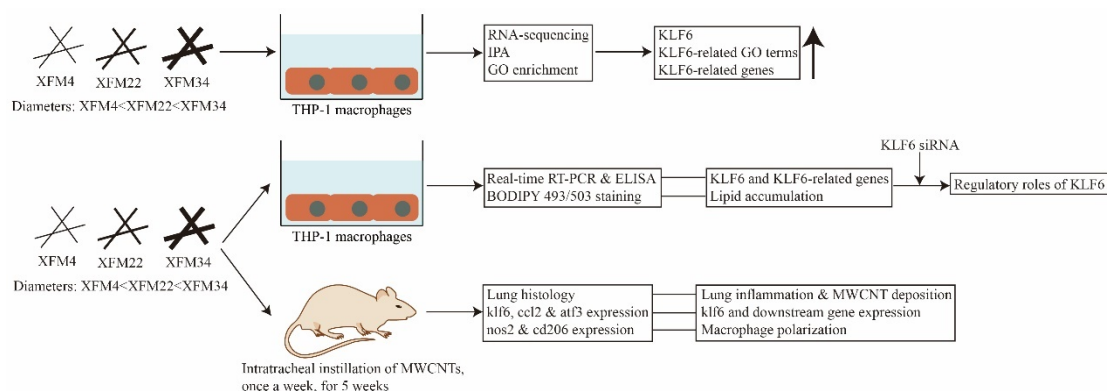
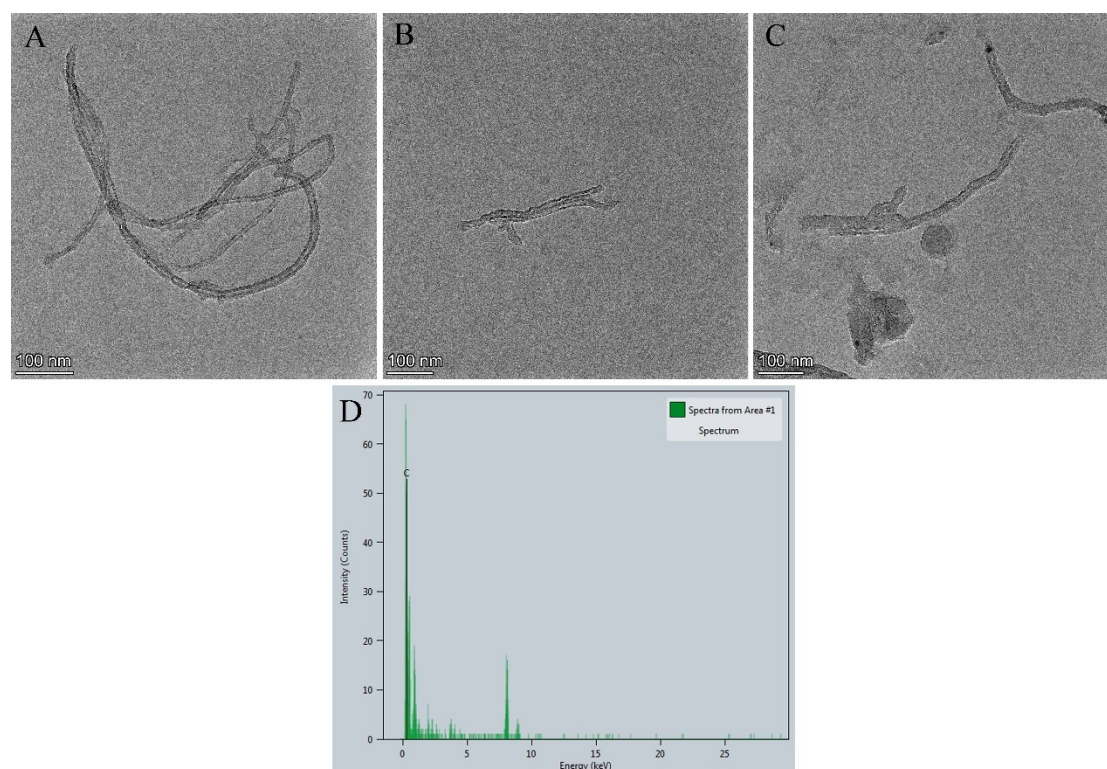


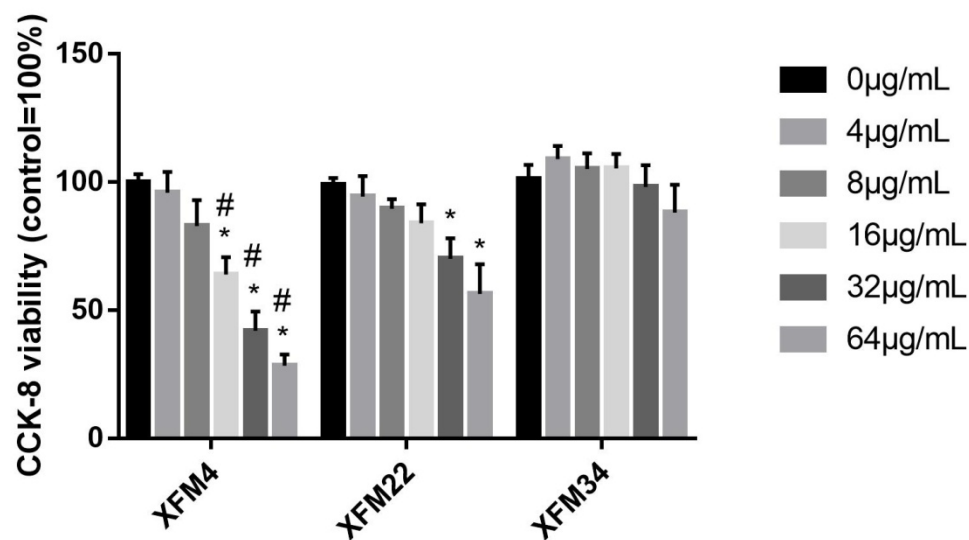
Supporting information



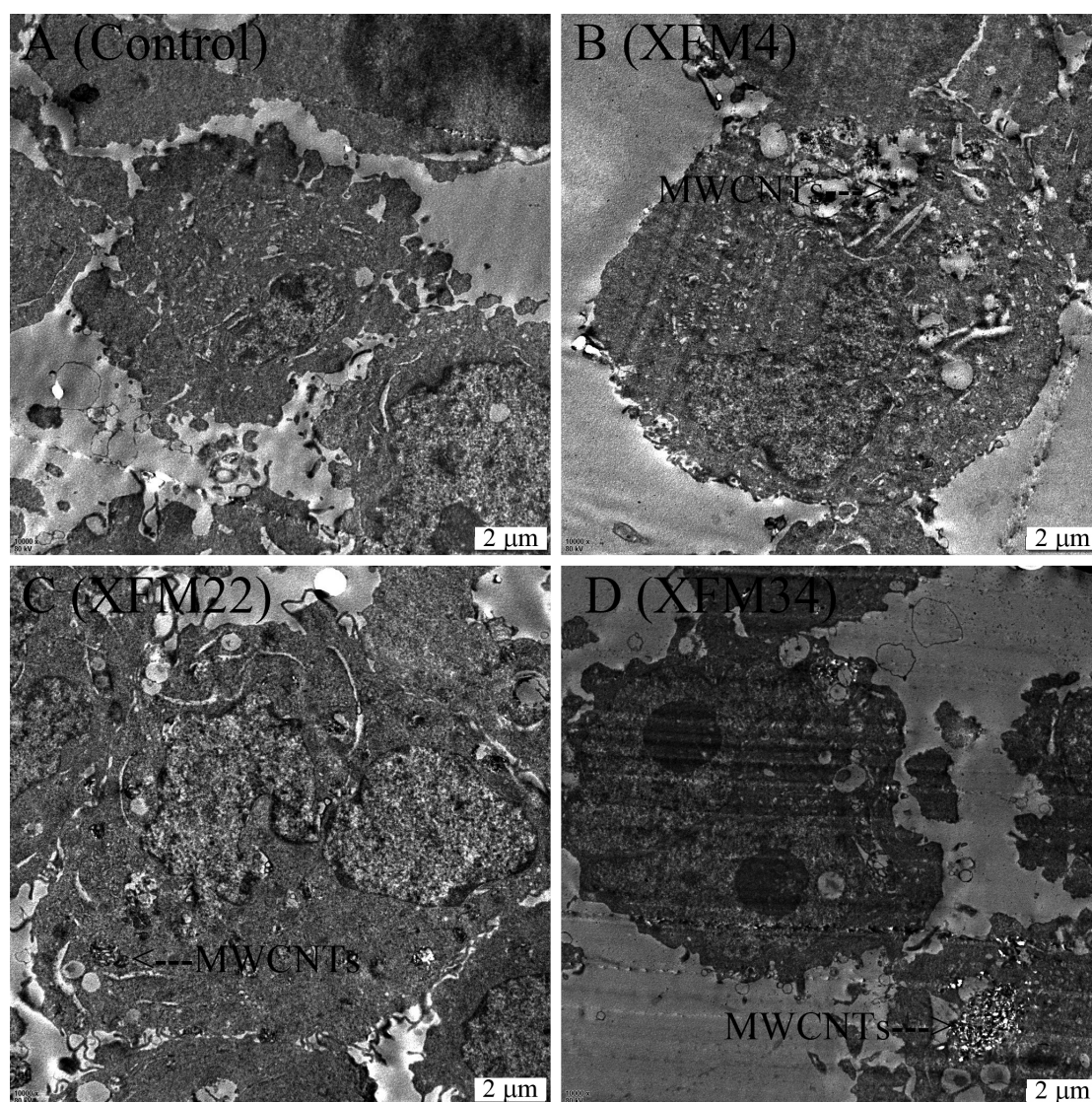
Supplemental Fig. S1. Schematic illustration of study design. This study first analyzed the RNA-sequencing data and found that KLF6 and KLF6-related GO terms/genes were activated in THP-1 macrophages. Then, the activation of KLF6 and regulatory roles of KLF6 on downstream genes and lipid accumulation were verified in THP-1 macrophages. Finally, mice were intratracheally instilled with MWCNTs, and *klf6* and *klf6*-regulated downstream events were verified in bronchoalveolar lavage cells. See more in main text.



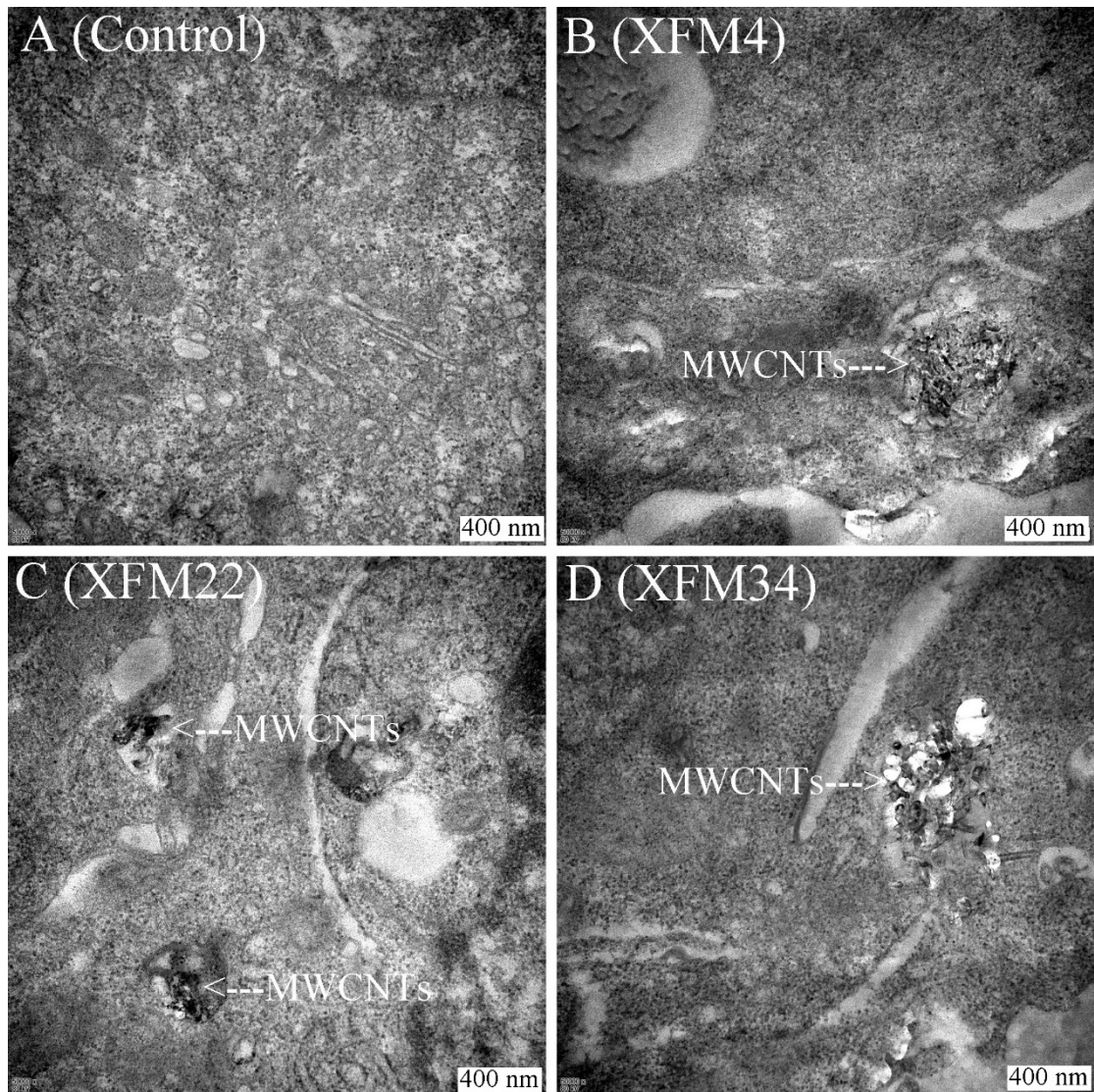
Supplemental Fig. S2. The TEM images of XFM4 (S2A), XFM22 (S2B) and XFM34 (S2C). S2D, the EDS spectrum of XFM4.



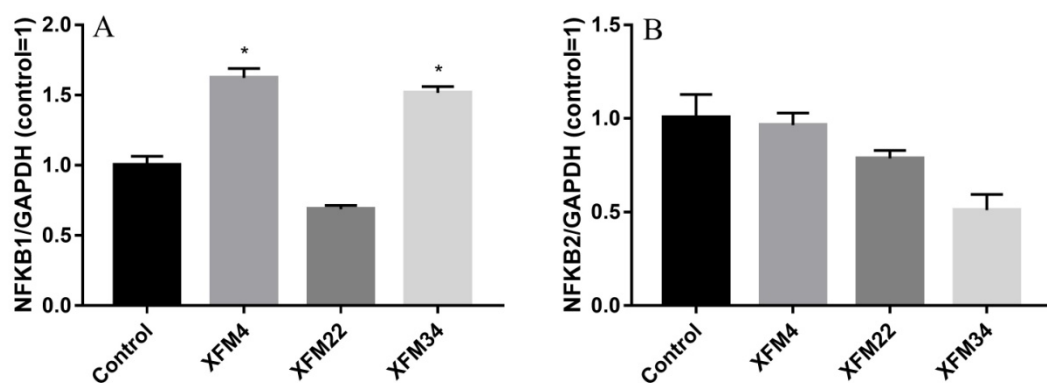
Supplemental Fig. S3. The changes of cellular viability. THP-1 macrophages were exposed to various concentrations of XFM4, XFM22 or XFM34 for 24 h. After the exposure, the cellular viability was measured by CCK-8 assay. *, $p < 0.01$, compared with control; #, $p < 0.01$, compared with XFM22 or XFM34 at the same mass concentrations.



Supplemental Fig. S4. The representative TEM images of THP-1 macrophages (lower magnification). THP-1 macrophages were incubated with cell culture medium (S4A, control), 32 $\mu\text{g/mL}$ XFM4 (S4B), XFM22 (S4C) or XFM34 (43D) for 24 h, and TEM was used to observe the internalized MWCNTs (arrows in Supplemental Fig. S4).

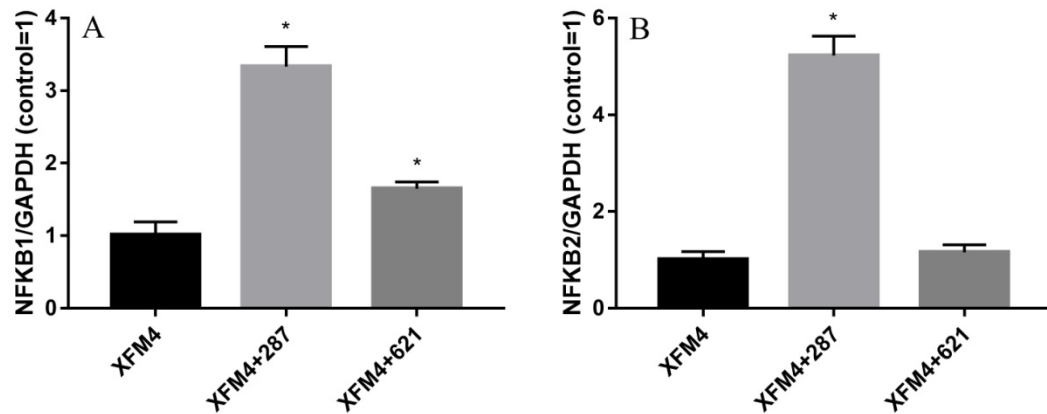


Supplemental Fig. S5. The TEM images of THP-1 macrophages (higher magnification).

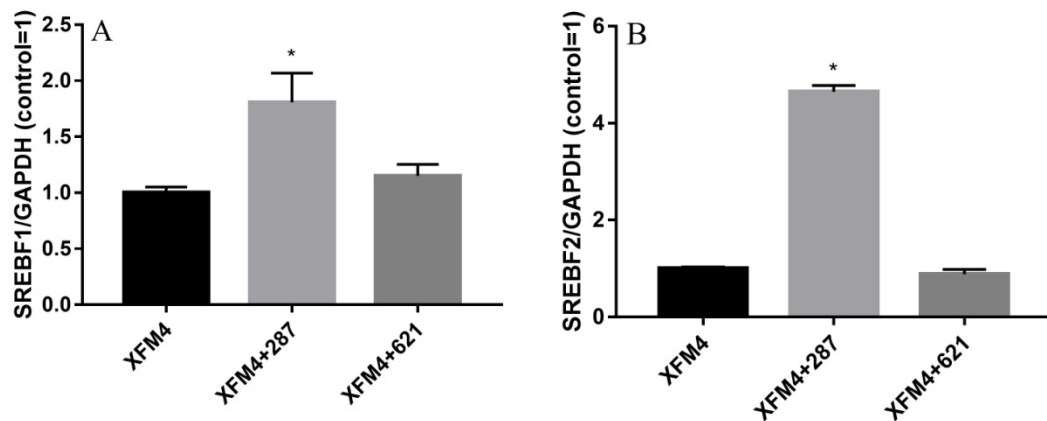


Supplemental Fig. S6. The expression of NFKB1 (S6A) and NFKB2 (S6B). THP-1 macrophages were exposed to 32 μ g/mL XFM4, XFM22 or XFM34 for 24 h, and the expression of NFKB1 and NFKB2 was measured by real-time RT-PCR. *, $p < 0.01$,

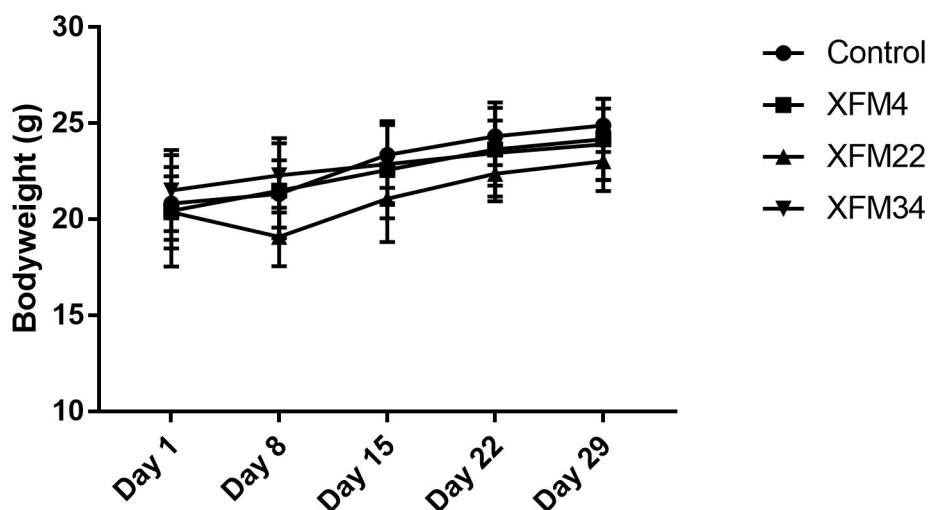
compared with control.



Supplemental Fig. S7. The influence of KLF6 siRNA (labeled as 287 and 621, respectively) on the expression of NFKB1 (S7A) and NFKB2 (S7B). THP-1 macrophages were transfected with KLF6 siRNA 287 and 621 before 24 h exposure to 32 µg/mL XFM4, and then the expression of NFKB1 and NFKB2 was measured by real-time RT-PCR. *, $p < 0.01$, compared with control.



Supplemental Fig. S8. The influence of KLF6 siRNA (labeled as 287 and 621, respectively) on the expression of SREBF1 (S8A) and SREBF2 (S8B). THP-1 macrophages were transfected with KLF6 siRNA 287 and 621 before 24 h exposure to 32 µg/mL XFM4, and then the expression of SREBF1 and SREBF2 was measured by real-time RT-PCR. *, $p < 0.01$, compared with control.



Supplemental Fig. S9. The changes of bodyweight. Mice under slight anaesthesia were intratracheally instilled with 50 μ L vehicles (control) or 2.56 mg/mL MWCNTs (6.4 mg/kg bodyweight), once a week, totally 5 weeks. The bodyweight was measured before each exposure. Data were expressed as mean $\pm$ SD (n=8).

Table S1. The physicochemical properties of XFM4, XFM22 and XFM34 provided by the suppliers

Code	Purity	Diameter	Length	SSA	Tap density	True density	EC
XFM4	>95%	<8 nm	0.5-2 μ m	>500 m^2/g	0.27 g/cm^3	$\sim 2.1 \text{ g}/\text{cm}^3$	>100 s/cm
XFM22	>95%	20-30 nm	0.5-2 μ m	>110 m^2/g	0.28 g/cm^3	$\sim 2.1 \text{ g}/\text{cm}^3$	>100 s/cm
XFM34	>95%	>50 nm	0.5-2 μ m	>40 m^2/g	0.18 g/cm^3	$\sim 2.1 \text{ g}/\text{cm}^3$	>100 s/cm

Abbreviations: EC: electric conductivity; SSA: special surface area. Data are available from Nanjing XFNANO Materials Tech Co., Ltd at (<https://en.xfnano.com/>)

Table S2. The physicochemical properties of MWCNTs according to our previous report.

Code	SSA (m^2/g)	Ion impurity	Primary size (nm)	Hydrodynamic size (nm)	Zeta potential (mV)	PDI
XFM4	283.66	Fe 0.29%, Ni 0.004%	D: 8.92 ± 2.87 ; L: 1135.25 ± 476.89	280.23 ± 8.11 (water); 297.40 ± 2.87 (medium)	1.43 ± 0.13 (water); -7.17 ± 0.15 (medium)	0.489 ± 0.027 (water); 0.479 ± 0.015 (medium)
XFM22	208.02	Fe 0.05%	D: 14.79 ± 3.84 ; L: 14.79 ± 3.84	217.53 ± 3.88 (water);	-	0.284 ± 0.032 (water);

		Ni 1.23%	902.27±812.6 6	219.30±2.80 (medium)	1 (water); -7.07±0.31 (medium)	0.265±0.02 4 (medium)
XFM3 4	79.93	Fe 0.01%, Ni 4.33%	D: 32.96±11.02; L: 1137.67±589. 54	193.47±4.15 (water); 222.33±3.18 (medium)	-3.68±0.34 (water); - 8.41±0.18 (medium)	0.213±0.02 7 (water); 0.234±0.01 5 (medium)

Abbreviations: D, diameter; L, length; PDI: polydispersity index; SSA: special surface area. Data were reproduced from the reference Yang et al, Toxicol Lett, 2020, 332:65-73.

Table S3. The primers used for *in vitro* studies.

Gene names	Forward primers	Reverse primers	Product length
ATF3	AAAACCAGGATGCC CACCGTT	CCACATCCCCTACG AGTGACA	112bp
CCL2	CCTAGCTTTCCCCAG ACACC	AAAAGCAATTTCCC CAAGTCTC	171bp
GAPDH	ACAGCCTCAAGATC ATCAGC	GGTCATGAGTCCTT CCACGAT	104bp
KLF6	CCCACGGCCAAGTTT ACCTC	AAGGCTTTTCTCCT GGCTTCC	202bp
NFKB1	TGGGAAGGCCTGAA CAAATG	TATGGGCCATCTGT TGGCAG	106bp
NFKB2	TGGCCGGGACAAGA GAAAAG	CCAGAATTTTAGAC GCCCCG	167bp
SREBF1	TCCCAGCCCCTCAGA TACCAC	CCCATTGAGCAGCC AGACCAC	127bp
SREBF2	CCCTCACCACCCTA TCCAGA	CTCTTGCCCCATCA TTACAGG	101bp

Table S4. The primers used for *in vivo* studies.

Gene names	Forward primers	Reverse primers	Product length
gapdh	CGACTTCAACAGCA ACTCCCACTCTTCC	TGGGTGGTCCAGGG TTTCTTACTCCTT	175bp
klf6	CTGCAGGAAAGTTTA CACGAAA	GTCAACTCATCACT TCTTGCAA	126bp
atf3	GAGGATTTTGCTAAC CTGACACC	GAGGATTTTGCTAA CCTGACACC	110bp
ccl2	TTTTTGTCACCAAGC TCAAGAG	TTCTGATCTCATTG GTTCCGA	101bp
cd206	CAAGGAAGGTTGGC ATTTGT	CCTTTCAGTCCTTTG CAAGC	111bp
nos2	TTGGCTCCAGCATGT	TCCTGCCCCACTGAG	121bp

	ACCCT	TTCGTC	
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Table S5. The KLF6 siRNA sequences (labeled as 287 and 621, respectively) used in this study.

	Sense (5'-3')	Antisense (5'-3')
287	GmsUmsUmAmCfAmAfCfUfUmA mGmAmGmAmCmCmAmAm	UmsUfsGmGmUmCfUmCfUfAmAm GmUmUfGmUfAmAmCmsAmsAm
621	CmsAmsGmGmAfAmAfGfUfUmU mAmCmAmCmCmAmAmAm	UmsUfsUmGmGmUfGmUfAfAmAm CmUmUfUmCfCmUmGmsCmsAm

Note: The modifications: m means the modifications with methoxy groups at 2', f means the modifications with F groups at 2'; and s means thiophosphate groups between the bases.

Table S6. The complete list of KLF6-related genes (FPKM>1 in at least one group).

Name	Control	XFM4	XFM22	XM34
CCL2	2.46±0.36	10.09±0.31	4.56±0.15	4.57±1.06
PTGS2	3.95±0.26	5.25±0.24	1.98±0.29	2.78±0.35
CXCL2	41.40±5.32	34.63±1.89	17.73±0.02	28.60±2.28
ATF3	20.42±0.47	31.34±1.38	16.19±0.39	18.04±0.54
COL1A1	2.03±0.07	0.59±0.09	0.71±0.01	1.12±0.05
CXCL8	2578.67±58.83	2278.52±67.63	947.23±27.25	1501.19±69.26
TNFAIP3	124.32±4.14	225.98±6.05	149.24±0.42	155.99±1.77
KLF4	1.64±0.21	2.88±0.16	3.09±0.06	2.36±0.09
NFKB2	29.68±1.18	35.76±1.42	29.48±1.19	31.04±1.19
PLAU	6.33±0.18	6.32±0.26	4.03±0.57	4.71±0.55
TNIP1	38.36±0.59	50.70±1.45	39.85±1.79	42.19±1.40
PCNA	6.30±0.61	8.33±0.14	8.22±1.46	7.15±1.52
JUN	26.43±0.20	71.81±2.80	43.17±1.59	39.17±1.37
NFKBIA	138.51±5.33	181.23±3.50	148.34±7.10	155.02±9.07
PMAIP1	5.03±0.56	18.02±0.57	10.23±2.32	7.43±0.33
E2F1	0.51±0.17	1.35±0.08	1.46±0.20	0.75±0.15
TGFBI	17.11±0.57	10.73±0.14	16.54±0.99	15.27±2.20
MNT	1.96±0.13	2.30±0.02	2.35±0.01	2.39±0.07
TFPI2	15.45±0.91	24.78±0.76	14.84±1.41	16.47±0.73
MAX	7.67±0.32	9.19±0.37	8.34±0.12	8.06±0.27
VEGFA	37.23±1.15	20.87±0.79	20.16±0.02	24.47±1.43
RELA	20.89±0.315	23.13±0.95	20.37±1.81	21.01±1.37
KLF6	41.70±1.66	59.85±1.25	46.67±0.81	47.48±1.84
CDK2	3.44±0.25	2.74±0.20	2.65±0.11	2.63±0.10
RUNX1	11.23±0.22	12.54±0.41	11.54±0.35	11.70±0.33
MCL1	453.41±8.67	399.12±13.68	360.85±11.72	391.60±14.11
NSD1	8.14±0.48	10.16±0.65	9.44±0.02	9.92±0.14
NFKB1	14.65±0.16	17.37±0.31	13.21±0.31	14.91±1.01

BCL6	54.01±1.00	61.61±0.27	50.35±2.85	54.90±3.13
TAF9	9.56±0.886	9.51±0.55	8.74±0.46	8.12±0.49
GSK3B	12.56±0.81	13.10±0.35	12.27±0.56	12.34±0.20
FBL	18.54±1.48	19.53±1.03	21.30±0.65	20.46±0.89
NOP56	8.35±0.45	10.35±0.77	9.267±0.467	9.797±1.287
CTNNB1	34.84±0.56	38.55±0.75	39.08±2.205	36.24±0.96
CREBBP	7.12±0.64	7.19±0.13	6.54±0.38	7.22±0.25
TNIP2	28.64±1.75	33.18±1.90	28.34±0.75	27.97±0.75
HDAC3	20.63±0.69	16.52±0.39	18.71±0.37	16.79±1.01
BAX	18.05±1.99	17.51±1.08	18.21±0.54	17.80±0.89
BCL2L11	0.60±0.00	1.17±0.17	1.06±0.12	1.00±0.06
SERPINH1	27.48±1.43	21.43±0.90	23.95±1.00	25.53±0.48
NUFIP1	1.46±0.24	1.55±0.23	2.01±0.15	1.61±0.13
NR2F6	5.24±0.43	4.90±0.59	5.82±0.12	4.88±0.35
NFKBIE	60.80±2.31	59.82±1.71	54.31±2.78	60.34±0.72
HDAC1	37.52±1.92	36.68±0.76	36.50±0.89	35.58±0.35
NR1H2	11.87±0.59	11.85±0.81	12.32±0.33	11.74±0.63
TRIM25	4.18±0.16	9.40±0.58	5.35±0.41	5.20±0.24
NFKBIZ	16.64±0.91	17.54±0.28	13.45±0.05	15.31±0.59
SIN3B	6.88±0.14	6.52±0.15	5.99±0.18	6.72±0.18
TGFR1	4.93±0.30	4.98±0.31	4.62±0.13	4.80±0.37
CDKN1A	797.34±27.59	540.08±24.82	569.08±19.49	626.66±22.82
SIN3A	5.66±0.43	6.15±0.20	5.84±0.04	5.96±0.15
RAC1	62.51±8.17	60.80±0.79	65.75±3.17	61.61±3.38
ENG	92.10±1.57	71.23±1.75	90.14±3.12	90.25±2.87
NFKBIB	17.47±1.18	20.02±1.36	16.46±1.01	18.05±1.09
CDH2	1.48±0.16	1.72±0.19	1.76±0.03	1.79±0.34
HRAS	10.88±1.78	10.56±1.13	12.00±0.80	10.40±1.00
LCOR	4.04±0.35	4.34±0.14	3.88±0.07	4.14±0.14
CCND1	37.87±1.51	43.95±1.02	38.95±0.03	42.11±1.02
MDM2	6.47±0.80	9.38±0.96	8.31±0.19	8.55±0.53
PNO1	9.91±0.50	10.76±0.33	9.91±1.84	9.14±0.53
BCL2L1	14.25±0.47	15.28±0.26	16.27±1.25	15.80±0.85
PDCD1LG2	1.28±0.35	2.58±0.24	2.51±0.29	2.10±0.21
PTCH1	1.25±0.04	1.05±0.13	1.11±0.01	1.17±0.06
PPARG	25.35±1.02	35.73±0.56	39.41±0.32	32.76±0.82
RARG	2.45±0.25	0.89±0.09	1.39±0.14	1.55±0.16
MYC	9.13±0.56	17.72±0.34	16.13±1.26	15.82±1.71
EHMT2	3.28±0.14	4.56±0.34	4.76±0.20	4.13±0.38
CDKN1B	8.29±0.55	9.76±0.22	9.07±0.96	7.56±0.27
PRDM1	10.42±0.64	6.72±0.53	5.36±0.00	6.86±0.47
APP	44.94±0.82	59.26±0.45	62.04±0.22	55.74±2.78
BAK1	44.92±3.29	47.31±4.10	49.39±0.82	44.49±0.53

CDK4	11.90±0.49	15.35±1.53	14.55±0.156	13.44±0.34
ESRRA	17.13±1.29	17.02±0.94	17.10±1.36	17.07±1.05
RB1	34.36±0.95	33.96±1.85	32.88±2.31	34.15±0.55
NCOA1	2.31±0.08	2.68±0.22	2.38±0.04	2.47±0.15
PTEN	9.01±0.46	6.97±0.63	8.25±0.28	7.73±0.31
NFKBIL1	6.00±0.21	6.36±1.06	6.42±0.53	5.99±0.26
KAT2B	7.14±0.35	9.32±0.42	9.72±0.28	8.25±0.48
VAV3	53.45±1.06	43.23±1.00	42.88±0.54	48.24±1.53
SRSF2	38.59±1.48	36.49±1.05	38.37±2.55	34.40±2.39
GTF3C1	16.26±0.84	15.57±0.06	16.76±0.62	18.32±0.35
CHI3L1	1333.58±27.07	907.44±9.84	1145.90±53.00	1139.98±42.10
MMP9	2641.03±104.31	1944.52±62.09	2212.17±196.44	2578.97±116.94
OLIG2	19.38±1.96	41.02±4.97	29.24±2.18	25.70±4.07
TNF	35.69±0.60	33.94±0.81	29.84±1.25	35.16±3.28
ALOX5	79.38±4.58	45.98±1.57	59.99±0.72	66.54±3.72
APOM	1.36±0.23	1.00±0.26	0.73±0.39	0.89±0.30
IRF8	3.15±0.66	5.14±0.264	5.20±0.91	3.91±0.23

Note: THP-1 macrophages were exposed to 32 µg/mL MWCNTs for 24 h before transcriptomics analysis. IPA was used to identify KLF6-related genes. Data represent mean±SD of triplicate.