

Locus	Tag SNP	Lead trait	Other traits
<i>ANGPTL3</i>	rs2131925	TG	TC, LDL
<i>GALNT2</i>	rs4846914	HDL	TG
<i>APOB</i>	rs1042034	TG	HDL
<i>GCKR</i>	rs1260326	TG	TC
<i>COBLL1/LOC101929615/GRB14</i>	rs10195252	TG	
<i>IRS1/CUL3</i>	rs2972146	HDL	TG
<i>MSL2L1/PCCB</i>	rs645040	TG	
<i>KLHL8</i>	rs442177	TG	
<i>MAP3K1</i>	rs9686661	TG	
<i>TIMD4</i>	rs6882076	TC	LDL, TG
<i>HLA/WASF5P</i>	rs2247056	TG	
<i>TYW1B</i>	rs13238203	TG	
<i>MLXIPL/TBL2/BCL7B</i>	rs17145738	TG	HDL
<i>PINX1</i>	rs11776767	TG	
<i>NAT2/PSD3</i>	rs1495741	TG	TC
<i>LPL/SLC18A1</i>	rs12678919	TG	HDL
<i>TRIB1/LOC101927634</i>	rs2954029	TG	TC, LDL, HDL
<i>JMJD1C</i>	rs10761731	TG	
<i>CYP26A1/NIP7P1</i>	rs2068888	TG	
<i>FADS1-2-3</i>	rs174546	TG	HDL, TC, LDL
<i>APOA1</i>	rs964184	TG	TC, HDL, LDL
<i>LRP1</i>	rs11613352	TG	HDL
<i>ZNF664</i>	rs4765127	HDL	TG
<i>CAPN3</i>	rs2412710	TG	
<i>FRMD5</i>	rs2929282	TG	
<i>LIPC</i>	rs1532085	HDL	TC, TG
<i>CTF1</i>	rs11649653	TG	
<i>CETP/HERPUD1</i>	rs3764261	HDL	TC, LDL, TG
<i>CILP2/TM6SF2/SUGP1</i>	rs10401969	TC	TG, LDL
<i>APOE/APOC1</i>	rs439401	TG	
<i>PLTP/PCIF1</i>	rs6065906	HDL	TG
<i>PLA2G6</i>	rs5756931	TG	

FIG. 1

Chr	Position	rsID	Gene	Amino acid substitution	Nucleotide substitution	N0	N1	N2	MAF [^]	MAF EUR ^{^^}	P-value	Beta	SE
2	27730940	rs1260326	GCKR*	L446P	G/A	1,515	972	247	27%	41%	0.007	0.03	0.01
8	18872307-08	rs71519934	PSD3	L186T AC/CT		1,907	728	101	17%	33%	0.049	-0.02	0.01
19	19379549	rs58542926	TM6SF2	E167K	G/A	2,470	259	7	5%	7%	5.7 x 10 ⁻⁸	0.12	0.02

FIG. 2

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Liver Biopsy Cohort	N	1,951
Anthropometrical traits	Age, years	47±12
	Male gender, n(%)	909(47)
	BMI, Kg/m ²	37±9
Metabolic traits	Diabetes presence, n(%)	507(26)
	Total cholesterol, mmol/L	4.90±1.14
	HDL, mmol/L	1.25±0.36
	LDL, mmol/L	2.93±0.99
	Triglycerides, mmol/L	1.35(0.99-1.91)
Liver histology	ALT, UI/L	38(23-63)
	Steatosis presence, n(%)	1551(79)
	Fibrosis presence, n(%)	1074(55)
	Inflammation presence, n(%)	1134(58)
	Ballooning presence*, n(%)	652(36)
Recruitment centre	Kuopio, Finland, n(%)	410(21)
	Helsinki, Finland, n(%)	145(7)
	Palermo, Italy, n(%)	374(19)
	Milan, Italy n(%)	1022(52)
Central European Cohort	N	674
Anthropometrical traits	Age, years	45±12
	Male gender, n(%)	236(35)
	BMI, Kg/m ²	46±10
Metabolic traits	Diabetes presence, n(%)	192(31)
	Total cholesterol, mmol/L	-
	HDL, mmol/L	-
	LDL, mmol/L	-
	Triglycerides, mmol/L	-
Liver histology	ALT, UI/L	29(20-46)
	Steatosis presence, n(%)	549(81)
	Fibrosis presence, n(%)	255(38)
	Inflammation presence, n(%)	212(31)
	Ballooning presence, n(%)	196(29)
Recruitment centre	Germany, n(%)	559(83)
	Austria, n(%)	83(12)
	Switzerland, n(%)	32(5)

FIG. 3

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	<i>P-value</i>	OR	CI	
Steatosis presence	5.9×10^{-6}	0.67	0.57	0.80
Fibrosis presence	0.006	0.82	0.72	0.94
Inflammation presence	9.9×10^{-7}	0.70	0.61	0.81
Ballooning presence*	0.002	0.79	0.68	0.92

FIG. 4

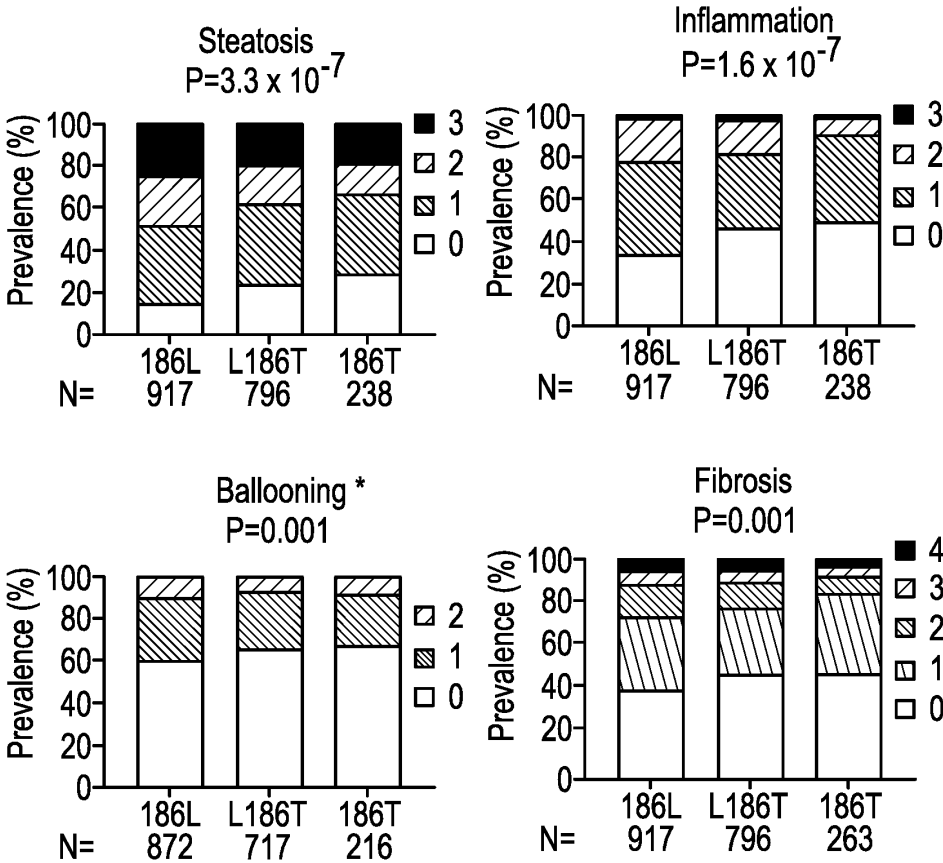


FIG. 5A

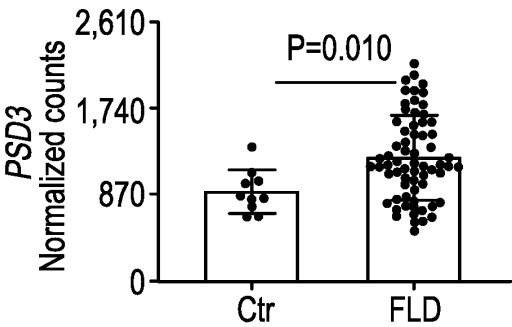


FIG. 5B

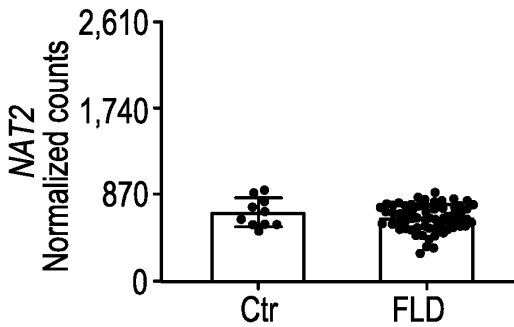


FIG. 5C

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	<i>P-value</i>	OR	CI	
Disease presence				
Steatosis	0.024	0.69	0.50	0.95
Fibrosis	0.049	0.77	0.59	1.00
Inflammation	<u>0.524</u>	0.92	0.70	1.20
Ballooning	0.047	0.75	0.56	1.00
Disease severity				
Steatosis	<u>0.158</u>	0.85	0.69	1.06
Fibrosis	0.040	0.77	0.60	0.99
Inflammation	<u>0.355</u>	0.88	0.68	1.15
Ballooning	0.048	0.75	0.57	1.00

FIG. 6

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Liver biopsy cohort	186L	L186T	186T	P-value
N	917	796	238	
Age, years	47±13	47±12	48±13	0.101
Male gender, n(%)	434(47)	376(47)	99(42)	0.218
BMI, Kg/m2	35.7±9.0	37.1±8.8	38.2±8.9	2.1 x 10 ⁻⁵
Diabetes presence, n(%)	222(24)	212(27)	73(31)	0.571
Total cholesterol, mmol/L	5.08±1.13	4.78±1.14	4.62±1.09	1.4 x 10 ⁻⁶
HDL, mmol/L	1.29±0.39	1.22±0.33	1.2±0.33	0.001
LDL, mmol/L	3.05±0.99	2.86±0.98	2.71±0.94	0.001
Triglycerides, mmol/L	1.35(0.99-1.91)	1.36(1.00-1.96)	1.32(0.98-1.85)	0.828
ALT, UI/L	39(23-66)	38(23-61)	37(24-58)	0.173
Central European cohort				
N	330	282	62	
Age, years	44±13	46±12	43±12	0.955
Male gender, n(%)	111(34)	102(36)	23(37)	0.469
BMI, Kg/m2	46±9	46±11	45±11	0.837
Diabetes presence, n(%)	89(30)	82(32)	21(36)	0.295
Total cholesterol, mmol/L	-	-	-	-
HDL, mmol/L	-	-	-	-
LDL, mmol/L	-	-	-	-
Triglycerides, mmol/L	-	-	-	-
ALT, UI/L	31(21-46)	28(19-45)	27(20-44)	0.985

FIG. 7

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Steatosis Severity	P	OR	CI	
LBC	3,3E-07	0,729	0,645	0,823
Replication	0,158	0,850	0,690	1,060
<i>Meta analyses</i>				
Fixed-effect	2,4E-07	0,755	0,678	0,840
Random-effects	1,24E-04	0,763	0,665	0,876

Fibrosis severity	P	OR	CI	
LBC	0,001	0,811	0,715	0,921
Replication	0,04	0,770	0,600	0,990
<i>Meta analyses</i>				
Fixed-effect	1,13E-04	0,803	0,718	0,898
Random-effects	1,13E-04	0,803	0,718	0,898

Inflammation severity	P	OR	CI	
LBC	1,6E-07	0,711	0,626	0,807
Replication	0,355	0,880	0,680	1,150
<i>Meta analyses</i>				
Fixed-effect	2,81E-07	0,739	0,659	0,829
Random-effects	0,008	0,764	0,627	0,931

Ballooning severity	P	OR	CI	
LBC	0,001	0,777	0,669	0,902
Replication	0,048	0,750	0,570	1,000
<i>Meta analyses</i>				
Fixed-effect	1,27E-04	0,771	0,675	0,881
Random-effects	1,27E-04	0,771	0,675	0,881

FIG. 8A

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Steatosis Presence	P	OR	CI	
LBC	5,90E-06	0,670	0,570	0,800
Replication	0,024	0,690	0,500	0,950
<i>Meta analyses</i>				
Fixed-effect	4,22E-07	0,674	0,579	0,786
Random-effects	4,22E-07	0,674	0,579	0,786

Fibrosis presence	P	OR	CI	
LBC	0,006	0,820	0,720	0,940
Replication	0,049	0,770	0,590	1,000
<i>Meta analyses</i>				
Fixed-effect	7,95E-04	0,808	0,714	0,915
Random-effects	7,95E-04	0,808	0,714	0,915

Inflammation presence	P	OR	CI	
LBC	9,90E-07	0,700	0,610	0,810
Replication	0,524	0,920	0,700	1,200
<i>Meta analyses</i>				
Fixed-effect	4,53E-06	0,747	0,659	0,846
Random-effects	0,073	0,785	0,603	1,023

Ballooning presence	P	OR	CI	
LBC	0,002	0,790	0,680	0,920
Replication	0,047	0,750	0,560	1,000
<i>Meta analyses</i>				
Fixed-effect	2,52E-04	0,781	0,684	0,892
Random-effects	2,52E-04	0,781	0,684	0,892

FIG. 8B

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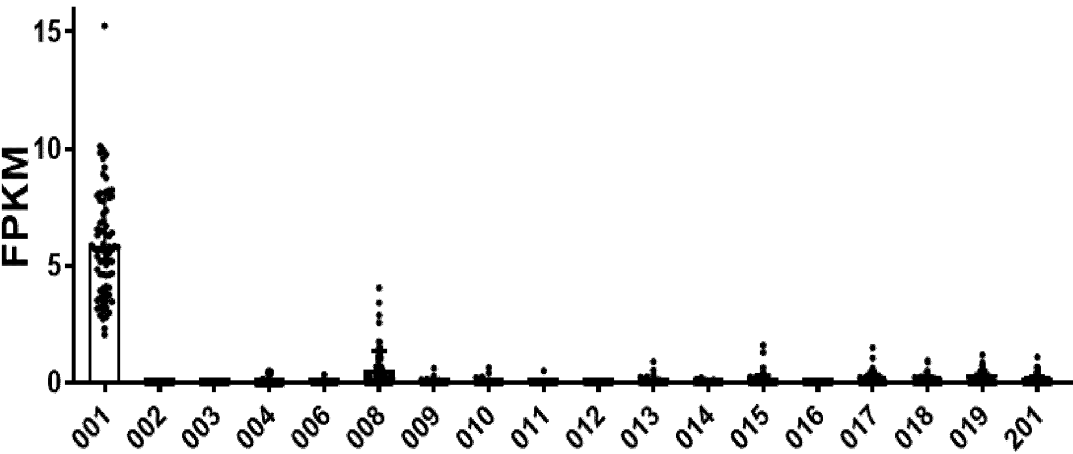


FIG. 9A

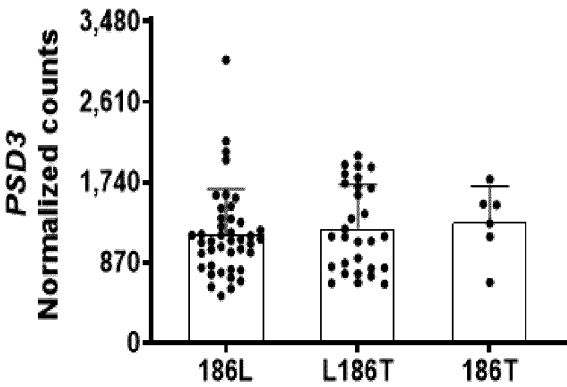


FIG. 9B

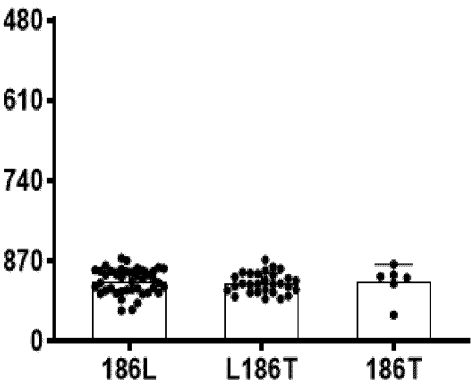


FIG. 9C

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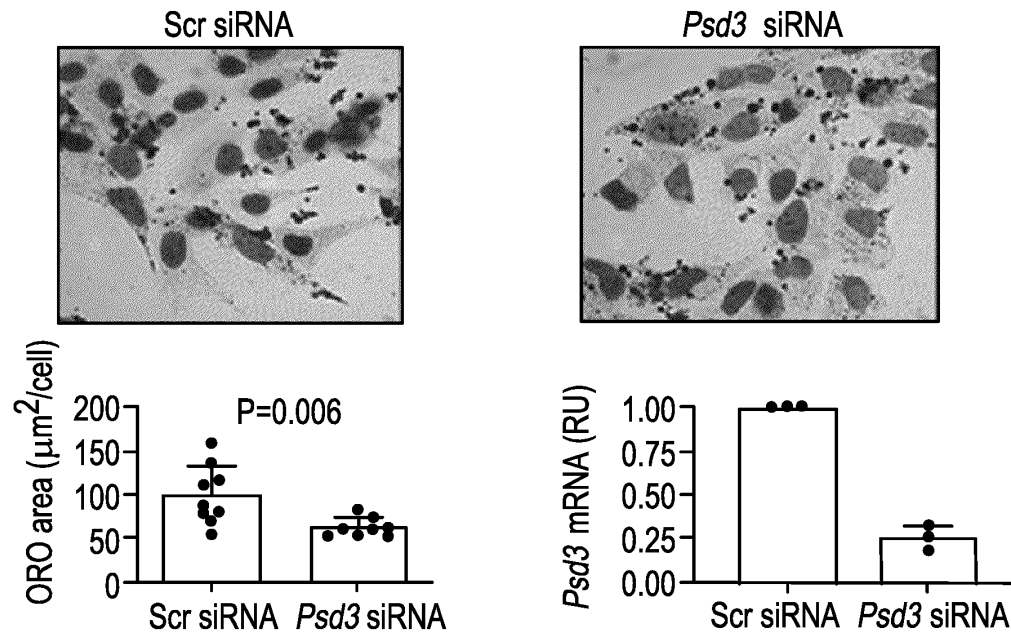


FIG. 10A

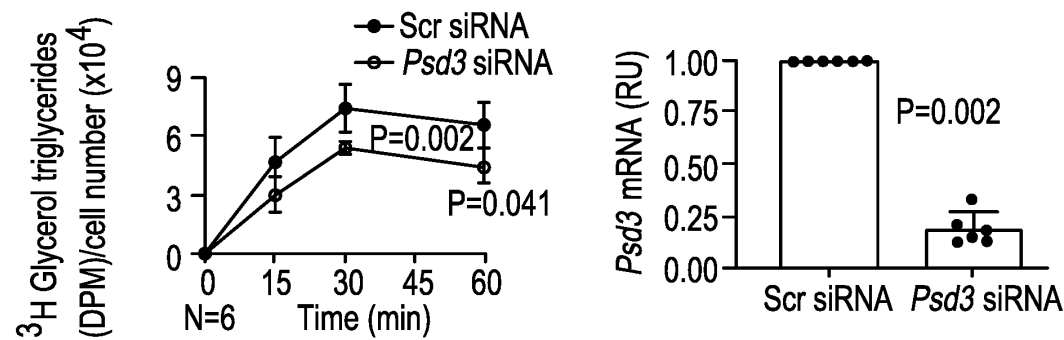


FIG. 10B

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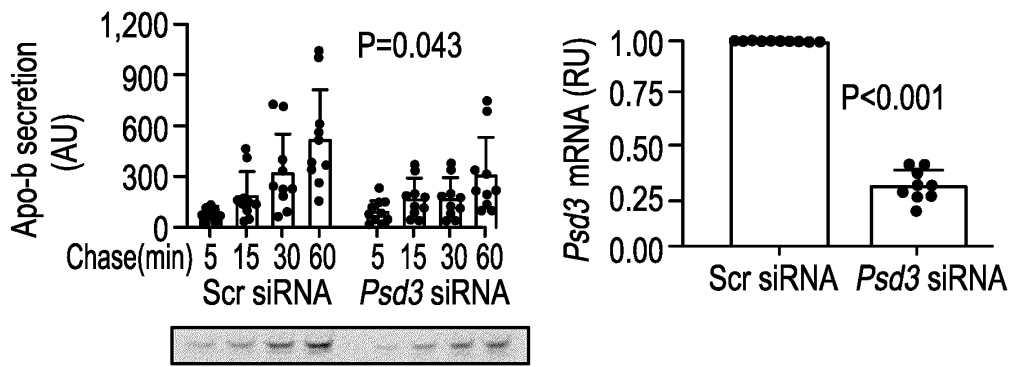


FIG. 10C

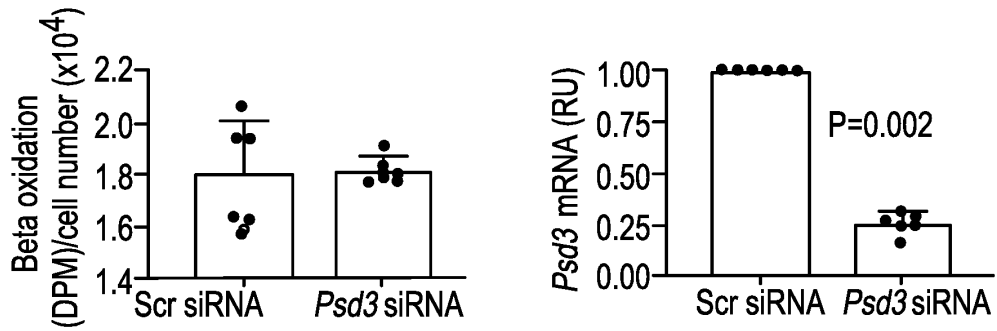


FIG. 10D

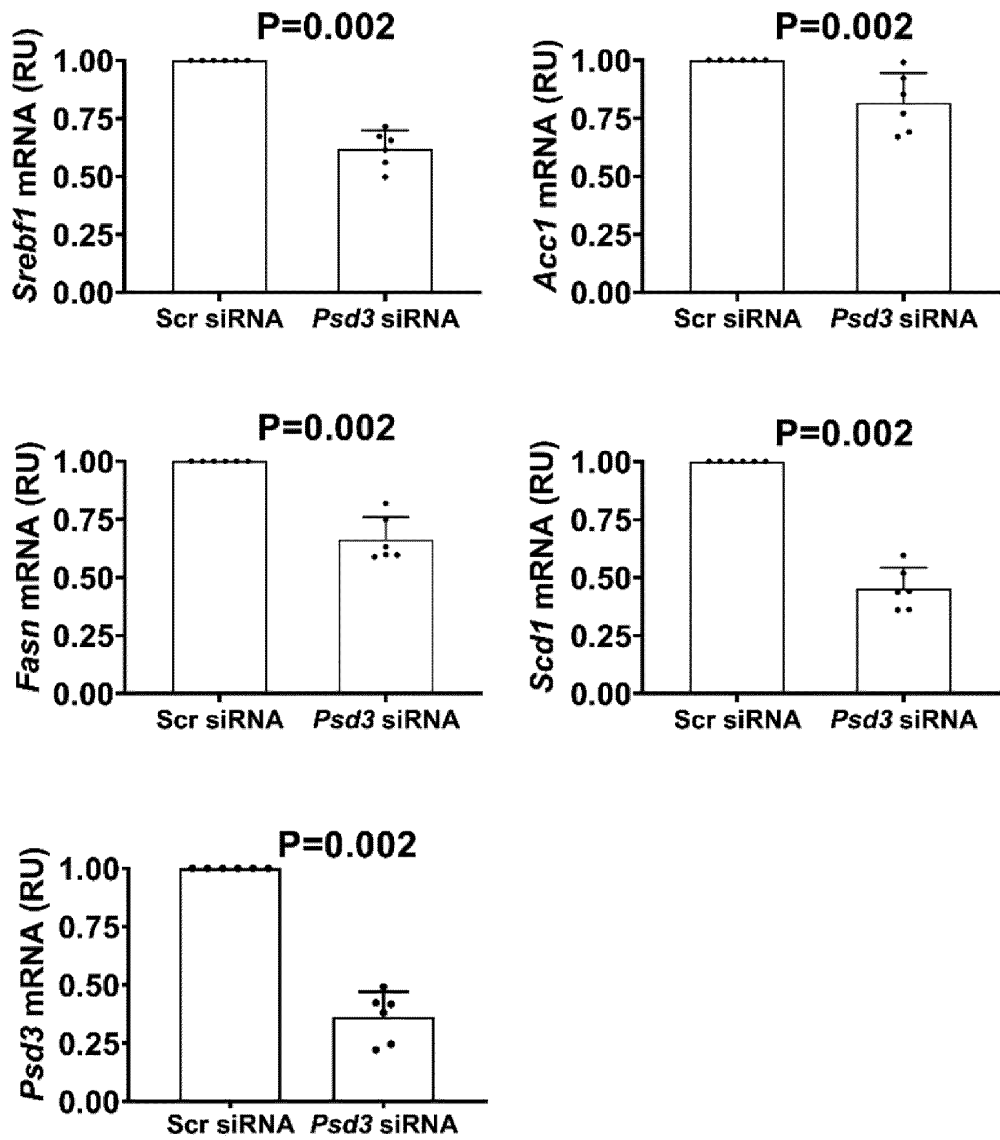


FIG. 11

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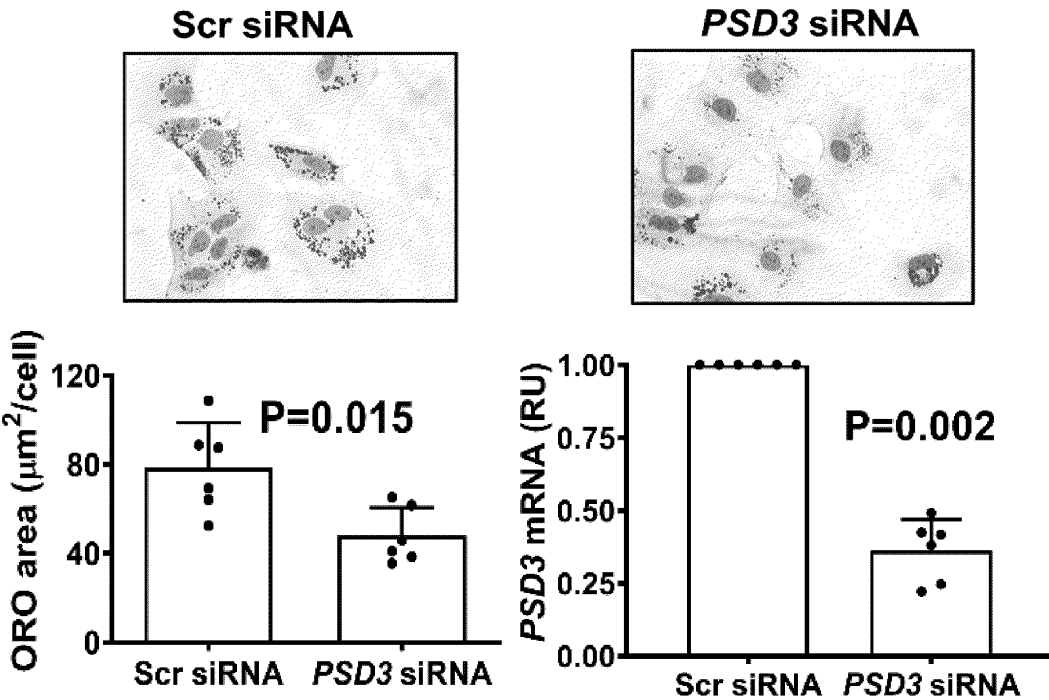


FIG. 12A

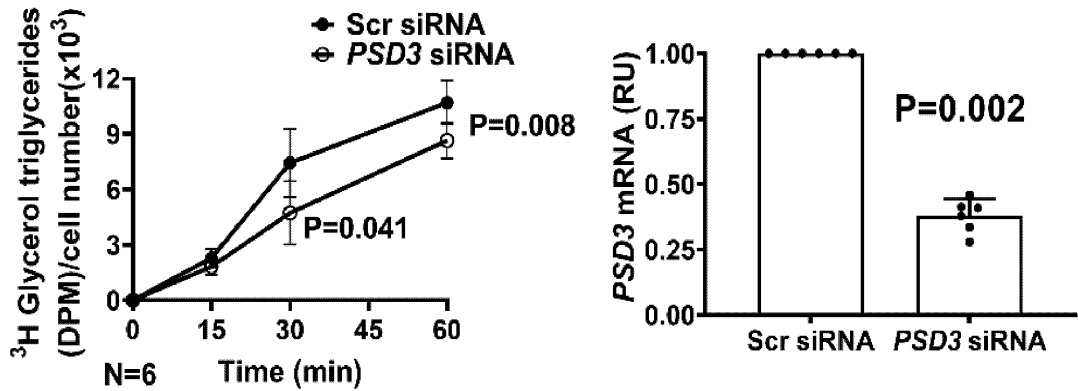


FIG. 12B

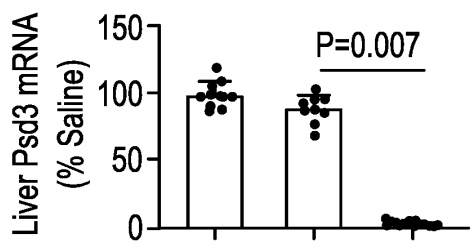


FIG. 13A

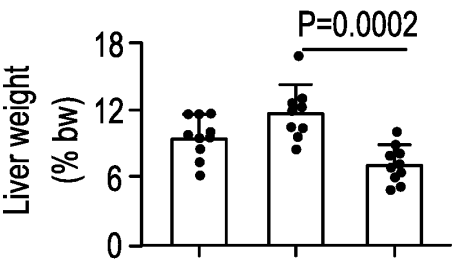


FIG. 13B

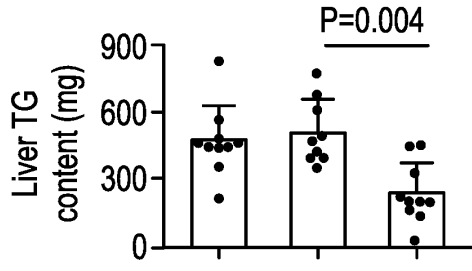


FIG. 13C

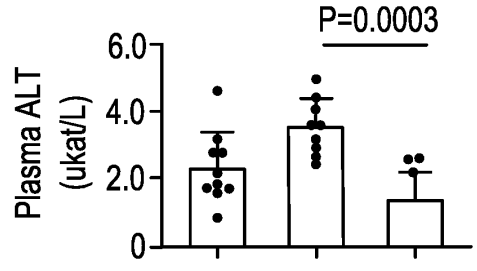


FIG. 13D

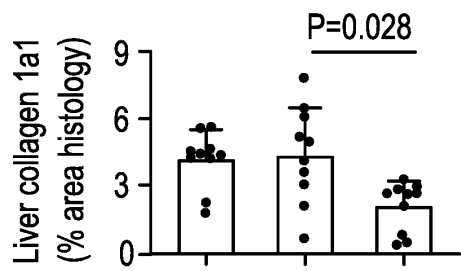


FIG. 13E

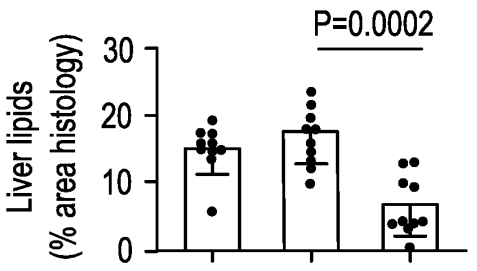


FIG. 13F

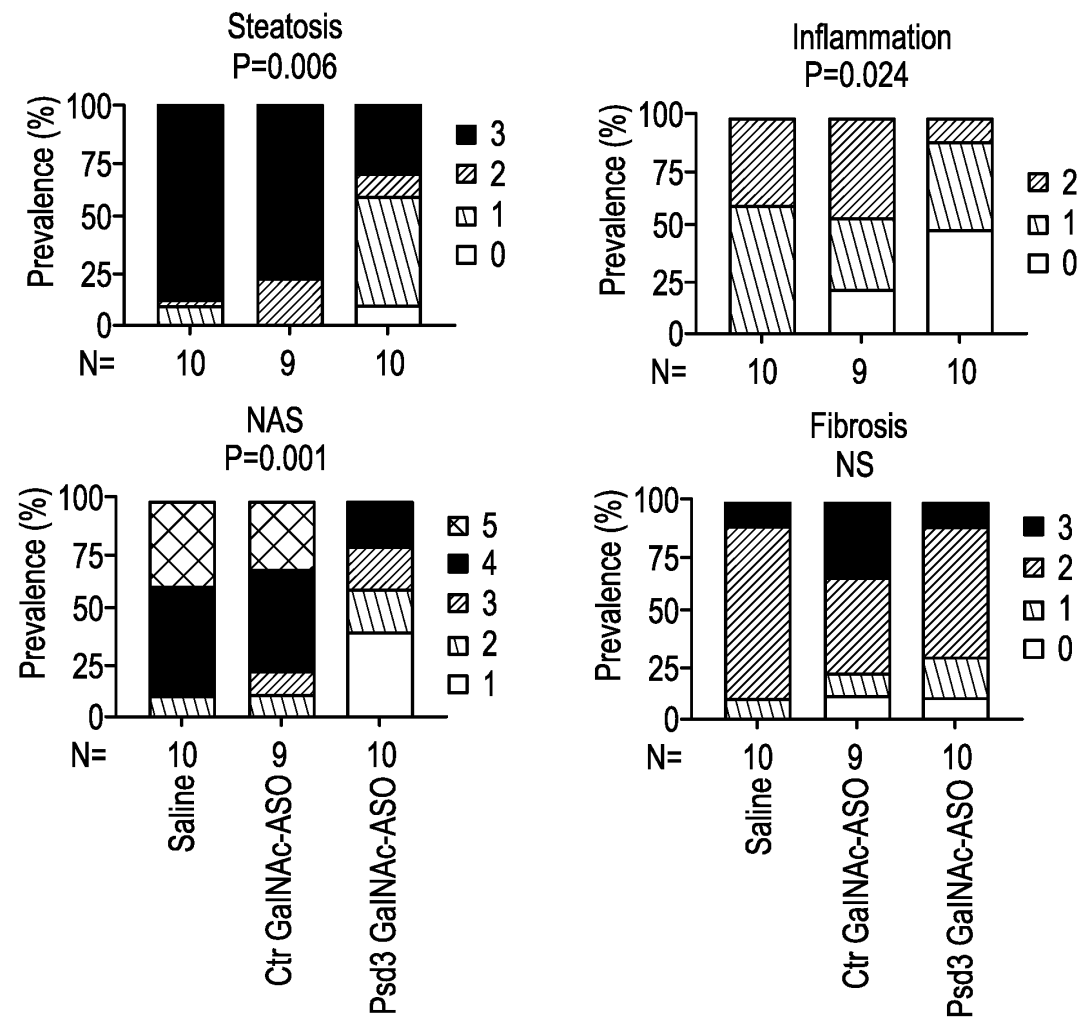


FIG. 13G

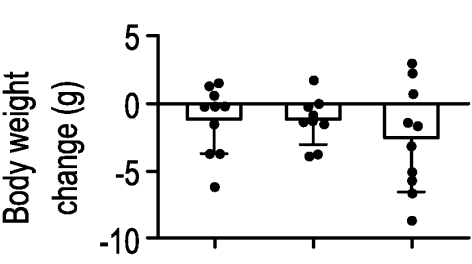


FIG. 14A

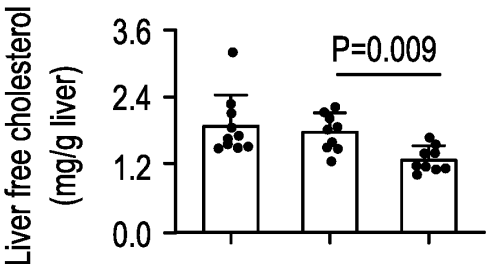


FIG. 14B

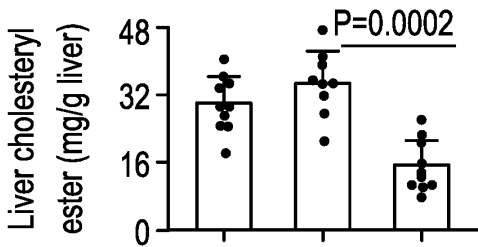


FIG. 14C

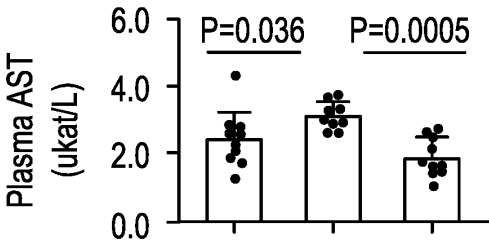


FIG. 14D

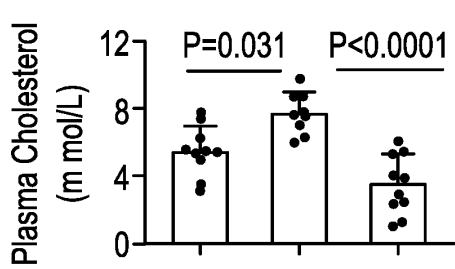


FIG. 14E

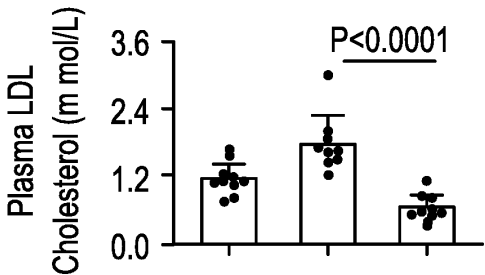


FIG. 14F

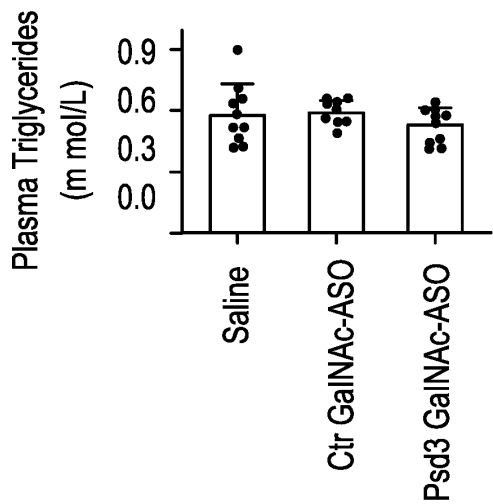


FIG. 14G

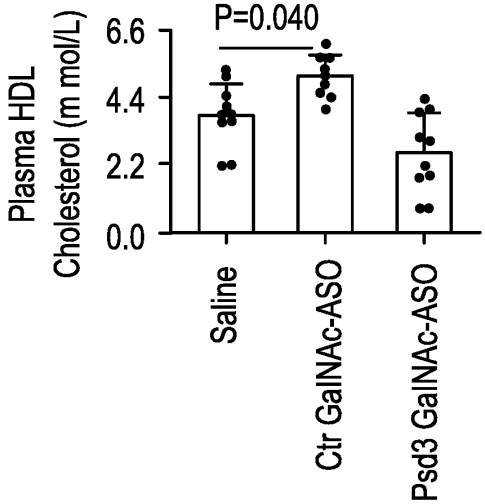


FIG. 14H

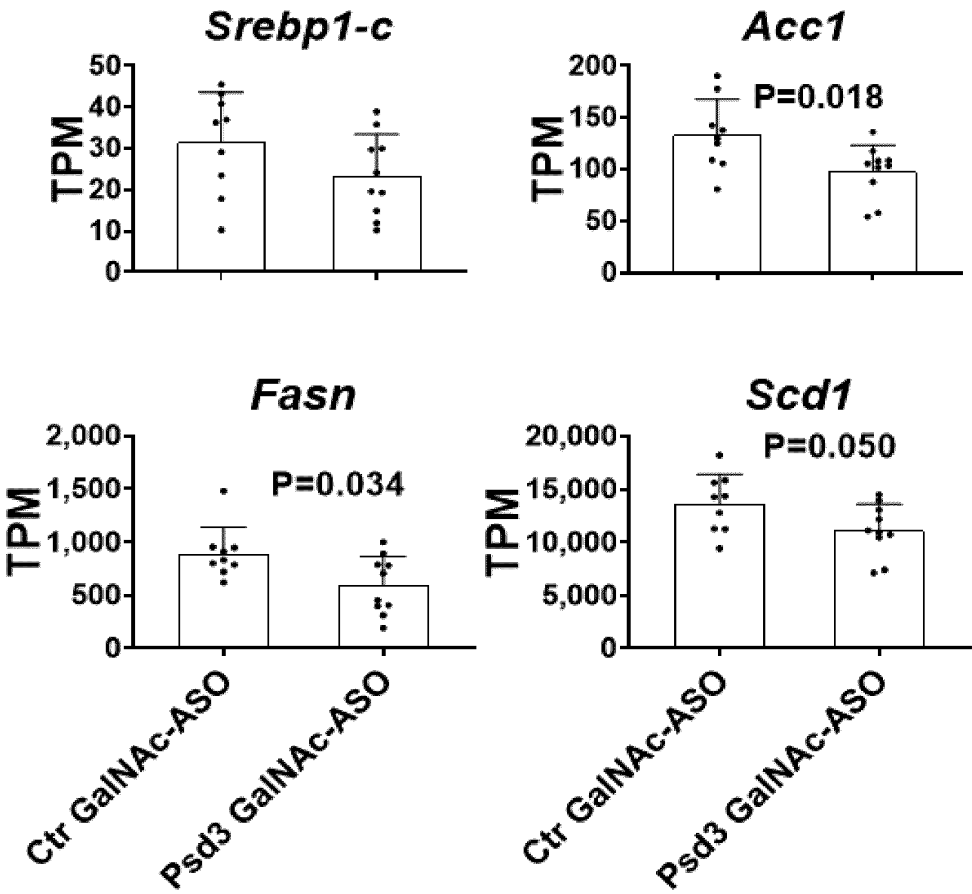


FIG. 15

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	<i>P-value</i>	OR	CI	
Steatosis severity	2.2E-06	0.74	0.65	0.84
Fibrosis severity	0.002	0.82	0.71	0.93
Inflammation severity	2.3E-06	0.73	0.64	0.83
Ballooning* severity	0.003	0.79	0.68	0.92

FIG. 16

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Characteristic	186L	L186T	186T	P-value
All ethnicities				
N	1907	728	101	
Age, years	45.6 ± 10.2	45.4 ± 10.4	47.5 ± 9.5	0.59
Female, n (%)	1077 (56.48)	403 (55.36)	53 (52.48)	0.67
BMI, kg/m ²	30.2 ± 6.8	30.2 ± 6.6	28.1 ± 6.1	0.49
TC, mg/dL	184.5 ± 40.9	184.2 ± 36.6	182.1 ± 39.1	0.18
LDL, mg/dL	109.7 ± 37.1	109 ± 33.9	108.9 ± 34.1	0.39
HDL, mg/dL	51 ± 14.9	49.8 ± 14.8	50.4 ± 15.4	0.69
TG, mg/dL	96 (68 - 144)	104 (73 - 155)	101 (72 - 140)	0.32
HTGC, %	3.49 (1.97 - 6.78)	3.74 (1.95 - 7.5)	3.01 (1.43 - 7.29)	0.049
African Americans				
N	1096	224	8	
Age, years	46.5 ± 10.1	45.8 ± 10.5	49.1 ± 11.7	0.52
Female, n (%)	642 (58.58)	142 (63.39)	3 (37.5)	0.19
BMI, kg/m ²	30.9 ± 7.2	31.9 ± 7.6	33.1 ± 7.9	0.072
TC, mg/dL	182.8 ± 41.2	181.9 ± 38.3	196.4 ± 42	0.78
LDL, mg/dL	109.4 ± 38.4	107.4 ± 36	120.8 ± 47.1	0.66
HDL, mg/dL	53 ± 15.5	53.4 ± 14.8	54.9 ± 29.1	0.41
TG, mg/dL	86 (63 - 121)	84 (66 - 128)	95 (78 - 136)	0.43
HTGC, %	3.2 (1.78 - 5.43)	3.1 (1.7 - 5.08)	5.39 (1.85 - 10.91)	0.57
European Americans				
N	457	344	81	
Age, years	46.7 ± 10.5	46.9 ± 10.1	47.3 ± 9.4	0.66
Female, n (%)	236 (51.64)	170 (49.42)	45 (55.56)	0.58
BMI, kg/m ²	28.6 ± 5.8	29.4 ± 6.1	27.7 ± 5.9	0.99
TC, mg/dL	189.9 ± 39.5	186.2 ± 35.7	179.2 ± 38.4	0.012
LDL, mg/dL	112.5 ± 36	110.7 ± 33.9	106.8 ± 32.3	0.20
HDL, mg/dL	50.1 ± 15.1	48.8 ± 15.4	49.6 ± 13.6	0.25
TG, mg/dL	113 (75 - 173)	112 (79 - 164)	101 (70 - 145)	0.11
HTGC, %	3.64 (2.09 - 7.42)	3.83 (2.02 - 7.98)	2.64 (1.28 - 5.51)	0.073
Hispanics				
N	308	149	8	
Age, years	41 ± 8.8	41.3 ± 9.5	49.6 ± 9.4	0.16
Female, n (%)	184 (59.74)	86 (57.72)	4 (50)	0.78
BMI, kg/m ²	30.4 ± 6.5	29.8 ± 5.5	28.5 ± 6	0.21
TC, mg/dL	183.9 ± 42.2	183.8 ± 36	189.6 ± 35.9	0.95
LDL, mg/dL	108 ± 34.3	107.8 ± 30.8	109.8 ± 28.1	0.92
HDL, mg/dL	45.7 ± 10.9	47.5 ± 12.3	52.2 ± 16.8	0.054
TG, mg/dL	122 (81 - 183)	119 (82 - 170)	116 (86 - 176)	0.57
HTGC, %	5.28 (2.7 - 12.54)	4.43 (2.36 - 9.92)	8.65 (4.35 - 12.36)	0.32

FIG. 17

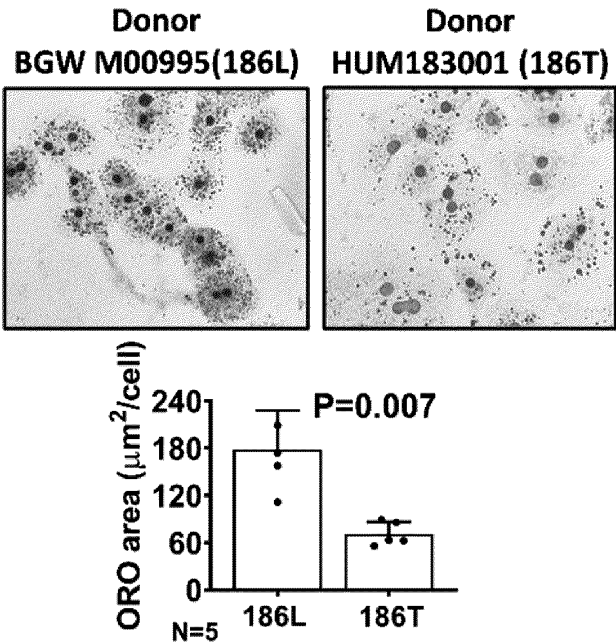


FIG. 19A

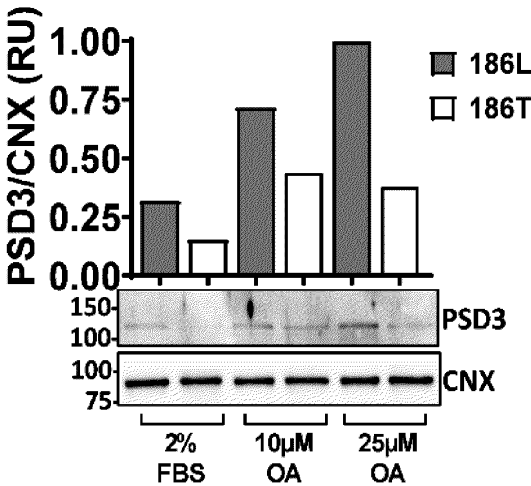


FIG. 19B

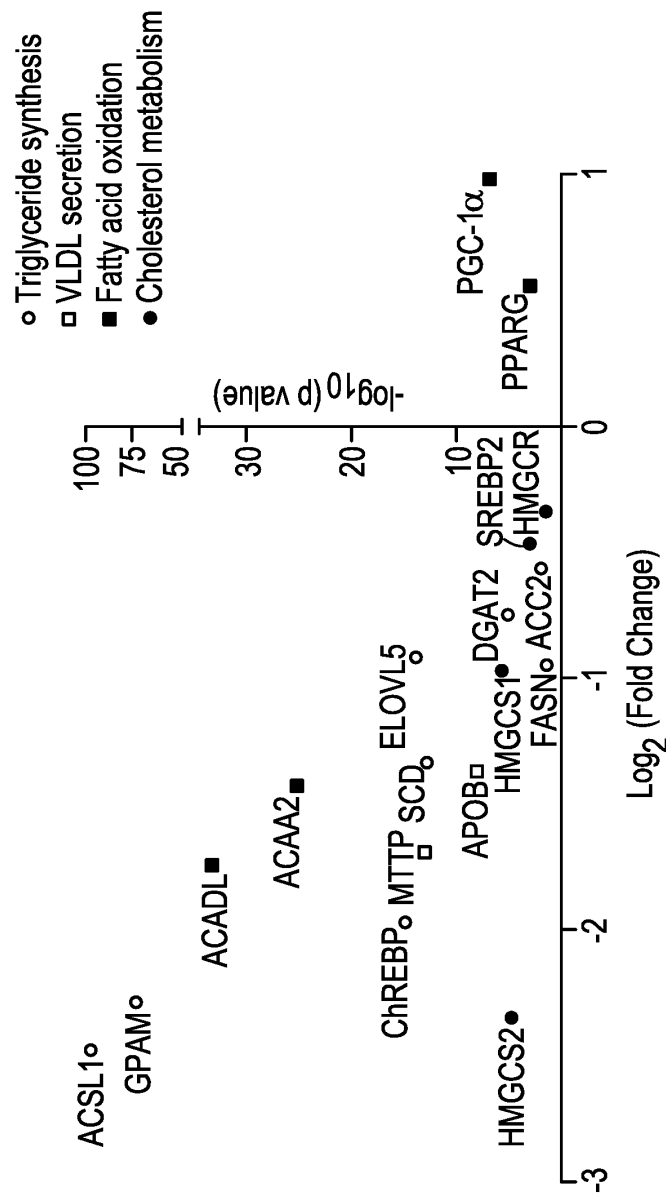


FIG. 19C

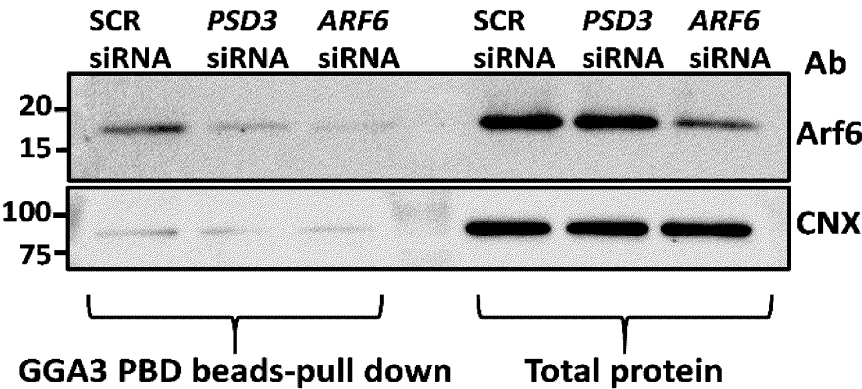


FIG. 20A

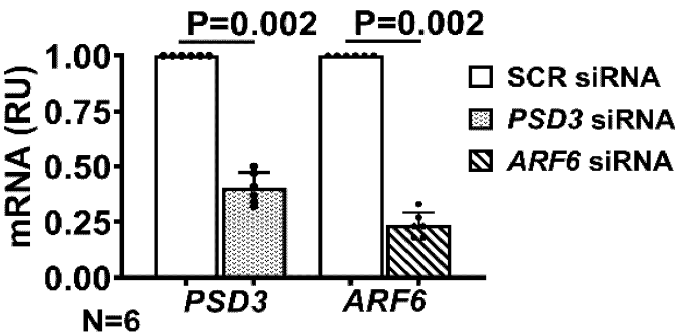


FIG. 20B

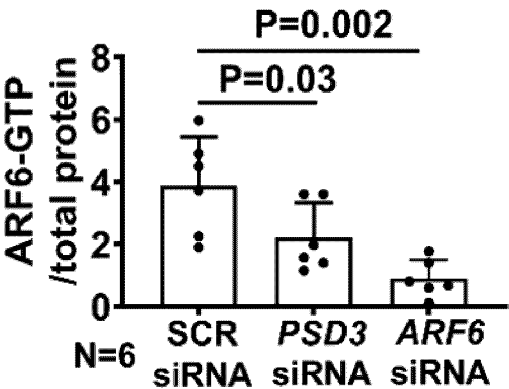


FIG. 20C

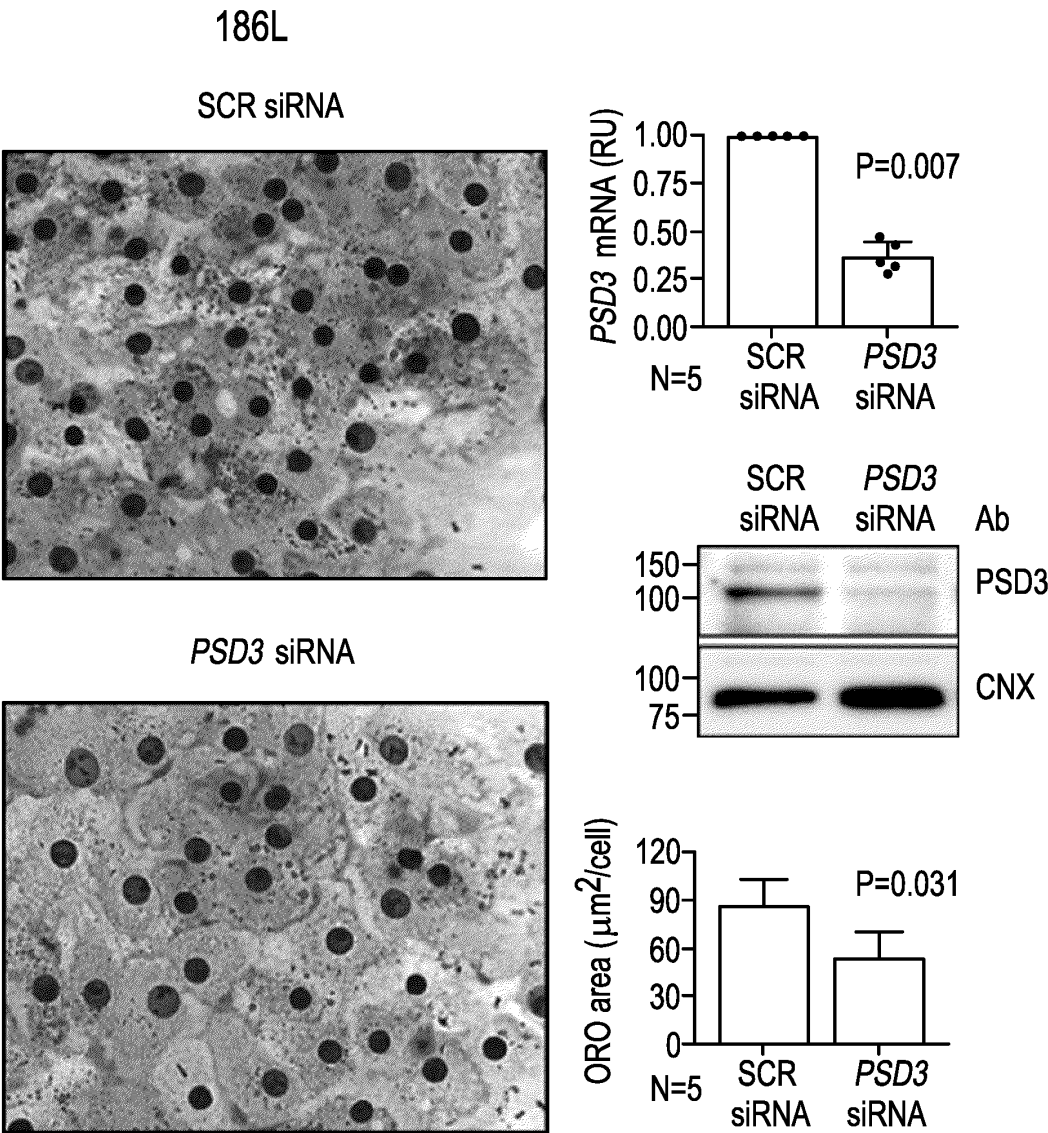


FIG. 21A

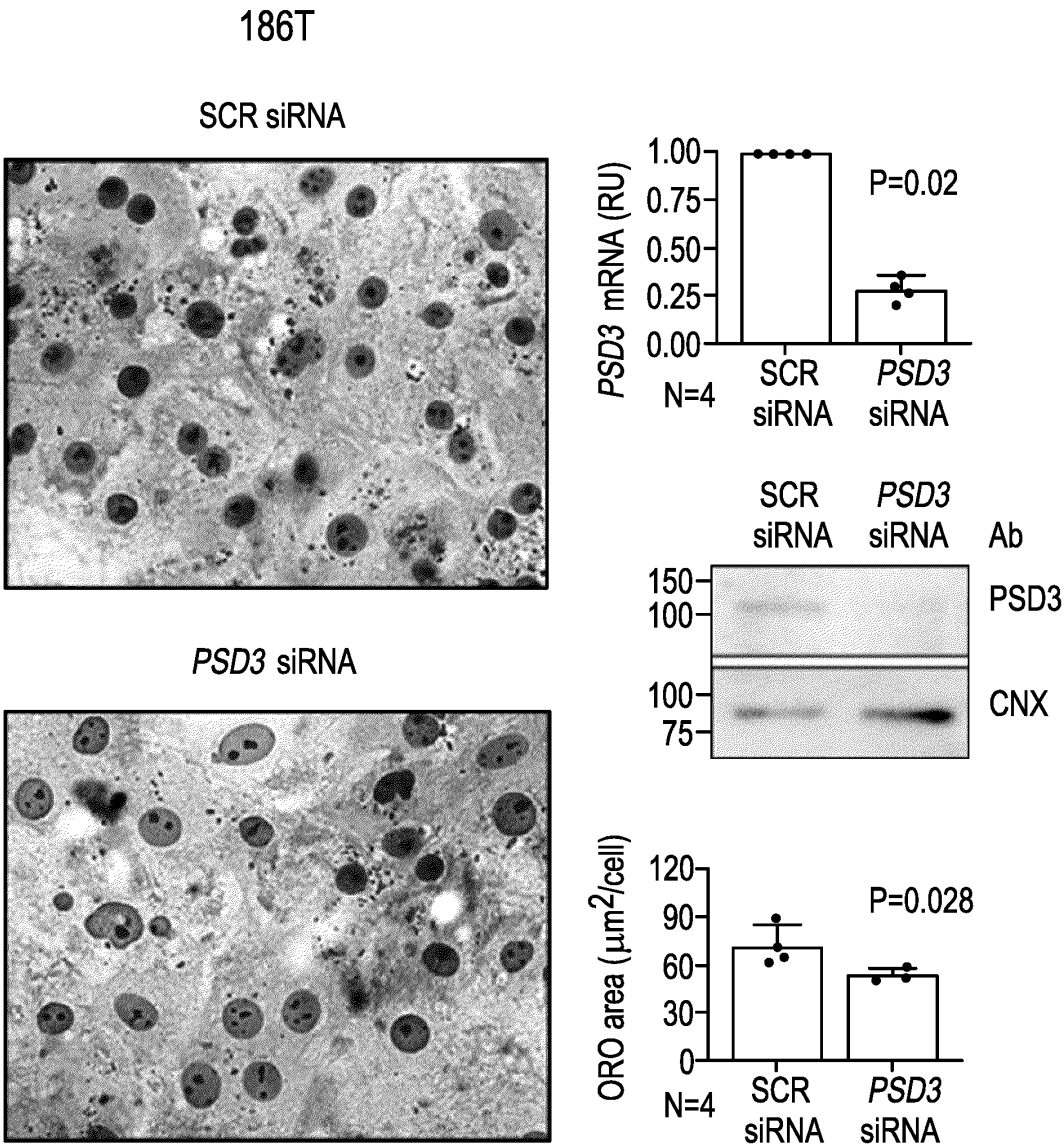


FIG. 21B

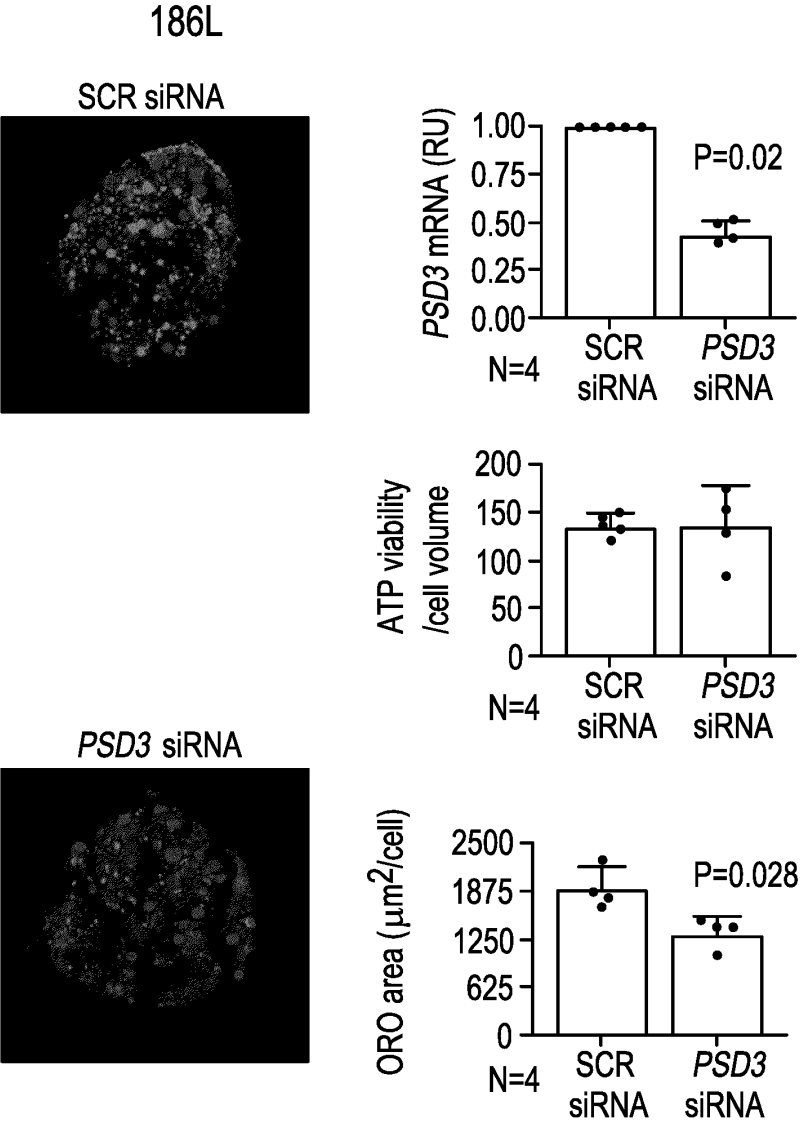


FIG. 21C

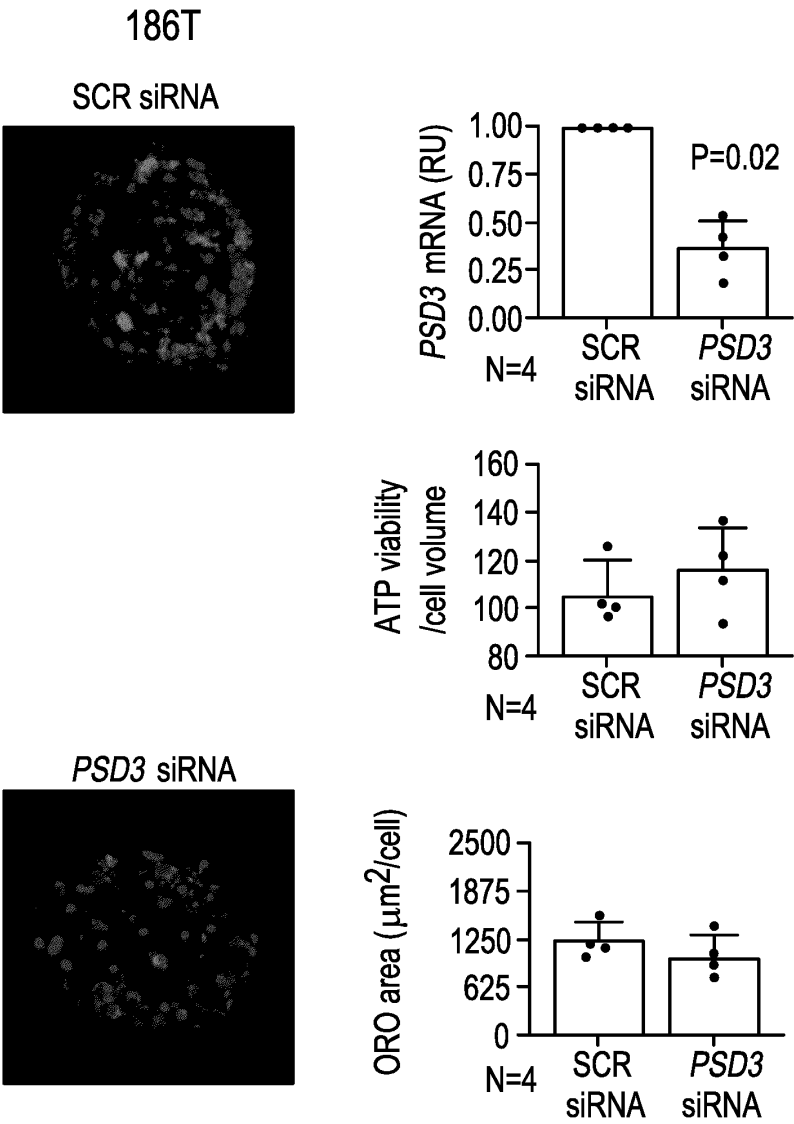


FIG. 21D