595638	3.162838301	0.002747018	NA	NA	NA
10462603	3.159684141	0.004661133	14102	Fas	Fas (TNF receptor superfamily member 6)
10566346	3.159465799	0.003863885	319236	Trim12c	tripartite motif-containing 12C
10404422	3.15880096	0.003961516	20708	Serpinb6b	serine (or cysteine) peptidase inhibitor, clade B, member 6b
10389238	3.134136871	0.012741859	56405	Dusp14	dual specificity phosphatase 14
10516064	3.123868311	0.010994906	76574	Mfsd2a	major facilitator superfamily domain containing 2A
10448278	3.120203298	0.003392094	240047	Mmp25	matrix metalloproteinase 25
10462398	3.119277684	0.00257849	58205	Pdcd1lg2	programmed cell death 1 ligand 2
10511282	3.11205471	0.003464695	22163	Tnfrsf4	tumor necrosis factor receptor superfamily, member 4
10403273	3.109923171	0.008660395	142688	Asb13	ankyrin repeat and SOCS box-containing 13
10587665	3.109445896	0.003554753	NA	NA	NA
10455784	3.079694197	0.003324094	107022	Gramd3	GRAM domain containing 3
10349081	3.057654213	0.002422501	98432	Phlpp1	PH domain and leucine rich repeat protein phosphatase 1
10542677	3.047284898	0.003901539	75320	Etnk1	ethanolamine kinase 1
10500378	3.023112594	0.004208873	78373	Nudt17	nudix (nucleoside diphosphate linked moiety X)-type motif 17
10569890	3.019457438	0.004367116	108909	Aida	axin interactor, dorsalization associated
10375331	3.017606879	0.003453201	16160	Il12b	interleukin 12b
10366407	3.014450881	0.005570598	100038558	Gm10752	predicted gene 10752
10502071	3.012985163	0.006851472	70617	5730508B09Rik	RIKEN cDNA 5730508B09 gene
10544891	3.012124845	0.003155165	107607	Nod1	nucleotide-binding oligomerization domain containing 1
10340350	3.008346061	0.031077453	NA	NA	NA
10560174	2.998580144	0.005317021	20364	Sepw1	selenoprotein W, muscle 1
10537227	2.998418862	0.005148528	68487	Tmem140	transmembrane protein 140
10354054	2.997759119	0.007061181	69028	Mitd1	MIT, microtubule interacting and transport, domain containing 1
10338178	2.993796647	0.027543146	NA	NA	NA
10493565	2.962925961	0.003050484	56417	Adar	adenosine deaminase, RNA-specific
10412562	2.959365033	0.00313588	286940	Flnb	filamin, beta
10450145	2.954523961	0.003112809	16912	Psmb9	proteasome (prosome, macropain) subunit, beta type 9 (large multifunctional peptidase 2)
10490826	2.953139477	0.01308743	229055	Zbtb10	zinc finger and BTB domain containing 10
10396831	2.949011441	0.002601433	11847	Arg2	arginase type II
10432190	2.947953231	0.003464695	11512	Adcy6	adenylate cyclase 6
10485624	2.946432582	0.006964294	228413	Prrg4	proline rich Gla (G-carboxyglutamic acid) 4 (transmembrane)
10542911	2.939213894	0.028731993	209086	Samd9l	sterile alpha motif domain containing 9-like
10345913	2.937369145	0.003370281	17974	Nck2	non-catalytic region of tyrosine kinase adaptor protein 2
10347948	2.936960251	0.003592662	20684	Sp100	nuclear antigen Sp100
10360391	2.925465502	0.014703404	NA	NA	NA
10342727	2.923187784	0.005871742	NA	NA	NA
10478678	2.920823745	0.007526959	21939	Cd40	CD40 antigen
10346562	2.917656069	0.007472686	12633	Cflar	CASP8 and FADD-like apoptosis regulator
10370000	2.917464048	0.009196537	14871	Gstt1	glutathione S-transferase, theta 1
10368534	2.915285105	0.008106866	211329	Ncoa7	nuclear receptor coactivator 7
10548345	2.91133817	0.025004936	27007	Klrk1	killer cell lectin-like receptor subfamily K, member 1

10356262	2.908181902	0.002735366	NA	NA	NA
10414514	2.89231567	0.005681459	18950	Pnp	purine-nucleoside phosphorylase
10563891	2.891760237	0.003752271	NA	NA	NA
10467182	2.886435806	0.004367116	15566	Htr7	5-hydroxytryptamine (serotonin) receptor 7
10566358	2.885522152	0.002735366	20128	Trim30a	tripartite motif-containing 30A
10486448	2.884753552	0.005335022	271844	Pla2g4f	phospholipase A2, group IVF
10462791	2.881417533	0.00687639	69104	05-mars	membrane-associated ring finger (C3HC4) 5
10363541	2.878978346	0.002747018	NA	NA	NA
10367919	2.878318295	0.004058421	74732	Stx11	syntaxin 11
10460767	2.875031631	0.019470053	74481	Batf2	basic leucine zipper transcription factor, ATF-like 2
10566574	2.872454944	0.003961516	NA	NA	NA
10388902	2.867061796	0.005040262	16859	Lgals9	lectin, galactose binding, soluble 9
10414374	2.866041692	0.010367375	16709	Ktn1	kinectin 1
10471154	2.865250433	0.003069664	NA	NA	NA
10444268	2.856569992	0.003145004	21355	Tap2	transporter 2, ATP-binding cassette, sub-family B (MDR/TAP)
10344015	2.855000955	0.039680772	NA	NA	NA
10570855	2.854729007	0.008454783	18791	Plat	plasminogen activator, tissue
10479411	2.850056642	0.002735366	72075	Ogfr	opioid growth factor receptor
10361828	2.848606714	0.016406184	17684	Cited2	Cbp/p300-interacting transactivator, with Glu/Asp-rich carboxy-terminal domain, 2
10372069	2.839764516	0.003191557	216233	Socs2	suppressor of cytokine signaling 2
10462390	2.838942694	0.00310807	60533	Cd274	CD274 antigen
10369102	2.837801876	0.004058421	100038725	Cep85l	centrosomal protein 85-like
10566326	2.834945593	0.003866706	76681	Trim12a	tripartite motif-containing 12A
10523012	2.833092305	0.003392094	13178	Dck	deoxycytidine kinase
10514289	2.828438065	0.004661133	NA	NA	NA
10510509	2.816427022	0.003940443	269604	Gpr157	G protein-coupled receptor 157
10369911	2.809229327	0.003967809	68778	Gucd1	guanylyl cyclase domain containing 1
10355246	2.792359215	0.016725023	11363	Acadl	acyl-Coenzyme A dehydrogenase, long-chain
10530633	2.790604541	0.010101046	24051	Sgcb	sarcoglycan, beta (dystrophin-associated glycoprotein)
10363498	2.790312335	0.004103856	67895	Ppa1	pyrophosphatase (inorganic) 1
10425808	2.786123986	0.003192109	12257	Tspo	translocator protein
10467149	2.770508921	0.011416892	112419	2010002M12Rik	RIKEN cDNA 2010002M12 gene
10578763	2.768893678	0.008660395	60406	Sap30	sin3 associated polypeptide
10526459	2.762479283	0.003370281	54153	Rasa4	RAS p21 protein activator 4
10444244	2.759392505	0.003060713	21354	Tap1	transporter 1, ATP-binding cassette, sub-family B (MDR/TAP)
10341111	2.758583895	0.004161345	NA	NA	NA
10596492	2.758007285	0.009844316	235587	Parp3	poly (ADP-ribose) polymerase family, member 3
10598152	2.749543373	0.008660395	625360	BC147527	cDNA sequence BC147527
10533304	2.749192142	0.005347979	231712	Traf1	TRAF type zinc finger domain containing 1
10477717	2.743817672	0.013800125	19124	Procr	protein C receptor, endothelial
10607950	2.739046505	0.038031971	654820	G530011O06Rik	RIKEN cDNA G530011O06 gene
10451613	2.732034171	0.012680239	74123	Foxp4	forkhead box P4
10356876	2.729325424	0.037385881	NA	NA	NA
10545930	2.721617942	0.004058421	NA	NA	NA
10583820	2.717019995	0.013981906	619310	Zfp872	zinc finger protein 872
10608650	2.709481673	0.003460976	15051	H2-T9	histocompatibility 2, T region locus 9
10406598	2.708010551	0.003535142	218442	Serinc5	serine incorporator 5
10519219	2.707484185	0.008262506	79554	Ctp	ceramide-1-phosphate transfer protein
10545623	2.707257115	0.017740989	13448	Dok1	docking protein 1
10468992	2.690383189	0.00334505	209630	Frmf4a	FERM domain containing 4A
10476945	2.689996554	0.006948414	13011	Cst7	cystatin F (leukocystatin)
10590791	2.689884801	0.009483476	11797	Birc2	baculoviral IAP repeat-containing 2
10399202	2.680581975	0.003460976	238455	Macc1	metastasis associated in colon cancer 1
10608680	2.673692873	0.003324094	15024	H2-T10	histocompatibility 2, T region locus 10
10481627	2.657469265	0.014276122	16819	Lcn2	lipocalin 2
10367982	2.657088992	0.003961516	215798	Gpr126	G protein-coupled receptor 126
10552252	2.640880796	0.003535142	72244	1600014C10Rik	RIKEN cDNA 1600014C10 gene
10595805	2.640329381	0.007468949	114713	Rasa2	RAS p21 protein activator 2
10367532	2.640150462	0.012413816	67596	Tespa1	thymocyte expressed, positive selection associated 1
10538993	2.63801695	0.005383416	12525	Cd8a	CD8 antigen, alpha chain
10521832	2.630543461	0.013088068	67073	Pi4k2b	phosphatidylinositol 4-kinase type 2 beta
10385511	2.621816718	0.004341377	NA	NA	NA

10394054	2.620075201	0.020748755	12516	Cd7	CD7 antigen
10371607	2.600145085	0.012741859	71712	Dram1	DNA-damage regulated autophagy modulator 1
10355456	2.59341845	0.003638095	381269	Mreg	melanoregulin
10584435	2.592112795	0.005347979	67776	Vwa5a	von Willebrand factor A domain containing 5A
10549544	2.585591084	0.008199033	100038707	Gm10388	predicted gene 10388
10361133	2.585376971	0.005141245	NA	NA	NA
10339773	2.585376249	0.00653615	NA	NA	NA
10368175	2.580684546	0.011990618	29863	Pde7b	phosphodiesterase 7B
10596960	2.575140215	0.007029423	NA	NA	NA
10442075	2.573484534	0.004661133	626942	Vmn2r90	vomeronasal 2, receptor 90
10439845	2.573189786	0.004977567	433024	Gm5486	predicted gene 5486
10519527	2.571406392	0.004058421	18671	Abcb1a	ATP-binding cassette, sub-family B (MDR/TAP), member 1A
10562605	2.56679863	0.005747821	233168	AI987944	expressed sequence AI987944
10416566	2.565621325	0.012190127	108670	Epsti1	epithelial stromal interaction 1 (breast)
10574153	2.561264424	0.005210168	434341	Nlr5	NLR family, CARD domain containing 5
10581378	2.559309374	0.005570598	19171	Psmb10	proteasome (prosome, macropain) subunit, beta type 10
10462406	2.559024101	0.008047332	226089	Ric1	RAB6A GEF complex partner 1
10588836	2.539132884	0.012692718	331026	Gmppb	GDP-mannose pyrophosphorylase B
10608715	2.539051577	0.004719034	74183	Perm1	PPARGC1 and ESRR induced regulator, muscle 1
10339806	2.534985581	0.004661133	NA	NA	NA
10516852	2.53320841	0.005347979	18386	Oprd1	opioid receptor, delta 1
10507933	2.532728114	0.008199033	16330	Inpp5b	inositol polyphosphate-5-phosphatase B
10514285	2.53075578	0.009854249	15977	Ifnb1	interferon beta 1, fibroblast
10351588	2.530267138	0.00541337	71740	Pvrl4	poliovirus receptor-related 4
10584460	2.517652631	0.00585028	258778	Olfir921	olfactory receptor 921
10574147	2.517128458	0.017886472	NA	NA	NA
10601581	2.513325059	0.0136789	NA	NA	NA
10579744	2.505342161	0.011192203	16795	Large	like-glycosyltransferase
10378816	2.50504166	0.005149359	15567	Slc6a4	solute carrier family 6 (neurotransmitter transporter, serotonin), member 4
10429573	2.504323107	0.038723398	NA	NA	NA
10439854	2.504116224	0.008670295	70508	Bbx	bobby sox homolog (Drosophila)
10606730	2.503928103	0.005239272	278097	Armxc6	armadillo repeat containing, X-linked 6
10344135	2.496190874	0.033275059	NA	NA	NA
10381872	2.492472073	0.025443758	24086	Tlk2	tousled-like kinase 2 (Arabidopsis)
10469276	2.490759466	0.004987651	100038528	Gm10851	predicted gene 10851
10495574	2.487255258	0.008738242	72776	Sass6	spindle assembly 6 homolog (C. elegans)
10359339	2.4834765	0.009285291	29809	Rabgap11	RAB GTPase activating protein 1-like
10577586	2.482009737	0.004367116	64933	Ap3m2	adaptor-related protein complex 3, mu 2 subunit
10450694	2.478645989	0.004296272	NA	NA	NA
10490923	2.476527365	0.005455572	12349	Car2	carbonic anhydrase 2
10460582	2.465679804	0.005347624	107242	AI837181	expressed sequence AI837181
10394674	2.465399568	0.004661133	NA	NA	NA
10487238	2.462559492	0.01063193	15186	Hdc	histidine decarboxylase
10371616	2.45970534	0.006283358	212862	Chpt1	choline phosphotransferase 1
10483081	2.458608798	0.006082292	14089	Fap	fibroblast activation protein
10591482	2.458145126	0.005040262	50868	Keap1	kelch-like ECH-associated protein 1
10425890	2.456789459	0.015255057	73167	Arhgap8	Rho GTPase activating protein 8
10459455	2.455887648	0.027292651	225638	Alpk2	alpha-kinase 2
10445767	2.443091298	0.019886416	328833	Trem12	triggering receptor expressed on myeloid cells-like 2
10547807	2.441539343	0.02483647	13807	Eno2	enolase 2, gamma neuronal
10426611	2.437988255	0.004719034	12297	Cacnb3	calcium channel, voltage-dependent, beta 3 subunit
10469816	2.437116039	0.032607999	16181	Il1m	interleukin 1 receptor antagonist
10437668	2.433966171	0.010367375	12703	Socs1	suppressor of cytokine signaling 1
10539739	2.432503133	0.032741434	67855	Asprv1	aspartic peptidase, retroviral-like 1
10340333	2.432396585	0.013973984	NA	NA	NA
10364030	2.430176842	0.004459738	11540	Adora2a	adenosine A2a receptor
10556280	2.428432812	0.004850495	20947	Swap70	SWA-70 protein
10373502	2.420521431	0.005018746	22781	Ikzf4	IKAROS family zinc finger 4
10490838	2.419553129	0.006152069	NA	NA	NA
10379401	2.417993008	0.00724137	71956	Rnf135	ring finger protein 135
10567987	2.415484228	0.027913412	246779	Il27	interleukin 27
10445774	2.410935678	0.015276296	320148	B430306N03Rik	RIKEN cDNA B430306N03 gene

10518735	2.410025712	0.006744163	74646	Spsb1	splA/ryanodine receptor domain and SOCS box containing 1
10436561	2.40480671	0.009003267	30940	Usp25	ubiquitin specific peptidase 25
10429580	2.404263425	0.012314958	546643	I830127L07Rik	RIKEN cDNA I830127L07 gene
10374197	2.402334866	0.038923804	56089	Ramp3	receptor (calcitonin) activity modifying protein 3
10469167	2.402035809	0.009137706	353282	Sfmbt2	Scm-like with four mbt domains 2
10469046	2.400216654	0.008974675	16922	Phyh	phytanoyl-CoA hydroxylase
10414527	2.397468034	0.006954094	NA	NA	NA
10555862	2.392821016	0.005161892	NA	NA	NA
10522976	2.391363409	0.010101046	52822	Rufy3	RUN and FYVE domain containing 3
10341058	2.389717329	0.008974675	NA	NA	NA
10585699	2.389650618	0.005732831	NA	NA	NA
10427997	2.388706884	0.010036963	67434	Ankrd33b	ankyrin repeat domain 33B
10569020	2.381246272	0.008974675	213002	Ifitm6	interferon induced transmembrane protein 6
10400072	2.380489556	0.012978515	20259	Scin	scinderin
10482762	2.3804032	0.005141245	319554	Idi1	isopentenyl-diphosphate delta isomerase
10525271	2.379962505	0.008738242	231713	Naa25	N(alpha)-acetyltransferase 25, NatB auxiliary subunit
10437684	2.379869345	0.036642937	19118	Prrm1	protamine 1
10580754	2.379703383	0.012190127	320377	9330175E14Rik	RIKEN cDNA 9330175E14 gene
10340015	2.377532467	0.049226151	NA	NA	NA
10340394	2.376303298	0.023558498	NA	NA	NA
10407126	2.374753378	0.005747821	20620	Plk2	polo-like kinase 2
10476775	2.373841295	0.021030707	67877	Naa20	N(alpha)-acetyltransferase 20, NatB catalytic subunit
10393573	2.373474255	0.012669515	19039	Lgals3bp	lectin, galactoside-binding, soluble, 3 binding protein
10557342	2.371954304	0.016771103	60504	Il21r	interleukin 21 receptor
10488655	2.360268758	0.008454783	12048	Bcl2l1	BCL2-like 1
10461594	2.360062572	0.019943327	64380	Ms4a4c	membrane-spanning 4-domains, subfamily A, member 4C
10438749	2.35950994	0.008670295	NA	NA	NA
10374236	2.356540254	0.005832067	22271	Upp1	uridine phosphorylase 1
10344032	2.352262074	0.006866161	NA	NA	NA
10435982	2.351369286	0.017161237	208154	Btla	B and T lymphocyte associated
10433578	2.350037205	0.021982442	20621	Snn	stannin
10572932	2.346320469	0.016926394	67877	Naa20	N(alpha)-acetyltransferase 20, NatB catalytic subunit
10588786	2.345592537	0.006866161	NA	NA	NA
10350159	2.340733371	0.005239272	16763	Lad1	ladinin
10342144	2.339469963	0.042437524	NA	NA	NA
10462343	2.332125766	0.00937864	100503337	Gm9895	predicted gene 9895
10399632	2.321659233	0.016725023	100038492	F630048H11Rik	RIKEN cDNA F630048H11 gene
10339069	2.320359227	0.010965862	NA	NA	NA
10587554	2.320216711	0.013432759	21983	Tpbp	trophoblast glycoprotein
10497265	2.319555255	0.036721903	11770	Fabp4	fatty acid binding protein 4, adipocyte
10514315	2.317826772	0.022025973	15965	Ifna2	interferon alpha 2
10588849	2.317297185	0.005317021	320844	Amigo3	adhesion molecule with Ig like domain 3
10415293	2.315280984	0.008047332	NA	NA	NA
10524866	2.313083252	0.0083059	231668	Vsig10	V-set and immunoglobulin domain containing 10
10429491	2.311966586	0.006016093	11838	Arc	activity regulated cytoskeletal-associated protein
10381445	2.310258409	0.009483476	217203	Tmem106a	transmembrane protein 106A
10572730	2.307760909	0.008820599	170938	Zfp617	zinc finger protein 617
10359917	2.304001844	0.007061181	15490	Hsd17b7	hydroxysteroid (17-beta) dehydrogenase 7
10582694	2.292505764	0.012190127	69627	Fam89a	family with sequence similarity 89, member A
10408616	2.290309272	0.005570598	73102	Slc22a23	solute carrier family 22, member 23
10420030	2.290205783	0.031316593	19188	Psme2	proteasome (prosome, macropain) activator subunit 2 (PA28 beta)
10403743	2.289107018	0.022817019	16323	Inhba	inhibin beta-A
10492957	2.288266152	0.011990618	12480	Cd1d2	CD1d2 antigen
10402080	2.286064892	0.009483476	217827	Nrde2	nrde-2 necessary for RNA interference, domain containing
10341173	2.281214884	0.021446615	NA	NA	NA
10363007	2.280569642	0.015241699	77987	Ascc3	activating signal cointegrator 1 complex subunit 3
10436941	2.275262095	0.01063193	NA	NA	NA
10566333	2.273386727	0.011652729	NA	NA	NA
10531653	2.269401393	0.009748851	231503	Tmem150c	transmembrane protein 150C
10524878	2.266156102	0.009168579	231668	Vsig10	V-set and immunoglobulin domain containing 10
10353524	2.265507017	0.01963389	70155	Ogfrl1	opioid growth factor receptor-like 1
10575745	2.264254926	0.009239149	234776	Atmin	ATM interactor

10493193	2.263339111	0.009642795	12462	Cct3	chaperonin containing Tcp1, subunit 3 (gamma)
10346551	2.256699607	0.012692718	12633	Cflar	CASP8 and FADD-like apoptosis regulator
10501164	2.252871689	0.013765287	12977	Csf1	colony stimulating factor 1 (macrophage)
10389207	2.24891375	0.006114385	20304	Ccl5	chemokine (C-C motif) ligand 5
10403413	2.248329616	0.008617214	319554	Idi1	isopentenyl-diphosphate delta isomerase
10379482	2.245971311	0.019518582	12569	Cdk5r1	cyclin-dependent kinase 5, regulatory subunit 1 (p35)
10412466	2.245738402	0.007239238	208715	Hmgcs1	3-hydroxy-3-methylglutaryl-Coenzyme A synthase 1
10342081	2.245201629	0.024564848	NA	NA	NA
10369989	2.238693557	0.015285777	13202	Ddt	D-dopachrome tautomerase
10439471	2.23625049	0.007149913	224143	Poglut1	protein O-glucosyltransferase 1
10542557	2.232114729	0.025443758	11569	Aebp2	AE binding protein 2
10508465	2.230155151	0.008047332	17357	Marcksl1	MARCKS-like 1
10529133	2.230040848	0.006152069	101023	Zfp513	zinc finger protein 513
10371662	2.229638575	0.01645636	20728	Spic	Spi-C transcription factor (Spi-1/PU.1 related)
10536505	2.228659133	0.016771103	17295	Met	met proto-oncogene
10514347	2.227940447	0.006948414	12579	Cdkn2b	cyclin-dependent kinase inhibitor 2B (p15, inhibits CDK4)
10443561	2.227911691	0.006866161	NA	NA	NA
10414612	2.224082816	0.008393305	214922	Slc39a2	solute carrier family 39 (zinc transporter), member 2
10338302	2.222895264	0.040475569	NA	NA	NA
10525452	2.222428016	0.019038597	80751	Rnf34	ring finger protein 34
10564631	2.21955791	0.038031971	108116	Slco3a1	solute carrier organic anion transporter family, member 3a1
10372177	2.21803187	0.014688597	278279	Tmtc2	transmembrane and tetratricopeptide repeat containing 2
10390535	2.217888929	0.014483811	217151	Arl5c	ADP-ribosylation factor-like 5C
10375463	2.214006507	0.014415098	171283	Havcr1	hepatitis A virus cellular receptor 1
10428004	2.210204302	0.00724137	67434	Ankrd33b	ankyrin repeat domain 33B
10552743	2.20317185	0.019518582	NA	NA	NA
10408613	2.198124981	0.040592722	73710	Tubb2b	tubulin, beta 2B class IIB
10504450	2.196305654	0.008036644	384009	Glipr2	GLI pathogenesis-related 2
10342823	2.195088758	0.035062175	NA	NA	NA
10504918	2.194725097	0.012741859	230162	Zfp189	zinc finger protein 189
10342200	2.193585808	0.016535203	NA	NA	NA
10436442	2.193115651	0.022771528	NA	NA	NA
10442027	2.185134254	0.010186487	NA	NA	NA
10421488	2.176966359	0.007526959	319448	Fndc3a	fibronectin type III domain containing 3A
10356878	2.174878159	0.007042897	NA	NA	NA
10545958	2.168830965	0.025443758	11746	Anxa4	annexin A4
10554938	2.167061636	0.00894422	75985	Rab30	RAB30, member RAS oncogene family
10562812	2.165706626	0.010367375	272382	Spib	Spi-B transcription factor (Spi-1/PU.1 related)
10589886	2.163724326	0.01645636	75116	4930520O04Rik	RIKEN cDNA 4930520O04 gene
10501420	2.161976119	0.008795077	20912	Stxbp3a	syntaxin binding protein 3A
10505890	2.16061165	0.029679368	15967	Ifna4	interferon alpha 4
10341284	2.15718638	0.015459503	NA	NA	NA
10387111	2.157080612	0.026565879	66358	Adprm	ADP-ribose/CDP-alcohol diphosphatase, manganese dependent
10444258	2.156871226	0.025797958	16913	Psmb8	proteasome (prosome, macropain) subunit, beta type 8 (large multifunctional peptidase 7)
10398075	2.151936171	0.032741434	20716	Serpina3n	serine (or cysteine) peptidase inhibitor, clade A, member 3N
10500388	2.151715132	0.012669515	74414	Polr3c	polymerase (RNA) III (DNA directed) polypeptide C
10412909	2.150932899	0.012680239	14137	Fdft1	farnesyl diphosphate farnesyl transferase 1
10348424	2.146657848	0.010224915	98402	Sh3bp4	SH3-domain binding protein 4
10342407	2.143315074	0.008738242	NA	NA	NA
10389674	2.14183075	0.011389965	68097	Dynll2	dynein light chain LC8-type 2
10560575	2.141111955	0.007627903	19698	Relb	avian reticuloendotheliosis viral (v-rel) oncogene related B
10437695	2.141018696	0.007472686	NA	NA	NA
10478875	2.14012683	0.021203747	NA	NA	NA
10548105	2.13944077	0.008331107	12444	Ccnd2	cyclin D2
10520450	2.137865129	0.007472686	100038472	Gm10469	predicted gene 10469
10385513	2.135078496	0.01385698	NA	NA	NA
10385526	2.134624358	0.014751863	NA	NA	NA
10338769	2.130065623	0.02652949	NA	NA	NA
10385325	2.129709433	0.007799583	30939	Pttg1	pituitary tumor-transforming gene 1
10599576	2.128699401	0.010704611	66496	Pdpdf	pancreatic progenitor cell differentiation and proliferation factor homolog (zebrafish)RIKEN cDNA 2700038C09 gene
10607832	2.126431624	0.027292651	56382	Rab9	RAB9, member RAS oncogene family
10374706	2.126009036	0.021547794	74467	Pus10	pseudouridylate synthase 10

10420637	2.123914068	0.008047332	16648	Kpna3	karyopherin (importin) alpha 3
10339752	2.122439015	0.034653838	NA	NA	NA
10449386	2.12158579	0.009088799	224647	D17Wsu92e	DNA segment, Chr 17, Wayne State University 92, expressed
10497381	2.121063411	0.017539143	13123	Cyp7b1	cytochrome P450, family 7, subfamily b, polypeptide 1
10424213	2.120666095	0.009542598	387609	Zhx2	zinc fingers and homeoboxes 2
10344551	2.120374344	0.012669515	NA	NA	NA
10536949	2.118107445	0.012642958	320609	Strip2	striatin interacting protein 2
10582997	2.11514212	0.010218713	12363	Casp4	caspase 4, apoptosis-related cysteine peptidase
10415319	2.103788902	0.009251199	16391	Irf9	interferon regulatory factor 9
10549497	2.102802311	0.018360544	NA	NA	NA
10339978	2.101662886	0.030870783	NA	NA	NA
10351095	2.101220932	0.033463153	22164	Tnfsf4	tumor necrosis factor (ligand) superfamily, member 4
10608649	2.101216989	0.009398512	547347	Gm6034	predicted gene 6034
10343855	2.100974141	0.025915589	NA	NA	NA
10584977	2.100934774	0.018328892	70661	Sik3	SIK family kinase 3
10363845	2.100886619	0.007931638	76551	Ccdc6	coiled-coil domain containing 6
10342494	2.100561191	0.046676897	NA	NA	NA
10574100	2.099601151	0.018900935	434341	Nlrc5	NLR family, CARD domain containing 5
10570201	2.095253462	0.010367375	50770	Atp11a	ATPase, class VI, type 11A
10523466	2.095219634	0.026984898	NA	NA	NA
10593842	2.095154573	0.009440173	NA	NA	NA
10346799	2.09386101	0.01278705	54167	Icos	inducible T cell co-stimulator
10519949	2.091837463	0.018685266	320770	A630072M18Rik	RIKEN cDNA A630072M18 gene
10499329	2.091615959	0.042773959	58176	Rhbg	Rhesus blood group-associated B glycoprotein
10497931	2.090954767	0.011753267	12633	Cflar	CASP8 and FADD-like apoptosis regulator
10439312	2.086062606	0.009802409	12524	Cd86	CD86 antigen
10444814	2.084957626	0.012741859	15015	H2-Q4	histocompatibility 2, Q region locus 4
10444068	2.083944446	0.008670295	21356	Tapbp	TAP binding protein
10341698	2.083082145	0.008738242	NA	NA	NA
10453867	2.082841929	0.022030903	225182	Rbbp8	retinoblastoma binding protein 8
10531544	2.082034383	0.012741859	231474	Paqr3	progesterin and adipoQ receptor family member III
10406859	2.081510035	0.011867775	238803	Zfp366	zinc finger protein 366
10481711	2.080287207	0.025443758	20910	Stxbp1	syntaxin binding protein 1
10380793	2.080208091	0.009802409	246198	Mllt6	myeloid/lymphoid or mixed-lineage leukemia (trithorax homolog, Drosophila); translocated to, 6
10479550	2.077076818	0.020357964	66496	Pdpdf	pancreatic progenitor cell differentiation and proliferation factor homolog (zebrafish)RIKEN cDNA 2700038C09 gene
10342558	2.076483564	0.009183206	NA	NA	NA
10410435	2.075907614	0.024464102	210106	Papd7	PAP associated domain containing 7
10494527	2.075509235	0.008547698	67845	Rnf115	ring finger protein 115
10342519	2.072479928	0.016955028	NA	NA	NA
10344319	2.071210861	0.040243542	NA	NA	NA
10339409	2.069553921	0.024407119	NA	NA	NA
10338502	2.069239792	0.023293593	NA	NA	NA
10379630	2.068999105	0.017457708	20556	Slfn2	schlafen 2
10407145	2.068896798	0.01063193	218613	Mier3	mesoderm induction early response 1, family member 3
10404531	2.06735337	0.01063193	69666	Psmg4	proteasome (prosome, macropain) assembly chaperone 4
10343490	2.066208086	0.014276122	NA	NA	NA
10369176	2.06610144	0.025151124	544696	Tbc1d32	TBC1 domain family, member 32
10341151	2.065684042	0.014963376	NA	NA	NA
10344369	2.065591735	0.013071088	NA	NA	NA
10395287	2.064819242	0.024349892	380753	Atxn7l1	ataxin 7-like 1
10451167	2.06283015	0.025930288	224807	Tmem63b	transmembrane protein 63b
10420730	2.061631485	0.011990618	14137	Fdft1	farnesyl diphosphate farnesyl transferase 1
10374485	2.061227868	0.011768406	67245	Peli1	pellino 1
10338968	2.06050132	0.039154418	NA	NA	NA
10507137	2.05992471	0.027655547	67182	Pdzk1ip1	PDZK1 interacting protein 1
10528090	2.059072178	0.013345983	242819	Rundc3b	RUN domain containing 3B
10401149	2.058593847	0.010704611	27260	Plek2	pleckstrin 2
10435508	2.050654212	0.021909654	76770	2010005H15Rik	RIKEN cDNA 2010005H15 gene
10554655	2.047821844	0.039241938	108797	Mex3b	mex3 homolog B (C. elegans)
10565994	2.046696175	0.010855451	11872	Art2b	ADP-ribosyltransferase 2b
10527896	2.04549286	0.013075978	70797	Ankib1	ankyrin repeat and IBR domain containing 1
10497441	2.042757782	0.019820076	27357	Gyg	glycogenin

10480760	2.042102259	0.013981906	22030	Traf2	TNF receptor-associated factor 2
10486172	2.041912599	0.013134543	67809	Rmdn3	regulator of microtubule dynamics 3
10511703	2.03832348	0.014669336	192656	Ripk2	receptor (TNFRSF)-interacting serine-threonine kinase 2
10519983	2.035613179	0.031508413	14190	Fgl2	fibrinogen-like protein 2
10523674	2.035065732	0.013333463	74167	Nudt9	nudix (nucleoside diphosphate linked moiety X)-type motif 9
10472782	2.03205826	0.01011529	107435	Hat1	histone aminotransferase 1
10403420	2.031417307	0.025915589	320581	Idi2	isopentenyl-diphosphate delta isomerase 2
10547906	2.029729546	0.025151124	16768	Lag3	lymphocyte-activation gene 3
10353947	2.029118511	0.010843602	56030	Tmem131	transmembrane protein 131
10490653	2.028969515	0.010097141	229004	Gmeb2	glucocorticoid modulatory element binding protein 2
10520250	2.027053438	0.015274562	53312	Nub1	negative regulator of ubiquitin-like proteins 1
10359097	2.026390937	0.012741859	208263	Tor1aip1	torsin A interacting protein 1
10592719	2.023067337	0.010855451	102644	Oaf	OAF homolog (Drosophila)
10376060	2.018097748	0.029932506	16362	Irf1	interferon regulatory factor 1
10517996	2.015498883	0.010166331	69582	Plekhm2	pleckstrin homology domain containing, family M (with RUN domain) member 2
10544687	2.015048227	0.021446615	13063	Cycs	cytochrome c, somatic
10571325	2.014955357	0.020483717	52065	Mfhas1	malignant fibrous histiocyoma amplified sequence 1
10377841	2.0149088	0.020616041	75604	Tm4sf5	transmembrane 4 superfamily member 5
10577655	2.01300081	0.01798657	15930	Ido1	indoleamine 2,3-dioxygenase 1
10500345	2.01263237	0.038342143	21748	Terc	telomerase RNA component
10341296	2.011477119	0.021446615	NA	NA	NA
10418991	2.011223544	0.016920547	72972	Ccser2	coiled-coil serine rich 2
10424781	2.01078259	0.01682735	66168	Grina	glutamate receptor, ionotropic, N-methyl D-aspartate-associated protein 1 (glutamate binding)
10475517	2.010191863	0.03558164	NA	NA	NA
10512766	2.007643884	0.014339236	74735	Trim14	tripartite motif-containing 14
10601473	2.00553719	0.017249188	68117	Apool	apolipoprotein O-like
10338116	2.001085415	0.015868368	NA	NA	NA
10523297	2.000775381	0.009844316	12452	Ccng2	cyclin G2
10469867	0.499769925	0.044578438	241274	Pnpla7	patatin-like phospholipase domain containing 7
10446763	0.499555387	0.021446615	77889	Lbh	limb-bud and heart
10546891	0.499486388	0.012692718	52163	Camk1	calcium/calmodulin-dependent protein kinase I
10573082	0.499253604	0.030687511	234515	Inpp4b	inositol polyphosphate-4-phosphatase, type II
10557177	0.498906626	0.033694632	18751	Prkcb	protein kinase C, beta
10368886	0.498800493	0.027292651	56484	Foxo3	forkhead box O3
10380560	0.497905178	0.009802409	268469	Zfp652	zinc finger protein 652
10481574	0.497885819	0.022492207	241303	Fam78a	family with sequence similarity 78, member A
10351781	0.497752299	0.032105591	16513	Kcnj10	potassium inwardly-rectifying channel, subfamily J, member 10
10396671	0.49768805	0.016725023	263406	Plekhg3	pleckstrin homology domain containing, family G (with RhoGef domain) member 3
10484402	0.49767253	0.012329744	12388	Ctnnd1	catenin (cadherin associated protein), delta 1
10365344	0.497266059	0.013442282	216198	Tcp11l2	t-complex 11 (mouse) like 2
10447317	0.497209058	0.045882324	13819	Epas1	endothelial PAS domain protein 1
10554574	0.496063769	0.017203915	107769	Tm6sf1	transmembrane 6 superfamily member 1
10598004	0.49560314	0.025151124	12768	Ccr1	chemokine (C-C motif) receptor 1
10537410	0.494847414	0.019805848	21391	Tbxas1	thromboxane A synthase 1, platelet
10547894	0.494759531	0.024989069	12504	Cd4	CD4 antigen
10470446	0.494382625	0.010659696	20181	Rxra	retinoid X receptor alpha
10343251	0.493816947	0.020194916	NA	NA	NA
10529375	0.492826541	0.015229292	17122	Mxd4	Max dimerization protein 4
10480842	0.49211798	0.012741859	51875	Tmem141	transmembrane protein 141
10567580	0.491521424	0.026179229	80719	Igsf6	immunoglobulin superfamily, member 6
10492682	0.491517536	0.010473946	68659	Fam198b	family with sequence similarity 198, member B
10431697	0.491354467	0.013385496	26874	Abcd2	ATP-binding cassette, sub-family D (ALD), member 2
10593225	0.490148224	0.010186487	235320	Zbtb16	zinc finger and BTB domain containing 16
10462237	0.490061147	0.020616041	67155	Smarca2	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 2
10574976	0.490033208	0.021358932	192654	Pla2g15	phospholipase A2, group XV
10464560	0.489967115	0.020690153	67689	Aldh3b1	aldehyde dehydrogenase 3 family, member B1
10447383	0.489883444	0.028660977	17075	Epcam	epithelial cell adhesion molecule
10524266	0.489687611	0.011139974	50883	Chek2	checkpoint kinase 2
10341304	0.489407534	0.031661875	NA	NA	NA
10474545	0.489271634	0.017249188	107723	Slc12a6	solute carrier family 12, member 6
10450226	0.489212704	0.020068165	54397	Ppt2	palmitoyl-protein thioesterase 2
10531794	0.488354521	0.012190127	72145	Wdfy3	WD repeat and FYVE domain containing 3

10554094	0.487689159	0.020389139	16001	Igf1r	insulin-like growth factor I receptor
10571142	0.486761857	0.012846919	78560	Gpr124	G protein-coupled receptor 124
10501229	0.486310336	0.031661875	14862	Gstm1	glutathione S-transferase, mu 1
10373223	0.486262989	0.01034251	16971	Lrp1	low density lipoprotein receptor-related protein 1
10399924	0.485206423	0.037613592	30955	Pik3cg	phosphoinositide-3-kinase, catalytic, gamma polypeptide
10448676	0.483711486	0.016389409	65962	Slc9a3r2	solute carrier family 9 (sodium/hydrogen exchanger), member 3 regulator 2
10340943	0.483355741	0.039438678	NA	NA	NA
10542993	0.48325769	0.021108214	269823	Pon3	paraoxonase 3
10499560	0.482528829	0.013973984	11490	Adam15	a disintegrin and metallopeptidase domain 15 (metargidin)
10544002	0.481904174	0.016115809	208647	Creb3l2	cAMP responsive element binding protein 3-like 2
10438445	0.481136574	0.027499387	239743	Klhl6	kelch-like 6
10503410	0.47992535	0.02357631	100201	Tmem64	transmembrane protein 64
10557862	0.479746514	0.011801326	16409	Itgam	integrin alpha M
10462796	0.479531155	0.049309731	16551	Kif11	kinesin family member 11
10494565	0.479093441	0.011753267	14263	Fmo5	flavin containing monooxygenase 5
10526783	0.479078654	0.017093115	381680	Nxpe5	neurexophilin and PC-esterase domain family, member 5
10502205	0.478826189	0.00901517	15107	Hadh	hydroxyacyl-Coenzyme A dehydrogenase
10449893	0.478719598	0.01325626	320484	Rasal3	RAS protein activator like 3
10341424	0.478508591	0.022612719	NA	NA	NA
10489569	0.478362088	0.018269849	18830	Pltp	phospholipid transfer protein
10583326	0.478159518	0.025797958	234967	Slc36a4	solute carrier family 36 (proton/amino acid symporter), member 4
10344528	0.477809116	0.02415125	NA	NA	NA
10572647	0.477196513	0.012915551	26457	Slc27a1	solute carrier family 27 (fatty acid transporter), member 1
10467068	0.476526589	0.011704514	208449	Sgms1	sphingomyelin synthase 1
10506031	0.475402863	0.015459503	18027	Nfia	nuclear factor I/A
10586616	0.475113906	0.015014874	320528	Vps13c	vacuolar protein sorting 13C (yeast)
10432511	0.473841118	0.019755569	26934	Racgap1	Rac GTPase-activating protein 1
10434758	0.473692145	0.017136239	20440	St6gal1	beta galactoside alpha 2,6 sialyltransferase 1
10356172	0.473146554	0.014500934	98496	Pid1	phosphotyrosine interaction domain containing 1
10556598	0.473079772	0.013432759	233781	Xylt1	xylosyltransferase 1
10429114	0.472009068	0.018685266	213068	Tmem71	transmembrane protein 71
10517287	0.471551381	0.044223832	230815	Man1c1	mannosidase, alpha, class 1C, member 1
10500666	0.47119751	0.013973984	19221	Ptgfrn	prostaglandin F2 receptor negative regulator
10576774	0.470681904	0.01214911	75863	Clec4g	C-type lectin domain family 4, member g
10527213	0.470653639	0.025036918	231871	Daglb	diacylglycerol lipase, beta
10359571	0.470540341	0.027292651	14261	Fmo1	flavin containing monooxygenase 1
10559248	0.470409153	0.009802409	27027	Tspan32	tetraspanin 32
10451123	0.470070699	0.028214956	63959	Slc29a1	solute carrier family 29 (nucleoside transporters), member 1
10431872	0.469813265	0.020043504	105727	Slc38a1	solute carrier family 38, member 1
10354649	0.469250278	0.020439616	241062	Pgap1	post-GPI attachment to proteins 1
10412298	0.469150965	0.045787882	109700	Itga1	integrin alpha 1
10508829	0.468853694	0.009382022	53608	Map3k6	mitogen-activated protein kinase kinase kinase 6
10532741	0.468561143	0.041110307	231633	Tmem119	transmembrane protein 119
10426479	0.468073551	0.012741859	105722	Ano6	anoctamin 6
10512022	0.468031287	0.027249839	214944	Mob3b	MOB kinase activator 3B
10366043	0.465604236	0.011043378	67603	Dusp6	dual specificity phosphatase 6
10358421	0.465197047	0.024163987	64214	Rgs18	regulator of G-protein signaling 18
10369453	0.4638969	0.007215556	27355	Pald1	phosphatase domain containing, paladin 1
10376216	0.462950138	0.007532687	215335	Slc36a1	solute carrier family 36 (proton/amino acid symporter), member 1
10557481	0.462935489	0.009196537	66090	Ypel3	yippee-like 3 (Drosophila)
10579799	0.462862631	0.02415125	234463	Tmem184c	transmembrane protein 184C
10568328	0.462739171	0.012145921	27973	Vkorc1	vitamin K epoxide reductase complex, subunit 1
10590631	0.462670425	0.025944986	12772	Ccr2	chemokine (C-C motif) receptor 2
10456071	0.462164612	0.015564211	12978	Csf1r	colony stimulating factor 1 receptor
10525419	0.461518347	0.012190127	18439	P2rx7	purinergic receptor P2X, ligand-gated ion channel, 7
10563085	0.461321633	0.018399423	NA	NA	NA
10563178	0.461107635	0.0083059	12493	Cd37	CD37 antigen
10390103	0.461017713	0.007472686	18604	Pdk2	pyruvate dehydrogenase kinase, isoenzyme 2
10411235	0.460637554	0.025151124	544963	Iqgap2	IQ motif containing GTPase activating protein 2
10393648	0.46010546	0.008858383	27029	Sgsh	N-sulfoglucosamine sulfohydrolase (sulfamidase)
10492815	0.460078841	0.022829866	320782	Tmem154	transmembrane protein 154
10544932	0.460002434	0.007820198	21743	Inmt	indolethylamine N-methyltransferase

10351477	0.459962538	0.048542148	26904	Sh2d1b1	SH2 domain containing 1B1
10592067	0.459908035	0.010367375	14247	Fli1	Friend leukemia integration 1
10380285	0.459728924	0.016725023	67888	Tmem100	transmembrane protein 100
10453636	0.459420438	0.008974675	225115	Svil	supervillin
10362422	0.457979948	0.047189984	76757	Trdn	triadin
10543802	0.457842238	0.017457708	243743	Plxna4	plexin A4
10604932	0.455038242	0.012068896	171486	Cd99l2	CD99 antigen-like 2
10558345	0.454925726	0.007468949	330662	Dock1	dedicator of cytokinesis 1
10341538	0.454914709	0.008331107	NA	NA	NA
10416355	0.454664618	0.008877937	105670	Rcbtb2	regulator of chromosome condensation (RCC1) and BTB (POZ) domain containing protein 2
10338168	0.454511349	0.044147061	NA	NA	NA
10548286	0.4536282	0.007029423	NA	NA	NA
10342264	0.453591601	0.013765287	NA	NA	NA
10372988	0.453136232	0.015229292	20503	Slc16a7	solute carrier family 16 (monocarboxylic acid transporters), member 7
10351679	0.452353983	0.007448624	12523	Cd84	CD84 antigen
10576799	0.451493237	0.017475969	170780	Cd209e	CD209e antigen
10488482	0.450714064	0.018159615	68738	Acsc1	acyl-CoA synthetase short-chain family member 1
10342017	0.448311738	0.021319697	NA	NA	NA
10349661	0.447481359	0.040421061	226421	5430435G22Rik	RIKEN cDNA 5430435G22 gene
10483679	0.446791108	0.021108214	68526	Gpr155	G protein-coupled receptor 155
10607868	0.446657849	0.017475969	170744	Tlr8	toll-like receptor 8
10388591	0.446495473	0.007468949	12874	Cpd	carboxypeptidase D
10461439	0.446487383	0.008370724	NA	NA	NA
10475229	0.444971222	0.010511335	668880	Stard9	START domain containing 9
10573747	0.443577125	0.012069025	11513	Adcy7	adenylate cyclase 7
10341710	0.443421387	0.042054955	NA	NA	NA
10571601	0.443164254	0.007861992	53318	Pdlim3	PDZ and LIM domain 3
10561128	0.442665598	0.007059114	74134	Cyp2s1	cytochrome P450, family 2, subfamily s, polypeptide 1
10350753	0.442572498	0.007634691	14645	Glul	glutamate-ammonia ligase (glutamine synthetase)
10541799	0.44253656	0.007468949	381810	Lpar5	lysophosphatidic acid receptor 5
10533145	0.442079827	0.006851472	252972	Tpcn1	two pore channel 1
10568001	0.441959027	0.013981906	20887	Sult1a1	sulfotransferase family 1A, phenol-preferring, member 1
10415818	0.441071616	0.007931638	268752	Wdfy2	WD repeat and FYVE domain containing 2
10479852	0.440487931	0.011192203	227541	Camk1d	calcium/calmodulin-dependent protein kinase ID
10471721	0.440283454	0.010531655	19224	Ptgs1	prostaglandin-endoperoxide synthase 1
10608654	0.439661089	0.012067355	545366	Cfhr2	complement factor H-related 2
10470614	0.438223951	0.015487705	68870	Ak8	adenylate kinase 8
10564909	0.434874022	0.005871742	140481	Man2a2	mannosidase 2, alpha 2
10555235	0.433285413	0.007468949	109689	Arb1	arrestin, beta 1
10416199	0.433169971	0.022812171	NA	NA	NA
10528038	0.431354891	0.012915551	11496	Adam22	a disintegrin and metallopeptidase domain 22
10441565	0.429837195	0.028838941	20112	Rps6ka2	ribosomal protein S6 kinase, polypeptide 2
10381514	0.429708016	0.009572497	52685	Cd300lg	CD300 antigen like family member G
10480090	0.429574148	0.020429267	241226	Itga8	integrin alpha 8
10425726	0.429448619	0.029772901	24050	O3-sept	septin 3
10579636	0.428215177	0.017457708	72054	Cyp4f18	cytochrome P450, family 4, subfamily f, polypeptide 18
10541587	0.427629306	0.007472686	26888	Clec4a2	C-type lectin domain family 4, member a2
10413710	0.426707503	0.008047332	70021	Nt5dc2	5'-nucleotidase domain containing 2
10489705	0.426668785	0.016926394	114644	Slc13a3	solute carrier family 13 (sodium-dependent dicarboxylate transporter), member 3
10499394	0.424581966	0.020260337	16905	Lmna	lamin A
10475226	0.423682912	0.032031908	668880	Stard9	START domain containing 9
10407327	0.423487193	0.009284838	13723	Emb	embigin
10445781	0.423235498	0.015285777	83433	Trem2	triggering receptor expressed on myeloid cells 2
10347335	0.422759311	0.03783199	18173	Slc11a1	solute carrier family 11 (proton-coupled divalent metal ion transporters), member 1
10599696	0.41816792	0.018162614	236790	Ddx26b	DEAD/H (Asp-Glu-Ala-Asp/His) box polypeptide 26B
10542738	0.418045426	0.007114452	71323	Rassf8	Ras association (RalGDS/AF-6) domain family (N-terminal) member 8
10406334	0.41776729	0.0242129	78771	Mctp1	multiple C2 domains, transmembrane 1
10436456	0.417387451	0.006826856	19128	Pros1	protein S (alpha)
10378216	0.416367651	0.019484087	53313	Atp2a3	ATPase, Ca++ transporting, ubiquitous
10555297	0.413908622	0.046395737	57442	Kcne3	potassium voltage-gated channel, Isk-related subfamily, gene 3
10598626	0.413422653	0.044625345	21912	Tspan7	tetraspanin 7
10345807	0.412840754	0.038502299	16182	Il18r1	interleukin 18 receptor 1

10367611	0.412126229	0.022673374	100504234	Ccdc170	coiled-coil domain containing 170
10500204	0.411651733	0.023795689	13601	Ecm1	extracellular matrix protein 1
10374453	0.411523957	0.016771103	NA	NA	NA
10360040	0.411062736	0.015274562	14131	Fcgr3	Fc receptor, IgG, low affinity III
10500677	0.410362212	0.00798688	12481	Cd2	CD2 antigen
10481845	0.4099225	0.009483476	72543	Mvb12b	multivesicular body subunit 12B
10378855	0.407707098	0.020616041	237860	Ssh2	slingshot homolog 2 (Drosophila)
10547641	0.407460626	0.004987651	20527	Slc2a3	solute carrier family 2 (facilitated glucose transporter), member 3
10412921	0.405967626	0.005913785	18074	Nid2	nidogen 2
10514275	0.405448443	0.008051812	66775	Ptplad2	protein tyrosine phosphatase-like A domain containing 2
10431266	0.40479962	0.005161892	223753	Cerk	ceramide kinase
10581434	0.402541425	0.006851472	319446	Dpep2	dipeptidase 2
10340074	0.402082021	0.004661133	NA	NA	NA
10547153	0.398686994	0.017645701	11689	Alox5	arachidonate 5-lipoxygenase
10599654	0.398452215	0.014828685	72865	Cxx1c	CAAX box 1C
10475218	0.393283098	0.020617046	668880	Stard9	START domain containing 9
10466712	0.39252372	0.007472686	71738	Mamdc2	MAM domain containing 2
10377215	0.391062141	0.00600988	14457	Gas7	growth arrest specific 7
10342889	0.388995203	0.012387927	NA	NA	NA
10577641	0.385993731	0.006114385	69068	1810011O10Rik	RIKEN cDNA 1810011O10 gene
10565819	0.384929564	0.017983901	101488	Slco2b1	solute carrier organic anion transporter family, member 2b1
10378649	0.384596853	0.004459738	215113	Slc43a2	solute carrier family 43, member 2
10358339	0.384098777	0.007004578	12628	Cfh	complement component factor h
10571840	0.383146764	0.014483811	15446	Hpgd	hydroxyprostaglandin dehydrogenase 15 (NAD)
10587854	0.380969231	0.027543146	331004	Slc9a9	solute carrier family 9 (sodium/hydrogen exchanger), member 9
10500808	0.380829568	0.045882324	99543	Olfml3	olfactomedin-like 3
10362294	0.380076827	0.012190127	73910	Arhgap18	Rho GTPase activating protein 18
10564646	0.379275941	0.023780477	64176	Sv2b	synaptic vesicle glycoprotein 2 b
10596148	0.378991467	0.02155072	NA	NA	NA
10344019	0.378955133	0.009062231	NA	NA	NA
10443690	0.378767024	0.031692822	14652	Glp1r	glucagon-like peptide 1 receptor
10570018	0.377767838	0.005141245	24099	Tnfsf13b	tumor necrosis factor (ligand) superfamily, member 13b
10344219	0.370960429	0.041328938	NA	NA	NA
10458382	0.370494503	0.04196954	12475	Cd14	CD14 antigen
10562709	0.370438551	0.009993751	12489	Cd33	CD33 antigen
10469457	0.367835677	0.003171864	67448	Plxdc2	plexin domain containing 2
10562720	0.361634726	0.005335022	83382	Siglece	sialic acid binding Ig-like lectin E
10590031	0.361598881	0.030400008	104099	Itga9	integrin alpha 9
10419170	0.361091255	0.022612719	70561	Txndc16	thioredoxin domain containing 16
10418506	0.361034601	0.027655547	192187	Stab1	stabilin 1
10576816	0.360429691	0.014497298	69165	Cd209b	CD209b antigen
10576807	0.357234484	0.003324094	170779	Cd209d	CD209d antigen
10422822	0.355630574	0.004367116	16880	Lifr	leukemia inhibitory factor receptor
10393559	0.355303072	0.005367911	21858	Timp2	tissue inhibitor of metalloproteinase 2
10587012	0.35312922	0.029523072	72278	Ccpg1	cell cycle progression 1
10424126	0.345915654	0.010750705	NA	NA	NA
10339491	0.345611412	0.003965494	NA	NA	NA
10436095	0.336151925	0.033632204	57262	Retnla	resistin like alpha
10355403	0.335540592	0.004661133	14268	Fn1	fibronectin 1
10389894	0.333743968	0.004554071	76408	Abcc3	ATP-binding cassette, sub-family C (CFTR/MRP), member 3
10597743	0.332055881	0.011307051	13051	Cx3cr1	chemokine (C-X3-C motif) receptor 1
10576829	0.330746804	0.025542383	170776	Cd209c	CD209c antigen
10392601	0.329180968	0.029060157	76184	Abca6	ATP-binding cassette, sub-family A (ABC1), member 6
10422598	0.322096924	0.007123182	NA	NA	NA
10549635	0.317258162	0.004661133	232801	Lilra5	leukocyte immunoglobulin-like receptor, subfamily A (with TM domain), member 5
10438753	0.313964848	0.00257849	210530	Leprel1	leprecan-like 1
10345762	0.313817788	0.018685266	16177	Il1r1	interleukin 1 receptor, type I
10542917	0.310562367	0.012680239	101202	Hepacam2	HEPACAM family member 2
10382300	0.308060177	0.002712038	26399	Map2k6	mitogen-activated protein kinase kinase 6
10500656	0.304950004	0.038380225	630146	Cd101	CD101 antigen
10395414	0.301713606	0.016771103	319660	Agmo	alkylglycerol monooxygenase
10345791	0.296266694	0.02161299	17082	Il1r1	interleukin 1 receptor-like 1

10360684	0.29486293	0.028731993	13849	Ephx1	epoxide hydrolase 1, microsomal
10469358	0.294510729	0.004165248	17533	Mrc1	mannose receptor, C type 1
10523134	0.281837092	0.013333463	56744	Pf4	platelet factor 4
10342604	0.278564119	0.033152007	NA	NA	NA
10466200	0.27341299	0.028531699	109225	Ms4a7	membrane-spanning 4-domains, subfamily A, member 7
10343187	0.265154318	0.013088068	NA	NA	NA
10541644	0.260370493	0.004076463	93671	Cd163	CD163 antigen
10345777	0.255314962	0.015984845	107527	Il1rl2	interleukin 1 receptor-like 2
10435305	0.251249603	0.007825797	16419	Itgb5	integrin beta 5
10560624	0.249234475	0.013071088	11816	ApoE	apolipoprotein E
10408693	0.247707904	0.001514742	74145	F13a1	coagulation factor XIII, A1 subunit
10446282	0.245282085	0.002130807	13733	Emr1	EGF-like module containing, mucin-like, hormone receptor-like sequence 1
10499189	0.2377482	0.002735366	80891	Fcrls	Fc receptor-like S, scavenger receptor
10392560	0.220060318	0.004165248	217262	Abca9	ATP-binding cassette, sub-family A (ABC1), member 9
10424140	0.196400699	0.004987651	12818	Col14a1	collagen, type XIV, alpha 1
10344363	0.191369393	0.034272673	NA	NA	NA

Supporting Information Table 2. TRANSFAC analysis for the enrichment of transcription factor binding sites in the proximal promoter region of the HDM signature genes

Matrix	Factor name	P-value	Fold enrichment
V\$IRF1_05	Irf1	1.51E-13	46.9213
V\$IRF_Q6	Irf	1.10E-12	43.9888
V\$IRF1_03	Irf-1	1.52E-09	33.236
V\$IRF1_Q5	Irf-1	2.07E-08	29.3258
V\$ICSBP_Q6	Icsbp	7.59E-08	27.3708
V\$IRF_Q6_01	Irf	1.45E-07	26.3933
V\$ISRE_01	Isgf-3	2.77E-07	24.4157
V\$ISGF3F_03	Irf-9	2.77E-07	24.4157
V\$CEBPB_04	C/EBPbeta	5.28E-07	24.4382
V\$IRF7_01	Irf-7	1.12E-09	18.573
V\$HNF3_Q6_01	HNF3	2.11E-09	18.0843
V\$CEBPE_02	Cebpe	1.63E-04	15.6404
V\$LBP9_01	Lbp9 (Tcfcp211)	3.04E-04	14.6629
V\$IRF2-Q6	Irf-2	3.04E-04	14.6629
V\$GKLF_Q3	Gklf	5.66E-04	13.6854
V\$GATA5_04	Gata5 secondary motif	5.66E-04	13.6854
V\$IRF4_Q5	Irf-4	5.83E-07	13.6854
V\$IRF5_Q5	Irf5	1.05E-03	12.7079
V\$PAX_Q6	Pax	1.05E-03	12.7079
V\$RREB1_Q5	Rreb1	1.05E-03	12.7079
V\$FOXO4_01	Foxo4	1.94E-03	11.7303
V\$HOXA3_07	Hoxa3 secondary motif	1.94E-03	11.7303
V\$PREP1_01	Prep1	3.56E-03	10.7528
V\$MRG2_01	Mrg2	3.56E-03	10.7528
V\$MEIS2_01	Meis2	6.50E-03	9.7753
V\$SPIB_03	Spi-B	6.50E-03	9.7753
V\$NFY_Q6_01	Nf-γ	6.50E-03	9.7753
V\$FOXL1_06	Foxl1	6.50E-03	9.7753
V\$MEIS1AHOXA9_	Meis1a:Hoxa9	6.50E-03	9.7753
V\$HIC1_08	Hic1	6.50E-03	9.7753
V\$FOXC2_02	Foxc2	6.50E-03	9.7753
V\$EP300_03	p300	6.50E-03	9.7753
V\$BLIMP1_Q6	Blimp-1	1.34E-04	9.2865
V\$FOXM1_04	Foxm1 secondary motif	4.33E-04	8.309
V\$HNF3ALPHA_Q6	Hnf3alpha	4.33E-04	8.309
V\$ZNF460_01	Znf460	4.33E-04	8.309
V\$TGIF_02	Tgif2	4.70E-04	7.8202
V\$IRF4_03	Irf4	9.73E-05	7.1685
V\$ZFP281_04	Zfp281	1.80E-12	6.9404
V\$VAX2_01	Vax-2	2.40E-03	6.8427
V\$HNF3B_Q6	Hnf-3beta	2.40E-03	6.8427
V\$NFE2L2_03	Nfe2l2	4.19E-03	6.3539

V\$IK3_01	Ik-3	4.19E-03	6.3539
V\$RELA_02	RelA	4.19E-03	6.3539
V\$NFKB1_03	Nf-kappaB1	4.19E-03	6.3539
V\$CFOSJUN_Q5	c-Fos:c-Jun	5.14E-04	6.191
V\$TBX5_02	Tbx5	7.27E-03	5.8652
V\$NFE2_q6	Nf-e2	7.27E-03	5.8652
V\$PAX6_Q2	Pax-6	7.27E-03	5.8652
V\$HFH3_01	Hfh3 (Foxi 1)	8.85E-04	5.8652
V\$SIX2_01	Six-2	7.27E-03	5.8652
V\$NFKAPPAB65_0	Nf-kappaB (p65)	1.13E-04	5.8652
V\$NFKB_C	Nf-kappaB	7.27E-03	5.8652
V\$GFI1_Q6_01	Gfi1	7.27E-03	5.8652
V\$NF1_Q6	Nf-1	1.51E-03	5.5393
V\$NRF2_Q6	Nrf2	1.51E-03	5.5393
V\$SMAD3_Q6	Smad3	1.51E-03	5.5393
V\$CREL_Q6	c-Rel	3.28E-04	5.3764
V\$RAX_03	Rax	2.57E-03	5.2135
V\$CEBPB_Q6	C/EBPbeta	2.57E-03	5.2135
V\$HNF3_Q6	Hnf3	4.33E-03	4.8876
V\$SIX6_02	Six-6	4.33E-03	4.8876
V\$NFE2_01	Nf-e2	1.73E-05	4.748
V\$ZFP740_03	Zfp740	8.33E-19	4.6921
V\$CHOP_01	Chop:C/EBPalpha	7.24E-03	4.5618
V\$FOXJ1_03	Foxj1	7.24E-03	4.5618
V\$SPI_10	Spi1	5.62E-04	4.4966
V\$RELA_Q6	RelA-p65	2.56E-03	4.3989
V\$HOXA9_Q5	Hoxa9	1.50E-03	4.1056
V\$PKNOX2_01	Pknox2	1.50E-03	4.1056
V\$HNF4G_02	Hnf-4gamma	4.77E-09	4.0826
V\$DAX1_01	Dax1	6.80E-09	3.9101
V\$NRF2_Q4	Nrf-2	6.80E-09	3.9101
V\$CEBPD_Q3	C/EBPdelta	2.43E-03	3.9101
V\$SIX1_01	Six-1	6.80E-03	3.9101
V\$DOBOX5_01	Dobox5	2.43E-03	3.9101
V\$IRF3_05	Irf-3	9.13E-07	3.9101
V\$HDAC2_02	Hdac2	5.18E-04	3.7705
V\$PAX5_Q6	Pax5	3.89E-03	3.7146
V\$WT1_Q4	Wt1	4.20E-09	3.6774
V\$PITX1_01	Pitx1	2.24E-03	3.5843
V\$FOXO3A_Q1	FOXO3A	2.24E-03	3.5843
V\$CFOS_Q4	c-Fos	8.97E-06	3.5341
V\$AML_Q6	Aml	6.19E-03	3.5191
V\$SPIC_03	Spic	6.19E-03	3.5191
V\$BLIMP1_Q6_01	Blimp-1	1.30E-03	3.4912
V\$CUX1_07	Cdp	2.81E-04	3.4757
V\$SIX6_01	Six-6	3.53E-03	3.4213

V\$TBX5_01	Tbx5	3.53E-03	3.4213
V\$OTX2_01	Otx2	3.53E-03	3.4213
V\$FOXA2_04	Hnf3-beta	3.53E-03	3.4213
V\$IK1_01	Ik-1	3.53E-03	3.4213
V\$FOXA2_05	Foxa2	4.39E-04	3.367
V\$FOSL1	Fra-1	2.03E-03	3.3515
V\$FOXO1_01	Foxo1	9.74E-03	3.3236
V\$SINA_01	sin3A	9.74E-03	3.3236
V\$PITX2_01	Pitx2	9.74E-03	3.3236
V\$TTF1_Q5_01	Ttf-1	7.63E-06	3.3236
V\$IRF2_01	Irf-2	9.74E-03	3.3236
V\$FREAC3_01	Freac-3	5.52E-03	3.2584
V\$SPIB_01	Spi-B	5.52E-03	3.2584
V\$CARRXR_Q2	Car_Rxr (dimer)	8.54E-03	3.0955
V\$NFKB_Q6_01	Nf-kappab	8.54E-03	3.0955
V\$NANOG_07	nanog	8.54E-03	3.0955
V\$PITX1_04	Pitx1	4.85E-03	3.072
V\$SPI1_03	Spi1	4.85E-03	3.072
V\$SPI1_07	PU.1	4.85E-03	3.072
V\$TFII_Q6_01	Tfii-i	4.85E-03	3.072
V\$OTX2_Q3_01	Otx2	4.85E-03	3.072
V\$PITX3_03	Pitx3	4.85E-03	3.072
V\$RHOXF1_02	RHOXF1	4.85E-03	3.072
V\$EP300_06	p300	2.78E-03	3.0548
V\$IRF3_Q3	Irf-3	2.78E-03	3.0548

Supporting Information Table 3: List of differentially expressed probesets in lung cDC2s of wild-type and Irf3-deficient mice exposed to intranasal house dust mite as determined by microarray analysis. Only probesets upregulated in the "HDM signature" were considered for comparison here.

Probe ID	Fold change	P-value	ENTREZ ID	MGI symbol	Description
10379633	32.30368589	0.001406661	20555	Slfn1	schlafen 1
10462621	26.91392776	0.001070116	667370	I830012O16Rik	RIKEN cDNA I830012O16 gene
10524631	18.61992824	0.000606561	231655	Oas1l	2'-5' oligoadenylate synthetase-like 1
10360373	17.26492571	0.000869035	623121	Pydc4	pyrin domain containing 4
10451287	17.04498554	0.001070116	677168	Gm9706	predicted gene 9706
10395039	16.56673194	0.000606561	22169	Cmpk2	cytidine monophosphate (UMP-CMP) kinase 2, mitochondrial
10569102	15.62326624	0.000606561	54123	Irf7	interferon regulatory factor 7
10360367	15.58312298	0.001889188	NA	NA	NA
10533213	14.26993145	0.000802248	246727	Oas3	2'-5' oligoadenylate synthetase 3
10439009	13.6946494	0.001076007	11815	Apod	apolipoprotein D
10554240	12.88377005	0.000606561	57444	Isg20	interferon-stimulated protein
10429560	12.66844384	0.000606561	57248	Ly6i	lymphocyte antigen 6 complex, locus I
10531420	12.21137813	0.002379478	56066	Cxcl11	chemokine (C-X-C motif) ligand 11
10437224	12.19084379	0.000606561	17858	Mx2	MX dynamin-like GTPase 2
10496539	12.09605955	0.000606561	229898	Gbp5	guanylate binding protein 5
10351880	11.97095625	0.001768381	NA	NA	NA
10490150	11.40932997	0.000606561	58203	Zbp1	Z-DNA binding protein 1
10420497	10.82452432	0.001734551	628705	Phf11c	PHD finger protein 11C
10376324	10.62104629	0.000685255	631323	Gm12250	predicted gene 12250
10360370	10.5949625	0.000759202	545384	BC094916	cDNA sequence BC094916
10544982	10.25830911	0.001406661	107569	Nt5c3	5'-nucleotidase, cytosolic III
10490903	10.06375732	0.000634536	71934	Car13	carbonic anhydrase 13
10599598	9.99538093	0.004365243	100504594	A630012P03Rik	RIKEN cDNA A630012P03 gene
10466314	9.687852919	0.002614397	NA	NA	NA
10531987	9.675738414	0.001191975	NA	NA	NA
10580752	9.602062859	0.00687446	320377	9330175E14Rik	RIKEN cDNA 9330175E14 gene
10385518	9.553555966	0.000869035	NA	NA	NA
10450325	9.262423381	0.000606561	NA	NA	NA
10490632	9.027057153	0.000606561	229003	Helz2	helicase with zinc finger 2, transcriptional coactivator
10571984	8.738741577	0.001070116	234311	Ddx60	DEAD (Asp-Glu-Ala-Asp) box polypeptide 60
10455954	8.662600339	0.002115596	240327	Gm4951	predicted gene 4951
10385533	8.544926349	0.001070116	NA	NA	NA
10378068	8.450572543	0.000685255	327959	Xaf1	XIAP associated factor 1
10455961	8.217903621	0.002289775	NA	NA	NA
10538590	8.149333868	0.001070116	67138	Herc6	hect domain and RLD 6
10375515	8.080305002	0.002585338	NA	NA	NA
10533198	8.028864675	0.000781347	246728	Oas2	2'-5' oligoadenylate synthetase 2
10450675	7.9667018	0.000781347	15042	H2-T24	histocompatibility 2, T region locus 24
10400299	7.834283703	0.002747018	14762	Gpr33	G protein-coupled receptor 33
10524621	7.499126058	0.000869035	23962	Oasl2	2'-5' oligoadenylate synthetase-like 2
10420488	7.440779524	0.001070116	219132	Phf11d	PHD finger protein 11D
10389190	7.423194716	0.000869035	629303	Heatr9	HEAT repeat containing 9
10531724	7.268350206	0.01063193	231507	Plac8	placenta-specific 8
10389143	6.79625176	0.001459533	276950	Slfn8	schlafen 8
10360382	6.787685875	0.001352589	NA	NA	NA
10541307	6.740559725	0.001070116	24110	Usp18	ubiquitin specific peptidase 18
10376326	6.708296615	0.001070116	NA	NA	NA
10582862	6.697066701	0.001406661	NA	NA	NA
10531994	6.635611706	0.001070116	NA	NA	NA
10391207	6.587645772	0.000869035	80861	Dhx58	DEXH (Asp-Glu-X-His) box polypeptide 58
10466932	6.535661007	0.001070116	27356	InsI6	insulin-like 6
10537426	6.480601771	0.000887825	75379	4930599N23Rik	RIKEN cDNA 4930599N23 gene
10584458	6.394981035	0.002487495	258783	Olfir920	olfactory receptor 920
10530692	6.260308532	0.001406661	16542	Kdr	kinase insert domain protein receptor
10592888	6.233919388	0.001076007	12145	Cxcr5	chemokine (C-X-C motif) receptor 5

10441233	6.195850065	0.001070116	17857	Mx1	MX dynamin-like GTPase 1
10385500	6.118736892	0.001070116	15944	Irgm1	immunity-related GTPase family M member 1
10444056	6.10082253	0.004015715	13163	Daxx	Fas death domain-associated protein
10379708	6.045683812	0.000887825	NA	NA	NA
10466127	6.001897464	0.001691006	107350	AW112010	expressed sequence AW112010
10473356	5.984793145	0.001070116	56791	Ube2l6	ubiquitin-conjugating enzyme E2L 6
10496975	5.979656939	0.001070116	242259	Slc44a5	solute carrier family 44, member 5
10496592	5.849712025	0.001070116	14469	Gbp2	guanylate binding protein 2
10531407	5.819565165	0.001070116	17329	Cxcl9	chemokine (C-X-C motif) ligand 9
10512067	5.794083821	0.001076007	230073	Ddx58	DEAD (Asp-Glu-Ala-Asp) box polypeptide 58
10420483	5.74865494	0.007029423	219131	Phf11a	PHD finger protein 11A
10483110	5.677673279	0.002379478	71586	Ifih1	interferon induced with helicase C domain 1
10434291	5.632928715	0.001191975	108105	B3gnt5	UDP-GlcNAc:betaGal beta-1,3-N-acetylglucosaminyltransferase 5
10533246	5.621170566	0.001489965	23960	Oas1g	2'-5' oligoadenylate synthetase 1G
10533256	5.5841972	0.001070116	246730	Oas1a	2'-5' oligoadenylate synthetase 1A
10383210	5.573955522	0.001070116	672511	Rnf213	ring finger protein 213
10579532	5.544998568	0.001710547	69550	Bst2	bone marrow stromal cell antigen 2
10389134	5.536501717	0.00245221	237886	Slfn9	schlafen 9
10398039	5.534738342	0.002204659	NA	NA	NA
10417526	5.528563175	0.001986809	13421	Dnase1l3	deoxyribonuclease 1-like 3
10469289	5.494607911	0.001070116	16169	Il15ra	interleukin 15 receptor, alpha chain
10582860	5.41911381	0.003250833	NA	NA	NA
10582877	5.41911381	0.003250833	NA	NA	NA
10594053	5.404374127	0.001070116	18854	Pml	promyelocytic leukemia
10347919	5.361067961	0.002712038	NA	NA	NA
10356291	5.361067961	0.002712038	NA	NA	NA
10513722	5.330276671	0.001406661	326623	Tnfsf15	tumor necrosis factor (ligand) superfamily, member 15
10383206	5.322475737	0.001070116	672511	Rnf213	ring finger protein 213
10579958	5.310383596	0.003069664	16168	Il15	interleukin 15
10500911	5.303033909	0.001070116	17454	Mov10	Moloney leukemia virus 10
10506714	5.255083217	0.001070116	16975	Lrp8	low density lipoprotein receptor-related protein 8, apolipoprotein e receptor
10383200	5.245599688	0.001070116	672511	Rnf213	ring finger protein 213
10439651	5.242218444	0.001070116	17470	Cd200	CD200 antigen
10429564	5.172555186	0.001125923	110454	Ly6a	lymphocyte antigen 6 complex, locus A
10383192	5.035554479	0.001214385	672511	Rnf213	ring finger protein 213
10566366	5.021989721	0.001070116	209387	Trim30d	tripartite motif-containing 30D
10469278	4.979956986	0.001352589	16184	Il2ra	interleukin 2 receptor, alpha chain
10497689	4.965553567	0.001076007	14696	Gnb4	guanine nucleotide binding protein (G protein), beta 4
10452980	4.963079662	0.003392094	19106	Eif2ak2	eukaryotic translation initiation factor 2-alpha kinase 2
10367224	4.944398011	0.001070116	20847	Stat2	signal transducer and activator of transcription 2
10542287	4.929957956	0.001489965	66813	Bcl2l14	BCL2-like 14 (apoptosis facilitator)
10574145	4.918277439	0.001459533	434341	Nlrc5	NLR family, CARD domain containing 5
10389151	4.901933305	0.001889188	NA	NA	NA
10368616	4.89863521	0.002204659	72580	Zufsp	zinc finger with UFM1-specific peptidase domain
10458028	4.87112763	0.001070116	71683	Gypc	glycophorin C
10383196	4.856467547	0.001070116	672511	Rnf213	ring finger protein 213
10574135	4.844080397	0.002632952	434341	Nlrc5	NLR family, CARD domain containing 5
10383212	4.839713869	0.001076007	672511	Rnf213	ring finger protein 213
10383204	4.76870472	0.001150617	672511	Rnf213	ring finger protein 213
10395273	4.754869616	0.002422501	100504486	Gdap10	ganglioside-induced differentiation-associated-protein 10
10419578	4.751715153	0.010684631	29811	Ndrp2	N-myc downstream regulated gene 2
10379615	4.702892393	0.003554753	327978	Slfn5	schlafen 5
10406852	4.679543838	0.003967809	NA	NA	NA
10346191	4.64936483	0.001788881	20846	Stat1	signal transducer and activator of transcription 1
10435514	4.615368679	0.001352589	106347	Ildr1	immunoglobulin-like domain containing receptor 1
10383194	4.605652877	0.001070116	672511	Rnf213	ring finger protein 213
10347933	4.533135489	0.001150617	NA	NA	NA
10356269	4.5300949308	0.001125923	381287	A530032D15Rik	RIKEN cDNA A530032D15Rik gene
10379646	4.518738699	0.001734551	20557	Slfn3	schlafen 3
10439249	4.48052992	0.001710547	547253	Parp14	poly (ADP-ribose) polymerase family, member 14
10383198	4.446159426	0.001282074	672511	Rnf213	ring finger protein 213

10574139	4.431131939	0.001734551	434341	Nlrc5	NLR family, CARD domain containing 5
10587659	4.420492016	0.002451309	NA	NA	NA
10474181	4.397634116	0.002422501	99382	Abtb2	ankyrin repeat and BTB (POZ) domain containing 2
10383233	4.373951436	0.001556066	672511	Rnf213	ring finger protein 213
10383152	4.371624302	0.001150617	672511	Rnf213	ring finger protein 213
10429140	4.350550452	0.00334505	17988	Ndrp1	N-myc downstream regulated gene 1
10545135	4.322547706	0.001989563	16162	Il12rb2	interleukin 12 receptor, beta 2
10383202	4.295674111	0.001191975	672511	Rnf213	ring finger protein 213
10496580	4.241246919	0.008738242	55932	Gbp3	guanylate binding protein 3
10574157	4.234604866	0.002735366	434341	Nlrc5	NLR family, CARD domain containing 5
10595371	4.193107338	0.007204029	94353	Hmgn3	high mobility group nucleosomal binding domain 3
10435457	4.185100382	0.001489965	80285	Parp9	poly (ADP-ribose) polymerase family, member 9
10482517	4.177400289	0.001851186	64685	Nmi	N-myc (and STAT) interactor
10483381	4.168978783	0.002163126	53416	Stk39	serine/threonine kinase 39
10462683	4.154878884	0.004987651	76073	Pcgf5	polycomb group ring finger 5
10461093	4.145865381	0.019855197	225845	Pla2g16	phospholipase A2, group XVI
10574163	4.103628449	0.00245221	434341	Nlrc5	NLR family, CARD domain containing 5
10566050	4.101267039	0.007029423	16068	Il18bp	interleukin 18 binding protein
10531980	4.069886721	0.005317021	236573	Gbp9	guanylate-binding protein 9
10437205	4.025962955	0.004661133	NA	NA	NA
10359181	3.995818583	0.002311838	30935	Tor3a	torsin family 3, member A
10544133	3.994826017	0.001691006	243771	Parp12	poly (ADP-ribose) polymerase family, member 12
10574104	3.983607934	0.001489965	434341	Nlrc5	NLR family, CARD domain containing 5
10383214	3.964881396	0.002268952	672511	Rnf213	ring finger protein 213
10356248	3.95630021	0.001691006	NA	NA	NA
10383168	3.955767839	0.001734551	672511	Rnf213	ring finger protein 213
10411459	3.94635148	0.002721248	380863	Tmem171	transmembrane protein 171
10350800	3.901821576	0.001734551	240832	Tor1aip2	torsin A interacting protein 2
10363195	3.890477182	0.003849533	15500	Hsf2	heat shock factor 2
10560608	3.859097053	0.004554071	11813	Apoc2	apolipoprotein C-II
10519270	3.817594914	0.001710547	11603	Agm	agrin
10547976	3.792859932	0.001691006	213233	Tapbpl	TAP binding protein-like
10566350	3.755201355	0.002379478	244183	Trim30b	tripartite motif-containing 30B
10351873	3.749121612	0.001889188	236312	Pyhin1	pyrin and HIN domain family, member 1
10346960	3.740597221	0.002601433	227210	Ccn1l	cyclin Y-like 1
10510270	3.719397087	0.004661133	17769	Mthfr	5,10-methylenetetrahydrofolate reductase
10574137	3.70711745	0.002146606	434341	Nlrc5	NLR family, CARD domain containing 5
10574133	3.691502976	0.003324094	434341	Nlrc5	NLR family, CARD domain containing 5
10420503	3.678487972	0.012177093	239122	Setdb2	SET domain, bifurcated 2
10574143	3.675991772	0.002379478	434341	Nlrc5	NLR family, CARD domain containing 5
10356271	3.673574282	0.001710547	381287	A530032D15Rik	RIKEN cDNA A530032D15Rik gene
10574159	3.671515152	0.002632952	434341	Nlrc5	NLR family, CARD domain containing 5
10377010	3.649375742	0.00585028	52892	Sco1	SCO cytochrome oxidase deficient homolog 1 (yeast)
10574098	3.648562383	0.003523902	434341	Nlrc5	NLR family, CARD domain containing 5
10402347	3.646589092	0.011307051	76933	Ifi2712a	interferon, alpha-inducible protein 27 like 2A
10405125	3.644432014	0.004937269	109082	Fbxw17	F-box and WD-40 domain protein 17
10347968	3.614727958	0.001994407	20684	Sp100	nuclear antigen Sp100
10608719	3.603637745	0.001734551	231002	Plekhn1	pleckstrin homology domain containing, family N member 1
10360410	3.586687712	0.002163126	404222	Olfir231	olfactory receptor 231
10574102	3.584106007	0.002130807	434341	Nlrc5	NLR family, CARD domain containing 5
10356267	3.567188836	0.002422501	381287	A530032D15Rik	RIKEN cDNA A530032D15Rik gene
10395259	3.561677748	0.001710547	59027	Nampt	nicotinamide phosphoribosyltransferase
10420362	3.56045298	0.002487495	14619	Gjb2	gap junction protein, beta 2
10452613	3.558194473	0.002614397	268970	Arhgap28	Rho GTPase activating protein 28
10574151	3.521947914	0.00242761	434341	Nlrc5	NLR family, CARD domain containing 5
10381408	3.516796519	0.00242761	70110	Ifi35	interferon-induced protein 35
10461622	3.502363777	0.008311382	69774	Ms4a6b	membrane-spanning 4-domains, subfamily A, member 6B
10574149	3.496574565	0.002735366	434341	Nlrc5	NLR family, CARD domain containing 5
10429843	3.489910836	0.002146606	NA	NA	NA
10572772	3.481651985	0.002311838	209488	Hsh2d	hematopoietic SH2 domain containing
10574161	3.480342325	0.00209843	434341	Nlrc5	NLR family, CARD domain containing 5

10532019	3.480290308	0.002320223	NA	NA	NA
10453049	3.4716421	0.010529111	260409	Cdc42ep3	CDC42 effector protein (Rho GTPase binding) 3
10500335	3.461714713	0.015229292	14129	Fcgr1	Fc receptor, IgG, high affinity 1
10439268	3.457544666	0.002601433	NA	NA	NA
10423593	3.440783102	0.002379478	114128	Laptm4b	lysosomal-associated protein transmembrane 4B
10461605	3.426654688	0.003069664	60361	Ms4a4b	membrane-spanning 4-domains, subfamily A, member 4B
10569168	3.408835124	0.00310807	68267	Slc25a22	solute carrier family 25 (mitochondrial carrier, glutamate), member 22
10574141	3.408121626	0.002268952	434341	Nlrc5	NLR family, CARD domain containing 5
10347921	3.406638493	0.004686384	621875	A530040E14Rik	RIKEN cDNA A530040E14 gene
10566144	3.397984954	0.002445448	20821	Trim21	tripartite motif-containing 21
10534909	3.373842246	0.002204659	624083	Gm15753	predicted gene 15753
10608646	3.359480366	0.010904597	435565	Iigp1b	interferon inducible GTPase 1B
10347928	3.350419154	0.002059091	NA	NA	NA
10582874	3.350419154	0.002059091	NA	NA	NA
10582868	3.333193281	0.002204659	664787	LOC664787	Sp110 nuclear body protein-like
10574155	3.322691196	0.002747018	434341	Nlrc5	NLR family, CARD domain containing 5
10356278	3.290134614	0.002146606	NA	NA	NA
10545154	3.25569707	0.018950042	209590	Il23r	interleukin 23 receptor
10576034	3.252426367	0.002735366	15900	Irf8	interferon regulatory factor 8
10350792	3.235107952	0.002311838	240832	Tor1aip2	torsin A interacting protein 2
10504672	3.232308257	0.002268952	100121	Tdrd7	tudor domain containing 7
10531972	3.231876133	0.002422501	76074	Gbp8	guanylate-binding protein 8
10499811	3.190975778	0.008858383	18160	Npr1	natriuretic peptide receptor 1
10489850	3.17600705	0.004661133	98999	Znfx1	zinc finger, NFX1-type containing 1
10535065	3.174423518	0.002735366	231821	Adap1	ArfGAP with dual PH domains 1
10560644	3.169756247	0.003849533	19294	Pvrl2	poliovirus receptor-related 2
10542040	3.163406928	0.002268952	101187	Parp11	poly (ADP-ribose) polymerase family, member 11
10522368	3.162926916	0.002735366	70701	Nipal1	NIPA-like domain containing 1
10462603	3.159684141	0.004661133	14102	Fas	Fas (TNF receptor superfamily member 6)
10566346	3.159465799	0.003863885	319236	Trim12c	tripartite motif-containing 12C
10448278	3.120203298	0.003392094	240047	Mmp25	matrix metallopeptidase 25
10511282	3.11205471	0.003464695	22163	Tnfrsf4	tumor necrosis factor receptor superfamily, member 4
10403273	3.109923171	0.008660395	142688	Asb13	ankyrin repeat and SOCS box-containing 13
10455784	3.079694197	0.003324094	107022	Gramd3	GRAM domain containing 3
10349081	3.057654213	0.002422501	98432	Phlpp1	PH domain and leucine rich repeat protein phosphatase 1
10542677	3.047284898	0.003901539	75320	Etnk1	ethanolamine kinase 1
10500378	3.023112594	0.004208873	78373	Nudt17	nudix (nucleoside diphosphate linked moiety X)-type motif 17
10569890	3.019457438	0.004367116	108909	Aida	axin interactor, dorsalization associated
10502071	3.012985163	0.006851472	70617	5730508B09Rik	RIKEN cDNA 5730508B09 gene
10544891	3.012124845	0.003155165	107607	Nod1	nucleotide-binding oligomerization domain containing 1
10560174	2.998580144	0.005317021	20364	Sepw1	selenoprotein W, muscle 1
10537227	2.998418862	0.005148528	68487	Tmem140	transmembrane protein 140
10354054	2.997759119	0.007061181	69028	Mitd1	MIT, microtubule interacting and transport, domain containing 1
10493565	2.962925961	0.003050484	56417	Adar	adenosine deaminase, RNA-specific
10412562	2.959365033	0.00313588	286940	Flnb	filamin, beta
10450145	2.954523961	0.003112809	16912	Psmb9	proteasome (prosome, macropain) subunit, beta type 9 (large multifunctional peptidase 2)
10490826	2.953139477	0.01308743	229055	Zbtb10	zinc finger and BTB domain containing 10
10396831	2.949011441	0.002601433	11847	Arg2	arginase type II
10432190	2.947953231	0.003464695	11512	Adcy6	adenylate cyclase 6
10485624	2.946432582	0.006964294	228413	Prrg4	proline rich Gla (G-carboxyglutamic acid) 4 (transmembrane)
10542911	2.939213894	0.028731993	209086	Samd9l	sterile alpha motif domain containing 9-like
10345913	2.937369145	0.003370281	17974	Nck2	non-catalytic region of tyrosine kinase adaptor protein 2
10342727	2.923187784	0.005871742	NA	NA	NA
10414514	2.89231567	0.005681459	18950	Pnp	purine-nucleoside phosphorylase
10486448	2.884753552	0.005335022	271844	Pla2g4f	phospholipase A2, group IVF
10462791	2.881417533	0.00687639	69104	05-mars	membrane-associated ring finger (C3HC4) 5
10363541	2.878978346	0.002747018	NA	NA	NA
10566574	2.872454944	0.003961516	NA	NA	NA
10444268	2.856569992	0.003145004	21355	Tap2	transporter 2, ATP-binding cassette, sub-family B (MDR/TAP)
10479411	2.850056642	0.002735366	72075	Ogfr	opioid growth factor receptor
10369102	2.837801876	0.004058421	100038725	Cep85l	centrosomal protein 85-like

10523012	2.833092305	0.003392094	13178	Dck	deoxycytidine kinase
10514289	2.828438065	0.004661133	NA	NA	NA
10510509	2.816427022	0.003940443	269604	Gpr157	G protein-coupled receptor 157
10369911	2.809229327	0.003967809	68778	Gucd1	guanylyl cyclase domain containing 1
10355246	2.792359215	0.016725023	11363	Acadl	acyl-Coenzyme A dehydrogenase, long-chain
10530633	2.790604541	0.010101046	24051	Sgcb	sarcoglycan, beta (dystrophin-associated glycoprotein)
10363498	2.790312335	0.004103856	67895	Ppa1	pyrophosphatase (inorganic) 1
10425808	2.786123986	0.003192109	12257	Tspo	translocator protein
10467149	2.770508921	0.011416892	112419	2010002M12Rik	RIKEN cDNA 2010002M12 gene
10526459	2.762479283	0.003370281	54153	Rasa4	RAS p21 protein activator 4
10444244	2.759392505	0.003060713	21354	Tap1	transporter 1, ATP-binding cassette, sub-family B (MDR/TAP)
10341111	2.758583895	0.004161345	NA	NA	NA
10596492	2.758007285	0.009844316	235587	Parp3	poly (ADP-ribose) polymerase family, member 3
10598152	2.749543373	0.008660395	625360	BC147527	cDNA sequence BC147527
10533304	2.749192142	0.005347979	231712	Trafd1	TRAF type zinc finger domain containing 1
10583820	2.717019995	0.013981906	619310	Zfp872	zinc finger protein 872
10608650	2.709481673	0.003460976	15051	H2-T9	histocompatibility 2, T region locus 9
10545623	2.707257115	0.017740989	13448	Dok1	docking protein 1
10590791	2.689884801	0.009483476	11797	Birc2	baculoviral IAP repeat-containing 2
10608680	2.673692873	0.003324094	15024	H2-T10	histocompatibility 2, T region locus 10
10481627	2.657469265	0.014276122	16819	Lcn2	lipocalin 2
10552252	2.640880796	0.003535142	72244	1600014C10Rik	RIKEN cDNA 1600014C10 gene
10385511	2.621816718	0.004341377	NA	NA	NA
10355456	2.59341845	0.003638095	381269	Mreg	melanoregulin
10584435	2.592112795	0.005347979	67776	Vwa5a	von Willebrand factor A domain containing 5A
10596960	2.575140215	0.007029423	NA	NA	NA
10439845	2.573189786	0.004977567	433024	Gm5486	predicted gene 5486
10519527	2.571406392	0.004058421	18671	Abcb1a	ATP-binding cassette, sub-family B (MDR/TAP), member 1A
10416566	2.565621325	0.012190127	108670	Epsti1	epithelial stromal interaction 1 (breast)
10574153	2.561264424	0.005210168	434341	Nlr5	NLR family, CARD domain containing 5
10581378	2.559309374	0.005570598	19171	Psmb10	proteasome (prosome, macropain) subunit, beta type 10
10588836	2.539132884	0.012692718	331026	Gmppb	GDP-mannose pyrophosphorylase B
10608715	2.539051577	0.004719034	74183	Perm1	PPARGC1 and ESRR induced regulator, muscle 1
10516852	2.53320841	0.005347979	18386	Oprd1	opioid receptor, delta 1
10351588	2.530267138	0.00541337	71740	Pvrl4	poliovirus receptor-related 4
10601581	2.513325059	0.0136789	NA	NA	NA
10378816	2.50504166	0.005149359	15567	Slc6a4	solute carrier family 6 (neurotransmitter transporter, serotonin), member 4
10439854	2.504116224	0.008670295	70508	Bbx	bobby sox homolog (Drosophila)
10606730	2.503928103	0.005239272	278097	Armxc6	armadillo repeat containing, X-linked 6
10344135	2.496190874	0.033275059	NA	NA	NA
10577586	2.482009737	0.004367116	64933	Ap3m2	adaptor-related protein complex 3, mu 2 subunit
10450694	2.478645989	0.004296272	NA	NA	NA
10460582	2.465679804	0.005347624	107242	AI837181	expressed sequence AI837181
10487238	2.462559492	0.01063193	15186	Hdc	histidine decarboxylase
10371616	2.45970534	0.006283358	212862	Chpt1	choline phosphotransferase 1
10483081	2.458608798	0.006082292	14089	Fap	fibroblast activation protein
10591482	2.458145126	0.005040262	50868	Keap1	kelch-like ECH-associated protein 1
10425890	2.456789459	0.015255057	73167	Arhgap8	Rho GTPase activating protein 8
10437668	2.433966171	0.010367375	12703	Socs1	suppressor of cytokine signaling 1
10556280	2.428432812	0.004850495	20947	Swap70	SWA-70 protein
10379401	2.417993008	0.00724137	71956	Rnf135	ring finger protein 135
10469167	2.402035809	0.009137706	353282	Sfmbt2	Scm-like with four mbt domains 2
10414527	2.397468034	0.006954094	NA	NA	NA
10555862	2.392821016	0.005161892	NA	NA	NA
10522976	2.391363409	0.010101046	52822	Rufy3	RUN and FYVE domain containing 3
10476775	2.373841295	0.021030707	67877	Naa20	N(alpha)-acetyltransferase 20, NatB catalytic subunit
10461594	2.360062572	0.019943327	64380	Ms4a4c	membrane-spanning 4-domains, subfamily A, member 4C
10433578	2.350037205	0.021982442	20621	Snn	stannin
10572932	2.346320469	0.016926394	67877	Naa20	N(alpha)-acetyltransferase 20, NatB catalytic subunit
10588786	2.345592537	0.006866161	NA	NA	NA
10514315	2.317826772	0.022025973	15965	Ifna2	interferon alpha 2

10588849	2.317297185	0.005317021	320844	Amigo3	adhesion molecule with Ig like domain 3
10415293	2.315280984	0.008047332	NA	NA	NA
10524866	2.313083252	0.0083059	231668	Vsig10	V-set and immunoglobulin domain containing 10
10429491	2.311966586	0.006016093	11838	Arc	activity regulated cytoskeletal-associated protein
10420030	2.290205783	0.031316593	19188	Psme2	proteasome (prosome, macropain) activator subunit 2 (PA28 beta)
10402080	2.286064892	0.009483476	217827	Nrde2	nrde-2 necessary for RNA interference, domain containing
10341173	2.281214884	0.021446615	NA	NA	NA
10363007	2.280569642	0.015241699	77987	Ascc3	activating signal cointegrator 1 complex subunit 3
10531653	2.269401393	0.009748851	231503	Tmem150c	transmembrane protein 150C
10524878	2.266156102	0.009168579	231668	Vsig10	V-set and immunoglobulin domain containing 10
10353524	2.265507017	0.01963389	70155	Ogfrl1	opioid growth factor receptor-like 1
10493193	2.263339111	0.009642795	12462	Cct3	chaperonin containing Tcp1, subunit 3 (gamma)
10389207	2.24891375	0.006114385	20304	Ccl5	chemokine (C-C motif) ligand 5
10443561	2.227911691	0.006866161	NA	NA	NA
10525452	2.222428016	0.019038597	80751	Rnf34	ring finger protein 34
10372177	2.21803187	0.014688597	278279	Tmtc2	transmembrane and tetratricopeptide repeat containing 2
10436442	2.193115651	0.022771528	NA	NA	NA
10421488	2.176966359	0.007526959	319448	Fndc3a	fibronectin type III domain containing 3A
10545958	2.168830965	0.025443758	11746	Anxa4	annexin A4
10554938	2.167061636	0.00894422	75985	Rab30	RAB30, member RAS oncogene family
10505890	2.16061165	0.029679368	15967	Ifna4	interferon alpha 4
10444258	2.156871226	0.025797958	16913	Psmb8	proteasome (prosome, macropain) subunit, beta type 8 (large multifunctional peptidase 7)
10500388	2.151715132	0.012669515	74414	Polr3c	polymerase (RNA) III (DNA directed) polypeptide C
10389674	2.14183075	0.011389965	68097	Dynll2	dynein light chain LC8-type 2
10560575	2.141111955	0.007627903	19698	Relb	avian reticuloendotheliosis viral (v-rel) oncogene related B
10478875	2.14012683	0.021203747	NA	NA	NA
10548105	2.13944077	0.008331107	12444	Ccnd2	cyclin D2
10385325	2.129709433	0.007799583	30939	Pttg1	pituitary tumor-transforming gene 1
10599576	2.128699401	0.010704611	66496	Pdpdf	pancreatic progenitor cell differentiation and proliferation factor homolog (zebrafish)RIKEN cDNA 2700038C09 gene
10374706	2.126009036	0.021547794	74467	Pus10	pseudouridylylase synthase 10
10420637	2.123914068	0.008047332	16648	Kpna3	karyopherin (importin) alpha 3
10449386	2.12158579	0.009088799	224647	D17Wsu92e	DNA segment, Chr 17, Wayne State University 92, expressed
10424213	2.120666095	0.009542598	387609	Zhx2	zinc fingers and homeoboxes 2
10344551	2.120374344	0.012669515	NA	NA	NA
10582997	2.11514212	0.010218713	12363	Casp4	caspase 4, apoptosis-related cysteine peptidase
10415319	2.103788902	0.009251199	16391	Irf9	interferon regulatory factor 9
10549497	2.102802311	0.018360544	NA	NA	NA
10608649	2.101216989	0.009398512	547347	Gm6034	predicted gene 6034
10574100	2.099601151	0.018900935	434341	Nlrc5	NLR family, CARD domain containing 5
10593842	2.095154573	0.009440173	NA	NA	NA
10444814	2.084957626	0.012741859	15015	H2-Q4	histocompatibility 2, Q region locus 4
10444068	2.083944446	0.008670295	21356	Tapbp	TAP binding protein
10479550	2.077076818	0.020357964	66496	Pdpdf	pancreatic progenitor cell differentiation and proliferation factor homolog (zebrafish)RIKEN cDNA 2700038C09 gene
10494527	2.075509235	0.008547698	67845	Rnf115	ring finger protein 115
10342519	2.072479928	0.016955028	NA	NA	NA
10407145	2.068896798	0.01063193	218613	Mier3	mesoderm induction early response 1, family member 3
10404531	2.06735337	0.01063193	69666	Psmg4	proteasome (prosome, macropain) assembly chaperone 4
10528090	2.059072178	0.013345983	242819	Rundc3b	RUN domain containing 3B
10401149	2.058593847	0.010704611	27260	Plek2	pleckstrin 2
10527896	2.04549286	0.013075978	70797	Ankib1	ankyrin repeat and IBR domain containing 1
10497441	2.042757782	0.019820076	27357	Gyg	glycogenin
10480760	2.042102259	0.013981906	22030	Traf2	TNF receptor-associated factor 2
10486172	2.041912599	0.013134543	67809	Rmdn3	regulator of microtubule dynamics 3
10519983	2.035613179	0.031508413	14190	Fgl2	fibrinogen-like protein 2
10547906	2.029729546	0.025151124	16768	Lag3	lymphocyte-activation gene 3
10490653	2.028969515	0.010097141	229004	Gmeb2	glucocorticoid modulatory element binding protein 2
10520250	2.027053438	0.015274562	53312	Nub1	negative regulator of ubiquitin-like proteins 1
10359097	2.026390937	0.012741859	208263	Tor1aip1	torsin A interacting protein 1
10376060	2.018097748	0.029932506	16362	Irf1	interferon regulatory factor 1
10517996	2.015498883	0.010166331	69582	Plekhn2	pleckstrin homology domain containing, family M (with RUN domain) member 2
10577655	2.01300081	0.01798657	15930	Ido1	indoleamine 2,3-dioxygenase 1

10500345	2.01263237	0.038342143	21748	Terc	telomerase RNA component
10341296	2.011477119	0.021446615	NA	NA	NA
10424781	2.01078259	0.01682735	66168	Grina	glutamate receptor, ionotropic, N-methyl D-aspartate-associated protein 1 (glutamate binding)
10601473	2.00553719	0.017249188	68117	Apool	apolipoprotein O-like
10523297	2.000775381	0.009844316	12452	Ccng2	cyclin G2

Supporting Information Table 4. List of the antibodies used

Antigen	Fluorochrome	Clone	Isotype	Provider
CD11c	APC-Cy7	HL3	Hamster IgG	BD bioscience
CD3e	PE	145-2C11	Hamster IgG1, κ	BD bioscience
Ly6g	PE	1A8	Rat IgG2a, κ	BD bioscience
CD64	PE	X54-5/7.1.1	Mouse IgG1, κ	BD bioscience
Siglec-f	PE	E50-2440	Rat IgG2a, κ	BD bioscience
CD11b	V450	M1/70	Rat IgG2b, κ	BD bioscience
CD11b	PE-Cy7	M1/70	Rat IgG2b, κ	BD bioscience
Ly6c	FITC	AL21	Rat IgM, κ	BD bioscience
Ly6c	PE-CF594	AL21	Rat IgM, κ	BD bioscience
Nk1.1	PE	Pk136	Mouse IgG2a, κ	BD bioscience
CD19	PE	1D3	Rat IgG2a, κ	BD bioscience
CD24	BV421	M1/69	Rat IgG2b, κ	BD bioscience
Sirp α	APC	P84	Rat IgG1, κ	BD bioscience
CD252 (OX40L)	Biotin	RM134L	Rat IgG2b, κ	BD bioscience
Rory-T	BV786	Q31-378	Mouse IgG2a, κ	BD bioscience
Gata3	BV421	L50-863	Mouse IgG1, κ	BD bioscience
T-bet	BV650	O4-46	Mouse IgG1, κ	BD bioscience
MHCII	Percp-Cy5.5	M5/14.15.2	Rat IgG2b, κ	Biolegend
Pdl1	Biotin	10F.962	Rat IgG2b, κ	Biolegend
CD86	Biotin	GL-1	Rat IgG2a, κ	Ebioscience
CD4	FITC	GK1.5	Rat IgG2a, κ	Ebioscience
Foxp3	PE	FJK-16S	Rat IgG2a, κ	Ebioscience
CD86	Unconjugated	GL-1	Rat IgG2a, κ	Sony

Interferon response factor-3 promotes the pro-Th2 activity of mouse lung CD11b⁺ conventional dendritic cells in response to house dust mite allergens

Thibaut Janss, Claire Mesnil, Dimitri Pirottin, Pierre Lemaitre, Thomas Marichal, Fabrice Bureau & Christophe J. Desmet

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Review Timeline:	Submission date:	4 May 2016
	First editorial decision:	6 June 2016
	Revision received:	7 July 2016
	Accepted:	16 August 2016

Handling Executive Committee member: Prof. Ken Murphy

Please note that the correspondence below does not include the standard editorial instructions regarding preparation and submission of revised manuscripts, only the scientific revisions requested and addressed.

First Editorial Decision – 6 June 2016

Dear Dr. Bureau, Dr. Desmet, Mr. Janss,

Manuscript ID ejj.201646513 entitled "Interferon response factor-3 promotes the pro-Th2 activity of mouse lung CD11b⁺ conventional dendritic cells in response to house dust mite allergens" which you submitted to the European Journal of Immunology has been reviewed. The comments of the referees are included at the bottom of this letter.

You will see that Referee 1 feels that although your submission is technically sound, it repeats some experiments reported in a previous article, is confirmatory and as such, doesn't justify publication. The Executive Editor disagrees regarding the rejection recommendation but wants to note:

"Note that one reviewer felt that the present study did not go far beyond your previous study published and also made comments that suggested that other signals besides CD86 could be at work in the skewing phenomenon you describe. Although no specific experiments are suggested, I would like the authors to try

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to 1) highlight the findings here that are new relative to your previous study, and 2) make an attempt to address the essential nature of the reviewers concern. This may not be possible in a reasonable period of time, and if this is the case, I would suggest that you include a discussion of the points raised and an outline of the possibilities and future direction, but if it is possible to address experimentally, then additional data are certainly welcome."

Therefore a revised version of your manuscript that takes into account the comments of both the referees will be reconsidered for publication. Should you disagree with any of the referees' concerns, you should address this in your point-by-point response and provide solid scientific reasons for why you will not make the requested changes.

You should also pay close attention to the editorial comments included below. *In particular, please edit your figure legends to follow Journal standards as outlined in the editorial comments. Failure to do this will result in delays in the re-review process.*

Please note that submitting a revision of your manuscript does not guarantee eventual acceptance, and that your revision will be re-reviewed by the referees before a decision is rendered.

If the revision of the paper is expected to take more than three months, please inform the editorial office. Revisions taking longer than six months may be assessed by new referee(s) to ensure the relevance and timeliness of the data.

Once again, thank you for submitting your manuscript to European Journal of Immunology and we look forward to receiving your revision.

Yours sincerely,
Karen Chu

On behalf of Prof. Kenneth Murphy

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Reviewer: 1

Comments to the Author

-The authors come up with the hypothesis that it is all CD86 that's driving the Th2 skew of HDM exposed DCs. In fact, they do not block Ox40L or any of the other potential candidates. Showing that the blockade of CD86 does something is not really terribly exciting, rather confirmatory. It could very well be that CD86 is a crucial signal 2, but that other signals really do the polarizing.

-the authors offer no explanation or comparison why these data are different from their earlier work on IRF3^{-/-} DCs, (Marchall et al. JACI) where DC migration was affected in the HDM model.

Reviewer: 2

Comments to the Author

The manuscript describes the very interesting finding that in the house dust mite (HDM) allergy model, the CD11b⁺ lung resident cDCs express antiviral defense genes (i.e. Irf7, Ifnb1, Mx1) regulated by IRF3. Remarkably, the IRF3^{-/-} CD11b⁺ cDCs displayed reduced Th2-promoting activity upon in vivo transfer, and induced less Th2 differentiation in vitro than WT DCs. The reduced Th2 promoting activity of the IRF3^{-/-} CD11b⁺ cDCs was associated with decreased expression of CD86 RNA and protein. While transcription of genes encoding Th2-promoting cytokines such as IL-10 and IL-33 was apparently not affected by Irf3 deficiency, the expression of IFNb RNA was reduced, and the expression of IL-12p40 RNA was increased in IRF3^{-/-} DCs. Thus, upon stimulation with HDM, IRF3 regulates an antiviral gene expression program in lung CD11b⁺ cDCs, which appears to be important to promote Th2 responses and eosinophilia in vivo. The experiments are well performed, the data shown are convincing and the manuscript is clearly written.

The following concerns should be addressed:

1. CD11b⁺ cDCs have been shown to promote Th2 or Th17 responses in several studies. This may be due to the fact that CD11b⁺ cDCs in the skin and lung have been shown to be heterogeneous in expression of surface markers, and differentially dependent on transcription factors such as IRF4 and KLF4. Does Irf3 deficiency differentially affect these CD11b⁺ cDC subsets?
2. It is interesting that Irf3 deficiency did not lead to a reduction in CD11b⁺ cDC expression of cytokines (i.e. IL-10, IL-6, IL-33) reported to be produced by this DC subset in the HDM model. Ideally expression of these genes would be shown in Fig. 6A. One concern is that the 12 hr time point was not optimal for detecting transcripts of these cytokines, or that cytokine protein production is regulated differently than the cytokine mRNA. It would be useful to know if the production of IL-10, IL-6, IL-33 or other Th2-promoting cytokines was altered in the CD11b⁺ cDCs exposed to HDM.

3. Related to point 2 above, it is notable that the expression of the IL-12p40 gene is increased in the *Irf3*^{-/-} mice. Do the CD11b⁺ cDCs express more IL-12p70 or IL-23? Would this account for the increase in IFN γ response shown in Fig. 5B?

4. DC migration was assessed after 24 hr. However, DC migration likely continues for multiple days post-HDM challenge, and differences in WT and *Irf3*^{-/-} DC migration may become more apparent later. Curiously, the authors (J Allergy Clin Immunol 2010) previously showed that *IRF3*^{-/-} lung DCs had a deficiency in migration to the LN 24 hr after HDM challenge. If this measurement included total DCs, perhaps the CD103⁺ DCs are affected by *Irf3* deficiency more than the CD11b⁺ DCs shown in the current paper?

5. It is possible that the lyophilized HDM extracts contain nucleic acids that might trigger cytosolic sensors upstream of *Irf3*. If so, this might be discussed. Would other type 2 promoting allergens that are free of nucleic acids also promote this *Irf3*-dependent response? Would the CD103⁺ lung DCs also show these *Irf3*-dependent antiviral responses?

Minor points:

1. The gating of LN migratory DCs to support Fig. 4D,E should be shown.

2. In Fig. 4, it would be helpful to also show the gating of the CD103⁺ lung DCs, and their numbers, to support the conclusion that this DC subset does not differ. Fig. 4C shows that the CD11c⁺ MHCII⁺ population contains two subsets – are these the CD11b⁺ and CD103⁺ DC subsets, or does the CD11b⁺ population also contain alveolar macrophages?

3. In the results section description of the CD86 blocking experiment in Fig. 6, it should be stated that cDCs were cocultured with anti-CD86 and T cells because the cytokines measured were from T cells. This is stated in the legend but not in the results section

First revision – authors' response – 7 July 2016

Reviewer: 1

Comments to the Author

-The authors come up with the hypothesis that it is all CD86 that's driving the Th2 skew of HDM exposed DCs. In fact, they do not block Ox40L or any of the other potential candidates. Showing that the blockade

of CD86 does something is not really terribly exciting, rather confirmatory. It could very well be that CD86 is a crucial signal 2, but that other signals really do the polarizing.

We fully agree with the reviewer. Although our data supports that it is a major contributor, we however did not aim to claim an exclusive role of CD86 in driving the pro-Th2 activity of HDM-exposed lung CD11b+ cDC2s, which we feel was explicitly stated in the discussion section of the original manuscript (page 17, lines 377 to 378). We adapted this statement for more clarity (added text underlined).

" Based on these observations, we propose that downregulation of CD86 expression likely is a major contributor to the decreased pro-Th2 activity of *Irf3*-deficient lung cDC2s. We however do not argue that altered expression of CD86 is the sole explanation for the reduced pro-Th2 activity of *Irf3*-deficient lung cDC2s. Other molecules not investigated here, such as other costimulatory/coinhibitory molecules or cytokines, could also contribute. One likely possibility is that in order to optimally induce Th2 responses, cDC2s need a fine-tuning of their co-stimulatory/co-inhibitory activity, which is perturbed in the absence of *Irf3* signalling."

-the authors offer no explanation or comparison why these data are different from their earlier work on *IRF3*^{-/-} DCs, (Marchall et al. JACI) where DC migration was affected in the HDM model.

We apologize for not discussing this matter in the original manuscript. In our JACI paper, we identified DCs as CD11c+ MHCII+ autofluorescence-negative cells, which we now know contains a mixture of cDC1s, cDC2s and inflammatory-monocyte-derived DCs (moDCs). We observed that in *Irf3*^{-/-} mice, moDC recruitment to the lung and lung draining lymph nodes was severely impaired following HDM treatment. We also observed reduced numbers of CD103+ cDC1s in the lung and draining lymph nodes of *Irf3*^{-/-} mice in the steady-state and following HDM treatment. If considering the DC population as a whole, we hence could conclude that DC recruitment to the draining lymph nodes is reduced in *Irf3*^{-/-} mice, in line with our conclusions in the JACI paper. Yet, migration of lung cDC2s was not affected in *Irf3*^{-/-} mice following HDM exposure. In line with comment 4 of Reviewer 2, we added this information in Supplemental Figure 1 and adapted the results and discussion sections accordingly (page 10, lines 196 to 208 and page 15, lines 325 to 331)

Reviewer: 2

Comments to the Author

The manuscript describes the very interesting finding that in the house dust mite (HDM) allergy model, the CD11b+ lung resident cDCs express antiviral defense genes (i.e. *Irf7*, *Ifnb1*, *Mx1*) regulated by *IRF3*. Remarkably, the *IRF3*^{-/-} CD11b+ cDCs displayed reduced Th2-promoting activity upon in vivo transfer, and induced less Th2 differentiation in vitro than WT DCs. The reduced Th2 promoting activity of the

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IRF3^{-/-} CD11b⁺ cDCs was associated with decreased expression of CD86 RNA and protein. While transcription of genes encoding Th2-promoting cytokines such as IL-10 and IL-33 was apparently not affected by Irf3 deficiency, the expression of IFN γ RNA was reduced, and the expression of IL-12p40 RNA was increased in IRF3^{-/-} DCs. Thus, upon stimulation with HDM, IRF3 regulates an antiviral gene expression program in lung CD11b⁺ cDCs, which appears to be important to promote Th2 responses and eosinophilia in vivo. The experiments are well performed, the data shown are convincing and the manuscript is clearly written.

We thank the reviewer for his kind appreciation of our work and for his constructive comments.

The following concerns should be addressed:

1. CD11b⁺ cDCs have been shown to promote Th2 or Th17 responses in several studies. This may be due to the fact that CD11b⁺ cDCs in the skin and lung have been shown to be heterogeneous in expression of surface markers, and differentially dependent on transcription factors such as IRF4 and KLF4. Does Irf3 deficiency differentially affect these CD11b⁺ cDC subsets?

We further subdivided CD11b⁺ cDC2s in the lung of wild type and Irf3^{-/-} mice based on their expression of Sirp α and CD24. This allowed us to identify 2 populations of CD11b⁺ cDC2s, namely Sirp α ⁺ CD24⁻ cDC2s and Sirp α ⁺ CD24⁺. This latter Sirp α ⁺ CD24⁺ subset should contain Klf4-dependent cDC2s, as recently reported (Tussiwand et al., 2015, Immunity 42, 916–928). Of note, we excluded from our analysis most monocyte-derived DCs (moDCs) through the exclusion of Ly6c⁺ cells. Using this strategy, we observed no significant differences in the number of either of these 2 subsets of cDC2s following saline or HDM treatment in the lung of wild type or Irf3^{-/-} mice. We added this information in Supplemental Figure 2 and adapted the results section accordingly (page 10, lines 207 to 210).

2. It is interesting that Irf3 deficiency did not lead to a reduction in CD11b⁺ cDC expression of cytokines (i.e. IL-10, IL-6, IL-33) reported to be produced by this DC subset in the HDM model. Ideally expression of these genes would be shown in Fig. 6A. One concern is that the 12 hr time point was not optimal for detecting transcripts of these cytokines, or that cytokine protein production is regulated differently than the cytokine mRNA. It would be useful to know if the production of IL-10, IL-6, IL-33 or other Th2-promoting cytokines was altered in the CD11b⁺ cDCs exposed to HDM.

As suggested by the Reviewer, we added microarray-derived data on the expression of IL-10, IL-6 and IL-33 in revised Figure 6A. We agree with the referee that assessing expression (ideally at the protein level) of IL-10, IL-6 and IL-33 would be interesting in potentially identifying additional levels of regulation of the pro-Th2 activity of lung cDC2s by Irf3. However, we feel that this goes beyond the scope of this study, as it would require extensive new experiments on limiting biological samples and would not change the key

messages of the present study. We hence modified the discussion in order to open this interesting perspective for future study (page 17, lines 375 to 376).

3. Related to point 2 above, it is notable that the expression of the IL-12p40 gene is increased in the *Irf3*^{-/-} mice. Do the CD11b⁺ cDCs express more IL-12p70 or IL-23? Would this account for the increase in IFN γ response shown in Fig. 5B?

We did not address expression of IL-12p70 or IL-23 at the protein level but our microarray data does not indicate differential expression of IL12p35 and IL23p19, which would argue against upregulated expression of these cytokines. We added this information in revised Figure 6. As above however, we agree with the reviewer that direct assessment of protein expression of these cytokines would be most conclusive and discuss this point in the revised discussion (page 16, lines 335 to 337).

4. DC migration was assessed after 24 hr. However, DC migration likely continues for multiple days post-HDM challenge, and differences in WT and *Irf3*^{-/-} DC migration may become more apparent later. Curiously, the authors (J Allergy Clin Immunol 2010) previously showed that *IRF3*^{-/-} lung DCs had a deficiency in migration to the LN 24 hr after HDM challenge. If this measurement included total DCs, perhaps the CD103⁺ DCs are affected by *Irf3* deficiency more than the CD11b⁺ DCs shown in the current paper?

We apologize for not discussing this matter in the original manuscript. In our JACI paper, we identified DCs as CD11c⁺ F4/80⁻ autofluorescence-negative cells, which we now know contains a mixture of cDC1s, cDC2s and monocyte-derived "moDCs". We observed that in *Irf3*^{-/-} mice, moDC numbers in the lung and lung draining lymph nodes were significantly reduced following HDM treatment. We also observed reduced numbers of CD103⁺ cDC1s in the lung and draining lymph nodes of *Irf3*^{-/-} mice in the steady-state and following HDM treatment. If considering the DC population as a whole, we hence can conclude that DC recruitment to the draining lymph nodes is reduced in *Irf3*^{-/-} mice, in line with our conclusions in the JACI paper. We added this information in Supplemental Figure 1 and adapted the results and discussion sections accordingly (page 10, lines 194 to 210 and page 15, lines 323 to 329).

5. It is possible that the lyophilized HDM extracts contain nucleic acids that might trigger cytosolic sensors upstream of *Irf3*. If so, this might be discussed. Would other type 2 promoting allergens that are free of nucleic acids also promote this *Irf3*-dependent response? Would the CD103⁺ lung DCs also show these *Irf3*-dependent antiviral responses?

We estimated the DNA content of the HDM extracts used in this study using PicoGreen, a fluorescent intercalating agent. DNA content amounted to 10 μ g/mg dry weight HDM, meaning that mice received 1 μ g of DNA per intranasal injection of HDM. Hence, HDM contains significant concentrations of DNA and it

is could be tempting to speculate that they could be responsible for Irf3 activation in this context. As this demonstration would merit further investigation to notably identify the DNA sensors involved, we feel it is an interesting perspective that we discuss in the revised version of the manuscript (page 15, lines 319 to 321).

Minor points:

1. The gating of LN migratory DCs to support Fig. 4D,E should be shown.

This information was actually provided in Figure 4C. Gating for lung DCs (Figure 4A,B) was identical to that of Figure 1A and was hence not shown again.

2. In Fig. 4, it would be helpful to also show the gating of the CD103+ lung DCs, and their numbers, to support the conclusion that this DC subset does not differ. Fig. 4C shows that the CD11c+ MHCII+ population contains two subsets – are these the CD11b+ and CD103+ DC subsets, or does the CD11b- population also contain alveolar macrophages?

The comparison of lung cDC1 numbers in WT and Irf3-/- mice as well as the gating strategies used are now provided in Supplementary Figure 1. In the original Figure 4C, macrophages were excluded by the DUMP staining, which included anti-CD64 and anti-SiglecF antibodies.

3. In the results section description of the CD86 blocking experiment in Fig. 6, it should be stated that cDCs were cocultured with anti-CD86 and T cells because the cytokines measured were from T cells. This is stated in the legend but not in the results section

We adapted the results section accordingly (page 13, line 270 to 271).

Second Editorial Decision – 29 July 2016

Dear Dr. Desmet,

It is a pleasure to provisionally accept your manuscript entitled "Interferon response factor-3 promotes the pro-Th2 activity of mouse lung CD11b+ conventional dendritic cells in response to house dust mite allergens" for publication in the European Journal of Immunology. For final acceptance, please follow the instructions below and return the requested items as soon as possible as we cannot process your manuscript further until all items listed below are dealt with.

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Please note that EJI articles are now published online a few days after final acceptance (see Accepted Articles: [http://onlinelibrary.wiley.com/journal/10.1002/\(ISSN\)1521-4141/accepted](http://onlinelibrary.wiley.com/journal/10.1002/(ISSN)1521-4141/accepted)). The files used for the Accepted Articles are the final files and information supplied by you in Manuscript Central. You should therefore check that all the information (including author names) is correct as changes will NOT be permitted until the proofs stage.

We look forward to hearing from you and thank you for submitting your manuscript to the European Journal of Immunology.

Yours sincerely,
Karen Chu

on behalf of Prof. Kenneth Murphy

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