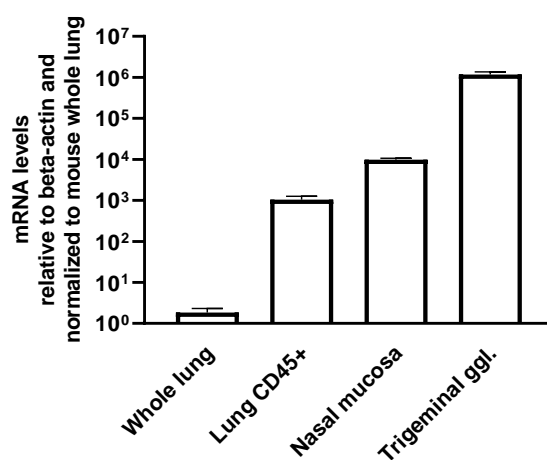


**Supplementary table 1. Comparison of TRPA1 expression of *Trpa1*<sup>+/+</sup> mouse lungs after 1, 2 and 3 months of smoke exposure.** The table shows the statistics performed using the means with SD of n=5-9 mice/group.  $p < 0.05$  (ordinary one-way ANOVA followed by Tukey's multiple comparisons 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 Hedges' <i>g</i>	0.9999 0.17		
2 months of CSE <i>p</i> value Hedges' <i>g</i>	0.0713 1.1 ↑↑	0.1772 0.92 ↑↑	
3 months of CSE <i>p</i> value Hedges' <i>g</i>	0.0753 1.74 ↑↑	0.1779 1.44 ↑↑	>0.9999 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'  $g$ .

Groups	Comparisons of CD68 immunostaining of CSE treated Trpa1 <sup>+/+</sup> mice			
	Intact	1 month of CSE		2 months of CSE
1 month of CSE <i>p</i> value Hedges' <i>g</i>	0.0048** 1.26 ↑			
2 months of CSE <i>p</i> value Hedges' <i>g</i>	0.2495 1.42 ↑	0.7989 0.46		
3 months of CSE <i>p</i> value Hedges' <i>g</i>	0.0028** 1.67 ↑	>0.9999 0.02		0.7133 0.6 ↑
Groups	Comparisons of CD68 immunostaining of CSE treated Trpa1 <sup>-/-</sup> mice			
	Intact	1 month of CSE		2 months of CSE
1 month of CSE <i>p</i> value Hedges' <i>g</i>	0.9998 0.14			
2 months of CSE <i>p</i> value Hedges' <i>g</i>	0.9892 0.35	0.9998 0.16		
3 months of CSE <i>p</i> value Hedges' <i>g</i>	>0.9999 0.07	0.9949 0.2		0.9295 0.38
	Intact	1 month of CSE	2 months of CSE	3 months of CSE
Comparisons of CD68 immunostaining of CSE treated Trpa1 <sup>+/+</sup> to Trpa1 <sup>-/-</sup> mice <i>p</i> value Hedges' <i>g</i>	0.06 1.37 ↑↑	0.946 0.3	>0.9999 0.04	0.9995 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*.

Groups	Comparisons of IL-1 $\beta$ mRNA expression of CSE treated Trpa1 <sup>+/+</sup> mice			
	Intact	1 month of CSE	2 months of CSE	
1 month of CSE <i>p</i> value Hedges' <i>g</i>	0.8141 1.1 $\uparrow\uparrow$			
2 months of CSE <i>p</i> value Hedges' <i>g</i>	0.9999 0.36	0.9604 0.74 $\downarrow$		
3 months of CSE <i>p</i> value Hedges' <i>g</i>	0.9999 0.37	>0.9999 0.75 $\downarrow$	>0.9999 0.0	
Groups	Comparisons of IL-1 $\beta$ mRNA expression of CSE treated Trpa1 <sup>-/-</sup> mice			
	Intact	1 month of CSE	2 months of CSE	
1 month of CSE <i>p</i> value Hedges' <i>g</i>	0.9997 0.22			
2 months of CSE <i>p</i> value Hedges' <i>g</i>	>0.9999 0.07	0.9987 0.31		
3 months of CSE <i>p</i> value Hedges' <i>g</i>	0.9931 0.45	0.9119 0.69 $\downarrow$	0.9978 0.44	
	Intact	1 month of CSE	2 months of CSE	3 months of CSE
Comparisons of IL-1 $\beta$ mRNA expression of CSE treated Trpa1 <sup>+/+</sup> to Trpa1 <sup>-/-</sup> mice <i>p</i> value Hedges' <i>g</i>	0.8693 0.83 $\uparrow\uparrow$	>0.9999 0.18	0.9913 0.56 $\uparrow$	>0.9999 0.75 $\uparrow$

**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*.

Groups	Comparisons of IL-23 mRNA expression of CSE treated Trpa1 <sup>+/+</sup> mice			
	Intact	1 month of CSE	2 months of CSE	
1 month of CSE <i>p</i> value Hedges' <i>g</i>	0.217 1.35 ↑↑			
2 months of CSE <i>p</i> value Hedges' <i>g</i>	0.9843 0.7 ↓	0.0316* 1.77 ↓↓		
3 months of CSE <i>p</i> value Hedges' <i>g</i>	0.9138 0.77 ↑	0.8932 0.6 ↓	0.4153 1.27 ↑↑	
Groups	Comparisons of IL-23 mRNA expression of CSE treated Trpa1 <sup>-/-</sup> mice			
	Intact	1 month of CSE	2 months of CSE	
1 month of CSE <i>p</i> value Hedges' <i>g</i>	0.9583 1.12 ↑↑			
2 months of CSE <i>p</i> value Hedges' <i>g</i>	0.8866 1.27 ↑↑	>0.9999 0.22		
3 months of CSE <i>p</i> value Hedges' <i>g</i>	0.4057 1.37 ↑↑	0.9564 0.79m ↑	0.9894 0.51 ↑	
	Intact	1 month of CSE	2 months of CSE	3 months of CSE
Comparisons of IL-23 mRNA expression of CSE treated Trpa1 <sup>+/+</sup> to Trpa1 <sup>-/-</sup> mice <i>p</i> value Hedges' <i>g</i>	0.964 0.87 m↑↑	0.2289 1.45 ↑↑	0.9348 0.83 ↑↑	>0.9999 0.07

**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*.

Groups	Comparisons of IL-10 mRNA expression of CSE treated Trpa1 <sup>+/+</sup> mice			
	Intact	1 month of CSE	2 months of CSE	
1 month of CSE <i>p</i> value Hedges' <i>g</i>	0.9107 0.91 ↓↓			
2 months of CSE <i>p</i> value Hedges' <i>g</i>	>0.9999 0.02	0.9025 0.89 ↑↑		
3 months of CSE <i>p</i> value Hedges' <i>g</i>	0.3554 2.05 ↓↓	0.9721 1.13 ↓↓	0.3427 1.95 ↓↓	
Groups	Comparisons of IL-10 mRNA expression of CSE treated Trpa1 <sup>-/-</sup> mice			
	Intact	1 month of CSE	2 months of CSE	
1 month of CSE <i>p</i> value Hedges' <i>g</i>	0.9125 0.51 ↑			
2 months of CSE <i>p</i> value Hedges' <i>g</i>	0.9851 0.71 ↓	0.4179 0.96 ↓↓		
3 months of CSE <i>p</i> value Hedges' <i>g</i>	0.3851 1.61 ↓↓	0.0318* 1.5 ↓↓	0.8923 1.38 ↓↓	
	Intact	1 month of CSE	2 months of CSE	3 months of CSE
Comparisons of IL-10 mRNA expression of CSE treated Trpa1 <sup>+/+</sup> to Trpa1 <sup>-/-</sup> mice <i>p</i> value Hedges' <i>g</i>	0.999 0.3654	0.0754 1.32 ↑↑	>0.9999 0.27	0.9983 0.7864 ↑

**Supplementary table 6. Comparison of TGF- $\beta$ 1 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			
	Intact	1 month of CSE		2 months of CSE
1 month of CSE <i>p</i> value Hedges' <i>g</i>	0.9949 0.61 ↓			
2 months of CSE <i>p</i> value Hedges' <i>g</i>	>0.9999 0.24	0.9578 0.67 ↑		
3 months of CSE <i>p</i> value Hedges' <i>g</i>	0.3173 2.16 ↑↑	0.0761 2.27 ↑↑		0.5098 1.32 ↑↑
Groups	Comparisons of TGF-β1 mRNA expression of CSE treated Trpa1 <sup>-/-</sup> mice			
	Intact	1 month of CSE		2 months of CSE
1 month of CSE <i>p</i> value Hedges' <i>g</i>	0.9768 0.52 ↑			
2 months of CSE <i>p</i> value Hedges' <i>g</i>	>0.9999 0.21	0.9982 0.32		
3 months of CSE <i>p</i> value Hedges' <i>g</i>	>0.9999 0.06	0.9875 0.45		>0.9999 0.14
	Intact	1 month of CSE	2 months of CSE	3 months of CSE
Comparisons of TGF-β1 mRNA expression of CSE treated Trpa1 <sup>+/+</sup> to Trpa1 <sup>-/-</sup> mice <i>p</i> value Hedges' <i>g</i>	0.9999 0.34	0.9018 0.69 ↑	0.9999 0.24	0.1785 1.86 ↓↓

**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'  $g$ .

Groups	TRPA1 immunostaining		
	Non-smoking SN	Smoking SN	Non-smoking SNM
Smoking SN $p$ value Hedges' $g$	0.5 1.29 $\uparrow\uparrow$		
Non-smoking SNM $p$ value Hedges' $g$	0.0039** 2.43 $\uparrow\uparrow$		
Smoking SNM $p$ value Hedges' $g$		<0.0001*** 6.29 $\uparrow\uparrow$	<0.0001*** 3.63 $\uparrow\uparrow$
Groups	TRPA1 mRNA expression		
	Non-smoking SN	Smoking SN	Non-smoking SNM
Smoking SN $p$ value Hedges' $g$	0.6065 1.22 $\uparrow\uparrow$		
Non-smoking SNM $p$ value Hedges' $g$	0.9747 0.52 $\uparrow$		
Smoking SNM $p$ value Hedges' $g$		0.1354 1.11 $\uparrow\uparrow$	0,0053** 2.0 $\uparrow\uparrow$
Groups	TGF $\beta$ mRNA expression		
	Non-smoking SN	Smoking SN	Non-smoking SNM
Smoking SN $p$ value Hedges' $g$	0,9994 0.09		
Non-smoking SNM $p$ value Hedges' $g$	>0.9999 0.00		
Smoking SNM $p$ value Hedges' $g$		0.7323 0.60 $\uparrow$	0.7933 0.52 $\uparrow$

