

Supplementary Table 1. The *PLCG2*-3'UTR cox regression model adjusted by sex in FinnGen.

	Hazard ratio (HR)	95% Confidence interval: lower-upper	p value
PLCG2-3'UTR heterozygous	0.8986	0.8462-0.9543	0.000497
PLCG2-3'UTR homozygous	0.8438	0.7950-0.8956	2.35x10 ⁻⁸
SEXmale	1.0909	1.0535-1.1296	9.87x10 ⁻⁷

Global Schoenfeld residual p=0.12

Supplementary Table 2. The *TREM2*-R62H cox regression model adjusted by sex in FinnGen.

	Hazard ratio (HR)	95% Confidence interval: lower-upper	p value
TREM2-R62H	1.091	0.9163-1.249	0.204
SEXmale	1.091	1.0536-1.130	9.71x10 ⁻⁷

Global Schoenfeld residual p=0.19

Supplementary Table 3. Summary statistics of UK biobank cohort

Total (n)	UK biobank cohort
Study subjects	486745
Mean age	70.3±8.0
Females/Males	263967/222778
APOE ε4 carriers	126137
PLCG2-P522R	6337
PLCG2-3'UTR	431218
TREM2-R62H	9290
AD cases	4742

n=total number

Supplementary Table 4. The *PLCG2*-P522R cox regression model adjusted by sex in UK biobank

	Hazard ratio (HR)	95% Confidence interval: lower-upper	p value
PLCG2-P522R	0.7854	0.5815-1.061	0.115
SEXmale	1.0052	0.9434- 1.071	0.872

Global Schoenfeld residual p=0.85

Supplementary Table 5. The *PLCG2*-3'UTR cox regression model adjusted by sex in UK biobank

	Hazard ratio (HR)	95% Confidence interval: lower-upper	p value
PLCG2-3'UTR heterozygous	0.9919	0.8507- 1.157	0.918
PLCG2-3'UTR homozygous	0.9318	0.8020- 1.083	0.356
SEXmale	0.9943	0.9312- 1.062	0.865

Global Schoenfeld residual p=0.076

Supplementary Table 6. The *PLCG2*-P522R *APOE* stratified cox regression model adjusted by sex in UK biobank. Different *APOE* groups were analyzed separately.

	Hazard ratio (HR)	95% Confidence interval: lower-upper	p value
PLCG2-P522R/ <i>APOE</i> 33	0.9160	0.5677-1.478	0.719
SEXmale/ <i>APOE</i> 33	1.2573	1.1289-1.400	3.09x10 ⁻⁵
PLCG2-P522R/ <i>APOE</i> 34	0.7026	0.4522-1.0916	0.116365
SEXmale/ <i>APOE</i> 34	0.8549	0.7813-0.9355	0.000646
PLCG2-P522R/ <i>APOE</i> 44	0.6644	0.2972-1.485	0.319
SEXmale/ <i>APOE</i> 44	0.9496	0.8058-1.119	0.537

Global Schoenfeld residuals: APOE33 p=0.42, APOE34 p=0.37, APOE44 p=0.13

Supplementary Table 7. The *PLCG2*-3'UTR *APOE* stratified cox regression model adjusted by sex in UK biobank. Different *APOE* groups were analyzed separately.

	Hazard ratio (HR)	95% Confidence interval: lower-upper	p value
PLCG2-3'UTR heterozygous/ <i>APOE</i> 33	1.1333	0.8625-1.489	0.369034
PLCG2-3'UTR homozygous/ <i>APOE</i> 33	1.0100	0.7728-1.320	0.942450
SEXmale/ <i>APOE</i> 33	1.2331	1.1029-1.379	0.000234
PLCG2-3'UTR heterozygous/ <i>APOE</i> 34	0.8305	0.6783-1.0168	0.072103
PLCG2-3'UTR homozygous/ <i>APOE</i> 34	0.8066	0.6628-0.9817	0.032010
SEXmale/ <i>APOE</i> 34	0.8476	0.7724-0.9302	0.000491
PLCG2-3'UTR heterozygous/ <i>APOE</i> 44	1.3603	0.8393-2.205	0.212
PLCG2-3'UTR homozygous/ <i>APOE</i> 44	1.3555	0.8431-2.179	0.209
SEXmale/ <i>APOE</i> 44	0.9595	0.8096-1.137	0.634

Global Schoenfeld residuals: *APOE*33 $p=0.16$., *APOE*34 $p=0.12$, *APOE*44 $p=0.132$

Supplementary Table 8. The *TREM2*-R62H cox regression model adjusted by sex in UK biobank

	Hazard ratio (HR)	95% Confidence interval: lower-upper	p value
<i>TREM2</i> -R62H	1.4366	1.1832- 1.747	0.00026
SEXmale	1.0026	0.9427- 1.070	0.89116

Global Schoenfeld residual $p=0.88$

Supplementary Table 9. The *TREM2*-R62H *APOE* stratified cox regression model adjusted by sex in UK biobank. Different *APOE* groups were analyzed separately.

	Hazard ratio (HR)	95% Confidence interval: lower-upper	p value
<i>TREM2</i> -R62H/ <i>APOE</i> 33	1.5270	1.106-2.108	0.0101
SEXmale/ <i>APOE</i> 33	1.2557	1.128-1.398	3.4×10^{-5}
<i>TREM2</i> -R62H / <i>APOE</i> 34	1.5595	1.1955-2.0344	0.001051
SEXmale/ <i>APOE</i> 34	0.8541	0.7806-0.9345	0.000592
<i>TREM2</i> -R62H / <i>APOE</i> 44	0.8712	0.4660-1.629	0.666
SEXmale/ <i>APOE</i> 44	0.9506	0.8069-1.120	0.545

Global Schoenfeld residuals: *APOE*33 $p=0.55$, *APOE*34 $p=0.41$, *APOE*44 $p=0.40$

Supplementary Table 10. Comparison of plasma ghrelin levels between genotypes with age, sex, or *APOE* $\epsilon 4$ status as co-variates in the FINGER cohort. Multilinear regression model was used.

	Unstandardized Coefficients		Standardized Coefficients	<i>t</i>	Sig. (<i>p</i>)	95,0% Confidence Interval for <i>B</i>	
	<i>B</i>	Std. Error	<i>Beta</i>			Lower Bound	Upper Bound
(Constant)	3,373	0,291		11,576	0,000	2,793	3,953
<i>PLCG2</i> P522R seq.16.81942028.C.G	0,227	0,079	0,312	2,862	0,005	0,069	0,385
<i>APOE</i> $\epsilon 4$ status	0,003	0,042	0,008	0,076	0,940	-0,080	0,086
Age	-0,003	0,004	-0,090	-0,815	0,418	-0,012	0,005
Sex	0,009	0,038	0,026	0,242	0,809	-0,067	0,086

Dependent variable: logarithmic ghrelin levels

Supplementary Table 11. Effect of *PLCG2*-P522R variant on plasma visfatin levels between genotypes with age, sex, or *APOE* $\epsilon 4$ status as co-variates in the FINGER cohort. Multilinear regression model was used.

	Unstandardized Coefficients		Standardized Coefficients	<i>t</i>	Sig. (<i>p</i>)	95,0% Confidence Interval for <i>B</i>	
	<i>B</i>	Std. Error	<i>Beta</i>			Lower Bound	Upper Bound
(Constant)	4,021	0,385		10,454	0,000	3,255	4,787
<i>PLCG2</i> P522R seq.16.81942028.C.G	0,198	0,105	0,212	1,894	0,062	-0,010	0,407
<i>APOE</i> $\epsilon 4$ status	-0,015	0,055	-0,031	-0,274	0,785	-0,125	0,095
Age	-0,005	0,005	-0,107	-0,945	0,348	-0,016	0,006
Sex	0,009	0,038	0,026	0,242	0,809	-0,067	0,086

Dependent variable: logarithmic visfatin levels

Supplementary Table 12. Effect of *PLCG2*-P522R on plasma leptin levels between genotypes with age, sex, or *APOE* ϵ 4 status as co-variates in the FINGER cohort. Multilinear regression model was used.

	Unstandardized Coefficients		Standardized Coefficients	<i>t</i>	Sig. (<i>p</i>)	95,0% Confidence Interval for <i>B</i>	
	<i>B</i>	Std. Error	<i>Beta</i>			Lower Bound	Upper Bound
(Constant)	2,714	0,515		5,271	0,000	1,689	3,739
<i>PLCG2</i> P522R seq.16.81942028.C.G	-0,100	0,140	-0,065	-0,716	0,476	-0,380	0,179
<i>APOE</i> ϵ 4status	0,110	0,074	0,135	1,488	0,141	-0,037	0,257
Age	0,004	0,007	0,045	0,500	0,618	-0,011	0,018
Sex	0,467	0,068	0,621	6,870	0,000	0,332	0,602

Dependent variable: logarithmic leptin levels