

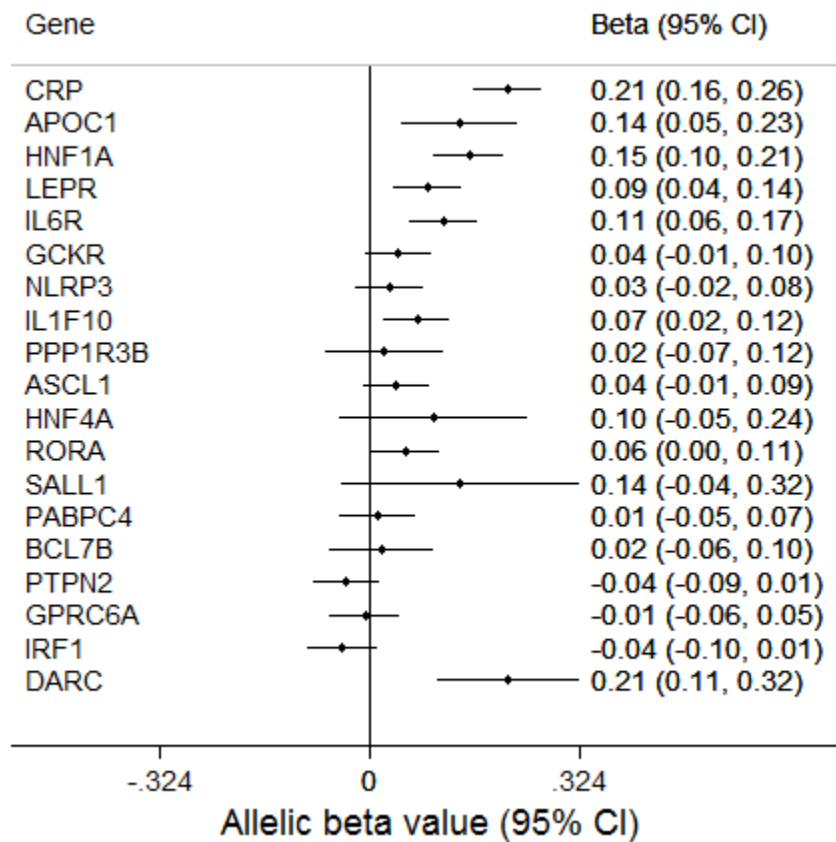
Do Genetic Markers of Inflammation Modify the Relationship between Periodontitis and Nonalcoholic Fatty Liver Disease? Findings from the SHIP Study

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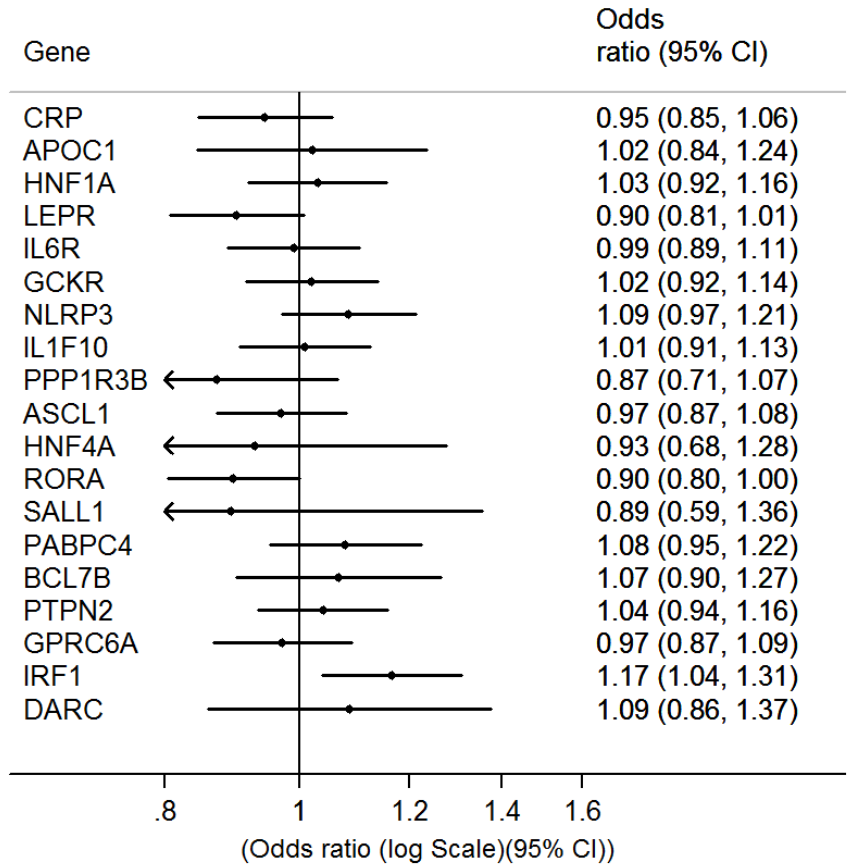
Appendix Table 1. List of SNPs used in constructing the weighted genetic scores with their original source of publication and the corresponding information used in constructing the scores

SNP	Chr	Position	Coded Allele	Beta	SE	P-value	Closest Gene	Study
C-reactive Protein								
rs2794520	1	157945440	C	0.160	0.006	2.0x10 ⁻¹⁸⁶	<i>CRP</i>	Dehghan et al 2011; Naitza et al 2012
rs4420638	19	50114786	A	0.236	0.009	8.8x10 ⁻¹³⁹	<i>APOC1</i>	Dehghan et al 2011
rs1183910	12	119905190	G	0.149	0.006	2.1x10 ⁻¹²⁴	<i>HNF1A</i>	Dehghan et al 2011
rs4420065	1	65934049	C	0.090	0.005	3.5x10 ⁻⁶²	<i>LEPR</i>	Dehghan et al 2011
rs4129267	1	152692888	C	0.079	0.005	2.1x10 ⁻⁴⁸	<i>IL6R</i>	Dehghan et al 2011;
rs1260326	2	27584444	T	0.072	0.005	4.6x10 ⁻⁴⁰	<i>GCKR</i>	Dehghan et al 2011
rs12239046	1	245668218	C	0.047	0.006	1.2x10 ⁻¹⁵	<i>NLRP3</i>	Dehghan et al 2011
rs6734238	2	113557501	G	0.050	0.006	1.8x10 ⁻¹⁷	<i>IL1F10</i>	Dehghan et al 2011
rs9987289	8	9220768	G	0.069	0.011	3.4x10 ⁻¹³	<i>PPP1R3B</i>	Dehghan et al 2011
rs10745954	12	102007224	A	0.039	0.006	1.6x10 ⁻¹¹	<i>ASCL1</i>	Dehghan et al 2011
rs1800961	20	42475778	C	0.088	0.015	2.2x10 ⁻⁹	<i>HNF4A</i>	Dehghan et al 2011
rs340029	15	58682257	T	0.032	0.006	4.1x10 ⁻⁹	<i>RORA</i>	Dehghan et al 2011
rs10521222	16	49716211	C	0.104	0.015	8.5x10 ⁻¹³	<i>SALL1</i>	Dehghan et al 2011
rs12037222	1	39837548	A	0.045	0.007	6.4x10 ⁻¹¹	<i>PABPC4</i>	Dehghan et al 2011
rs13233571	7	72609167	A	0.054	0.009	3.6x10 ⁻⁹	<i>BCL7B</i>	Dehghan et al 2011
rs2847281	18	12811593	A	0.031	0.006	2.2x10 ⁻⁸	<i>PTPN2</i>	Dehghan et al 2011
rs6901250	6	117220718	A	0.035	0.006	4.8x10 ⁻⁸	<i>GPRC6A</i>	Dehghan et al 2011
rs4705952	5	131867517	G	0.042	0.007	1.3x10 ⁻⁸	<i>IRF1</i>	Dehghan et al 2011
rs12068753		157959161	A	0.213	0.035	1.2x10 ⁻⁹	<i>DARC</i>	Naitza et al 2012
Interleukin-6 (IL-6)								
rs643434	9	135132176	G	0.245	0.026	2.7x10 ⁻²¹	<i>ABO</i>	Naitza et al 2012
Erythrocyte Sedimentation Rate (ESR)								
rs12034598	1	205824138	G	0.143	0.022	9.3x10 ⁻¹¹	<i>CR1</i>	Naitza et al 2012
rs4910742	11	5263085	A	0.229	0.042	6.3x10 ⁻⁸		Naitza et al 2012
Monocyte Chemoattractant Protein (MCP-1)								

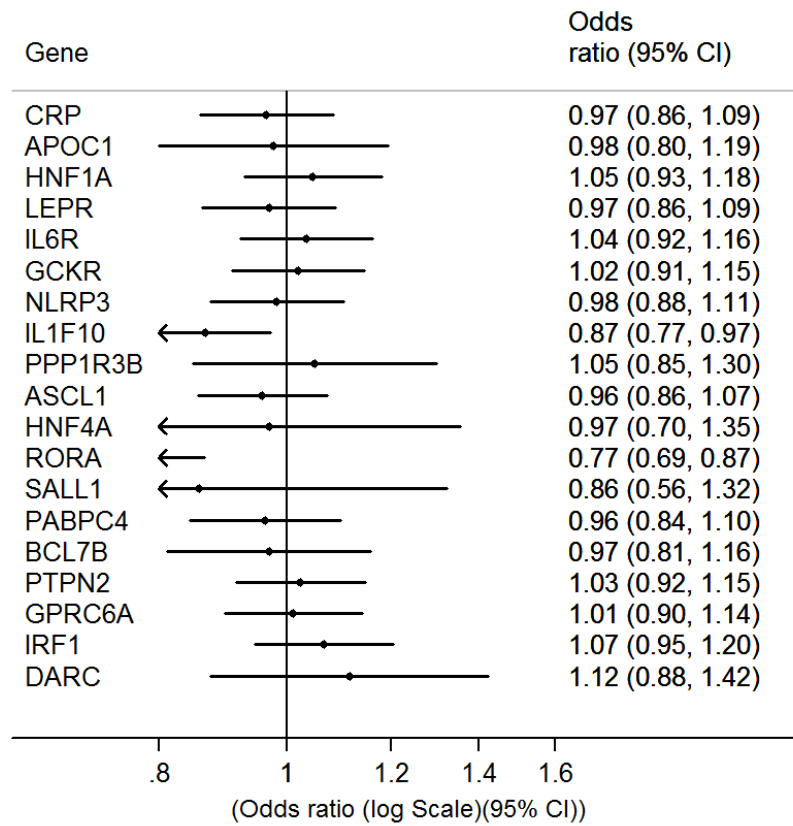
rs12075	1	157441978	A	0.303	0.026	1.7×10^{-30}	<i>DARC</i>	Naitza et al 2012
rs3026968	1	157414076	T	0.239	0.033	7.6×10^{-13}	<i>CADM3</i>	Naitza et al 2012



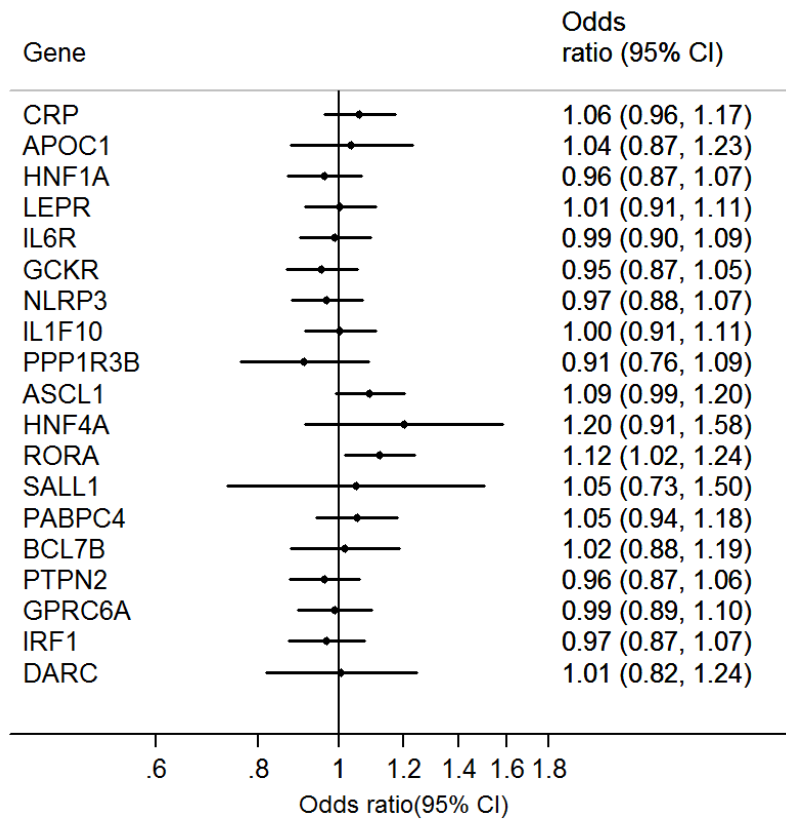
Appendix Figure 1. Associations between known CRP SNPs and log transformed serum CRP levels measured in the Study of Health in Pomerania (SHIP)



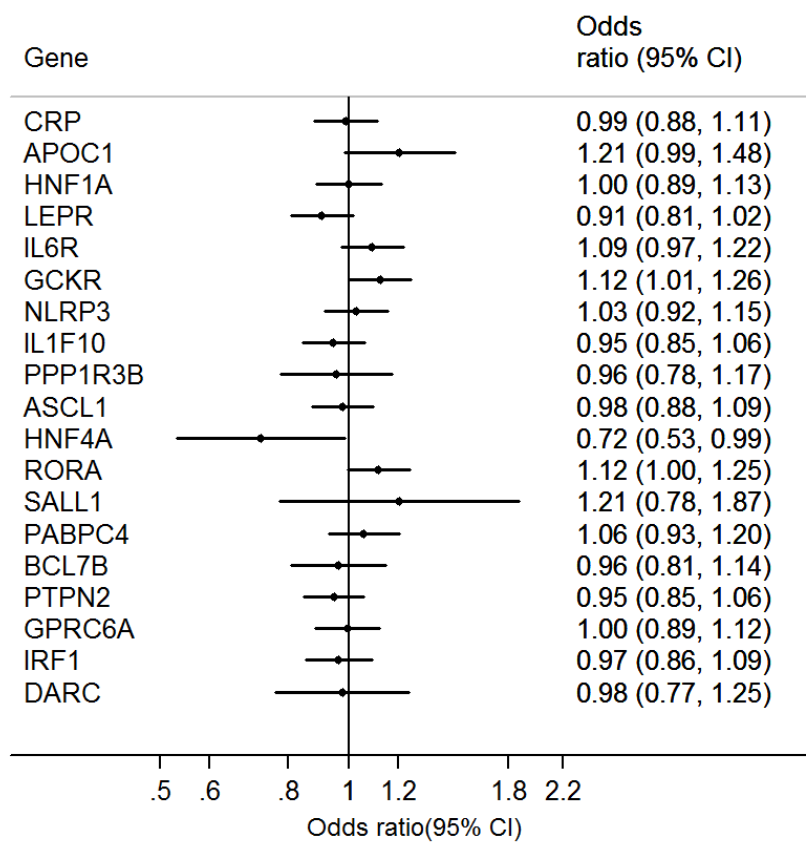
Appendix Figure 2. Associations between known CRP SNPs and periodontitis (proportion of sites with PD ≥ 4 mm) in the Study of Health in Pomerania (SHIP)



Appendix Figure 3. Associations between known CRP SNPs and periodontitis (proportion of sites with CAL \geq 3mm) in the Study of Health in Pomerania (SHIP)



Appendix Figure 4. Associations between known CRP SNPs and periodontitis (CDC-AAP moderate/severe) in the Study of Health in Pomerania (SHIP)



Appendix Figure 5. Associations between known CRP SNPs and Non-alcoholic Fatty Liver Disease (NAFLD) in the Study of Health in Pomerania (SHIP)

Appendix Table 2. Stratified analysis for the association between the proportion of periodontal sites with CAL ≥ 3 mm (0%, <30%, $\geq 30\%$) and non-alcoholic fatty liver disease according to categories of the weighted genetic CRP score and serum CRP levels, in the Study of Health in Pomerania, 1997-2001

	NAFLD		Prevalence Odds Ratio (95% CI)	
	Cases	Non-cases	Crude	Adjusted*
wGS_{CRP} ≤ 1.98 (N=1,222)				
No site (0%)	9	112	Ref.	Ref.
Moderate (<30%)	52	297	2.18 (1.04, 4.57)	1.34 (0.62, 2.93)
Extensive ($\geq 30\%$)	251	501	6.24 (3.11, 12.5)	1.44 (0.65, 3.19)
wGS_{CRP} >1.98 (N=1,259)				
No site (0%)	5	92	Ref.	Ref.
Moderate (<30%)	77	316	4.48 (1.76, 11.4)	2.99 (1.13, 7.86)
Extensive ($\geq 30\%$)	260	509	9.40 (3.77, 23.4)	2.85 (1.06, 7.64)
Serum CRP <1mg/L (N=972)				
No site (0%)	3	103	Ref.	Ref.
Moderate (<30%)	35	308	3.90 (1.18, 12.9)	2.43 (0.71, 8.31)
Extensive ($\geq 30\%$)	126	397	10.9 (3.40, 34.9)	2.58 (0.73, 9.10)
Serum CRP 1-3mg/L (N=887)				
No site (0%)	7	66	Ref.	Ref.
Moderate (<30%)	55	202	2.57 (1.12, 5.91)	1.67 (0.67, 4.13)
Extensive ($\geq 30\%$)	195	362	5.08 (2.29, 11.3)	1.39 (0.55, 3.52)
Serum CRP >3mg/L (N=622)				
No site (0%)	4	35	Ref.	Ref.
Moderate (<30%)	39	103	3.31 (1.11, 9.94)	2.02 (0.64, 6.34)
Extensive ($\geq 30\%$)	190	251	6.62 (2.31, 18.9)	2.22 (0.70, 7.03)

*Adjusted for age, gender, waist circumference, smoking, physical activity, alcohol consumption and diabetes

CAL-clinical attachment level

CRP-C-reactive protein

wGS_{CRP}- weighted genetic score for CRP

**Interaction p-value for the genetic CRP score=0.3

***Interaction p-value for serum CRP levels=0.2

Appendix Table 3. Stratified analysis investigating the relationship between periodontitis (CDC-AAP) and non-alcoholic fatty liver disease according to categories of the weighted genetic CRP score and serum CRP levels, in the Study of Health in Pomerania, 1997-2001

	NAFLD		Prevalence Odds Ratio (95% CI)	
	Cases	Non-cases	Crude	Adjusted*
wGS_{CRP} ≤1.98 (N=1,220)				
None/mild	91	463	Ref.	Ref.
Moderate/Severe	221	445	2.53 (1.92, 3.33)	1.26 (0.90, 1.76)
wGS_{CRP} >1.98 (N=1,259)				
None/mild	112	467	Ref.	Ref.
Moderate/ Severe	230	450	2.13 (1.64, 2.77)	1.09 (0.80, 1.50)
Serum CRP <1mg/L (N=971)				
None/mild	49	462	Ref.	Ref.
Moderate/ Severe	115	345	3.14 (2.19, 4.52)	1.43 (0.93, 2.19)
Serum CRP 1-3mg/L (N=887)				
None/mild	82	305	Ref.	Ref.
Moderate/ Severe	175	325	2.00 (1.48, 2.72)	1.05 (0.72, 1.52)
Serum CRP >3mg/L (N=621)				
None/mild	72	163	Ref.	Ref.
Moderate/severe	161	225	1.62 (1.15, 2.28)	0.86 (0.56, 1.32)

*Adjusted for age, gender, waist circumference, smoking, physical activity, alcohol consumption and diabetes

CRP-C-reactive protein

wGS_{CRP}- weighted genetic score for CRP

**Interaction p-value for the genetic CRP score=0.8

***Interaction p-value for serum CRP levels=0.014

Appendix Table 4. Distribution of baseline factors according to categories of serum CRP among participants of the Study of Health in Pomerania, 1997-2001

	Low	Intermediate	High
	(CRP <1mg/L)	(CRP 1-3mg/L)	(CRP >3mg/L)
CRP, mg/l	0.53 (0.32, 0.75)	1.84 (1.30, 2.54)	5.83 (4.05, 8.67)
Age, yrs.	43.0 (31.0, 56.0)	47.0 (35.0, 61.0)	52.0 (37.0, 63.0)
Waist circumference (cm)	82.8 (74.0, 92.5)	89.2 (78.8, 99.1)	94.9 (84.2, 103)
Alcohol*	4.65 (1.34, 7.71)	4.18 (1.31, 6.86)	3.35 (0.65, 5.33)
Abdominal obesity**	150 (15.5)	284 (32.1)	313 (50.5)
Physical activity	485 (50.2)	366 (41.4)	248 (40.1)
Men	472 (48.6)	408 (46.0)	235 (37.8)
Smoking			
Never	385 (39.8)	332 (37.6)	249 (40.2)
Former	289 (29.9)	307 (34.7)	184 (29.7)
Current	293 (30.3)	245 (27.7)	186 (30.1)
Diabetes mellitus	125 (12.9)	191 (21.5)	149 (24.0)

Data are presented as No. (%) or Median (lower quartile, upper quartile)

*Number of standard drinks in the past 30 days

**Gender-specific weight circumference defined as ≥ 88 cm for women and ≥ 102 cm for men (Grundy et al. 2005)

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