

# **Supplemental Material**

## **Genotype-based recall to study metabolic effects of genetic variation: A pilot study of PPARG Pro12Ala carriers**

Prasad G Kamble<sup>1</sup>, Stefan Gustafsson<sup>2</sup>, Maria J Pereira<sup>1</sup>, Per Lundkvist<sup>1</sup>, Naomi Cook<sup>2</sup>, Lars Lind<sup>3</sup>, Paul W Franks<sup>4</sup>, Tove Fall<sup>2</sup>, Jan W Eriksson<sup>1\*</sup> and Erik Ingelsson<sup>2,5\*</sup>

\*Contributed equally

### **Supplemental text**

#### **1. DETAILED INCLUSION/EXCLUSION CRITERIA**

##### **1.1 Inclusion criteria**

1. Males and females aged  $\geq 18$
2. The fasting plasma glucose should be in the range of 3-7.0 mmol/L on the morning of visit 1

##### **1.1.1 Exclusion criteria**

1. Known diabetes with/without medication
2. Treatment with glucocorticoids or other immune modulating agents.
3. Acute myocardial infarction (NSTEMI, STEMI) or unstable angina, during the last 3 months
4. Stroke (ischemic and hemorrhagic) during the last 3 months
5. Cancer during the last 12 months
6. Other serious or acute illness as judged by the investigator, that may either put the subject at risk because of participation in the study, or influence the results or the subject's ability to participate in the study
7. Pregnant or planning to be pregnant during the study
8. Known or suspected history of significant drug abuse
9. History of alcohol abuse or excessive intake of alcohol as judged by investigator
10. History of severe allergy/hypersensitivity or ongoing allergy/hypersensitivity, as judged by the investigator
11. Plasma donation within one month of screening or any blood donation during the 3 months prior to screening
12. Any other condition within the opinion of the investigator would render the patient unsuitable for inclusion in the study and /or for the patient's safety
13. Involvement in the planning and/or conduct of the study
14. Judgment by the investigator that the subject should not participate in the study if considers subject unlikely to comply with study procedures, restrictions and requirements

## **Supplemental Tables**

**Supplemental Table 1.** Baseline characteristics of the full EpiHealth cohort of participants enrolled at the Uppsala test center until the end of 2015, and the subset of participants selected for genotyping<sup>a</sup>

<b>Phenotype*</b>	<b>Full EpiHealth cohort, Uppsala center (N=13,426)</b>	<b>Genotyped subset (N=2,500)</b>
Age at blood draw (years)	60.4 (8.5)	61.2 (8.4)
Women (%)	56.8	50.0
BMI (kg/m <sup>2</sup> )	26.2 (4.0)	26.5 (3.9)
Waist-hip ratio	0.89 (0.08)	0.90 (0.08)
Body fat (%)	30.7 (8.1)	30.4 (8.2)
Plasma glucose (mmol/L)	5.96 (1.01)	6.00 (0.99)
Anti-diabetic medication (%)	2.8	2.6
Total cholesterol (mmol/L)	5.87 (1.09)	5.98 (1.11)
HDL cholesterol (mmol/L)	1.55 (0.40)	1.51 (0.39)
LDL cholesterol (mmol/L)	3.81 (0.96)	3.93 (0.98)
Triglycerides (mmol/L)	1.22 (0.72)	1.29 (0.75)
Lipid-lowering medication (%)	10.2	10.2
Systolic blood pressure (mmHg)	133 (17)	135 (17)
Diastolic blood pressure (mmHg)	82 (9)	83 (9)
Blood pressure-lowering medication (%)	20.8	22.6

<sup>a</sup>The numbers given are either counts, percentages, or means (standard deviations). Use of medication is self-reported. A varying number of missing observations is present for different phenotypes. Abbreviations: HDL, high-density lipoprotein; LDL, low-density lipoprotein.

**Supplemental Table 2.** Associations between the protein-altering variants and measures of adiposity, glucose, and lipid metabolism in unrelated, non-diabetic individuals from the EpiHealth and ULSAM studies <sup>a</sup>

rsID	BMI			WHR			Body fat percent			Fasting glucose			Total cholesterol			LDL			Triglycerides			ULSAMWt-value		
	Beta	95% CI	P	Beta	95% CI	P	Beta	95% CI	P	Beta	95% CI	P	Beta	95% CI	P	Beta	95% CI	P	Beta	95% CI	P	Beta	95% CI	P
rs1137101	0.003/-0.030/-0.089	0.33	0.04/-0.007/-0.087	0.10	0.002/-0.040/-0.044	0.94	0.049/-0.020/-0.06	0.18	-0.049/-0.018/-0.021	0.19	-0.05/-0.111/-0.007	0.09	-0.045/-0.101/-0.020	0.18	0.032/-0.032/-0.097	0.32	-0.044/-0.136/-0.047	0.34	LEPR					
rs1935	-0.008/-0.058/-0.052	0.18	-0.021/-0.058/-0.027	0.39	0.005/-0.038/-0.047	0.83	-0.03/-0.100/-0.026	0.25	0.002/-0.053/-0.057	0.95	-0.047/-0.106/-0.013	0.12	0.01/-0.055/-0.075	0.76	0.001/-0.054/-0.075	0.76	0.003/-0.090/-0.096	0.95	JMJD1C					
rs49594	0.018/-0.040/-0.076	0.15	-0.028/-0.075/-0.018	0.23	0.024/-0.017/-0.066	0.25	0.052/-0.069/-0.113	0.10	0.045/-0.018/-0.038	0.16	-0.012/-0.070/-0.046	0.68	0.058/-0.005/-0.023	0.07	0.03/-0.032/-0.083	0.34	-0.016/-0.108/-0.075	0.73	GPRC2					
rs13928	-0.004/-0.01/-0.020	0.19	-0.079/-0.27/-0.031	0.00	-0.023/-0.065/-0.020	0.30	0.029/-0.034/-0.092	0.37	0.032/-0.033/-0.097	0.33	0.079/-0.020/-0.019	0.01	0.006/-0.060/-0.071	0.87	-0.021/-0.085/-0.044	0.53	0.072/-0.059/-0.163	0.12	AEPPL					
rs378434	-0.002/-0.062/-0.057	0.94	-0.013/-0.060/-0.034	0.60	-0.008/-0.050/-0.034	0.71	0.007/-0.056/-0.069	0.83	0.018/-0.047/-0.082	0.59	-0.016/-0.075/-0.043	0.60	0.013/-0.052/-0.078	0.69	0.031/-0.032/-0.095	0.33	0.028/-0.064/-0.120	0.55	VPS3C					
rs085704	-0.029/-0.088/-0.031	0.35	-0.004/-0.052/-0.043	0.86	-0.023/-0.066/-0.019	0.28	-0.008/-0.072/-0.055	0.79	-0.008/-0.073/-0.057	0.82	0.016/-0.043/-0.076	0.59	-0.002/-0.068/-0.063	0.94	-0.046/-0.110/-0.019	0.17	-0.048/-0.139/-0.044	0.31	VPS3C					
rs1208	0.044/-0.017/-0.04	0.16	0.025/-0.023/-0.073	0.31	0.014/-0.029/-0.057	0.52	0.004/-0.060/-0.068	0.91	0.012/-0.054/-0.078	0.72	0.035/-0.055/-0.065	0.25	0.013/-0.053/-0.080	0.70	-0.053/-0.118/-0.033	0.11	0.042/-0.051/-0.134	0.37	NAT2					
rs5215	-0.027/-0.087/-0.032	0.37	0.02/-0.028/-0.067	0.41	-0.019/-0.062/-0.023	0.37	0.004/-0.059/-0.067	0.90	0.006/-0.059/-0.071	0.86	0.04/-0.019/-0.010	0.19	0.001/-0.064/-0.067	0.97	-0.045/-0.110/-0.019	0.17	-0.042/-0.133/-0.072	0.66	KCNV1					
rs5219	-0.006/-0.066/-0.034	0.39	0.02/-0.027/-0.068	0.40	-0.019/-0.061/-0.024	0.39	0.005/-0.059/-0.068	0.98	0.006/-0.059/-0.071	0.85	0.038/-0.021/-0.068	0.21	0.002/-0.054/-0.068	0.95	-0.045/-0.110/-0.020	0.17	-0.039/-0.111/-0.073	0.69	KCNV1					
rs12529	0.017/-0.044/-0.078	0.58	0.04/-0.038/-0.089	0.10	0.023/-0.015/-0.072	0.20	-0.021/-0.035/-0.044	0.53	0.016/-0.051/-0.082	0.64	-0.013/-0.074/-0.048	0.68	0.009/-0.058/-0.077	0.79	0.005/-0.040/-0.097	0.44	-0.006/-0.101/-0.089	0.90	AKR1C3					
rs9938550	-0.003/-0.066/-0.059	0.91	0.018/-0.031/-0.068	0.47	0.009/-0.035/-0.053	0.70	0.04/-0.026/-0.015	0.24	0.014/-0.053/-0.081	0.69	-0.026/-0.088/-0.036	0.41	0.014/-0.054/-0.082	0.68	0.057/-0.000/-0.134	0.05	-0.074/-0.171/-0.023	0.13	HDBB7					
rs1260226	-0.073/-0.35/-0.011	0.02	-0.033/-0.083/-0.016	0.18	-0.035/-0.080/-0.008	0.11	-0.03/-0.158/-0.028	0.032	0.074/-0.070/-0.140	0.03	-0.047/-0.015/-0.08	0.14	0.032/-0.036/-0.100	0.35	0.11/-0.040/-0.177	0.011	0.007/-0.080/-0.113	0.73	GCRR					
rs11057401	0.006/-0.057/-0.059	0.86	-0.007/-0.097/-0.003	0.06	0.032/-0.030/-0.077	0.16	-0.067/-0.133/-0.001	0.05	0.024/-0.030/-0.092	0.48	-0.007/-0.068/-0.055	0.83	0.022/-0.047/-0.090	0.53	0.033/-0.034/-0.101	0.33	0.011/-0.086/-0.108	0.82	CDCN92					
rs2626564	0.025/-0.039/-0.088	0.44	0.019/-0.032/-0.069	0.47	0.015/-0.034/-0.056	0.63	-0.016/-0.123/-0.039	0.008	0.038/-0.051/-0.087	0.62	0.007/-0.056/-0.070	0.82	0.005/-0.055/-0.075	0.89	0.034/-0.036/-0.103	0.33	-0.022/-0.122/-0.077	0.66	SCLCVA8					
rs1169288	-0.042/-0.07/-0.022	0.20	-0.022/-0.074/-0.029	0.39	-0.017/-0.062/-0.029	0.47	0.008/-0.059/-0.056	0.80	0.029/-0.059/-0.049	0.03	0.006/-0.033/-0.124	0.06	0.088/-0.030/-0.134	0.02	-0.031/-0.060/-0.039	0.39	0.065/-0.031/-0.161	0.19	HNF1A					
rs864557	0.004/-0.068/-0.060	0.90	0.016/-0.034/-0.067	0.35	0.003/-0.035/-0.055	0.20	-0.035/-0.120/-0.015	0.22	0.027/-0.046/-0.007	0.03	-0.046/-0.110/-0.007	0.15	0.068/-0.138/-0.002	0.06	0.079/-0.080/-0.079	0.78	0.039/-0.080/-0.117	0.70	PP2R3A					
rs17197552	-0.003/-0.067/-0.061	0.92	0.016/-0.034/-0.067	0.33	-0.003/-0.075/-0.015	0.20	0.052/-0.120/-0.015	0.13	-0.078/-0.147/-0.008	0.03	-0.046/-0.110/-0.018	0.16	0.069/-0.139/-0.001	0.06	0.089/-0.060/-0.078	0.79	0.038/-0.081/-0.117	0.72	PP2R3A					
rs6200889	0.067/-0.030/-0.032	0.04	0.015/-0.036/-0.066	0.56	0.041/-0.035/-0.086	0.08	-0.112/-0.180/-0.003	0.0014	-0.053/-0.123/-0.017	0.14	-0.038/-0.102/-0.027	0.25	-0.043/-0.114/-0.028	0.23	0.007/-0.070/-0.069	0.99	0.048/-0.052/-0.148	0.34	ARAP1					
rs6149245	0.042/-0.023/-0.108	0.21	-0.002/-0.054/-0.050	0.95	0.012/-0.034/-0.059	0.61	0.023/-0.046/-0.091	0.52	-0.042/-0.113/-0.029	0.24	0.011/-0.064/-0.066	0.98	-0.033/-0.105/-0.038	0.36	-0.025/-0.065/-0.045	0.48	-0.007/-0.106/-0.092	0.89	GRB14					
rs2464196	-0.039/-0.045/-0.026	0.24	-0.031/-0.083/-0.022	0.25	-0.003/-0.050/-0.043	0.89	0.018/-0.030/-0.016	0.61	0.015/-0.030/-0.176	0.0090	0.071/-0.056/-0.136	0.03	0.139/-0.049/-0.135	0.020	0.055/-0.055/-0.157	0.16	0.06/-0.038/-0.157	0.23	HNF4A					
rs1799330	-0.048/-0.114/-0.018	0.16	-0.027/-0.079/-0.026	0.32	-0.025/-0.072/-0.022	0.31	-0.02/-0.090/-0.049	0.56	-0.025/-0.097/-0.046	0.48	-0.038/-0.104/-0.007	0.25	-0.02/-0.084/-0.060	0.75	0.001/-0.069/-0.072	0.97	0.006/-0.088/-0.109	0.91	NAT2					
rs1137100	-0.086/-0.152/-0.020	0.01	-0.067/-0.120/-0.015	0.01	-0.046/-0.039/-0.002	0.06	-0.073/-0.143/-0.003	0.04	0.039/-0.033/-0.111	0.29	0.019/-0.025/-0.157	0.01	0.034/-0.039/-0.107	0.36	-0.072/-0.144/-0.000	0.05	NA	NA	NA	NA	NA			
rs677903	0.004/-0.063/-0.071	0.91	-0.048/-0.042/-0.005	0.08	0.014/-0.033/-0.062	0.56	-0.036/-0.070/-0.035	0.31	-0.026/-0.099/-0.047	0.49	0.048/-0.019/-0.114	0.16	-0.025/-0.099/-0.049	0.51	-0.074/-0.146/-0.002	0.05	-0.033/-0.118/-0.092	0.81	PPP2R3A					
rs321776	-0.036/-0.049/-0.031	0.29	-0.057/-0.110/-0.003	0.04	-0.017/-0.064/-0.031	0.50	-0.010/-0.050/-0.021	0.13	-0.01/-0.068/-0.065	0.97	-0.055/-0.129/-0.018	0.14	-0.038/-0.105/-0.039	0.37	-0.001/-0.105/-0.104	0.99	ANWRD5							
rs17570	0.025/-0.043/-0.033	0.46	-0.049/-0.039/-0.005	0.08	0.019/-0.030/-0.067	0.45	0.054/-0.115/-0.018	0.14	-0.032/-0.097/-0.050	0.54	0.037/-0.031/-0.010	0.29	-0.045/-0.119/-0.029	0.24	-0.002/-0.075/-0.071	0.96	PEPD							
rs1809337	-0.072/-0.43/-0.001	0.05	0.014/-0.042/-0.071	0.62	-0.061/-0.112/-0.011	0.02	0.008/-0.067/-0.083	0.83	0.083/-0.050/-0.159	0.04	0.005/-0.055/-0.076	0.88	0.069/-0.091/-0.047	0.08	0.085/-0.050/-0.162	0.03	0.058/-0.049/-0.165	0.29	GPR					
rs10761725	0.063/-0.011/-0.137	0.10	0.032/-0.026/-0.089	0.28	0.019/-0.034/-0.072	0.48	0.011/-0.067/-0.089	0.78	-0.079/-0.160/-0.001	0.05	0.006/-0.088/-0.079	0.88	-0.088/-0.169/-0.007	0.03	0.039/-0.077/-0.083	0.94	-0.057/-0.181/-0.046	0.24	JMJD1C					
rs1724632	0.049/-0.027/-0.125	0.21	-0.013/-0.074/-0.047	0.67	0.045/-0.050/-0.099	0.10	-0.045/-0.126/-0.035	0.27	0.036/-0.046/-0.119	0.39	0.018/-0.057/-0.094	0.63	0.016/-0.067/-0.099	0.71	-0.004/-0.147/-0.039	0.25	NA	NA	MEOWY					
rs1738343	0.015/-0.061/-0.092	0.70	-0.006/-0.067/-0.055	0.84	0.001/-0.044/-0.064	0.72	0.03/-0.050/-0.115	0.46	0.033/-0.050/-0.115	0.44	0.038/-0.037/-0.114	0.32	0.013/-0.066/-0.070	0.54	0.039/-0.053/-0.079	0.39	-0.004/-0.157/-0.087	0.53	CD30/G					
rs475661	-0.032/-0.110/-0.047	0.43	-0.034/-0.097/-0.029	0.29	0.018/-0.038/-0.073	0.54	0.02/-0.084/-0.083	0.99	0.032/-0.054/-0.118	0.47	0.023/-0.056/-0.102	0.57	0.031/-0.056/-0.118	0.49	-0.056/-0.101/-0.070	0.72	0.136/-0.049/-0.259	0.03	PPARG					
rs7657817	0.009/-0.001/-0.069	0.03	-0.004/-0.067/-0.059	0.89	0.056/-0.026/-0.115	0.04	0.022/-0.067/-0.016	0.61	-0.038/-0.123/-0.050	0.41	0.065/-0.044/-0.044	0.11	-0.047/-0.135/-0.040	0.29	-0.051/-0.145/-0.035	0.025	-0.072/-0.046/-0.189	0.23	FAM134					
rs9896862	-0.091/-0.177/-0.005	0.04	-0.004/-0.089/-0.028	0.25	-0.054/-0.115/-0.006	0.08	0.013/-0.070/-0.014	0.77	-0.028/-0.119/-0.068	0.59	0.025/-0.109/-0.080	0.76	0.044/-0.109/-0.080	0.76	-0.054/-0.147/-0.039	0.25	NA	NA	MEOWY					
rs12																								