

Figure S1. Validation of additional microarray targets (A) Quantification of FACS ADGRL4/ELTD1 surface. (B) Volcano plots and Venn diagram depicting differentially expressed genes for each siRNA. (C) *KIT* qPCR and FACS quantification of surface *KIT* protein expression. (D) *DLL4* qPCR and FACS quantification of surface *DLL4* protein expression. (E) *JAG1* qPCR and FACS quantification of surface *JAG1* protein expression. (F) *HES2* qPCR. (G) Representative western blot showing ADGRL4/ELTD1 overexpression in HUVECs (longer exposure, on the right, required to show endogenous expression in wild type HUVECs) and *ACLY* and *SLC25A1* qPCR quantification in ADGRL4/ELTD1 overexpressing HUVECs. (* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$)

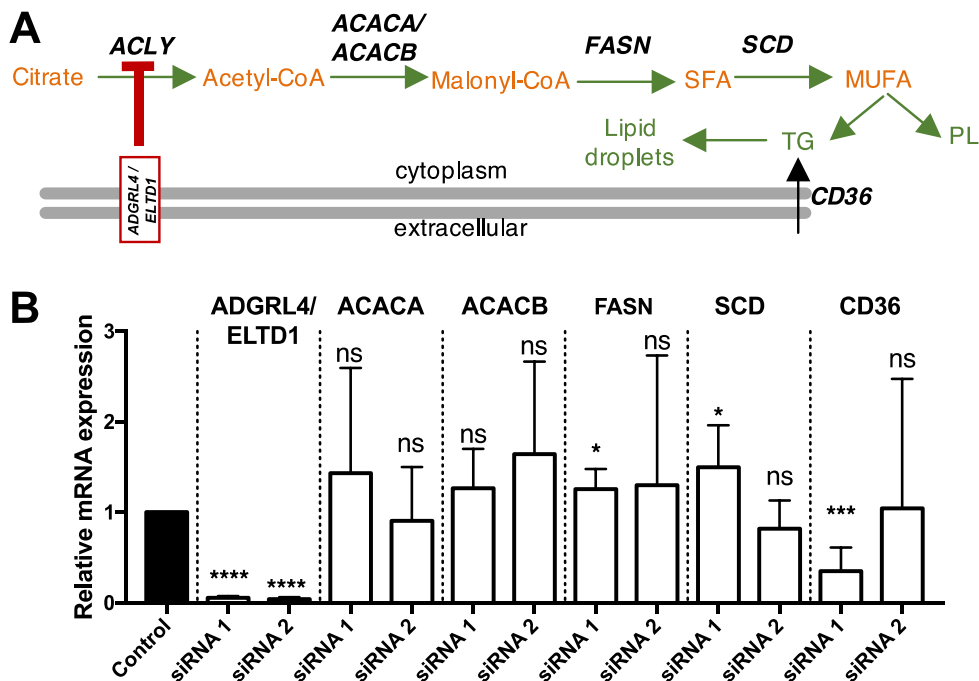


Figure S2. HUVEC ADGRL4/ELTD1 silencing does not affect fatty acid synthesis pathway genes. (A) The fatty acid synthesis and cholesterol pathways. Key fatty acid synthesis enzymes are in black and substrates are in orange. ADGRL4/ELTD1 labelled in red. (B) Fatty acid synthesis pathway qPCR results. (* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$) (Abbreviations: MUFA= monounsaturated fatty acid; PL=phospholipid; SFA=saturated fatty acid; TG=triglyceride).

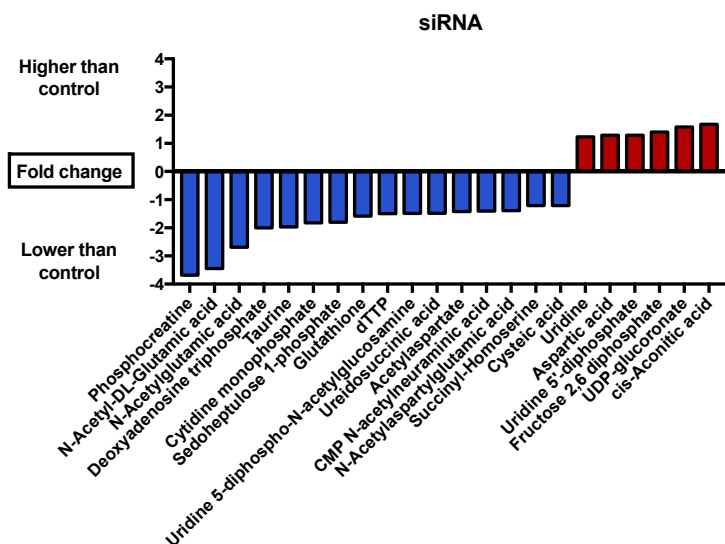


Figure S3: Maximum fold change for selected metabolites ($p \leq 0.05$ and fold change > 1.2).

Pathway Name	Match	p	FDR	Metabolites
Alanine, aspartate and glutamate metabolism	6/24	0.000002	1.67E-04	N-Acetyl-L-aspartic acid, L-Aspartic acid, Oxoglutaric acid, L-Glutamine; Gamma-Aminobutyric acid; Fumaric acid;
Pyrimidine metabolism	8/60	0.000005	2.25E-04	Uridine 5'-diphosphate; dCTP; L-Glutamine; Uridine; Cytidine monophosphate; Thymidine 5'-triphosphate; Thymidine; Malonic acid;
Arginine and proline metabolism	7/77	0.00004	0.007612	L-Glutamine; L-Aspartic acid; L-Arginine; N-Acetyl-L-alanine; Phosphocreatine; Gamma-Aminobutyric acid; Fumaric acid
beta-Alanine metabolism	4/28	0.001	0.024222	Malonic acid; L-Aspartic acid; Gamma-Aminobutyric acid; L-Histidine
Nitrogen metabolism	4/39	0.004	0.061099	Taurine; L-Aspartic acid; L-Glutamine; L-Histidine;
Citrate cycle (TCA cycle)	3/20	0.004	0.061099	Oxoglutaric acid; cis-Aconitic acid; Fumaric acid;
D-Glutamine and D-glutamate metabolism	2/11	0.01	0.15157	L-Glutamine; Oxoglutaric acid
Cysteine and methionine metabolism	4/56	0.01	0.15157	O-Succinyl-L-homoserine; Glutathione; Cysteic acid; L-Aspartic acid
Amino sugar and nucleotide sugar metabolism	5/88	0.01	0.15157	Uridine diphosphate glucuronic acid; Uridine diphosphate-N-acetylglucosamine; Glucose 1-phosphate; Cytidine monophosphate N-acetylneuraminic acid; Uridine diphosphategalactose;
Butanoate metabolism	3/40	0.03	0.24117	Gamma-Aminobutyric acid; Oxoglutaric acid; Fumaric acid
Galactose metabolism	3/41	0.03	0.24117	Glucose 1-phosphate; Uridine diphosphategalactose; Sorbitol
Aminoacyl-tRNA biosynthesis	4/75	0.03	0.24117	L-Histidine; L-Arginine; Glutamine; L-Aspartic acid;
Histidine metabolism	3/44	0.04	0.24117	L-Histidine; L-Aspartic acid; Oxoglutaric acid;
Ascorbate and aldarate metabolism	3/45	0.04	0.24117	Uridine diphosphate glucuronic acid; D-Glucarate; Oxoglutaric acid;
Taurine and hypotaurine metabolism	2/20	0.04	0.24699	taurine; cysteic acid
Pentose and glucuronate interconversions	3/53	0.06	0.31668	D-Xylulose; Glucose 1-phosphate; Uridine diphosphate glucuronic acid
Glycolysis or Gluconeogenesis	2/31	0.1	0.47174	L-Aspartic acid; Fumaric acid

Table S1: Metabolite pathway analysis with extended range of metabolites (FC >1.2 irrespective of *p* value).

Supplementary dataset

supplementary_raw_output_metabolomics.xlsx

Supplementary methods

Gene name	Forward primer (5'-3')	Reverse primer (5'-3')
ACACA	AACGTGAAGACGGATAAGCAG	CTTCTTCGGAGAATCTGACCA
ACACB	AGTTCGCCGACTTCCAT	TCTTCCACTCCAGGATGTCA
ACLY	CCAGCAGGACAGCATCTTTT	GGATCTTGGACTTGGGACTG
ACTB	ATGCTCTCCCTCACGCCATC	CACGCACGATTTCCCTCTCA
CD36	GTGCCTATTCTTTGGCTTAATGA	TTACTTGACTTCTGAACATGTTTG C
DLL4	CCCTGGCAATGTACTTGTGAT	TGGTGGGTGCAGTAGTTGAG
ADGRL4/ELTD 1	GCTCAAACCCACCCACATTAT	CACAGCCCTCTGAAGACCAG
FASN	CAGGCACACACAGGATGGAC	CGGAGTGAATCTGGGTTGA
GAPDH	AGCCACATCGCTCAGACAC	GCCCAATACGACCAAATCC
HES2	CCAACTGCTCGAAGCTAGAGA	AGCGCACGGTCATTTCCAG
JAG1	GAATGGCAACAAAACCTTGCAT	AGCCTTGTCGGCAAATAGC
KIT	AATCCTCTCGTCAAACTGAAG G	CCATCTCGCTTATCCAACAATGA
SCD	GACCTGCTTGCTGATCCTGT	CCATTCACGAAGCATCTCAC

Supplementary methods Table 1: qPCR primer sequences.

Target	Type	Dilution	Company
--------	------	----------	---------

Primary antibodies			
ADGRL4/ELTD1	Mouse IgG2 monoclonal	10 µg/mL	Professor Alison Banham, Oxford University (184.11)
DLL4	Rat IgG2 monoclonal	10 µg/mL	R&D Systems (MAB1506)
JAG1	Mouse IgG2 monoclonal	1 in 200	Professor Alison Banham, Oxford University (J1-65D)
KIT	Mouse IgG1 monoclonal	1 in 200	Invitrogen (17-1178-41)
IgG1 isotype control	Mouse IgG1 monoclonal	10 µg/mL	Invitrogen (17-4714-41)
IgG2 isotype control	Mouse IgG2 monoclonal	10 µg/mL	Invitrogen (17-4724-41)
Secondary antibodies			
anti-mouse APC	Goat IgG	1 in 100	Invitrogen (A-865)
anti-rat APC	Goat IgG	1 in 100	Invitrogen (A10540)

Supplementary methods Table 2: FACS antibodies.