

Supp. Table 1 The linear regression statistics of the bodyweight

Group (<i>n</i>)	R	R ²	Coef.	Coef. err.
FA (18)	0.96	0.93	1.1	±0.22
Low (19)	0.92	0.85	0.8	±0.26
Mod. Beirut (20)	0.93	0.86	1.0	±0.30
High (20)	0.98	0.95	1.0	±0.16

Shown is the linear regression statistics after linearized y-axis (\log_{10}). According to similar coefficients, the bodyweight remained unchanged in all groups after WP smoke exposure. Data reported used product 2. Bodyweight not measured from groups using product 1. FA= filtered air control, *n* = number of biological replicas.

Supp. Table 2 Results of differential cell count in BAL samples

Cell type	No. cells x 10 ⁴ ±SE (%) for each experimental group			
	Air (<i>n</i> = 10)	Low (<i>n</i> = 10)	Mod. Beirut (<i>n</i> = 10)	High (<i>n</i> = 10)
<i>Product 1</i>				
Total cells/mL	6.03 ± 0.77 (100.0)	5.36 ± 0.46 (100.0)	5.92 ± 1.00 (100.0)	5.61 ± 0.71 (100.0)
Lymphocytes	1.10 ± 0.14 (18.3)	0.72 ± 0.05 (13.6)	0.77 ± 0.21 (11.9)	0.62 ± 0.12 (10.6)
Macrophages	4.87 ± 0.62 (80.7)	4.74 ± 0.47 (86.1)	5.26 ± 0.94 (87.3)	4.92 ± 0.63 (88.2)
Neutrophils	0.07 ± 0.04 (00.9)	0.02 ± 0.01 (00.3)	0.05 ± 0.02 (00.8)	0.07 ± 0.06 (01.2)
<i>Product 2</i>				
Total cells/mL	8.13 ± 0.70 (100.0)	8.15 ± 0.71 (100.0)	8.05 ± 0.42 (100.0)	7.20 ± 0.42 (100.0)
Lymphocytes	1.57 ± 0.24 (18.4)	1.34 ± 0.25 (15.7)	1.05 ± 0.10 (13.2)	0.72 ± 0.06 (10.3)
Macrophages	6.29 ± 0.45 (79.0)	6.68 ± 0.50 (82.9)	6.96 ± 0.39 (86.3)	6.40 ± 0.32 (89.3)
Neutrophils	0.27 ± 0.10 (02.6)	0.13 ± 0.05 (01.4)	0.04 ± 0.01 (0.5)	0.09 ± 0.04 (00.3)

n = number of biological replicas

Supp. Table 3 Design of the exposure experiments

Product (experiment)	Date start	Date end
Product 1 (Chronic exposure)	6/5/17	11/27/17
Filtered air	10	
Low	10	
Mod. Beirut	10	
High	10	
Product 2 (Chronic exposure)	1/10/18	6/18/18
Filtered air	18 [#]	
Low	19 [#]	
Mod. Beirut	20	
High	20	
Product 2 (Acute exposure)	05/31/2018	05/31/2018
Filtered air	5	
Mod. Beirut	5	
Dry waterpipe	5	

[#] in FA group, 2 mice died on 2/26/18 and the other between 02/23/18-04/13/18 (exact dated missing). In the Low regimen group, 1 mouse died on 3/12/18.

Supp. Table 4. EIGs expressed uniquely either in waterpipe or dry waterpipe

Genes unique to waterpipe

<i>Gene</i>	<i>Symbol</i>	<i>WP</i>	<i>Loc</i>	<i>Fm</i>
cytochrome P450 family 1 subfamily A member 1	Cyp1a1	-2.7	C	Ez
major urinary protein 1	Mup20	-2.5	E.S	O
collagen type II alpha 1 chain	Col2a1	-2.5	E.S	O
serpin family A member 1	Serpina1e	-2.3	E.S	O
collagen type X alpha 1 chain	Col10a1	-2.3	E.S	O
fibrinogen beta chain	Fgb	-2.3	E.S	O
retinol binding protein 7	Rbp7	-2.2	C	O
apolipoprotein A1	Apoa1	-2.1	E.S	T
albumin	Alb	-2.0	E.S	T
serpin family A member 3	Serpina3k	-1.8	E.S	O
transthyretin	Ttr	-1.7	E.S	T
fibrinogen alpha chain	Fga	-1.6	E.S	O
prostaglandin-endoperoxide synthase 2	Ptgs2	-1.6	C	Ez
protein phosphatase 2 regulatory subunit Bgamma	Ppp2r2c	-1.5	N	P
orosomucoid 1	Orm1	-1.5	E.S	O
myocilin	Myoc	-1.5	C	O
ADAM metallopeptidase with thrombospondin type 1 motif 4	Adamts4	-1.4	E.S	Pp
fibrinogen gamma chain	Fgg	-1.4	E.S	O
alpha 2-HS glycoprotein	Ahsg	-1.4	E.S	O
iodothyronine deiodinase 2	Dio2	-1.4	C	Ez
lecithin-cholesterol acyltransferase	Lcat	-1.2	E.S	Ez
selectin E	Sele	-1.2	P.M	T.R
laminin subunit alpha 1	Lama1	-1.2	E.S	O
retinol dehydrogenase 12	Rdh12	1.3	C	Ez
matrix metallopeptidase 8	Mmp8	1.3	E.S	Pp
transmembrane protein 40	Tmem40	1.3	O	O
sodium voltage-gated channel alpha subunit 4	Scn4a	1.3	P.M	I.C. Gp.
C-X-C motif chemokine receptor 2	Cxcr2	1.3	P.M	C.R.
interleukin 1 receptor type 2	Il1r2	1.4	P.M	T.R
schlafen family member 12 like	Slfn4	1.4	O	Ez
S100 calcium binding protein A8	S100a8	1.5	C	O
schlafen 1	Slfn1	1.5	N	Ez
S100 calcium binding protein A9	S100a9	1.5	C	O
colony stimulating factor 3 receptor	Csf3r	1.5	P.M	T.R
D-box binding PAR bZIP transcription factor	Dbp	1.6	N	T. reg

death associated protein like 1	Dapl1	1.6	O	O
lymphocyte antigen 6 family member D	Ly6d	1.8	P.M	O
aspartic peptidase retroviral like 1	Asprv1	1.8	O	Pp
<i>Genes unique to dry smoke</i>				
collagen type IX alpha 2 chain	Col9a2	-7.4	E.S.	O
phosphoenolpyruvate carboxykinase 1	Pck1	-4.5	C	Kn
transmembrane protein 45B	Tmem45b	-3.3	E.S.	O
perilipin 1	Plin1	-3.2	C	O
BPI fold containing family A member 1	Bpifa1	-3.2	E.S.	O
hypoxia inducible factor 3 subunit alpha	Hif3a	-3.2	N	T. reg
glycoprotein 2	Gp2	-3.0	C	O
lactotransferrin	Ltf	-2.9	E.S.	Pp
adiponectin, C1Q and collagen domain containing	Adipoq	-2.8	E.S.	O
anterior gradient 2, protein disulphide isomerase family member	Agr2	-2.8	E.S.	O
regenerating family member 3 gamma	Reg3g	-2.3	E.S.	O
BPI fold containing family B member 1	Bpifb1	-2.2	E.S.	O
zinc finger protein 791	Zfp791	-2.1	O	O
patatin like phospholipase domain containing 3	Pnpla3	-2.0	C	Ez
calcium voltage-gated channel auxiliary subunit alpha2delta 4	Cacna2d4	-1.9	P.M.	I.C.
insulin receptor substrate 3	Irs3	-1.9	N	O
cell adhesion molecule 4	Cadm4	-1.8	P.M.	O
laminin subunit alpha 3	Lama3	-1.7	E.S.	O
zinc finger protein 365	Zfp365	-1.7	C	O
fibroblast growth factor 18	Fgf18	-1.6	E.S.	G.F.
secretoglobin family 3A member 1	Scgb3a1	-1.6	E.S.	Ck
rhotekin 2	Rtkn2	-1.5	P.M.	O
A-kinase anchoring protein 5	Akap5	-1.5	P.M.	O
prolyl 3-hydroxylase 2	P3h2	-1.5	C	Ez
cytochrome P450 family 2 subfamily B member 6	Cyp2b10	-1.5	C	Ez
phospholipase C epsilon 1	Plce1	-1.4	C	Ez
chromobox 8	Cbx8	-1.4	N	O
cell death inducing DFFA like effector c	Cidec	-1.3	C	O
HOP homeobox	Hopx	-1.3	N	T. reg
perilipin 4	Plin4	-1.2	C	O
cyclin dependent kinase like 5	Cdkl5	-1.2	N	Kn
mal, T cell differentiation protein 2 (gene/pseudogene)	Mal2	-1.2	P.M.	T
mitogen-activated protein kinase kinase kinase kinase 1	Map4k1	1.2	C	Kn
2'-5'-oligoadenylate synthetase 2	Oas2	1.2	C	Ez
POU class 2 associating factor 1	Pou2af1	1.2	N	T. reg

CD3d molecule	Cd3d	1.2	P.M.	T.R.
protein tyrosine phosphatase, receptor type C	Ptprc	1.2	P.M.	P
Rac family small GTPase 2	Rac2	1.2	C	Ez
interferon gamma inducible protein 47	Ifi47	1.2	C	O
TBC1 domain family member 10C	Tbc1d10c	1.3	N	O
Rho GTPase activating protein 15	Arhgap15	1.3	C	O
protein tyrosine phosphatase, receptor type C associated protein	Ptprcap	1.3	P.M.	O
sialophorin	Spn	1.3	P.M.	T.R.
major histocompatibility complex, class II, DO beta	H2-Ob	1.3	P.M.	T.R.
protein tyrosine phosphatase, non-receptor type 22	Ptpn22	1.3	C	P
serine/threonine kinase 17b	Stk17b	1.3	N	Kn
guanylate binding protein 4	Gbp3	1.3	C	Ez
janus kinase and microtubule interacting protein 1	Jakmip1	1.3	C	Tr. Reg
ST8 alpha-N-acetyl-neuraminide alpha-2,8-sialyltransferase 4	St8sia4	1.3	C	Ez
GIMAP1-GIMAP5 readthrough	Gimap3	1.3	C	O
FYN binding protein 1	Fyb	1.3	N	O
lymphocyte antigen 9	Ly9	1.3	P.M.	O
transmembrane protein 200A	Tmem200a	1.3	O	O
C-X-C motif chemokine receptor 5	Cxcr5	1.3	P.M.	GP.C.R.
T cell activation RhoGTPase activating protein	Tagap	1.3	C	O
kinesin family member 21B	Kif21b	1.3	C	O
triggering receptor expressed on myeloid cells like 2	Trem12	1.4	P.M.	O
ras homolog family member H	Rhoh	1.4	P.M.	Ez
Cas scaffold protein family member 4	Cass4	1.4	P.M.	O
membrane spanning 4-domains A1	Ms4a1	1.4	P.M.	O
G protein-coupled receptor 132	Gpr132	1.4	P.M.	GP.C.R.
NLR family CARD domain containing 5	Nlrc5	1.4	C	T. reg
ArfGAP with coiled-coil, ankyrin repeat and PH domains 1	Acap1	1.4	P.M.	O
protein phosphatase 1 regulatory subunit 15A	Ppp1r15a	1.4	C	O
lymphocyte transmembrane adaptor 1	Lax1	1.5	C	O
selectin L	Sell	1.5	P.M.	T.R.
B cell CLL/lymphoma 11A	Bcl11a	1.5	N	T. reg
CD274 molecule	Cd274	1.5	P.M.	Ez
	D16Ertd47			
chromosome 21 open reading frame 91	2e	1.5	O	O
cysteine and serine rich nuclear protein 1	Csrnp1	1.5	N	T. reg
membrane-spanning 4-domains, subfamily A, member 4B	Ms4a4b	1.5	P.M.	O
synaptotagmin like 3	Syt13	1.5	C	O
TNF receptor superfamily member 13C	Tnfrsf13c	1.5	P.M.	T.R.

protein kinase C beta	Prkcb	1.5	C	Kn
leukocyte associated immunoglobulin like receptor 1	Lair1	1.5	P.M.	T.R.
RAB37, member RAS oncogene family	Rab37	1.6	C	Ez
NFKB inhibitor delta	Nfkbid	1.6	N	T. reg
radical S-adenosyl methionine domain containing 2	Rsad2	1.6	C	Ez
zinc finger CCCH-type containing 12D	Zc3h12d	1.6	C	O
killer cell lectin-like receptor family E member 1	Klre1	1.6	P.M.	T.R.
myocardial infarction associated transcript 1	Mirt1	1.6	O	O
BLK proto-oncogene, Src family tyrosine kinase	Blk	1.6	C	Kn
B cell scaffold protein with ankyrin repeats 1	Bank1	1.6	E.S.	O
GTPase, very large interferon inducible 1	Gm4070	1.6	N	O
TNF alpha induced protein 3	Tnfaip3	1.6	N	Ez
H2.0 like homeobox	Hlx	1.7	N	T. reg
major histocompatibility complex, class I, A	H2-Q6	1.7	P.M.	O
C-C motif chemokine receptor 7	Ccr7	1.7	P.M.	GP.C.R.
C-C motif chemokine ligand 5	Ccl5	1.7	E.S.	Ck
solute carrier family 28 member 2	Slc28a2	1.7	P.M.	T
P2Y receptor family member 10	P2ry10	1.7	P.M.	GP.C.R.
interferon inducible GTPase 1	Iigp1	1.7	E.S.	Ez
killer cell lectin-like receptor subfamily K, member 1	Klrl1	1.7	P.M.	T.R.
granzyme B	Gzmb	1.8	C	Pp
CD28 molecule	Cd28	1.8	P.M.	T.R.
cathepsin W	Ctsw	1.8	C	Pp
Fc receptor like 1	Fcrl1	1.8	P.M.	O
adhesion G protein-coupled receptor E4	Adgre4	1.8	P.M.	O
sprouty RTK signaling antagonist 4	Spry4	1.8	P.M.	O
CD226 molecule	Cd226	1.8	P.M.	O
natural cytotoxicity triggering receptor 1	Ncr1	1.8	P.M.	T.R.
natural killer cell granule protein 7	Nkg7	1.8	P.M.	O
Z-DNA binding protein 1	Zbp1	1.9	C	O
guanylate binding protein family member 6	Gbp4	1.9	C	Ez
lymphocyte antigen 6 complex, locus A	Ly6i	1.9	P.M.	O
interferon induced transmembrane protein 6	Ifitm6	1.9	O	O
SH2 domain containing 2A	Sh2d2a	2.0	C	O
TXK tyrosine kinase	Txk	2.0	C	Kn
perforin 1	Prfl	2.0	C	T
cysteine rich angiogenic inducer 61	Cyr61	2.1	E.S.	O
killer cell lectin like receptor C1	Klrc1	2.1	P.M.	T.R.
killer cell lectin like receptor B1	Klrb1c	2.1	P.M.	T.R.
activating transcription factor 3	Atf3	2.1	N	T. reg

complement C3d receptor 2	Cr2	2.2	P.M.	T.R.
ATPase sarcoplasmic/endoplasmic reticulum Ca ²⁺ transporting 1	Atp2a1	2.2	C	T
granzyme A	Gzma	2.3	C	Pp
interleukin 2 receptor subunit beta	Il2rb	2.3	P.M.	T.R.
regulator of G protein signaling 1	Rgs1	2.3	P.M.	O
killer cell lectin-like receptor subfamily C, member 2	Klrc2	2.3	P.M.	T.R.
polo like kinase 2	Plk2	2.4	N	Kn
early growth response 3	Egr3	2.4	N	T. reg
G protein-coupled receptor 174	Gpr174	2.4	P.M.	GP.C.R.
killer cell lectin-like receptor, subfamily A, member 4	Klra9	2.5	P.M.	T.R.
cytotoxic T-lymphocyte associated protein 4	Ctla4	2.7	P.M.	T.R.
calcium voltage-gated channel subunit alpha1 I	Cacna1i	2.8	P.M.	I.C.
eomesodermin	Eomes	2.8	N	T. reg
oncostatin M	Osm	2.9	E.S.	Ck
C-X-C motif chemokine ligand 3	Cxcl2	3.0	E.S.	Ck
titin	Ttn	3.2	C	Kn
nebulin	Neb	4.3	C	O

¹Fold change (log₂) depicted for each exposure relative to filtered air control. ²Loc, location, ³Fm., family; E.S., extracellular space, P.M.; plasma membrane; N, nucleus; C.; cytoplasm; O, other; I.C., ion channel; T., transporter; T. reg., transcriptional regulator; Tr. reg., translation regulator; I.C., ion channel; T.R., transmembrane receptor; Kn, kinase; P., phosphatase; Pp, peptidase; G.f., growth factor; Gp. C.R., G-protein coupled receptor; Ck, cytokine, Ez, enzyme.

Supp. Table 5. Glycoprotein 6 platelet (GP6) signaling pathway

Gene name	Symbol	WP ¹	Dry ¹
collagen type X alpha 1 chain	Col10a1	-4.8	
collagen type II alpha 1 chain	Col2a1	-5.7	
fibrinogen alpha chain	Fga	-3.0	
fibrinogen beta chain	Fgb	-4.8	
fibrinogen gamma chain	Fgg	-2.7	
laminin subunit alpha 1	Lama1	-2.3	
collagen type IX alpha 2 chain	Col9a2		-174.0
laminin subunit alpha 3	Lama3		-3.2
protein kinase C beta	Prkcb		2.9

¹Fold change depicted for each exposure relative to filtered air control. WP = waterpipe mainstream smoke, Dry = dry smoke. Z-score = -2.4.

Supp. Table 6 Genes changes from the LXR/RXR activation pathway.

Gene Name	Symbol	WP ¹
alpha 2-HS glycoprotein	Ahsg	-2.6
albumin	Alb	-4.0
apolipoprotein A1	Apoa1	-4.4
fibrinogen alpha chain	Fga	-3.0
interleukin 1 receptor type 2	Il1r2	2.6
lecithin-cholesterol acyltransferase	Lcat	-2.4
prostaglandin-endoperoxide synthase 2	Ptgs2	-3.0
S100 calcium binding protein A8	S100a8	2.8
serpin family A member 1	Serpina1e	-5.1
transthyretin	Ttr	-3.2

¹Fold change depicted for each exposure relative to filtered air control. WP = waterpipe mainstream smoke. Z-score = -2.5.

Supp. Table 7 Protein kinase C theta Signaling in T Lymphocytes

Gene Name	Symbol	Dry ¹
calcium voltage-gated channel subunit alpha1 I	Cacna1i	7.1
calcium voltage-gated channel auxiliary subunit alpha2delta 4	Cacna2d4	-41.1
CD28 molecule	Cd28	3.5
CD3d molecule	Cd3d	2.3
major histocompatibility complex, class I, A	H2-Q6	3.2
major histocompatibility complex, class II, DO beta	H2-Ob	2.5
NFKB inhibitor delta	Nfkbid	3.0
Rac family small GTPase 2	Rac2	2.3

¹Fold change depicted for each exposure relative to filtered air control. Dry = dry smoke. Z-score = 2.5.