

Supporting Information

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SI Materials and Methods

Four percent formaldehyde solution, human signaling Pathway-Finder RT² Profiler PCR Array (SABiosciences, cat #PAHS-071Z), RT² First Strand kit (SABiosciences, cat #C-03), RT² SYBR Green/Fluorescein qPCR Mastermix (SABiosciences, cat #PA-011), and Qiagen RNeasy Mini Kit were purchased from Qiagen. Human breast cancer tissue (BR1503b, BR1505, and T088) and normal tissue (BN00011 and BN1002a) arrays were purchased from US Biomax. Dulbecco's PBS, DAPI, Quant-iT RNA Assay Kit, 0.25% trypsin/2.6 mM EDTA solution, Gibco DMEM, Gibco DMEM/F12(1:1) Roswell Park Memorial Institute (RPMI)-1640 medium, and McCoy's 5A medium were purchased from Invitrogen. MEGM Mammary Epithelial Cell Growth Medium was purchased from Lonza. Quantum Simply Cellular microbeads were purchased from Bangs Laboratory.

Mouse anti-human intercellular adhesion molecule-1 (ICAM-1) monoclonal antibody (aICAM1), IgG isotype control, and NorthernLights 557 (NL557)-conjugated donkey anti-mouse IgG were purchased from R&D Systems. Phycoerythrin (PE)-conjugated mouse anti-human ICAM-1 antibody (PE-aCXCR4) and PE-conjugated mouse IgG isotype (PE-IgG) were purchased from BioLegend. The 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride, *N*-hydroxysuccinimide, BSA, anhydrous DMSO, FITC, and Nanosep 300K Omega centrifugal device were purchased from Sigma-Aldrich. The Lab-Tek II Chamber Slide System was obtained from Thermo Fisher Scientific. Fluorogel with Tris buffer was purchased from Electron Microscopy Sciences. Activation Buffer and Coupling Buffer were purchased from Ocean Nanotech.

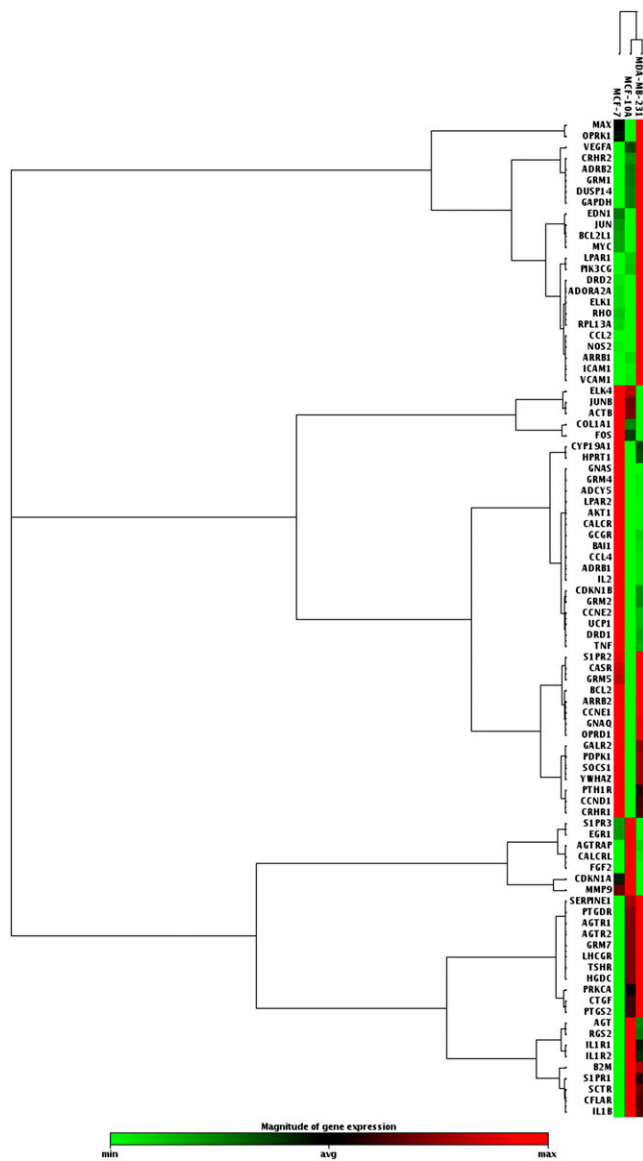


Fig. S1. Gene expression analysis for 84 G-protein coupled receptor signaling genes.

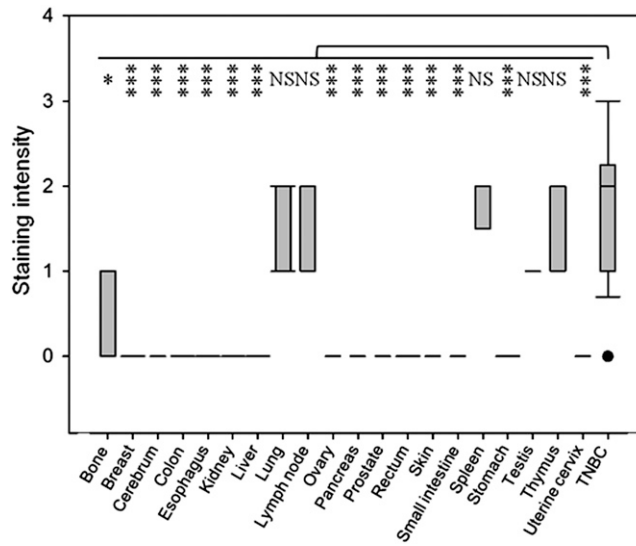


Fig. S2. Quantification of ICAM-1 staining intensities in various human normal organs: bone ($n = 5$), breast ($n = 14$), cerebrum ($n = 5$), colon ($n = 11$), esophagus ($n = 10$), kidney ($n = 11$), liver ($n = 11$), lung ($n = 11$), lymph node ($n = 5$), ovary ($n = 5$), pancreas ($n = 5$), prostate ($n = 4$), rectum ($n = 10$), skin ($n = 5$), small intestine ($n = 5$), spleen ($n = 5$), stomach ($n = 11$), testis ($n = 5$), thymus ($n = 5$), uterine cervix ($n = 5$), and triple negative breast cancer (TNBC) tissue ($n = 26$). Data are presented as a box-and-whisker plot. * $P < 0.05$; *** $P < 0.001$; NS, not significant compared with TNBC tissues.

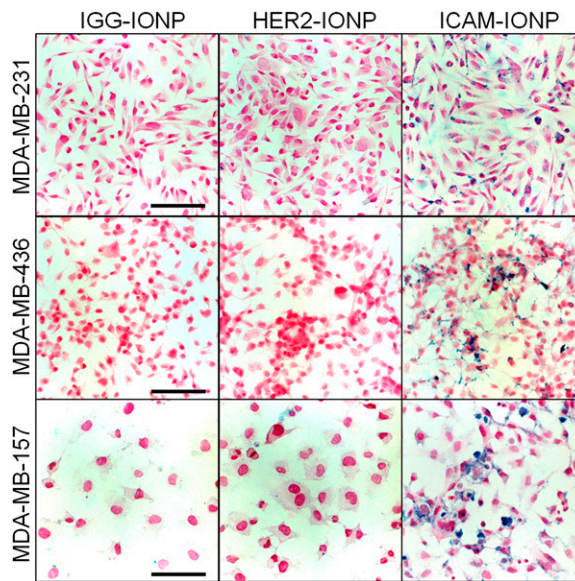


Fig. S3. Representative microscopic images of Prussian blue staining of ion oxide nanoparticles functionalized with IgG (IGG-IONP), human epidermal growth factor receptor 2 (HER2-IONP), and ICAM-1 (ICAM-IONP) demonstrating uptake by MDA-MB-231, MDA-MB-436, and MDA-MB-157. Scale bars represent 20 μm .

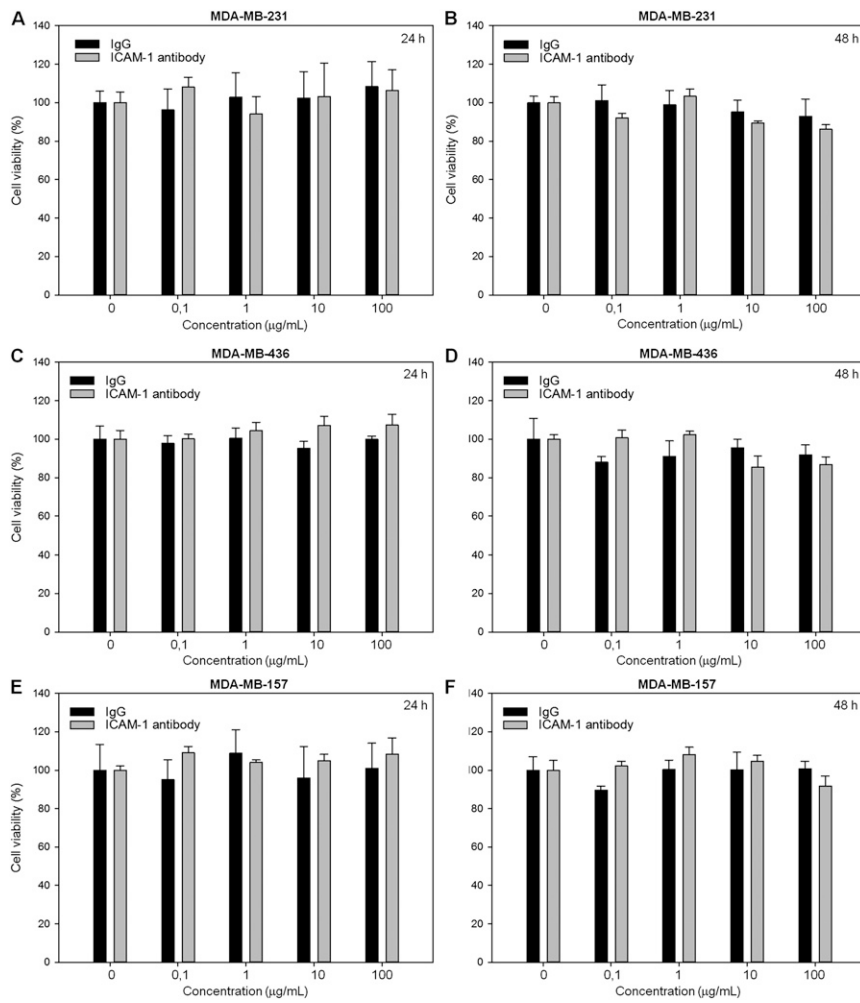


Fig. S4. Effect of the free ICAM-1 antibody on the proliferation of TNBC cells at different concentrations: MDA-MB-231 (A and B), MDA-MB-436 (C and D), MDA-MB-157 (E and F). Nonspecific IgG was used as control. The duration of cell proliferation was 24 h for A, C, and E and 48 h for B, D, and F.

Table S1. List of gene symbols

Symbol	Description
ADCY5	Adenylate cyclase 5
ADORA2A	Adenosine A2a receptor
ADRB1	Adrenergic β_1 -receptor
ADRB2	Adrenergic β_2 -receptor, surface
AGT	Angiotensinogen (serpin peptidase inhibitor, clade A, member 8)
AGTR1	Angiotensin II receptor, type 1
AGTR2	Angiotensin II receptor, type 2
AGTRAP	Angiotensin II receptor-associated protein
AKT1	V-akt murine thymoma viral oncogene homolog 1
ARRB1	Arrestin, β_1
ARRB2	Arrestin, β_2
BAI1	Brain-specific angiogenesis inhibitor 1
BCL2	B-cell CLL/lymphoma 2
BCL2L1	BCL2-like 1
CALCR	Calcitonin receptor
CALCRL	Calcitonin receptor-like
CASR	Calcium-sensing receptor
CCL2	Chemokine (C-C motif) ligand 2
CCL4	Chemokine (C-C motif) ligand 4
CCND1	Cyclin D1
CCNE1	Cyclin E1
CCNE2	Cyclin E2
CDKN1A	Cyclin-dependent kinase inhibitor 1A (p21, Cip1)
CDKN1B	Cyclin-dependent kinase inhibitor 1B (p27, Kip1)
CFLAR	CASP8 and FADD-like apoptosis regulator
COL1A1	Collagen, type I, α_1
CRHR1	Corticotropin-releasing hormone receptor 1
CRHR2	Corticotropin-releasing hormone receptor 2
CTGF	Connective tissue growth factor
CYP19A1	Cytochrome P450, family 19, subfamily A, polypeptide 1
DRD1	Dopamine receptor D1
DRD2	Dopamine receptor D2
DUSP14	Dual-specificity phosphatase 14
S1PR1	Sphingosine-1-phosphate receptor 1
LPAR1	Lysophosphatidic acid receptor 1
S1PR3	Sphingosine-1-phosphate receptor 3
LPAR2	Lysophosphatidic acid receptor 2
S1PR2	Sphingosine-1-phosphate receptor 2
EDN1	Endothelin 1
EGR1	Early growth response 1
ELK1	ELK1, member of ETS oncogene family
ELK4	ELK4, ETS-domain protein (SRF accessory protein 1)
FGF2	Fibroblast growth factor 2 (basic)
FOS	FBJ murine osteosarcoma viral oncogene homolog
GALR2	Galanin receptor 2
GCGR	Glucagon receptor
GNAQ	Guanine nucleotide binding protein (G protein), q polypeptide
GNAS	GNAS complex locus
GRM1	Glutamate receptor, metabotropic 1
GRM2	Glutamate receptor, metabotropic 2
GRM4	Glutamate receptor, metabotropic 4
GRM5	Glutamate receptor, metabotropic 5
GRM7	Glutamate receptor, metabotropic 7
ICAM1	Intercellular adhesion molecule 1
IL1B	Interleukin 1 β
IL1R1	Interleukin 1 receptor, type I
IL1R2	Interleukin 1 receptor, type II
IL2	Interleukin 2
JUN	Jun proto-oncogene
JUNB	Jun B proto-oncogene
LHCGR	Luteinizing hormone/choriogonadotropin receptor
MAX	MYC-associated factor X
MMP9	Matrix metalloproteinase 9 (gelatinase B, 92-kDa gelatinase, 92-kDa type IV collagenase)

Table S1. Cont.

Symbol	Description
MYC	V-myc myelocytomatosis viral oncogene homolog (avian)
NOS2	Nitric oxide synthase 2, inducible
OPRD1	Opioid receptor, δ_1
OPRK1	Opioid receptor, κ_1
PDPK1	3-Phosphoinositide-dependent protein kinase-1
PIK3CG	Phosphoinositide-3-kinase, catalytic, γ -polypeptide
PRKCA	Protein kinase C, α
PTGDR	Prostaglandin D2 receptor (DP)
PTGS2	Prostaglandin-endoperoxide synthase 2 (prostaglandin G/H synthase and cyclooxygenase)
PTH1R	Parathyroid hormone 1 receptor
RGS2	Regulator of G protein signaling 2, 24 kDa
RHO	Rhodopsin
SCTR	Secretin receptor
SERPINE1	Serpin peptidase inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 1
SOCS1	Suppressor of cytokine signaling 1
TNF	Tumor necrosis factor
TSHR	Thyroid-stimulating hormone receptor
UCP1	Uncoupling protein 1 (mitochondrial, proton carrier)
VCAM1	Vascular cell adhesion molecule 1
VEGFA	Vascular endothelial growth factor A
YWHAZ	Tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, ζ -polypeptide
B2M	β_2 -Microglobulin
HPRT1	Hypoxanthine phosphoribosyltransferase 1
RPL13A	Ribosomal protein L13a
GAPDH	Glyceraldehyde-3-phosphate dehydrogenase
ACTB	Actin, β
HGDC	Human genomic DNA contamination
RTC	Reverse transcription control
PPC	Positive PCR control

Table S2. ICAM-1 expression on human umbilical vein endothelial cells is experimentally lower than on TNBC cells by flow cytometry measurement

Cell line	ICAM-1, molecules/cell
MDA-MB-231	2,350,000 \pm 25,000
MDA-MB-157	751,000 \pm 4,400
MDA-MB-436	756,000 \pm 7,600
HUVEC	284,000 \pm 4,600
MCF10A	93,000 \pm 2,300

HUVEC, human umbilical vein endothelial cells.