Electronic Supplementary Information

Table S1 Representative NDs-interacting transmembrane receptors identified by mass spectrometry.

Transmembrane Receptors		
UniProtKB		Name
Q6IB11		Progesterone receptor membrane component 1
Q6I9U3		Mannose-6-phosphate receptor
O95944		Natural cytotoxicity triggering receptor 2
Q05BV5		Opoid growth factor receptor
F5GWR7		Receptor-type tyrosine-protein phosphatase receptor δ
D2JYI1		**TGFβ receptor type-2**
B4DDJ5		Similar to Macrophage scavenger receptor types
A8K1Z4		Leukemia inhibitory factor receptor
P42566		Epidermal growth factor receptor substrate 15
Q9UL62		Short transient receptor 5
A0A0A0MRB9		X-linked interleukin-1 receptor accessory protein-like 2
A0A087WX59		Proteasomal ubiquitin receptor ADRM1
A0A087WUV8		Signal recognition particle receptor subunit β
Q9NR97		Toll-like receptor 8
Q9GZP7		Vomeronasal type-1 receptor-1
Q7Z5H4		Vomeronasal type-1 receptor-5
P37288		Vasopressin V1a receptor
P58181		Olfactory receptor 10A3
Q17R88		Sortilin-related VPS10 domain containing receptor 3
Q01638		Interleukin-1 receptor-like 1
P51686		C-C chemokine receptor type 9
Q3S2J4		Macrophage scavenger receptor
P21757		Thyroid hormone receptor
F8VVC		TGFβ receptor type-1
O75330		Hyaluronan mediated motility receptor

Table S2 Representative NDs-interacting cytoskeletons identified by mass spectrometry.

Cytoskeletons		
UniProtKB		Name
Q5HY54		Filamin-A
Q5SU16		Tubulin-β
Q71U36		Tubulin-α-1A
B7Z1K5		Tubulin-α chain
Q8IZ29		Tubulin-β-4B chain
Q13885		Tubulin β-2A chain
P04350		Tubulin β-4A chain
C9J2C0_		Tubulin α-8 chain
E5RHG6		Tubulin-specific chaperone A
Q9H4B7		Tubulin β-1 chain
Q15813		Tubulin-specific chaperone
A6NHL2		Tubulin α chain-like 3
A4UCU2_		β-4 tubulin (Fragment)
H3BLT7		Tubulin monoglycylase TTLL3 (Fragment)
O95922		Tubulin polyglutamylase TTLL1
O75369		Filamin-B
P68133		Actin, α skeletal muscle
A0A0S2Z3G9		Actinin α 4 isoform 1
H9KV75		α-actinin-1
Q53GK6		β actin variant (Fragment)
Q14315		Filamin-C
A0A024R0E5		Capping protein (Actin filament) muscle Z-lineα1
B1AK88		Capping protein (Actin filament)muscle Z-lineβ
A4D0V4		Capping protein (Actin filament) muscle Z-lineα2
A5YM63		NEFM protein

Table S3 Representative NDs-interacting chaperones identified by mass spectrometry.

Chaperones		
UniProtKB		Name
V9HW96		Chaperonin containing TCP1
Q6FH24		Prefoldin subunit 3
F8W726		Ubiquitin-associated protein 2-like
Q9Y5K6		CD2-associated protein
P42167		Lamina-associated polypeptide 2
E9PAL7		Translocon-associated protein subunit α
A0A024RDL1		Chaperonin containing TCP1, subunit 6A
O95295		SNARE-associated protein Snapin
Q53G55		TNF receptor-associated protein 1
O15212		Prefoldin subunit 6
A0A024R6M6		BCL2-associated athanogene 5
Q9P0L0		Vesicle-associated membrane protein-associated protein
P78371		T-complex protein 1 subunit β
P50991		T-complex protein 1 subunit δ
P50990		T-complex protein 1 subunit θ
P49368		T-complex protein 1 subunit γ
P48643		T-complex protein 1 subunit ε
A0A024R3X4		Heat shock 60kDa protein 1 (Chaperonin)
E7EVA0		Microtubule-associated protein
Q96A49		Synapse-associated protein 1
Q9Y3F4		Serine-threonine kinase receptor-associated protein
A0A024R3V8		Translin-associated factor X
Q09666		Neuroblast differentiation-associated protein
P17987		T-complex protein 1 subunit α
Q9UNN5		FAS-associated factor 1

Table S4 Representative NDs-interacting enzymes identified by mass spectrometry.

Enzymes		
UniProtKB		Name
V9HWB8		Pyruvate kinase
P35520		Cystathionine β-synthase
Q15185		Prostaglandin E synthase 3
A0A0U1RQF0		Fatty acid synthase
Q9H2P9		Diphthine methyl ester synthase
Q6UB35		Monofunctional C1-tetrahydrofolate synthase
A0A024R1Y2		ATP-citrate synthase
Q15181		Inorganic pyrophosphatase
P36871		Adenylate kinase 2
P19623		Spermidine synthase
P30049		ATP synthase subunit δ, mitochondrial
P36871		Phosphoglucomutase-1
Q9NPH2		Inositol-3-phosphate synthase 1
P31153		S-adenosylmethionine synthase isoform type-2
P29401		Transketolase
Q8WWH5		Probable tRNA pseudouridine synthase 1
P12277		Creatine kinase B-type
O43175		D-3-phosphoglycerate dehydrogenase
V9HWH2		ATP synthase subunit β
P11586		C-1-tetrahydrofolate synthase
P56385		ATP synthase subunit e
P07195		L-lactate dehydrogenase
Q9NR45		Sialic acid synthase
P00558		Phosphoglycerate kinase 1
O75947		ATP synthase subunit d

Table S5 Representative NDs-interacting signal transducers identified by mass spectrometry.

Signal Transducers		
UniProtKB		Name
Q2M3K2		Regulator of G-protein signaling 6
Q7Z426		Putative MAPK activating protein
J3KQ34		COP9 signalosome complex subunit 7b
E7EM64		COP9 signalosome complex subunit 6
O76094		Signal recognition particle subunit
H0YLA2		Signal recognition particle 14 kDa protein
Q92905		COP9 signalosome complex subunit 5
D6RFN0		COP9 signalosome complex subunit 4
B2RAY1		5'-AMP-activated protein kinase catalytic subunit α-2
A0A024R3V8		Translin-associated factor X
A0A024QZF6		AKT1 substrate 1
F8W930		Insulin-like growth factor 2 mRNA-binding protein 2
Q9Y5X3		Sorting nexin-5
P54646		14-3-3 protein ζ/δ
P61011		Signal recognition particle 54 kDa protein
Q6NZ61		Ras homolog enriched in brain
Q07666		KH domain-containing transduction-associated protein 1
Q13158		FAS-associated death domain protein
Q9P055		JNK1/MAPK8-associated membrane protein
Q14160		Protein scribble homolog
Q92783		Signal transducing adapter molecule 1
P38919		Eukaryotic initiation factor 4A-III
B7Z4E1		Similar to X-linked interleukin-1 protein-like 2
P22234		Multifunctional protein ADE2
Q5TH30		NDRG family member 3

Table S6 Representative NDs-interacting transcription factors identified by mass spectrometry.

Transcription Factors		
UniProtKB		Name
O15370		Transcription factor SOX-12
P32519		ETS-related transcription factor Elf-1
A0A024RDU9		General transcription factor IIF subunit2
A0A0B4J1Z5		Transcription initiation factor IIA subunit 2
P20290		Transcription factor BTF3
Q96QR8		Transcriptional activator protein Pur
Q86YP4		Transcriptional repressor p66-α
A0A0U1RRM1		Transcriptional repressor p66-β
Q96K17		Transcription factor BTF3 homolog 4
Q12789		General transcription factor 3C polypeptide 1
Q8IYS3		GA binding protein transcription factor
A0A0A0MRX7		Transcription factor TFIIIB component B
C9JSJ3		Basic helix-loop-helix
O00268		Transcription initiation factor TFIID subunit 4
Q12962		Transcription initiation factor TFIID subunit 10
Q7Z7C8		Transcription initiation factor TFIID subunit 8
E7EVE9		TFIIH basal transcription factor complex
P53999		Activated RNA polymerase II transcriptional co-activator
B4DH52		Highly similar to General transcription factor II-I
A0A024RDU6		E74-like factor 1 (Ets domain transcription factor)
Q658N3		Down-regulator of transcription 1
B4DDB5		Transcription initiation factor IIF α subunit
Q9NUK2		Transcription regulatory protein SNF2
Q9NQ48		Leucine zipper transcription
E7EVE9		TFIIH basal transcription factor complex

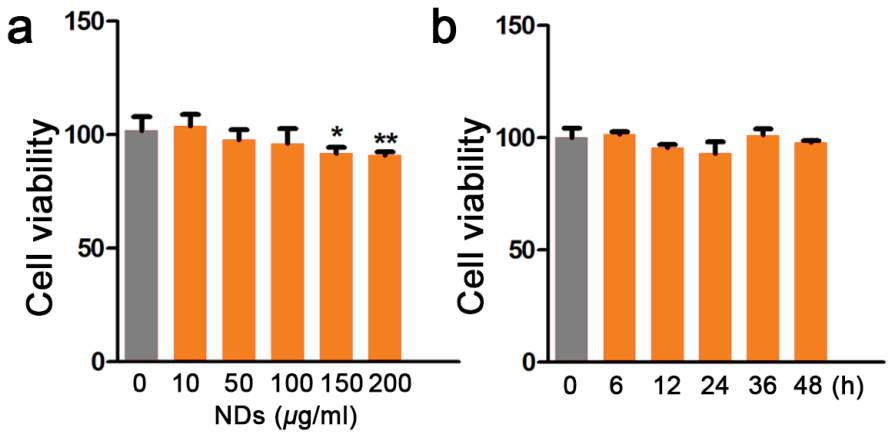

FIG. S1 Cytotoxicity of NDs in A549 cells. (a) The cytotoxicity of NDs at different concentrations (0, 10, 50, 100, 150, 200 μg/mL) was measured after 24-hour incubation. (b) Cell viability was examined at indicated time points after incubation with 100 μg/mL NDs. Data are represented as mean $\pm$SD (n=4). Student's *t*-test, *p<0.05, **p<0.01.

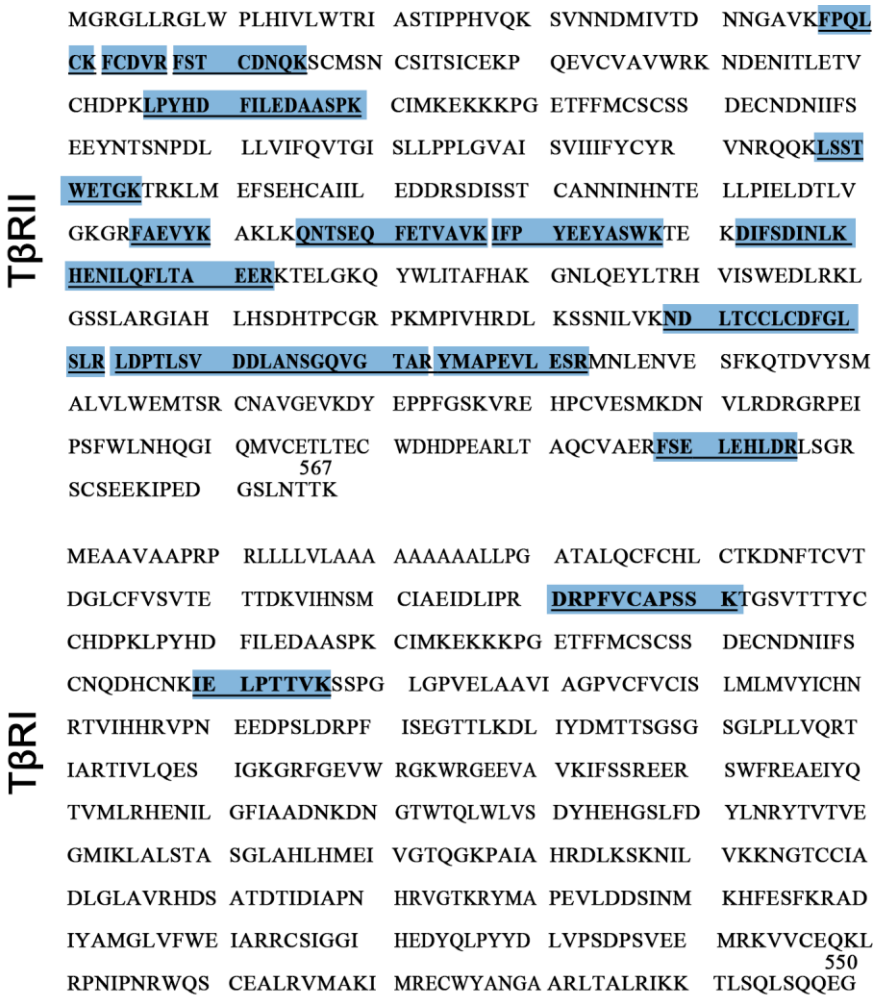

FIG. S2 Mass spectrometry-identified peptides from TGFβ receptors. The protein sequences of TGFβ receptors and the identified peptides (blue).

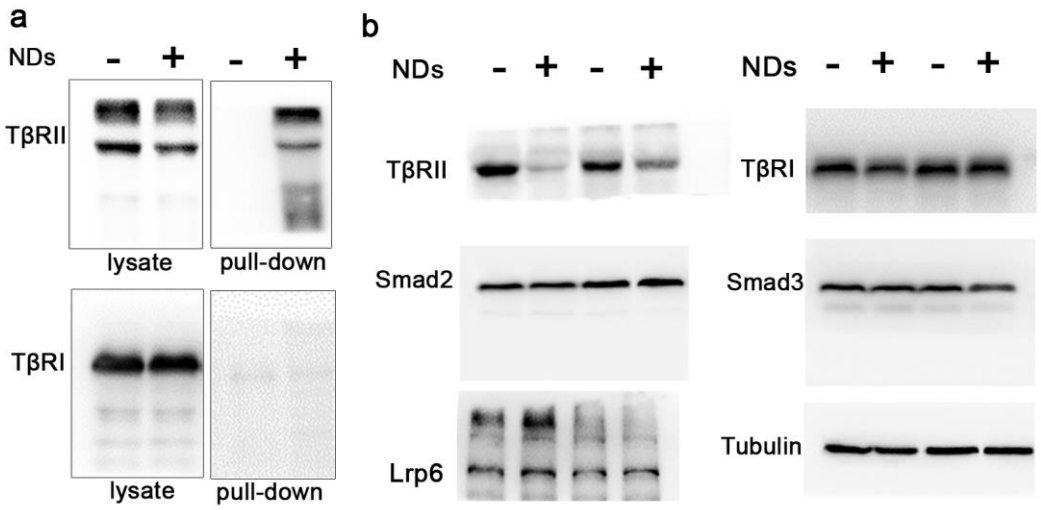

FIG. S3 The original images of figure 2b and 2e. (a) The pull-down of TGFβ receptors by NDs from the lysate of A549 cells. (b) The effects of NDs uptake on the protein levels of indicated proteins in A549 cells.

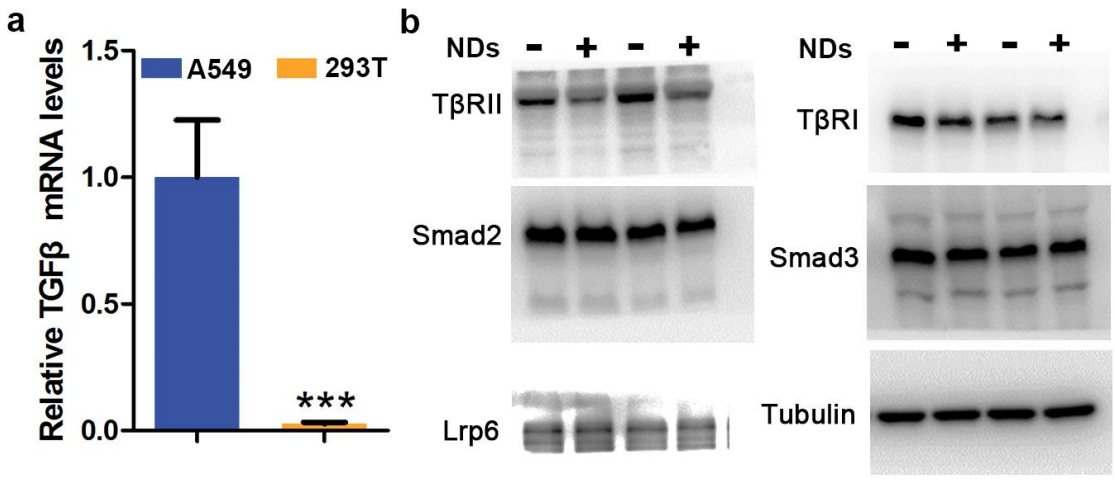

FIG. S4 (a) The mRNA levels of TGFβ1 cytokine in A549 cells and HEK-293T cells. (b) The effects of NDs uptake on the protein levels of indicated proteins in HEK-293T cells.

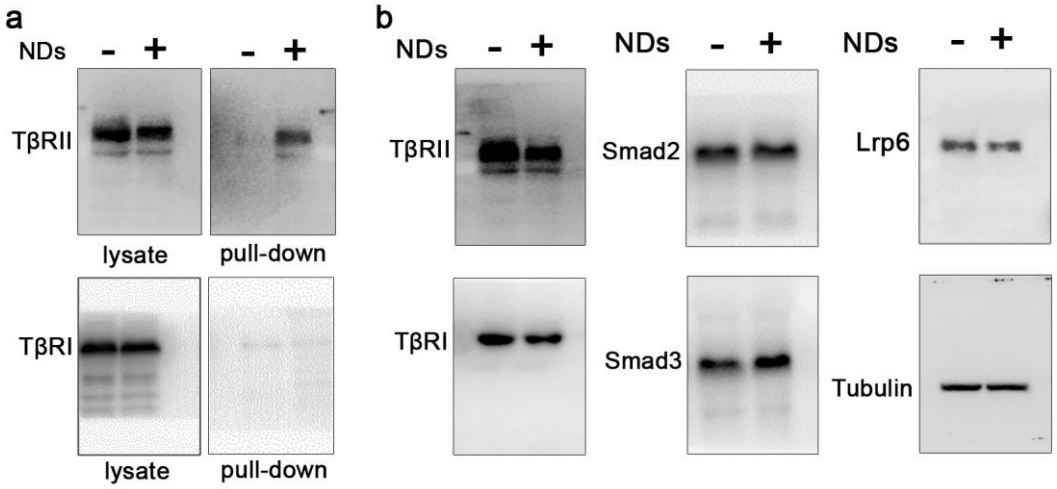

FIG. S5 (a) The pull-down of TGFβ receptors by NDs from the lysate of A549 cells cultured in serum-free medium. (b) The effects of NDs uptake on the protein levels of indicated proteins in A549 cells cultured in serum-free medium.

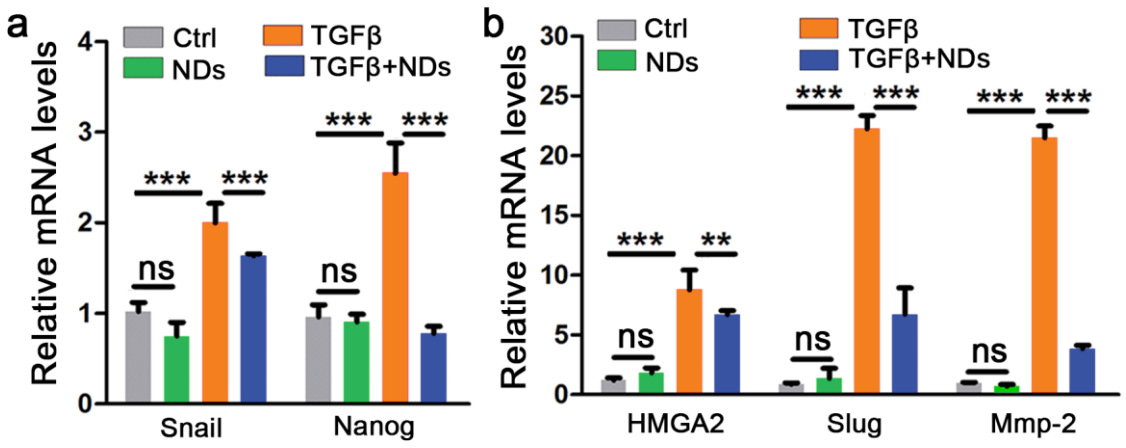

FIG. S6 NDs attenuate the transcriptional outputs of TGFβ signaling. (a, b) The effects of NDs on the expression of endogenous TGFβ target genes in the absence or presence of TGFβ. Data are represented as mean ±SD (n=3). Student's *t*-test, ns: not significant, ***p*<0.01, ****p*<0.001.

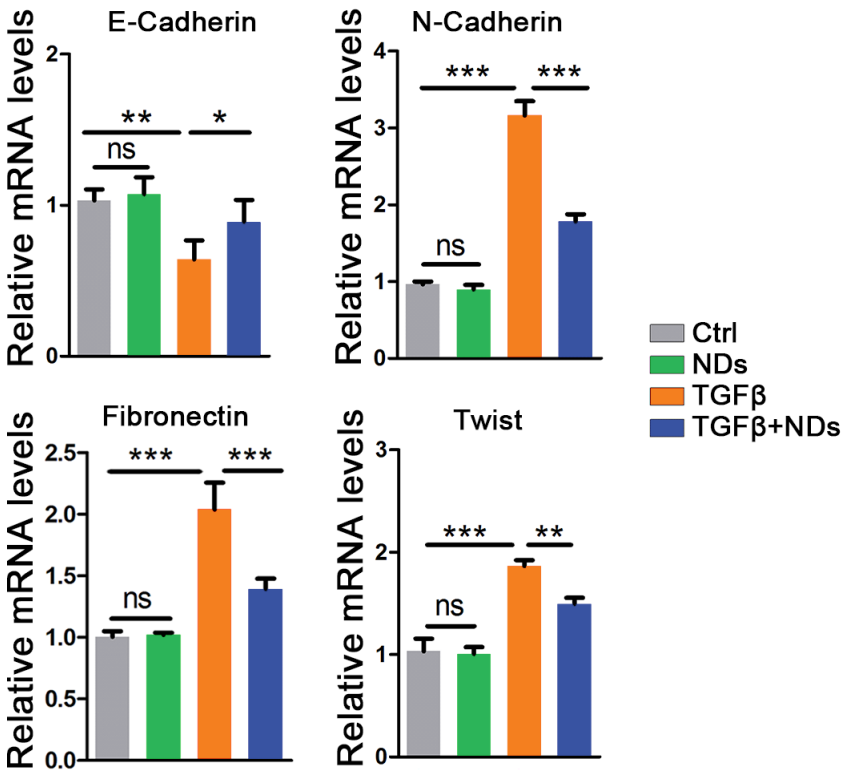

FIG. S7 NDs block TGFβ-mediated metastasis-associated gene expression in tumor organoids. The effects of NDs on the expression of E-Cadherin, N-Cadherin, Fibronectin and Twist in the absence or presence of TGFβ. Data are represented as mean ±SD (n=3). Student's *t*-test, ns: not significant, **p*<0.05, ***p*<0.01, ****p*<0.001.

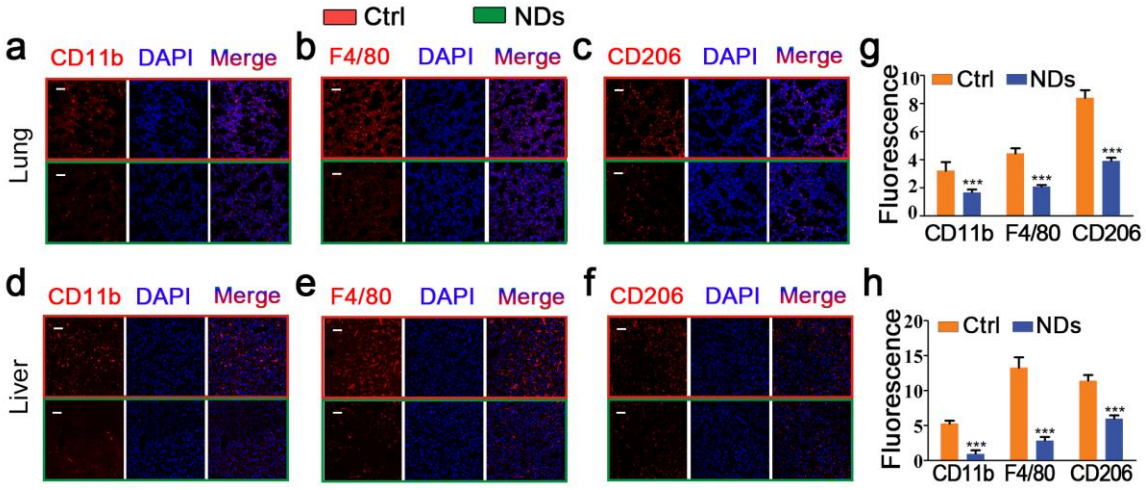

FIG. S8 NDs reduce TAMs recruitment and M2 macrophage polarization in the lung and liver. Immunofluorescence imaging shows the expression of CD11b, F4/80 and CD206 cell surface markers in the lung (a-c) and liver (d-f) tissue sections. Scale bars, 50 μm. (g, h) The quantification of fluorescence intensities from CD11b, F4/80 and CD206 markers in the lung (g) and liver (h) tissue sections. Data are represented as mean ±SD (n=3), Student's *t*-test, ***p<0.001.

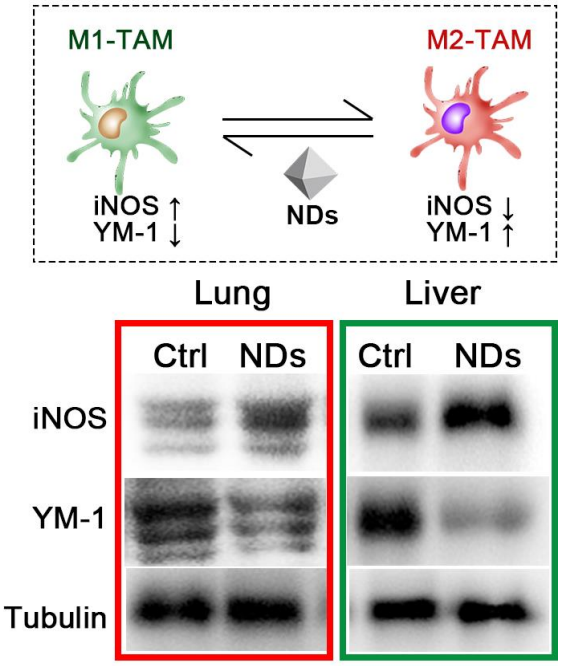

FIG. S9 NDs affect the expression of M1-TAM and M2-TAM markers. Upper panel: a scheme for the change of marker levels during M1/M2 polarization. Lower panel: the protein levels of M1-TAM marker iNOS and M2-TAM marker YM-1 are monitored by western blotting.

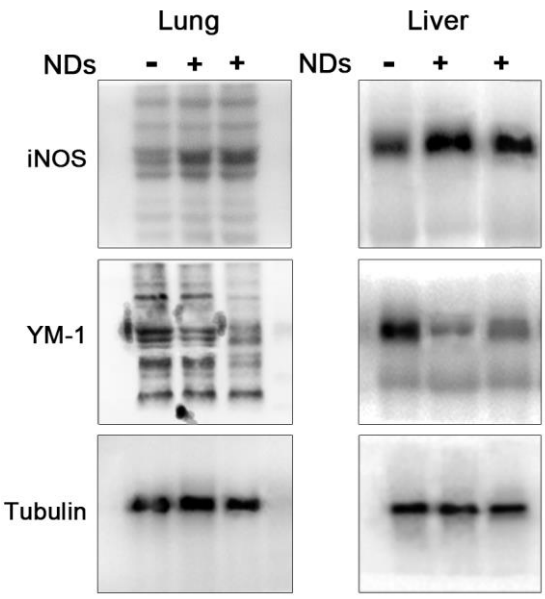

FIG. S10 The original images of figure S9.