

Supporting information

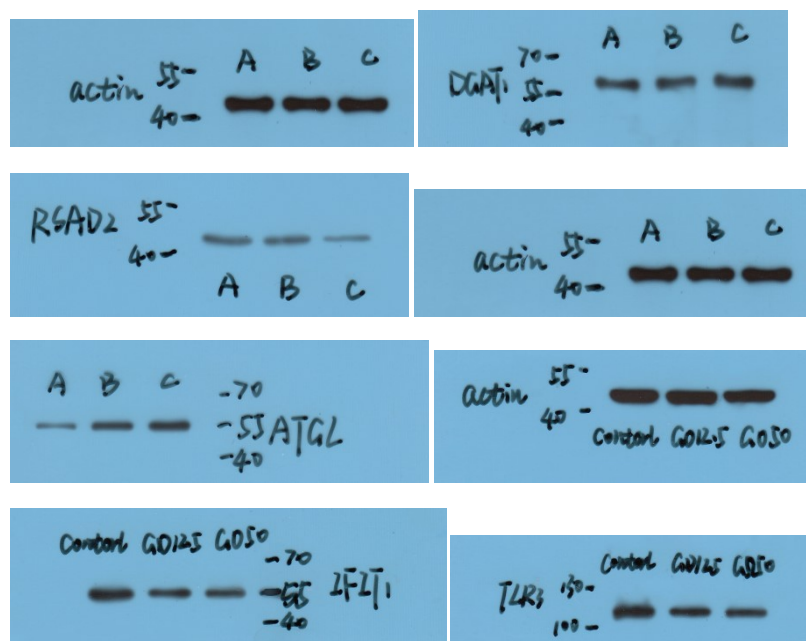
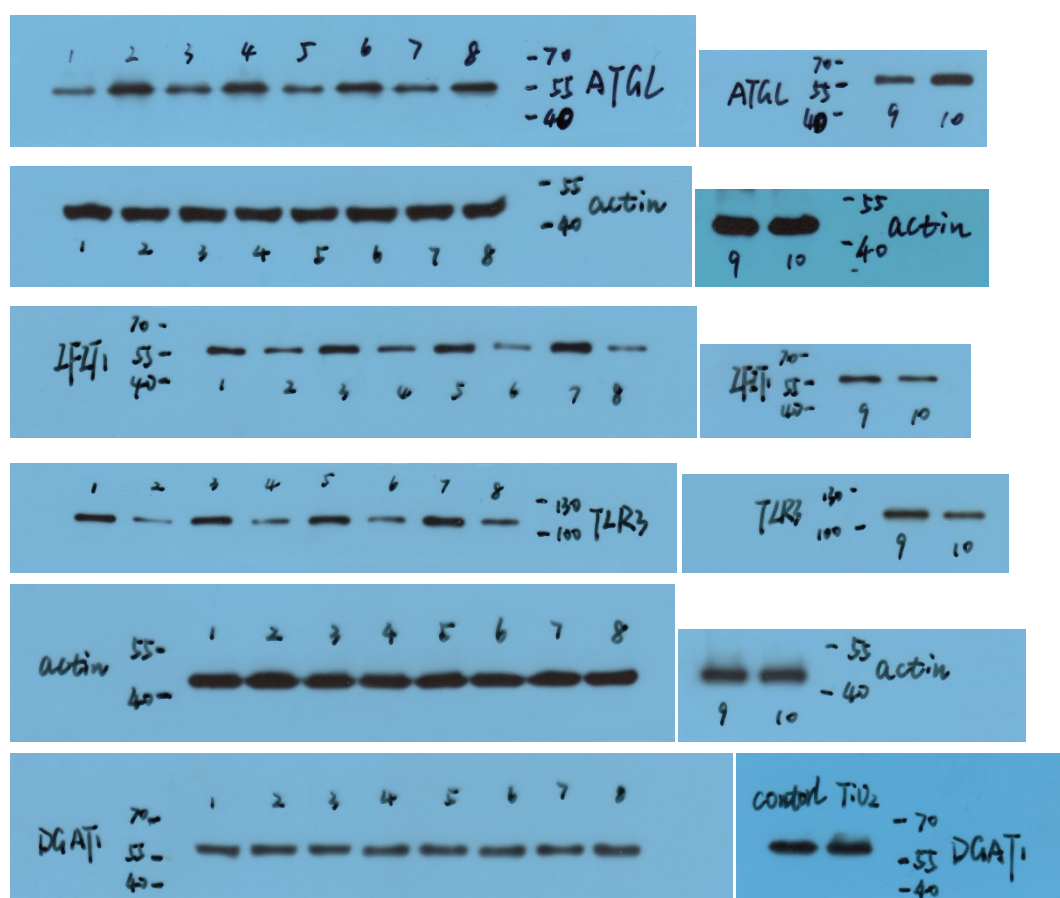


Figure S1. The unedited Western blot images for *in vitro* studies.



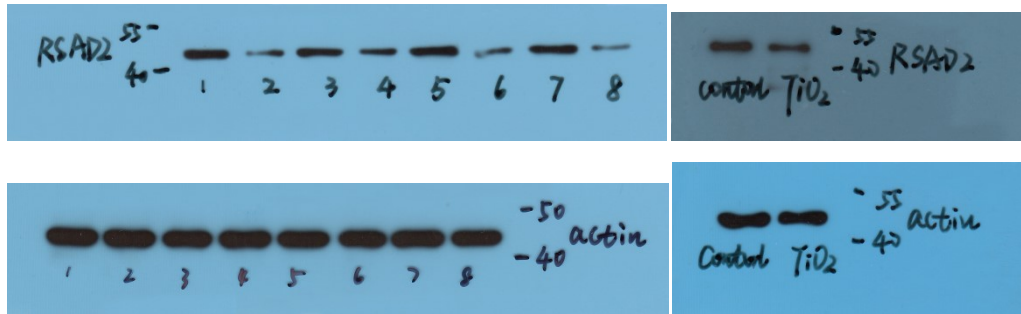


Figure S2. The unedited Western blot images for *in vivo* studies.

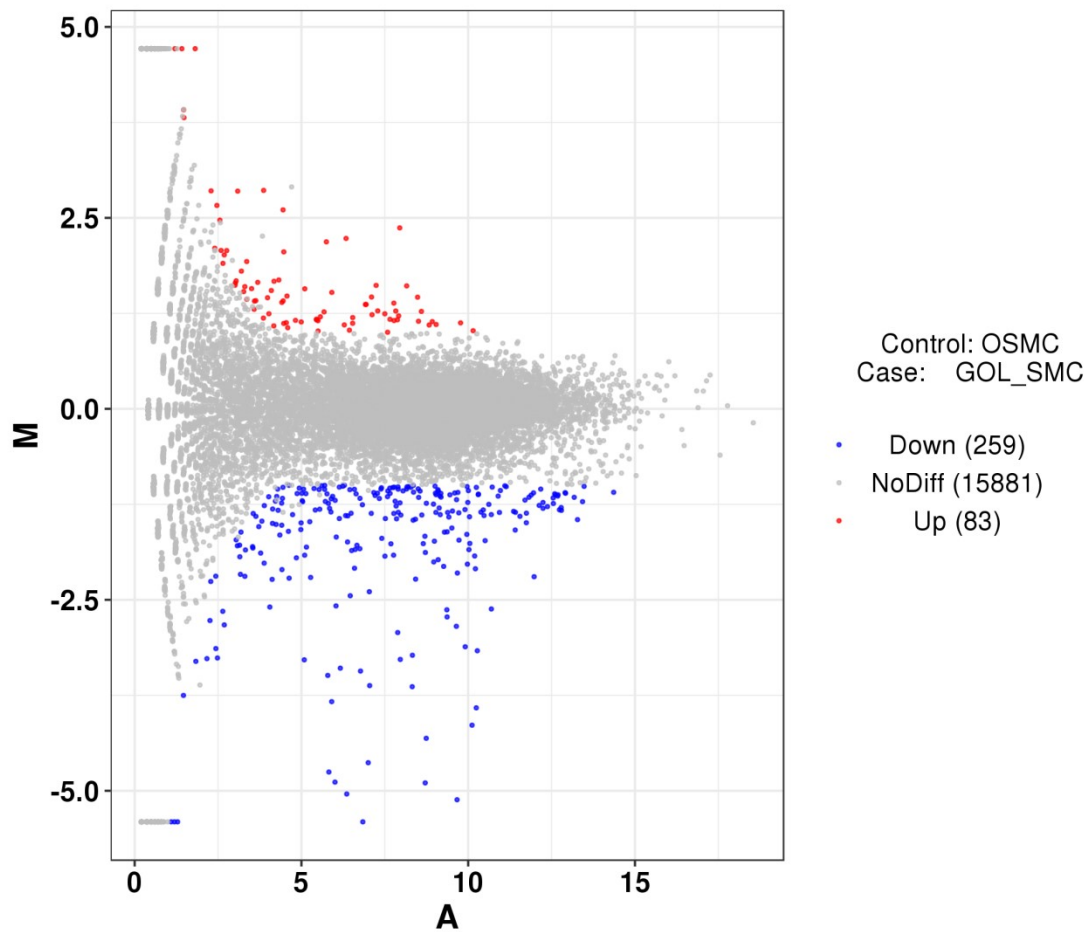


Figure S3. The MA plot showing the statistical changes of genes. Human VSMCs were exposed to 12.5 $\mu\text{g}/\text{mL}$ graphene oxide for 24 h before RNA-sequencing experiment.

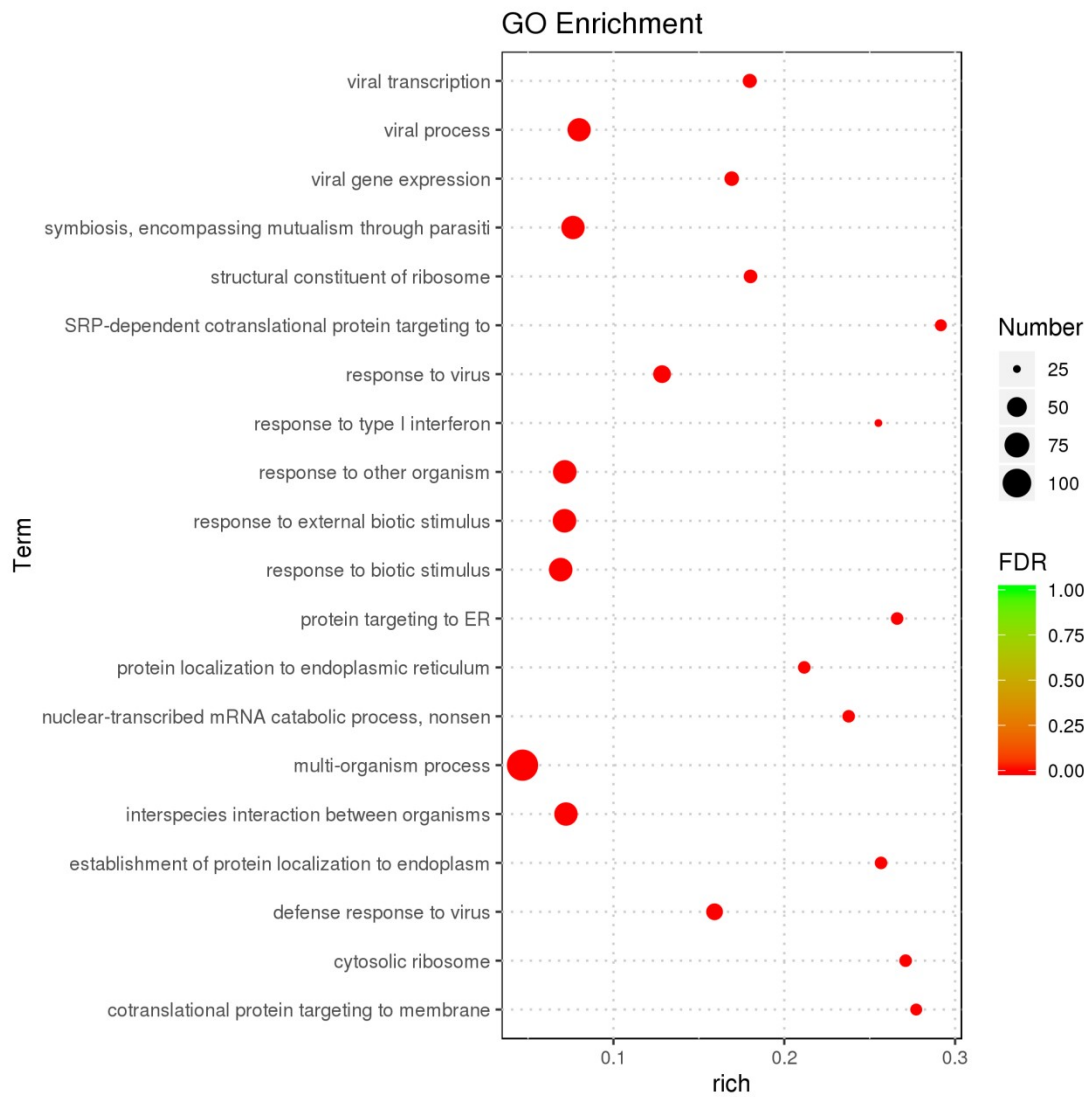


Figure S4. The most significantly changed GO terms. Human VSMCs were exposed to 12.5 $\mu\text{g}/\text{mL}$ graphene oxide for 24 h before RNA-sequencing experiment.

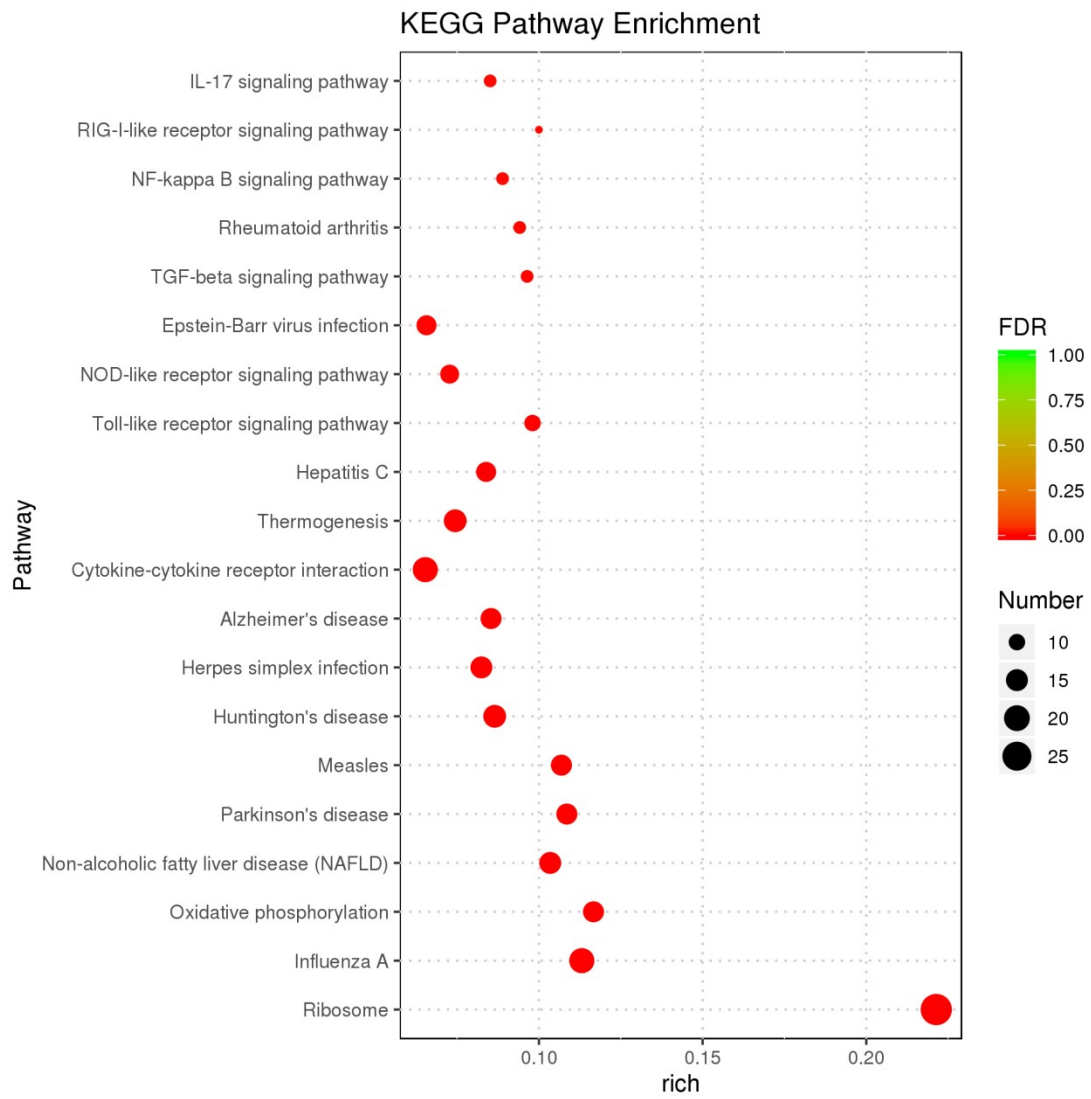


Figure S5. The most significantly changed KEGG pathways. Human VSMCs were exposed to 12.5 $\mu\text{g}/\text{mL}$ graphene oxide for 24 h before RNA-sequencing experiment.

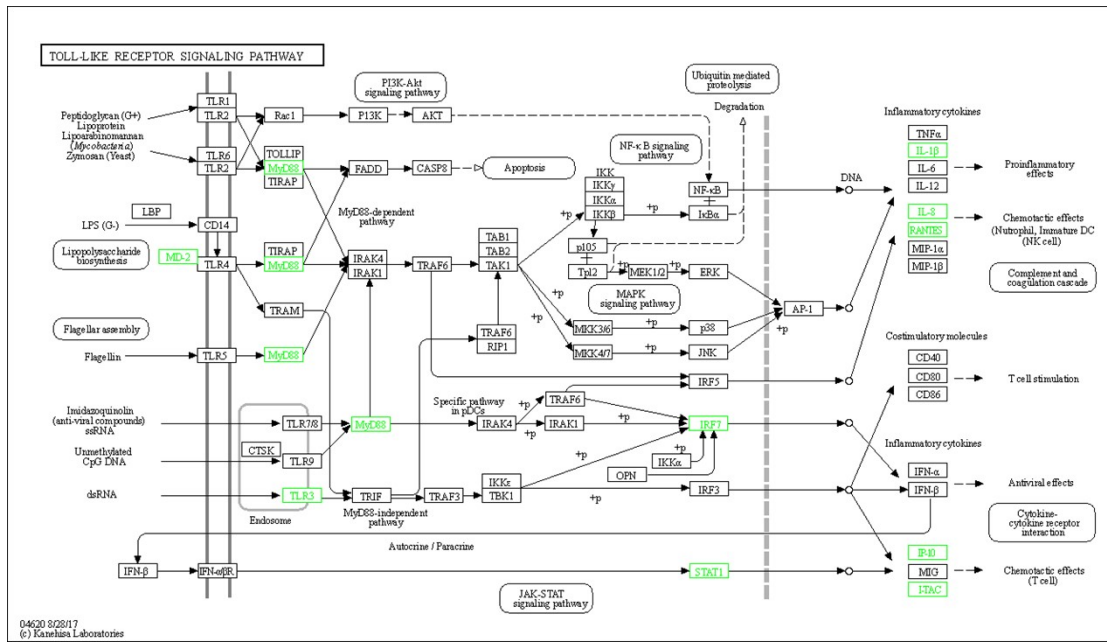


Figure S6. Toll-like receptor signaling pathway (hsa04620) in human VSMCs exposed to 12.5 $\mu\text{g}/\text{mL}$ graphene oxide for 24 h. The green color indicated the significantly down-regulated genes.

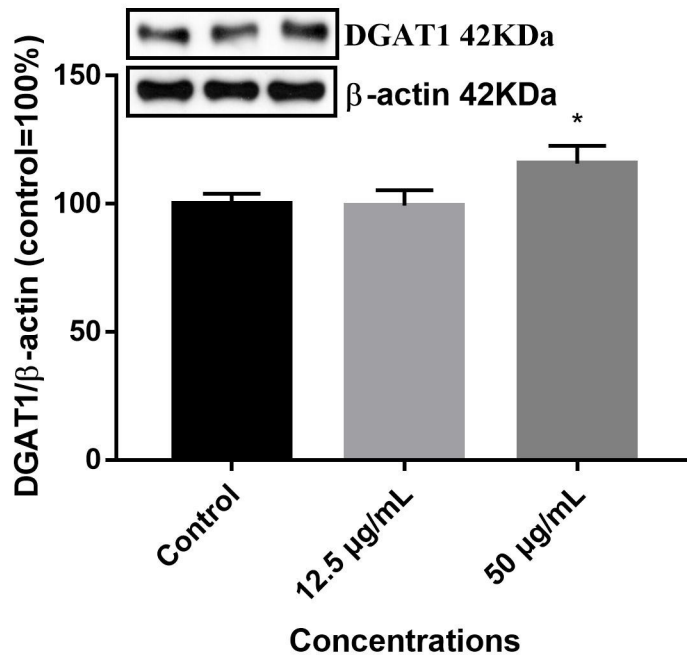


Figure S7. The changes of DGAT1 in human VSMCs after 24 h exposure to 12.5 or 50 $\mu\text{g}/\text{mL}$ graphene oxide. *, $p < 0.05$, compared with control.

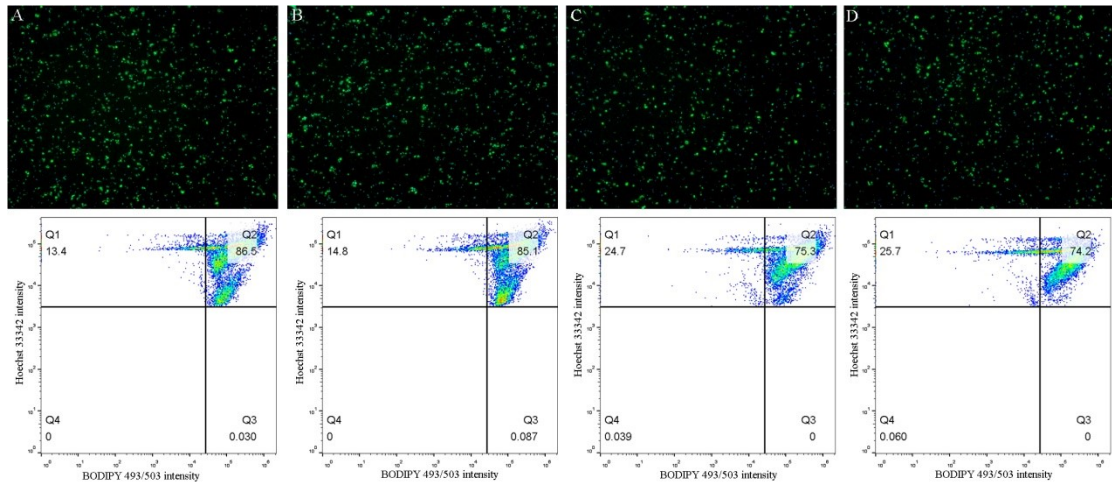


Figure S8. The changes of BODIPY493/503 staining. Human VSMCs were incubated with cell culture medium (control; S6A), 100 $\mu\text{g}/\text{mL}$ Poly IC (S6B), 12.5 $\mu\text{g}/\text{mL}$ graphene oxide (S6C), or graphene oxide plus Poly IC (S6D) for 24 h, and then counterstained by Hoechst 33342 (blue fluorescence) and BODIPY 493/503 (green fluorescence). The cells were imaged (upper panels) and the intensity of BODIPY 493/503 was analyzed (lower panels).

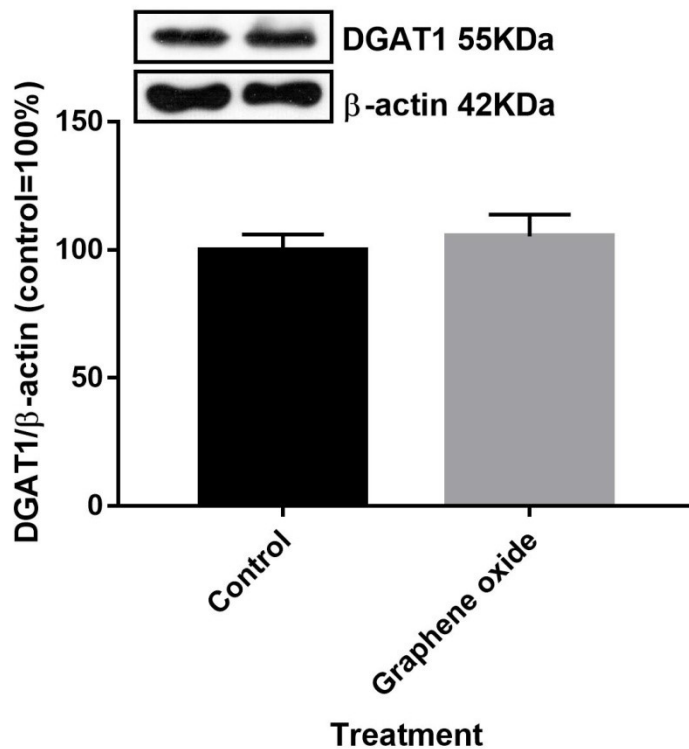


Figure S9. The changes of DGAT1 in mouse aortas. The mice were intravenously administrated with 20 μg graphene oxide per day, totally 5 days before Western blotting experiment.

Table S1. The complete list of TLR3-related GO terms in human VSMCs exposed to 12.5 µg/mL graphene oxide for 24 h. These GO terms were categorized according to biological process (BP), cellular component (CC) and molecular function (MF), respectively.

Category	GO.ID	Term	Up	Down	DEG	Total	P value	FDR
BP	GO:0051607	defense response to virus	1	38	39	245	2.3E-25	2.74E-22
BP	GO:0009615	response to virus	1	41	42	327	1.7E-23	9.77E-21
BP	GO:0006952	defense response	7	74	81	1610	2E-17	3.83E-15
BP	GO:0045087	innate immune response	3	54	57	912	2.9E-16	4.82E-14
BP	GO:0002376	immune system process	14	89	103	2914	6.5E-12	6.96E-10
MF	GO:0003723	RNA binding	4	65	69	1674	3.5E-11	3.57E-09
BP	GO:0071346	cellular response to interferon-gamma	0	18	18	177	4.8E-09	4.10E-07
MF	GO:0003725	double-stranded RNA binding	0	10	10	74	7.9E-07	4.71E-05
CC	GO:0005737	cytoplasm	55	194	249	11583	1.1E-06	6.15E-05
BP	GO:0001819	positive regulation of cytokine production	2	22	24	461	5.1E-06	2.27E-04
CC	GO:0005615	extracellular space	23	63	86	3145	2.7E-05	9.98E-04
BP	GO:0032755	positive regulation of interleukin-6 production	1	8	9	96	6.9E-05	2.31E-03
BP	GO:0032481	positive regulation of type I interferon production	0	8	8	79	1.0E-04	3.16E-03
BP	GO:0051092	positive regulation of NF-kappaB transcription factor activity	1	10	11	150	1.1E-04	3.34E-03
BP	GO:0009597	detection of virus	0	3	3	6	1.2E-04	3.55E-03
BP	GO:0007165	signal transduction	38	103	141	5985	2.0E-04	0.01
BP	GO:0071360	cellular response to exogenous dsRNA	0	4	4	18	2.8E-04	0.01

BP	GO:0006954	inflammatory response	5	22	27	716	3.5E-04	0.01
BP	GO:0007249	I-kappaB kinase/NF-kappaB signaling	2	12	14	274	5.8E-04	0.01
BP	GO:0050729	positive regulation of inflammatory response	0	9	9	129	6.4E-04	0.01
BP	GO:0002730	regulation of dendritic cell cytokine production	0	3	3	12	1.2E-03	0.02
BP	GO:0035666	TRIF-dependent toll-like receptor signaling pathway	0	4	4	29	1.9E-03	0.03
BP	GO:0043123	positive regulation of I-kappaB kinase/NF-kappaB signaling	1	9	10	184	2.2E-03	0.04
BP	GO:0032757	positive regulation of interleukin-8 production	0	5	5	51	2.4E-03	0.04
BP	GO:0032728	positive regulation of interferon-beta production	0	4	4	32	2.7E-03	0.04
BP	GO:0002756	MyD88-independent toll-like receptor signaling pathway	0	4	4	33	3.0E-03	0.04
BP	GO:0032722	positive regulation of chemokine production	0	5	5	56	3.6E-03	0.05
BP	GO:0043065	positive regulation of apoptotic process	8	14	22	646	4.29E-03	0.06
BP	GO:0032760	positive regulation of tumor necrosis factor production	1	5	6	85	4.81E-03	0.06
BP	GO:0035458	cellular response to interferon-beta	0	3	3	20	5.59E-03	0.07
BP	GO:0034128	negative regulation of MyD88-independent toll-like receptor signaling pathway	0	2	2	7	6.67E-03	0.08
BP	GO:0097190	apoptotic signaling pathway	5	15	20	597	7.54E-03	0.08
MF	GO:0005515	protein binding	58	188	246	12646	0.01	0.10
BP	GO:0045766	positive regulation of angiogenesis	1	7	8	165	0.01	0.11

BP	GO:0043330	response to exogenous dsRNA	0	4	4	48	0.01	0.11
BP	GO:1901224	positive regulation of NIK/NF-kappaB signaling	1	4	5	76	0.01	0.12
BP	GO:0034346	positive regulation of type III interferon production	0	1	1	1	0.02	0.13
BP	GO:0045080	positive regulation of chemokine biosynthetic process	0	2	2	12	0.02	0.13
CC	GO:0036020	endolysosome membrane	1	1	2	14	0.03	0.16
BP	GO:0070266	necroptotic process	0	3	3	35	0.03	0.16
BP	GO:0035690	cellular response to drug	1	3	4	71	0.04	0.21
BP	GO:0002224	toll-like receptor signaling pathway	0	6	6	145	0.05	0.23
BP	GO:0010628	positive regulation of gene expression	12	34	46	1979	0.06	0.24
BP	GO:0071260	cellular response to mechanical stimulus	0	4	4	80	0.06	0.24
BP	GO:0034123	positive regulation of toll-like receptor signaling pathway	0	2	2	23	0.07	0.25
BP	GO:0045356	positive regulation of interferon-alpha biosynthetic process	0	1	1	4	0.07	0.25
CC	GO:0005783	endoplasmic reticulum	11	32	43	1924	0.08	0.28
BP	GO:0045671	negative regulation of osteoclast differentiation	1	1	2	27	0.09	0.28
MF	GO:0042802	identical protein binding	7	32	39	1757	0.10	0.30
BP	GO:0097527	necroptotic signaling pathway	0	1	1	6	0.11	0.30
BP	GO:0046330	positive regulation of JNK cascade	1	4	5	138	0.11	0.32
CC	GO:0031012	extracellular matrix	4	5	9	317	0.12	0.33
BP	GO:0043331	response to dsRNA	0	4	4	103	0.12	0.33

BP	GO:0045359	positive regulation of interferon-beta biosynthetic process	0	1	1	8	0.14	0.34
BP	GO:0032735	positive regulation of interleukin-12 production	0	2	2	36	0.14	0.35
BP	GO:0042742	defense response to bacterium	1	6	7	261	0.21	0.42
BP	GO:0045944	positive regulation of transcription from RNA polymerase II promoter	3	23	26	1193	0.21	0.42
BP	GO:0045078	positive regulation of interferon-gamma biosynthetic process	0	1	1	13	0.21	0.42
CC	GO:0005789	endoplasmic reticulum membrane	2	21	23	1072	0.22	0.43
BP	GO:0097191	extrinsic apoptotic signaling pathway	0	6	6	223	0.23	0.44
BP	GO:0007250	activation of NF-kappaB-inducing kinase activity	0	1	1	18	0.28	0.49
BP	GO:0007252	I-kappaB phosphorylation	0	1	1	18	0.28	0.49
BP	GO:0034138	toll-like receptor 3 signaling pathway	0	1	1	20	0.31	0.51
CC	GO:0005765	lysosomal membrane	2	6	8	360	0.32	0.52
BP	GO:0006972	hyperosmotic response	0	1	1	29	0.42	0.60
CC	GO:0016020	membrane	42	129	171	9421	0.46	0.63
BP	GO:0008584	male gonad development	1	2	3	139	0.47	0.64
CC	GO:0010008	endosome membrane	1	8	9	477	0.49	0.65
BP	GO:0001774	microglial cell activation	0	1	1	45	0.57	0.71
CC	GO:0005769	early endosome	2	4	6	355	0.62	0.75
MF	GO:0038023	signaling receptor activity	11	14	25	1478	0.66	0.77
CC	GO:0005768	endosome	4	11	15	922	0.69	0.80

MF	GO:0004888	transmembrane signaling receptor activity	10	11	21	1276	0.70	0.80
CC	GO:0005887	integral component of plasma membrane	11	14	25	1667	0.86	0.92
CC	GO:0016021	integral component of membrane	23	66	89	5674	0.95	0.98
CC	GO:0000139	Golgi membrane	1	7	8	746	0.96	0.98

Table S2. The complete list of TLR3-related genes in human VSMCs exposed to 12.5 µg/mL graphene oxide for 24 h. Data were expressed as mean±SD of triplicate.

Gene name	Control	GO	Regulation	Log ₂ (fc)	P value	Significant
IFIT1	58.68±8.22	1.69±0.39	down	-5.12	0.00	Yes
MX1	14.92±1.47	0.50±0.15	down	-4.90	0.00	Yes
OAS1	8.28±0.88	0.20±0.06	down	-5.41	0.00	Yes
MX2	1.22±0.06	0.05±0.02	down	-4.75	0.00	Yes
USP18	23.56±1.05	2.43±0.47	down	-3.28	0.00	Yes
STAT1	81.05±10.91	17.76±0.83	down	-2.20	0.00	Yes
RSAD2	5.51±1.22	0.45±0.04	down	-3.62	0.00	Yes
ISG15	304.92±51.85	20.33±4.60	down	-3.91	0.00	Yes
IRF7	17.40±1.13	4.77±0.16	down	-1.88	0.00	Yes
IFI6	310.74±66.46	17.77±5.07	down	-4.14	0.00	Yes
HERC5	1.87±0.34	0.31±0.06	down	-2.58	0.00	Yes
CSF3	5.01±0.73	1.19±0.16	down	-2.09	0.00	Yes
IFIT3	83.32±24.50	9.25±0.79	down	-3.17	0.00	Yes
IL1B	10.13±0.40	3.73±0.91	down	-1.46	0.00	Yes
DHX58	2.71±0.13	0.76±0.03	down	-1.84	0.00	Yes
CXCL8	426.74±73.32	184.10±16.31	down	-1.21	0.00	Yes
IFIT2	29.98±8.77	4.17±0.48	down	-2.85	0.00	Yes
OASL	4.76±0.87	0.91±0.23	down	-2.39	0.00	Yes
MMP1	883.65±35.93	416.48±43.34	down	-1.09	0.00	Yes
MYD88	26.36±2.18	12.19±1.60	down	-1.12	0.00	Yes
ID1	74.38±17.42	12.16±0.86	down	-2.63	0.00	Yes
IFIH1	8.31±2.63	1.77±0.22	down	-2.23	0.00	Yes
ZNFX1	27.27±2.88	14.68±0.37	down	-0.91	0.00	Yes
CCL20	13.64±3.49	5.32±0.57	down	-1.35	0.00	Yes
CXCL10	3.91±1.25	0.85±0.27	down	-2.21	0.00	Yes
IFI44L	10.68±5.57	0.54±0.12	down	-4.31	0.00	Yes
IFI44	27.56±12.58	2.94±0.26	down	-3.23	0.00	Yes
EIF2AK2	22.24±6.37	8.81±1.25	down	-1.34	0.00	Yes
TFPI2	59.86±5.40	36.83±2.78	down	-0.71	0.00	Yes

DDX58	25.14±10.29	6.13±0.47	down	-2.03	0.00	Yes
NMI	6.33±1.57	3.41±0.23	down	-0.89	0.00	Yes
SOCS3	8.16±1.30	4.48±0.38	down	-0.88	0.00	Yes
ZC3HAV1	15.09±1.97	9.88±0.82	down	-0.62	0.00	Yes
IL1A	9.09±2.69	4.46±0.36	down	-1.02	0.00	Yes
TLR3	1.09±0.38	0.42±0.09	down	0.38	0.00	Yes
VEGFC	25.72±1.75	17.14±1.14	down	-0.60	0.00	Yes
CXCL11	1.31±0.12	0.51±0.19	down	-1.38	0.00	Yes
CD274	4.88±1.05	3.12±0.16	down	-0.64	0.00	Yes
GLRX3	30.02±0.83	20.71±1.62	down	-0.54	0.00	Yes
DUSP1	83.16±5.10	59.02±5.96	down	-0.50	0.01	no
PTGES	2.33±0.57	1.01±0.32	down	-1.21	0.01	no
CXCL3	5.14±0.63	3.33±0.28	down	-0.63	0.01	no
CXCL2	11.92±1.74	8.04±0.25	down	-0.58	0.01	no
PROCR	7.76±0.92	5.17±0.49	down	-0.60	0.01	no
IFI16	35.96±10.42	23.07±0.36	down	-0.64	0.01	no
SERPINB9	1.23±0.03	0.74±0.16	down	-0.76	0.01	no
CCL5	1.17±0.22	0.52±0.09	down	-1.17	0.02	no
CCL5	1.17±0.22	0.52±0.09	down	-1.17	0.02	no
LIPG	1.07±0.02	0.74±0.02	down	-0.54	0.02	no
ABCA1	12.19±2.25	8.91±1.64	down	-0.46	0.03	no
PECAM1	7.11±0.19	5.41±0.31	down	-0.40	0.03	no
GBP3	15.41±5.07	10.35±0.81	down	-0.57	0.05	no
CSF2	11.07±2.65	7.51±1.17	down	-0.58	0.06	no
LIPA	29.30±0.60	23.59±0.68	down	-0.32	0.07	no
CTH	1.13±0.06	1.67±0.18	up	0.55	0.09	no
IL6	5.58±0.96	4.27±0.55	down	-0.39	0.09	no
PFDN6	10.99±0.69	8.54±1.39	down	-0.37	0.10	no
CPM	1.67±0.10	1.33±0.15	down	-0.34	0.14	no
TNFRSF1B	4.45±0.74	3.65±0.17	down	-0.30	0.16	no
GCH1	1.64±0.15	1.23±0.12	down	-0.42	0.17	no
PMAIP1	14.85±2.18	12.84±0.69	down	-0.22	0.27	no
CALCOCO2	6.80±0.21	5.94±0.24	down	-0.20	0.28	no
AKT3	4.23±1.07	4.88±0.54	down	0.20	0.30	no
CD40	1.40±0.09	1.11±0.03	down	-0.34	0.31	no
BCAR3	9.45±0.65	8.38±0.12	down	-0.19	0.32	no
SRC	7.22±1.08	8.20±0.20	up	0.16	0.37	no
NFKBIZ	11.83±3.52	10.49±1.58	down	-0.18	0.47	no
CFLAR	5.80±1.25	5.31±0.84	down	-0.14	0.48	no
RIPK1	9.61±0.67	8.84±0.68	down	-0.13	0.48	no
N4BP1	5.78±0.53	5.32±0.56	down	-0.13	0.49	no
ATF3	1.18±0.19	1.37±0.11	down	0.19	0.49	no
LMNB1	11.36±0.65	10.50±0.69	down	-0.13	0.51	no

FAS	4.02±0.97	4.45±0.42	up	0.14	0.51	no
ZNF644	3.87±1.37	4.43±0.67	up	0.19	0.52	no
ZBTB22	9.37±0.74	10.26±1.40	up	0.12	0.59	no
MAP3K7	9.29±2.63	10.00±0.73	up	0.10	0.63	no
TSLP	1.02±0.20	0.94±0.11	down	-0.14	0.66	no
TIMP1	226.78±35.09	209.96±32.91	down	-0.12	0.66	no
FURIN	85.46±16.32	81.09±1.89	down	-0.10	0.67	no
DNMT1	12.74±0.46	12.24±0.48	down	-0.07	0.70	no
NFE2L3	20.33±2.21	17.91±0.22	down	0.06	0.71	no
LPIN2	7.76±0.46	8.15±0.37	up	0.06	0.76	no
WDR92	1.11±0.18	1.06±0.08	down	-0.07	0.79	no
PIK3R1	5.82±1.66	6.07±0.73	up	0.06	0.83	no
SOCS1	4.18±0.48	4.13±0.47	down	-0.03	0.94	no
RAE1	6.48±0.54	6.56±0.53	up	0.01	0.94	no
IRAK4	4.43±0.74	4.42±0.30	down	-0.01	0.95	no
PHLDA1	24.37±2.26	24.4±13.47	up	-0.01	0.95	no
TRAF3	10.79±0.15	10.84±0.18	up	0.00	0.98	no
IRF1	2.08±0.43	2.10±0.16	up	0.00	1.00	no