Supplementary Material

Supplementary Figure Legends

Figure S1: (A) Schematic illustration of our technical route approach to identify fatty-acid receptor CD36 functions as a H_2S-targeting receptor with its Cys333-Cys272 disulfide bond serving as a specific molecular switch to accelerate GC metastasis *in vitro*. (B) Veen analysis of up- and down-regulated genes in NaHS (50μM)-treated group compared with Vehicle-treated group. (C) Real-time PCR were performed to detect CD36 mRNA levels in AGS, HGC27, and SGC7901 cells with treated NaHS at various concentrations for 24 h (n=10, student's t-test). ***: $p<0.001$, **: $p<0.01$, *: $p<0.05$. (D) Western blots showing CD36 protein levels in HGC27 cells. H_2S promoted cell migration in the nonsense siRNA groups and this effect was inhibited in cells with CD36-specific siRNA knockdown (n=4, student's t-test). (E) H_2S induced HGC27 cells to release VEGF in nonsense siRNA groups, but this effect was inhibited in cells with CD36-specific siRNA knockdown (n=3, student's t-test). (F) Schematic illustration of our technical route approach to identify fatty-acid receptor CD36 functions as a H_2S-targeting receptor with its Cys333–Cys272 disulfide bond serving as a specific molecular switch to accelerate GC metastasis *in vivo*. (G) The expression level of CD36 in human GC cell lines by western blot and densitometric measurements of CD36 protein levels. n.s, no significant differences. Each bar represents the mean ± standard deviation (S.D.).

Figure S2: (A) Wound healing assayed that the effect of H_2S to migration for serum free stimulated GES-1 cells (n=6, student's t-test). (B) ELISA assayed that the effect of H_2S to release VEGF for serum free stimulated GES-1 cells (n=6, student's t-test). (C) TMRM analysis the effects of stable expression CD36(wt) on level of MMP in AGS cells (n=3, student's t-test). (D) IHC staining with anti-CSE antibody and anti-CD36 antibody was performed on human stomach normal tissues. Representative photos of staining are shown. Scale bar: 20μm. n.s, no significant differences. Each bar represents the mean ± standard deviation (S.D.).

Figure S3: (A) The structure of CD36, shown in purple. The nine N-linked glycosylation sites and associated sugars are green while two palmitic acids are shown as yellow sticks. (B) Prediction of the secondary structure of the CD36 sequence containing the LC-FAs second binding site using the I-TASSER platform. (C) Western blot assays the level of Fyn phosphorylation (n=3, student's t-test). (D)

Western blot was performed to detect CD36 protein levels in AGS cells that stably expressed CD36(wt) and CD36(C333A). (E) PA also promoted AGS cells migration in the stably expression CD36(C333A) groups (n=3, student's t-test). (F) The level of H_2S in the plasma of orthotropic xenotransplanted mice (student's t-test). (G) Western blot was performed to detect CD36 protein and CSE protein levels in AGS cells, and hypoxia promoted CD36 and CSE protein expression in the nonsense siRNA groups, and this effect which hypoxia promoted CD36 protein expression was decrease in the cells with CSE siRNA knock down. n.s, no significant differences. Each bar represents the mean ± standard deviation (S.D.).

Figure S4: (A) The expression level of Syk in human GC cell lines by western blot assay. (B) The phosphorylation level of Fyn in AGS cells with stable expressing Syk by western blot assay. (C) The phosphorylation level of CD36 in AGS cells by western blot assay. (D) Western blots showing CD36 precursor protein levels and mature protein levels in AGS cells. (E) A schematic illustration of our systems-reprogramming of lipid metabolism approach.

Supplementary Table Legend

***Table S1*:** Summary of patient characteristics and their correlation with CSE expression.

Supplementary Table Information

REAGENT or RESOURCE	SOURCE	IDENTIFIER
Antibodies		
Mouse polyclonal to CTH	Santa Cruz	Sc-365381
Mouse monoclonal to CD36	Proteintech	18836-1-AP
Rabbit polyclonal to Fyn	Abcam	ab 184276 ab 182661
Rabbit monoclonal to Nrf2	Abcam	ab 62352
Rabbit monoclonal to GAPDH	Abcam	ab 181602
Rabbit monoclonal to β-Actin	Abcam	ab 124964
Rabbit polyclonal to Lamin A	Abcam	ab 26300
Chemicals		
Sodium Hydrosulfide	Sigma	161527
Sulfo-*N*-succinimidyl 6-(biotinamido)hexanoate sodium salt (SSO)	Abcam	ab146111
BODIPY™ 558/568 Phalloidin	Invitrogen	B3475
Tetramethylrhodamine	Invitrogen	A1318
Test kit		
VEGF ELISA Kit	Abcam	ab 222510
CBS Assay Kit	Abcam	ab 241043
LC-FA Uptake Assay Kit	Abcam	ab 176768
Cell Counting Kit 8	Abcam	ab 228554
Oil Red O kit	Abcam	ab 150678
Human recombinant protein		
Human CD36 protein	Sino Biological Inc	10752-H08H
The sequences of RNAi		
siRNA CD36	Thermo Fisher	HSS101567
siRNA CSE	SEQUENCE	Sense: **5'** GCAUCUGAAUUUGGAUUAAtt **3'** antisense: **5'** UUAAUCCAAAUUCAGAUGCca **3'**
siRNA Nrf2	SEQUENCE	sense: **5'** GTAAGAAGCCAGATGTTAA **3'** antisense: **5'** GUAAGAAGCCAGAUGUUAAdUdU **3'**
shRNA CD36	SEQUENCE	**5'** GAAGTTACATATTAGGCCAT **3'**
PCR Primers pairs		
CD36	SEQUENCE	Forward: **5'** TGTCATTGGTGCTGTCCTGG **3'** Reverse: **5'** TCCTCAGCGTCCTGGGTTAC **3'**
GAPDH	SEQUENCE	Forward: **5'** CTGACTTCAACAGCGACACC **3'** Reverse: **5'** TGCTGTAGCCAAATTCGTTGT **3'**