

Supplementary Table 1. Demographics of the study groups (entire sample)

Variable	DA+	AWs	P value
N	132	148	
Sex (M/F)	114/18	138/10	0.0719
Age (years, SEM)	41.06, 1.02	30.46, 0.623	<0.0001
Exposure (HDI/MDI/TDI)	60/27/45	148/0/0	<0.0001
Exposure Duration (months, SEM)	135.6, 11.52	66.06, 2.22	<0.0001
Atopy (Yes/No)	72/52	78/57	1
Smoking (Current/Ex/Never)	22/50/59	54/29/65	<0.0001

AW (asymptomatic diisocyanate exposed controls), DA+ (exposed workers with SIC-confirmed diisocyanate asthma)

Supplementary Table 2. Distribution of genotype frequencies between the groups (entire sample)

Gene/SNP ID	DA+ (n = 130) N (%)	AWs (n=148) N (%)	Fisher's exact p-values
ADAM33 S1 (rs3918396)			0.4938
1.1	106 (81.5)	127 (85.8)	
1.2	17 (13.1)	17 (11.5)	
2.2	7 (5.4)	4 (2.7)	
ADAM33 ST+5 (rs597980)			0.4828
1.1	31 (23.8)	43 (29.1)	
1.2	69 (53.1)	68 (45.9)	
2.2	31 (23.8)	37 (25.0)	
ADAM33 T1 (rs2280091)			0.3080
1.1	98 (75.4)	116 (78.4)	
1.2	31 (23.8)	31 (20.9)	
2.2	2 (1.5)	0 (0.0)	
ALOX5 (G-1699A) (rs4986832)			0.5936
1.1	83 (63.8)	98 (66.2)	
1.2	38 (29.2)	45 (30.4)	
2.2	8 (6.2)	5 (3.4)	
PTGS1 (C644A) (rs5788)			0.9463
1.1	92 (70.8)	106 (71.6)	
1.2	34 (26.2)	36 (24.3)	
2.2	5 (3.8)	5 (3.4)	
PTGS2 (G-765C) (rs20417)			9.522E-05
1.1	74 (56.9)	93 (62.8)	
1.2	37 (28.5)	52 (35.1)	

2.2	19 (14.6)	2 (1.4)	
PTGS2 (G3050C) (rs5277)			0.2243
1.1	93 (71.5)	110 (74.8)	
1.2	37 (28.5)	34 (23.0)	
2.2	0 (0.0)	3 (2.0)	
NAG1/GDF15 (H6D) (rs1058587)			0.8576
1.1	71 (54.6)	80 (54.4)	
1.2	54 (41.5)	59 (40.1)	
2.2	5 (3.8)	8 (5.4)	
NAG1/GDF15 (V9L) (rs1059519)			0.5319
1.1	57 (43.5)	58 (39.2)	
1.2	57 (43.5)	74 (50.0)	
2.2	17 (13.0)	16 (10.8)	
IL10 (G-1082A) (rs1800896)			0.1328
1.1	46 (35.4)	41 (27.7)	
1.2	59 (45.4)	85 (57.4)	
2.2	25 (19.2)	22 (14.9)	
IL10 (C-819T) (rs1800871)			0.8474
1.1	68 (52.3)	76 (51.7)	
1.2	54 (41.5)	59 (40.1)	
2.2	8 (6.2)	12 (8.2)	
IL1 α (G+4845T) (rs17561)			0.5279
1.1	62 (48.1)	81 (54.7)	
1.2	54 (41.9)	53 (35.8)	
2.2	13 (10.1)	14 (9.5)	
IL1 β (C+3953T) (rs1143634)			0.1251
1.1	70 (53.8)	93 (62.8)	

	1.2	56 (43.1)	47 (31.8)	
	2.2	4 (3.1)	8 (5.4)	
IL1 β (C-511T) (rs16944)				0.3995
	1.1	46 (35.4)	64 (43.2)	
	1.2	60 (46.2)	62 (41.9)	
	2.2	24 (18.5)	22 (14.9)	
IL1 RN (T+2018C) (rs419598)				0.5124
	1.1	65 (49.6)	80 (54.1)	
	1.2	59 (45.0)	57 (38.5)	
	2.2	7 (5.3)	11 (7.4)	
TGFB (C-509T) (rs1800469)				0.1975
	1.1	68 (52.3)	64 (43.2)	
	1.2	51 (39.2)	63 (42.6)	
	2.2	11 (8.5)	21 (14.2)	
TGFB codon 10 (T/C) (rs1982073)				0.7824
	1.1	42 (34.4)	57 (38.8)	
	1.2	57 (46.7)	64 (43.5)	
	2.2	23 (18.9)	26 (17.7)	
TNF α (G-238A) (rs361525)				0.2399
	1.1	114 (87.7)	134 (90.5)	
	1.2	16 (12.3)	12 (8.1)	
	2.2	0 (0.00)	2 (1.4)	
TNF α (G-308A) (rs1800629)				0.0861
	1.1	79 (60.8)	108 (73.0)	
	1.2	47 (36.1)	37 (25.0)	
	2.2	4 (3.1)	3 (2.0)	

*1.1: homozygous for the major allele; 2.2: homozygous for the minor allele; 1.2 heterozygous

Supplementary Table 3. Logistic regression model for significant variations in HDI exposed workers: DA+ vs AW controls

Genetic Model	Additive		Dominant		Recessive	
	OR (95% CI)	p-value [†]	OR (95% CI)	p-value [†]	OR (95% CI)	p-value*
ADAM33/rs3918396	0.48 (0.10, 2.24)	0.347	0.55 (0.24, 1.25)	0.150	0.53 (0.12, 2.45)	0.417
ADAM33/rs597980	0.89 (0.39, 2.05)	0.784	1.23 (0.64, 2.37)	0.541	0.71 (0.35, 1.42)	0.327
ADAM33/rs2280091	1.51 (0.77, 2.95) [†]	0.229	1.62 (0.84, 3.14)	0.152	N/A	
ALOX5/rs4986832	2.19 (0.48, 9.91)	0.311	0.98 (0.53, 1.83)	0.951	2.28 (0.51, 10.18)	0.282
PTGS1/rs5788	0.48 (0.09, 2.46)	0.377	0.54 (0.27, 1.08)	0.081	0.58 (0.12, 2.85)	0.498
PTGS2/rs20417	16.94 (3.49, 82.17)	0.0004	1.54 (0.85, 2.79)	0.151	17.15 (3.58, 82.16)	0.0004
PTGS2/rs5277	1.29 (0.68, 2.46) [†]	0.441	1.16 (0.62, 2.20)	0.643	N/A	
GDF15/rs1058587	0.34 (0.06, 1.20)	0.233	0.87 (0.49, 1.54)	0.623	0.36 (0.06, 2.02)	0.243
GDF15/rs1059519	0.96 (0.37, 2.51)	0.935	1.02 (0.57, 1.83)	0.957	0.95 (0.38, 2.33)	0.903
IL10/rs1800896	1.06 (0.46, 2.45)	0.898	0.66 (0.36, 1.21)	0.178	1.49 (0.71, 3.16)	0.295
IL10/rs1800871	0.56 (0.16, 1.92)	0.359	1.02 (0.58, 1.82)	0.934	0.53 (0.16, 1.78)	0.307
IL1 α /rs17561	1.33 (0.52, 3.41)	0.552	1.32 (0.74, 2.34)	0.344	1.18 (0.48, 2.92)	0.716
IL1 β /rs1143634	0.72 (0.19, 2.78)	0.635	1.34 (0.76, 2.39)	0.316	0.62 (0.16, 2.36)	0.486
IL1 β /rs16944	1.22 (0.53, 2.78)	0.644	1.28 (0.72, 2.30)	0.402	1.06 (0.49, 2.27)	0.882
IL1RN/rs419598	0.70 (0.20, 2.42)	0.578	1.26 (0.71, 2.23)	0.426	0.61 (0.18, 2.06)	0.428
TGFB/rs1800469	0.28 (0.10, 0.76)	0.0125	0.48 (0.27, 0.87)	0.0159	0.37 (0.14, 0.95)	0.0388
TGFB/rs1982073	0.80 (0.34, 1.88)	0.607	0.92 (0.50, 1.69)	0.790	0.81 (0.38, 1.76)	0.598
TNF α /rs361525	1.33 (0.54, 3.30) [†]	0.537	1.04 (0.43, 2.51)	0.927	N/A	
TNF α /rs1800629	0.36 (0.04, 3.06)	0.353	1.99 (1.08, 3.70)	0.0286	0.29 (0.04, 2.39)	0.249

*Adjusted for smoking status, duration of exposure and age

[†]Marked ones: heterozygotes vs major genotype; others: major variant vs minor variant

Supplementary Table 4. Regulome DB scores of significant and correlated SNPs

Position	SNP ID	RegulomeDB score	Description
chr19:41860295	rs1800469	1b	eQTL + TF binding + any motif + DNase footprint + DNase peak
chr19:41864508	rs1982072	1f	eQTL + TF binding/DNase peak
chr6:31543030	rs1800629	1f	eQTL + TF binding/DNase peak
chr1:186650320	rs20417	2b	TF binding + any motif + DNase footprint + DNase peak
chr19:41869755	rs2241712	2b	TF binding + any motif + DNase footprint + DNase peak
chr9:125141706	rs10306141	2b	TF binding + any motif + DNase footprint + DNase peak
chr19:41856885	rs2241715	4	TF binding + DNase peak
chr9:125141785	rs10306143	4	TF binding + DNase peak
chr9:125145618	rs4240474	4	TF binding + DNase peak
chr19:41861673	rs2317130	5	TF binding or DNase peak
chr9:125144940	rs10306152	5	TF binding or DNase peak
chr19:41869391	rs2241714	6	Motif hit
chr9:125142708	rs60185476	6	Motif hit
chr9:125143791	rs5788	No Data	
chr19:41871141	rs1549933	No Data	
chr6:31496568	rs2516482	No Data	
chr9:125142480	rs7026055	No Data	
chr9:125143060	rs10306145	No Data	
chr9:125143146	rs10306146	No Data	
chr9:125143383	rs10306148	No Data	
chr9:125144422	rs10306150	No Data	

Bolded SNPs are significant study SNPs, the others are correlated SNPs ($r^2=1$)

Supplementary Table 5. SNPs with putative regulatory function (RegulomeDB Score 1-6)

Gene	RegulomeDB score	Significant and Correlated SNPs	Distance	eQTL	Protein Binding	Binding motif
<i>TGFB1</i>	1b	rs1800469	0	MGC4093	POLR2A, CREBBP, CTCF	COUPTF
	1f	rs1982072	1378	MGC4093		
	2b	rs2241712	3410		NFKB1, CDX2, USF1, SP1, EGR1, ZBTB7A, IRF1, POLR2A, ELF1, GAPBA, SPI1, MAX, NRF1, TBP,	SREBP, SREBP1
	4	rs2241715	4213		POLR2A, TAF1, GATA2, ZNF263, GABPA, GATA1, TAL1, SPI1, REST, MAX, MYC, MXI1	
	6	rs2241714	9460	MGC4093, B3GALT7	No data	No data
<i>TNFα</i>	1f	rs1800629	0	AIF1	No data	SP1
<i>PTGS2</i>	2b	rs20417	0	No data	TFAP2A, TFAP2C	STAT1, E2F-1:DP-1, E2F-1:DP-2, E2F-4:DP-2, EWSR1-FLI1
<i>ADAM33</i>	5	rs2280091	0	No data	No data	SREBP, SREBP1
<i>PTGS1</i>	2b	rs10306141	2085		CTCF, TRIM28, SMC3, RAD21	POU1F1
	4	rs4240474	1827	No data	E2F1	No data
	4	rs10306143	2006		CTCF, TRIM28, SMC3, RAD21	
	6	rs60185476	1083			HNF4, PPARG::RXRA, HNF4A, Zbtb3

eQTL, expression quantitative trait loci; bolded SNPs are significant SNPs