

## **Supplementary materials**

**Supplementary Table 1.** Sequences of the primers and TaqMan<sup>®</sup> probes

<b>Gene (GenBank accession)</b>	<b>Oligonucleotide sequence (5'-3')</b>
<i>CCL2</i> (NM_002982)	
Forward	GCTCATAGCAGCCACCTTCATT
Reverse	TCTGCACTGAGATCTTCCTATTGGT
TaqMan <sup>®</sup> Probe	FAM-TCGCTCAGCCAGATGCAATCAATGC-TAMRA
<i>CD68</i> (NM_001251)	
Forward	CACGCAGCACAGTGGACATT
Reverse	CGAGTTGCTGCAACTGAAGCT
TaqMan <sup>®</sup> Probe	FAM-TCGGCTCAGAATGCATCCCTTCGA-TAMRA
<i>IL1RN</i> (NM_173842)	
Forward	CCAGCTGGAGGCAGTTAACATC
Reverse	GCAGGCGGCAGACTCAA
TaqMan <sup>®</sup> Probe	FAM-CGCCTTCATCCGCTCAGACAGTGG-TAMRA
<i>MMP9</i> (NM_004994)	
Forward	GCCCGGACCAAGGATACAGT
Reverse	CCCCTCAGTGAAGCGGTACA
TaqMan <sup>®</sup> Probe	FAM-ACGCGCTGGGCTTAGATCATTCTCA-TAMRA
<i>SPP1</i> (NM_000582)	
Forward	CATCCAGTACCCTGATGCTACAGA
Reverse	GGCCTTGATGCACCATTCAA
TaqMan <sup>®</sup> Probe	FAM-ACATCACCTCACACATGGAAAGCGAGGA-TAMRA
<i>TNF</i> (NM_00594)	
Forward	CCCCAGGGACCTCTCTAATC
Reverse	ACATGGGCTACAGGCTTGTC
TaqMan <sup>®</sup> Probe	FAM-CCTCTGGCCAGGCAGTCAGATCAT-TAMRA
<i>VEGFA</i> (NM_004994)	
Forward	CAGCACAACAAATGTGAATGCA
Reverse	CAAATGCTTTCTCCGCTCTGA
TaqMan <sup>®</sup> Probe	FAM-AGCAAGACAAGAAAACCCTGTGGGCC-TAMRA

*CCL2*, C-C motif chemokine ligand 2 (MCP-1); *CD68*, CD68 molecule; *IL1RN*, interleukin-1 receptor antagonist; *MMP9*, matrix metalloproteinase 9; *SPP1*, secreted phosphoprotein 1 (osteopontin); *TNF*, tumor necrosis factor, *VEGFA*, vascular endothelial growth factor A.

**Supplementary Table 2.** Bivariate analysis of the correlation between IL-1RA and other variables, unadjusted and after adjusting for body fat

Variable	Serum IL-1RA			
	Unadjusted correlation		Adjusted correlation	
	<i>r</i>	<i>P</i> value	<i>r</i>	<i>P</i> value
Sex	-0.01	0.861	-0.20	<b>0.012</b>
Age	-0.07	0.422	-0.14	0.091
BMI	0.51	<b>&lt;0.001</b>	0.32	<b>&lt;0.001</b>
Body fat percentage	0.42	<b>&lt;0.001</b>	—	—
WC	0.50	<b>&lt;0.001</b>	0.33	<b>&lt;0.001</b>
SBP	0.16	<b>0.044</b>	0.01	0.983
DBP	0.20	<b>0.014</b>	0.04	0.665
Glucose	0.14	0.087	0.03	0.705
Insulin	0.31	<b>&lt;0.001</b>	0.20	<b>0.014</b>
HOMA	0.30	<b>&lt;0.001</b>	0.19	<b>0.018</b>
QUICKI	-0.37	<b>&lt;0.001</b>	-0.21	<b>0.011</b>
Triglycerides	0.13	0.115	0.08	0.306
Cholesterol	0.20	<b>0.013</b>	0.09	0.244
LDL-cholesterol	0.25	<b>0.002</b>	0.16	0.052
HDL-cholesterol	-0.27	<b>&lt;0.001</b>	-0.25	<b>0.002</b>
Uric acid	0.33	<b>&lt;0.001</b>	0.26	<b>0.001</b>
Fibrinogen	0.33	<b>&lt;0.001</b>	0.28	<b>&lt;0.001</b>
vWF	0.17	<b>0.045</b>	0.07	0.448
Homocysteine	0.14	0.101	0.14	0.104
CRP	0.49	<b>&lt;0.001</b>	0.33	<b>&lt;0.001</b>
WBC	0.55	<b>&lt;0.001</b>	0.47	<b>&lt;0.001</b>
ALT	0.05	0.545	0.16	<b>0.049</b>
AST	-0.07	0.387	0.09	0.257
AST/ALT ratio	-0.17	<b>0.033</b>	-0.15	0.067
γ-GT	0.23	<b>0.004</b>	0.23	<b>0.004</b>
Creatinine	0.02	0.800	0.14	0.098
SAA	0.35	<b>&lt;0.001</b>	0.18	<b>0.048</b>
Endotoxin	0.14	0.124	0.05	0.619
Osteopontin	0.24	<b>0.005</b>	0.26	<b>0.004</b>
VAI	0.18	<b>0.023</b>	0.11	0.178
TyG index	0.28	<b>&lt;0.001</b>	0.17	<b>0.038</b>
FLI	0.45	<b>&lt;0.001</b>	0.24	<b>0.002</b>
Adiponectin	-0.46	<b>&lt;0.001</b>	-0.46	<b>&lt;0.001</b>
Leptin	0.31	<b>&lt;0.001</b>	-0.02	0.806
Adpn/Lep ratio	-0.33	<b>&lt;0.001</b>	-0.10	0.243

BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; HOMA, homeostatic model assessment; QUICKI, quantitative insulin sensitivity check index; vWF, von Willebrand factor; CRP, C-reactive protein; ALT, alanine aminotransferase; WBC, white blood cells; AST, aspartate aminotransferase; γ-GT, γ-glutamyltransferase; SAA, serum amyloid A; VAI, visceral adipose index; TyG index, triglyceride glucose index; FLI, fatty liver index. Values are Pearson's correlation coefficients (*r*) and associated *P* values. *P* values lower than 0.05 are highlighted in bold.

**Supplementary Table 3.** Characteristics of individuals with normal weight or obesity included in the adipose tissue expression study

	NW	OB-NG	OB-IGT&T2D	<i>P</i>
n	7	10	19	
Sex, m/f	1/6	1/6	0/19	0.285
Age, y	54 ± 18	35 ± 10*	51 ± 9†	0.001
BMI, kg/m <sup>2</sup>	22.5 ± 2.4	45.8 ± 6.9*	43.2 ± 6.5*	<0.001
Glucose, mg/dL	89 ± 10	92 ± 11	120 ± 35†	0.035
2h OGTT Glucose, mg/dL		117 ± 17	207 ± 75†	0.002
Insulin, µU/mL	6.7 ± 1.6	16.8 ± 11.3	22.2 ± 13.7	0.150
HOMA	1.4 ± 0.3	4.0 ± 3.1	7.1 ± 7.1	0.228
QUICKI	0.36 ± 0.01	0.33 ± 0.03	0.30 ± 0.03*	0.012
Triglycerides, mg/dL	69 ± 27	110 ± 26	117 ± 54	0.168
HDL-cholest, mg/dL	61 ± 8	43 ± 7*	50 ± 10*	0.005
CRP, mg/L	2.0 ± 1.0	14.7 ± 22.7*	16.0 ± 17.2*	0.026
AST/ALT	1.13 ± 0.20	0.67 ± 0.21*	0.67 ± 0.16*	0.002
Leptin, ng/mL	8.4 ± 4.5	66.9 ± 21.4*	70.0 ± 21.2*	<0.001
<i>SPP1</i> mRNA, a. u.	1.0 ± 0.8	3.6 ± 2.5	8.9 ± 4.6*†	<0.001
<i>TNF</i> mRNA, a. u.	1.0 ± 1.5	3.1 ± 2.1	3.9 ± 2.5	0.073
<i>CCL2</i> mRNA, a. u.	1.0 ± 0.8	2.6 ± 2.4	3.9 ± 2.9	0.101
<i>CD68</i> mRNA, a. u.	1.0 ± 1.2	3.0 ± 1.9	3.8 ± 2.2*	0.028
<i>MMP9</i> mRNA, a. u.	1.0 ± 0.7	12.7 ± 12.2	31.0 ± 22.1*†	0.004
<i>VEGFA</i> mRNA, a. u.	1.0 ± 0.8	1.0 ± 0.5	1.1 ± 0.5	0.868

NW, normal weight; OB, obesity; NG, normoglycemia; IGT, impaired glucose tolerance; T2D, type 2 diabetes; BMI, body mass index; OGTT, oral glucose tolerance test; HOMA, homeostatic model assessment; QUICKI, quantitative insulin sensitivity check index; CRP, C-reactive protein; AST, aspartate aminotransferase; ALT, alanine aminotransferase; *SPP1*, secreted phosphoprotein 1 (osteopontin); a. u. arbitrary units; TNF, tumor necrosis factor, *CCL2*, C-C motif chemokine ligand 2 (MCP-1); *CD68*, CD68 molecule; *MMP9*, matrix metalloproteinase 9; *VEGFA*, vascular endothelial growth factor A. Data presented as mean ± SD. mRNA expression in visceral adipose tissue is expressed as the ratio to *18S* rRNA. The expression in NW subjects was assumed to be 1. Differences between groups were analyzed by ANOVA followed by LSD tests. \* *P* < 0.05 vs NW. †*P* < 0.05 vs OB-NG.

**Supplementary Table 4.** Effect of weight gain

	Before WG	After WG	P
Sex, male/female	5/15	—	—
Age, y	45.2 ± 15.6	46.7 ± 15.6	—
Body weight, kg	78.0 ± 18.9	83.3 ± 19.2	<0.001
BMI, kg/m <sup>2</sup>	29.4 ± 5.4	32.3 ± 6.3	<0.001
Body fat, %	38.1 ± 7.8	42.3 ± 6.9	<0.001
WC, cm	96 ± 15	100 ± 16	0.004
SBP, mm Hg	116 ± 14	113 ± 16	0.490
DBP, mm Hg	71 ± 10	70 ± 9	0.449
Glucose, mg/mL	94 ± 11	99 ± 15	0.052
Insulin, μU/mL	5.0 ± 3.6	4.7 ± 5.4	0.716
HOMA	1.2 ± 0.8	1.1 ± 1.3	0.834
QUICKI	0.390 ± 0.040	0.404 ± 0.044	0.267
Triglycerides, mg/dL	78 ± 21	85 ± 36	0.292
Total-cholesterol, mg/dL	153 ± 34	168 ± 37	0.014
LDL-cholesterol, mg/dL	80 ± 35	87 ± 40	0.185
HDL-cholesterol, mg/dL	57 ± 19	64 ± 16	0.003
Uric acid, mg/dL	4.0 ± 0.9	4.3 ± 1.0	0.105
Homocysteine, μmol/L	7.1 ± 1.7	7.9 ± 3.3	0.253
CRP, mg/L	1.0 ± 0.6	1.0 ± 0.8	0.924
WBC, 10 <sup>6</sup> cells/mL	5.6 ± 1.1	5.6 ± 0.9	0.895
ALT, IU/L	24 ± 14	15 ± 6	0.036
AST, IU/L	10 ± 8	15 ± 4	0.049
AST/ALT ratio	0.88 ± 0.23	1.08 ± 0.35	0.021
γ-GT, IU/L	13 ± 11	13 ± 12	0.898
VAI	1.19 ± 0.65	1.13 ± 0.70	0.557
TyG index	8.14 ± 0.33	8.20 ± 0.47	0.506
FLI	83.3 ± 6.4	84.5 ± 6.3	0.235
Leptin, ng/mL	19.3 ± 18.4	26.5 ± 17.6	0.003
Adiponectin, μg/mL	16.8 ± 6.4	17.4 ± 7.4	0.570
Adpn/Lep ratio	2.3 ± 2.3	1.2 ± 1.2	0.001

WG, weight gain; BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; HOMA, homeostasis model assessment; QUICKI, quantitative insulin sensitivity check index; CRP, C-reactive protein; WBC, white blood cells; ALT, alanine aminotransferase; AST, aspartate aminotransferase; γ-GT, γ-glutamyltransferase. Data presented as mean ± SD. Differences between after vs before weight gain (WG) were computed by two-tailed paired Student's *t* tests.

**Supplementary Table 5.** Effect of weight loss in patients with obesity after conventional dietary treatment or RYGB

	<i>Conventional dietary treatment</i>			<i>RYGB</i>		
	Before WL	After WL	P	Before WL	After WL	P
Sex, male/female	9/7	—	—	22/41	—	—
Age, y	40.5 ± 16.4	41.3 ± 16.2	—	47.2 ± 10.8	47.9 ± 10.8	—
Body weight, kg	95 ± 18	81 ± 15	<0.001	118 ± 21	81 ± 15	<0.001
BMI, kg/m <sup>2</sup>	32.8 ± 5.1	28.1 ± 3.5	<0.001	42.5 ± 5.7	29.1 ± 4.3	<0.001
Body fat, %	42.1 ± 7.1	33.9 ± 6.2	<0.001	51.9 ± 6.5	35.2 ± 9.8	<0.001
WC, cm	107 ± 13	95 ± 11	<0.001	124 ± 12	96 ± 13	<0.001
SBP, mm Hg	123 ± 13	115 ± 11	0.028	132 ± 17	117 ± 13	<0.001
DBP, mm Hg	77 ± 10	71 ± 7	0.011	84 ± 11	71 ± 8	<0.001
Glucose, mg/mL	94 ± 14	94 ± 13	0.930	102 ± 23	87 ± 13	<0.001
Insulin, μU/mL	16.4 ± 7.4	12.7 ± 5.9	0.171	19.9 ± 11.7	6.5 ± 3.8	<0.001
HOMA	3.9 ± 2.1	3.1 ± 1.9	0.190	5.2 ± 3.8	1.4 ± 0.8	<0.001
QUICKI	0.319 ± 0.023	0.335 ± 0.039	0.208	0.316 ± 0.036	0.382 ± 0.047	<0.001
Triglycerides, mg/dL	112 ± 49	84 ± 33	0.023	123 ± 50	71 ± 14	<0.001
Total-cholesterol, mg/dL	184 ± 30	168 ± 22	0.064	194 ± 35	160 ± 36	<0.001
LDL-cholesterol, mg/dL	114 ± 38	102 ± 23	0.188	117 ± 30	88 ± 24	<0.001
HDL-cholesterol, mg/dL	47 ± 14	50 ± 11	0.551	50 ± 13	54 ± 13	0.046
Uric acid, mg/dL	5.5 ± 0.9	5.0 ± 0.8	0.064	5.6 ± 1.4	4.4 ± 1.0	<0.001
CRP, mg/L				11.6 ± 12.8	2.6 ± 6.7	<0.001
WBC, 10 <sup>6</sup> cells/mL	7.1 ± 1.7	6.8 ± 1.5	0.536	7.4 ± 2.2	6.0 ± 1.5	<0.001
ALT, IU/L	28 ± 22	19 ± 12	0.057	26 ± 15	28 ± 19	0.557
AST, IU/L	15 ± 7	13 ± 3	0.146	19 ± 8	25 ± 18	0.013

AST/ALT ratio	0.68 ± 0.24	0.83 ± 0.32	0.099	0.81 ± 0.25	0.98 ± 0.28	0.019
γ-GT, IU/L	19 ± 11	18 ± 22	0.856	29 ± 36	23 ± 43	0.184
VAI	1.71 ± 0.87	1.29 ± 0.66	0.024	2.08 ± 1.87	1.03 ± 0.39	<0.001
TyG index	8.49 ± 0.43	8.20 ± 0.43	0.011	8.63 ± 0.40	8.01 ± 0.25	<0.001
FLI	89.7 ± 1.6	86.5 ± 3.5	0.016	91.8 ± 1.0	85.3 ± 3.8	<0.001
Leptin, ng/mL	26.2 ± 16.2	13.5 ± 7.4	0.003	45.1 ± 23.8	12.7 ± 11.6	<0.001
Adiponectin, μg/mL	9.8 ± 5.9	11.3 ± 7.6	0.215	10.7 ± 5.6	18.3 ± 7.8	<0.001
Adpn/Lep ratio	0.5 ± 0.3	1.5 ± 2.0	0.049	0.3 ± 0.2	3.6 ± 5.8	<0.001

RYGB, Roux-en-Y gastric bypass; WL, weight loss; BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; HOMA, homeostatic model assessment; QUICKI, quantitative insulin sensitivity check index; CRP, C-reactive protein; WBC, white blood cells; ALT, alanine aminotransferase; AST, aspartate aminotransferase; γ-GT, γ-glutamyltransferase. Data presented as mean ± SD. Differences between after vs before WL were computed by two-tailed paired Student's *t* tests.