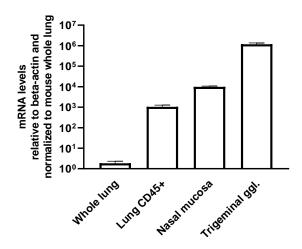
Supplementary table 1. Comparison of TRPA1 expression of Trpa1<sup>+/+</sup> mouse lungs after 1, 2 and 3 months of smoke exposure. The table shows the statistics performed using the means with SD of n=5-9 mice/group. p<0.05 (ordinary one-way ANOVA followed by Tukey's multiple comparisons test) was considered significant indicated by \* and effect size was calculated using Hedges' g.

Group comparisons	Intact	1 month of CSE	2 months of CSE
1 month of CSE			
<i>p</i> value	0.9999		
Hedges' g	0.17		
2 months of CSE			
<i>p</i> value	0.0713	0.1772	
Hedges' g	1.1 ↑↑	0.92 ↑↑	
3 months of CSE			
<i>p</i> value	0.0753	0.1779	>0.9999
Hedges' g	1.74 个个	1.44 ↑↑	0.02

**Supplementary figure 1. Expression of Trpa1.** A. Trpa1 mRNA levels in intact mouse tissue detected by qPCR. Each column represents mean±SEM, n=4.



Supplementary table 2. Comparison of CD68 immunostaining demonstrating macrophages in intact and cigarette smoke exposed mouse lung tissues. The table shows the statistics performed using the means with SD of n=5 tissue sections/group, 20 images/section. p<0.05 (two-way ANOVA followed by Tukey's multiple comparisons test) was considered significant indicated by \* and effect size was calculated using Hedges' g.

Comparisons of CD68 immunostaining of CSE treated Trpa1 <sup>+/+</sup>							
Groups	Companso	ilis of CDC	00 1111111	mice	CJL	ireated Irpai	
Croups	Intact		1 m	1 month of CSE		2 months of CSE	
1 month of CSE							
<i>p</i> value	0.0048	3**					
Hedges' g	1.26	$\uparrow$					
2 months of CSE							
<i>p</i> value	0.249	95		0.7989			
Hedges' g	1.42	$\uparrow$		0.46			
3 months of CSE							
<i>p</i> value	0.0028	3**		>0.9999		0.7133	
Hedges' g	1.67	$\uparrow$		0.02		0.6 个	
	Comparisons of CD68 immunostaining of CSE treated Trpa1 <sup>-/-</sup>						
Groups				mice			
	Intact		1 m	1 month of CSE 2		months of CSE	
1 month of CCT							
1 month of CSE	0.999	10					
p value Hedges' g	0.995						
Tieuges y	0.12						
2 months of CSE							
<i>p</i> value	0.989	92		0.9998			
Hedges' g	0.35	, )		0.16			
3 months of CSE							
<i>p</i> value	>0.99		0.9949			0.9295	
Hedges' g	0.07		0.2			0.38	
	Intact	1 mon CSI		2 months of (	CSE	3 months of CSE	
Comparisons of CD68							
immunostaining of CSE							
treated Trpa1+/+ to Trpa1-							
/- mice		_					
<i>p</i> value	0.06	0.94		>0.9999		0.9995	
Hedges' g	1.37 ↑↑	0.3	3	0.04		0.14	

Supplementary table 3. Comparison of IL-1 $\beta$  mRNA expression of intact and cigarette smoke exposed mouse lung tissues. The table shows the statistics performed using the means with SD of n=5. p<0.05 (two-way ANOVA followed by Tukey's multiple comparisons test) was considered significant indicated by \* and effect size was calculated using Hedges' g.

Crouns	Comparisons of IL-1 $\beta$ mRNA expression of CSE treated Trpa1 $^{+/+}$ mice					
Groups	Intac	·+	1 m	onth of CSE	2	months of CSE
	iiitat	, L	1111	OHUI OI CSL		IIIOIILIIS OI CSL
1 month of CSE						
p value	0.814	L1				
Hedges' g	1.1 ↑					
l licages g	1.1	'				
2 months of CSE						
<i>p</i> value	0.999	9		0.9604		
Hedges' g	0.36	5		0.74↓		
3 months of CSE						
<i>p</i> value	0.999	9		>0.9999		>0.9999
Hedges' g	0.37	7		0.75↓		0.0
	Comparisons of IL-1β mRNA expression of CSE treated Trpa1 <sup>-/-</sup>					
Groups				mice		·
·	Intact		1 month of CSE 2		2	months of CSE
1 month of CSE						
<i>p</i> value	0.999	97				
Hedges' g	0.22	<u>)</u>				
2 months of CSE						
<i>p</i> value	>0.99	99		0.9987		
Hedges' g	0.07	7		0.31		
3 months of CSE						
<i>p</i> value	0.993	31	0.9119			0.9978
Hedges' g	0.45	5		0.69↓		0.44
	Intact	1 mon		2 months of 0	CSE	3 months of CSE
Comparisons of IL-1β			_			552
mRNA expression of CSE						
treated Trpa1+/+ to Trpa1-						
/- mice						
<i>p</i> value	0.8693	>0.99	999	0.9913		>0.9999
Hedges' g	0.83 ↑↑	0.1		0.56 ↑		0.75 ↑

Supplementary table 4. Comparison of IL-23 mRNA expression of intact and cigarette smoke exposed mouse lung tissues. The table shows the statistics performed using the means with SD of n=5. p<0.05 (two-way ANOVA followed by Tukey's multiple comparisons test) was considered significant indicated by \* and effect size was calculated using Hedges' g.

	C	(11.2	2 DNI 4	·			
	Comparisons of IL-23 mRNA expression of CSE treated Trpa1 <sup>+/+</sup>					treated Irpa1"	
Groups				mice		2 1 (005	
	Intac	<u>t</u>	1 m	onth of CSE	2	months of CSE	
4							
1 month of CSE	0.24	<del>-</del>					
p value	0.21						
Hedges' g	1.35 1	`1`					
2 months of CSE							
<i>p</i> value	0.984	13	(	0.0316*			
Hedges' g	0.7 \	L		77 ↓↓			
				•			
3 months of CSE							
<i>p</i> value	0.913	38		0.8932		0.4153	
Hedges' g	0.77	$\uparrow$		0.6 ↓		1.27 个个	
	Compariso	ns of IL-2	3 mRNA	A expression of	CSE	treated Trpa1 <sup>-/-</sup>	
Groups	mice						
-	Intac	t	1 m	1 month of CSE		months of CSE	
1 month of CSE							
<i>p</i> value	0.958	33					
Hedges' g	1.12 1	$\uparrow$					
2 months of CSE							
<i>p</i> value	0.886	66	:	>0.9999			
Hedges' g	1.27 1	$\uparrow$	0.22				
3 months of CSE							
<i>p</i> value	0.405	57	0.9564			0.9894	
Hedges' g	1.37 1	$\uparrow$	C	).79m 个		0.51 个	
	laka ak	1 mon	th of	2		3 months of	
	Intact	CSE		E 2 months of		CSE	
Comparisons of IL-23							
mRNA expression of CSE							
treated Trpa1+/+ to Trpa1-							
/- mice							
p value	0.964	0.2289		0.9348		>0.9999	
Hedges' g	0.87			0.03 44		0.07	
Tieuges y	m↑↑	1.45 ↑		↑↑ 0.83 ↑↑			

Supplementary table 5. Comparison of IL-10 mRNA expression of intact and cigarette smoke exposed mouse lung tissues. The table shows the statistics performed using the means with SD of n=5. p<0.05 (two-way ANOVA followed by Tukey's multiple comparisons test) was considered significant indicated by \* and effect size was calculated using Hedges' g.

	Comparisons of IL-10 mRNA expression of CSE treated Trpa1 <sup>+/+</sup>						
Groups				mice		·	
·	Intac	ct	1 m	1 month of CSE		months of CSE	
1 month of CSE							
<i>p</i> value	0.910	)7					
Hedges' g	0.91 ↓	$\checkmark \downarrow$					
2 months of CSE							
<i>p</i> value	>0.99	99		0.9025			
Hedges' g	0.02	2	C	0.89 ↑↑			
3 months of CSE							
<i>p</i> value	0.355	54		0.9721		0.3427	
Hedges' g	2.05 ↓		1	13 ↓↓		1.95 ↓↓	
<u> </u>					CSE	treated Trpa1 <sup>-/-</sup>	
Groups	'		mice			•	
	Intact		1 month of CSE		2	2 months of CSE	
1 month of CSE							
p value	0.912	) [					
Hedges' g	0.912						
neuges y	0.51	1					
2 months of CSE							
p value	0.985	51		0.4179			
Hedges' g	0.71	$\downarrow$	0.96 ↓↓				
3 months of CSE	0.205	- 4		0.0240*		0.0022	
p value	0.385		0.0318*			0.8923	
Hedges' g	1.61 ↓			1.5 ↓↓		1.38 ↓↓	
	Intact	1 mon		2 months of 0	CSE	3 months of CSE	
Comparisons of IL-10							
mRNA expression of CSE							
treated Trpa1+/+ to Trpa1-							
<sup>/-</sup> mice							
<i>p</i> value	0.999	0.0754		>0.9999		0.9983	
Hedges' g	0.3654	1.32 ↑↑		0.27		0.7864 个	

Supplementary table 6. Comparison of TGF- $\beta1$  mRNA expression of intact and cigarette smoke exposed mouse lung tissues. The table shows the statistics performed using the means with SD of n=5. p<0.05 (two-way ANOVA followed by Tukey's multiple comparisons test) was considered significant indicated by \* and effect size was calculated using Hedges' g.

Groups	Comparisons of TGF-β1 mRNA expression of CSE treated Trpa1 <sup>+/+</sup> mice					f CSE treated
	Intact			onth of CSE	2	months of CSE
1 month of CSE p value Hedges' g	0.99 <sup>4</sup> 0.61					
2 months of CSE p value Hedges' g	>0.99 0.24			0.9578 0.67 个		
3 months of CSE p value Hedges' g	0.3173 2.16 ↑↑		2	0.0761 2.27 个个		0.5098 1.32 ↑↑
Cravina	Comparisons of TGF-β1 mRNA expression of CSE treated Tr					SE treated Trpa1 <sup>-</sup>
Groups	Intact		<sup>/-</sup> mice 1 month of CSE		2	months of CSE
1 month of CSE p value Hedges' g	0.976 0.52					
2 months of CSE p value Hedges' g	>0.9999 0.21			0.9982 0.32		
3 months of CSE p value Hedges' g	>0.9999 0.06		0.9875 0.45			>0.9999 0.14
	Intact	1 mon		2 months of (	CSE	3 months of CSE
Comparisons of TGF-β1 mRNA expression of CSE treated Trpa1+/+ to Trpa1-/- mice						
p value Hedges' g	0.9999 0.34	0.9018 0.69 ↑		0.9999 0.24		$0.1785$ $1.86 \downarrow \downarrow$

Supplementary table 7. Comparisons of TRPA1 and TGF- $\beta$ 1 expression changes in control and cigarette smoke-exposure (CSE) treated 3-dimensional SN/SNM spheroids. The table shows the statistics performed using the means with SD of n=4-15. p<0.05 (ordinary one-way ANOVA followed by Tukey's multiple comparisons test) was considered significant indicated by \* and effect size was calculated using Hedges' q.

by * and effect size was calculated using Hedges' g.							
Groups		TRPA1 immunostainin	g				
Огоирз	Non-smoking SN	Smoking SN	Non-smoking SNM				
Smoking SN							
<i>p</i> value	0.5						
Hedges' g	1.29 ↑↑						
Non-smoking SNM							
<i>p</i> value	0.0039**						
Hedges' g	2.43 ↑↑						
Smoking SNM							
<i>p</i> value		<0.0001***	<0.0001***				
Hedges' g		6.29 个个	3.63 ↑↑				
Groups		RPA1 mRNA expression					
Стопрэ	Non-smoking SN	Smoking SN	Non-smoking SNM				
Smoking SN							
<i>p</i> value	0.6065						
Hedges' g	1.22 ↑↑						
Non-smoking SNM							
<i>p</i> value	0.9747						
Hedges' g	0.52 ↑						
C L: CNINA							
Smoking SNM		0.405.4	0.0050##				
<i>p</i> value		0.1354	0,0053**				
Hedges' g		1.11 个个	2.0 个个				
Groups		TGFβ mRNA expression					
0.000	Non-smoking SN	Smoking SN	Non-smoking SNM				
Smoking SN							
p value	0,9994						
Hedges' g	0.09						
Niew annalde CAIAA							
Non-smoking SNM	. 0 0000						
p value	>0.9999						
Hedges' g	0.00						
Smoking CNIM							
Smoking SNM		0.7222	0.7022				
p value		0.7323	0.7933				
Hedges' g		0.60 个	0.52 ↑				