

PROTEOMICS

**Supporting Information
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**Proteomic characterization of thiazolidinedione regulation of obese adipose
secretome in Zucker obese rats**

Table S1. Adipose tissue secretome from lean and obese rats

Accession	Reference	Gene symbol	Lean adipose tissue	Obese adipose tissue
P01015	Angiotensinogen precursor	AGT	+	+
P00787	Cathepsin B precursor	CTSB	+	+
P05371	Clusterin precursor	CLU	+	+
P21180	Complement C2 precursor	C2	+	+
P08649	Complement C4 precursor	C4	+	+
P09006	Contrapsin-like protease inhibitor 6 precursor	SERPINA3	+	+
P20305	Gelsolin precursor	GSN	+	+
P19879	Mimecan precursor (Osteoglycin)	OGN	+	+
P20961	Plasminogen activator inhibitor-1 precursor)	SERPINE1	+	+
Q62009	Osteoblast-specific factor 2	POSTN	+	+
Q08519	serine proteinase inhibitor 1	PI	+	+
P07214	SPARC precursor	SPARC	+	+
P29447	Thioredoxin 3	TRX3	+	+
P16368	Metalloproteinase inhibitor 2 precursor (TIMP-2)	TIMP2	+	+
P02544	Vimentin	VIM	+	+
AAC35371	CD14	CD14	+	-
XP_213392	pigment epithelium-derived factor	SERPINF1	+	-
XP_226803	similar to Complement component C7 precursor	C7	+	-
A32827	fetuin precursor	AHSG	+	-
CAA29759	thyroid hormone binding protein	P4HB	+	-
AAA40964	C-reactive protein	CRP	+	-
NP_036869	apolipoprotein A-IV	APOA4	+	-
P12346	Serotransferrin precursor	TF	+	-
P20059	Hemopexin precursor	HPX	+	-
AAA41081	vitamin D-binding protein	GC	+	-
XP_236746	tetranectin	TNA	+	-

AAH02356	nucleobindin 1	NUCB1	+	-
XP_236631	dystroglycan 1	DAG1	+	-
P49141	Transthyretin precursor	TTR	+	-
CAA58858	lumican	LUM	+	-
AAH13651	serine protease inhibitor 2-2	HTRA3	+	-
PROTEASE				
P34955	Alpha-1-antiproteinase precursor		-	+
P14046	Alpha-1-inhibitor 3 precursor	MUG1	-	+
P05155	Plasma protease C1 inhibitor precursor	SERPING1	-	+
P05154	Plasma serine protease inhibitor precursor	SERPINA5	-	+
Q9VAC5	ADAM 17-like protease precursor	ADAM17	-	+
Q9P0K1	ADAM 22 precursor	ADAM22	-	+
O15072	ADAMTS-3 precursor	ADAMTS3	-	+
P24268	Cathepsin D precursor	CTSD	-	+
P08311	Cathepsin G precursor	CTSG	-	+
O46427	Cathepsin H precursor	CTSH	-	+
P07154	Cathepsin L precursor	CTSL	-	+
Q9JL96	Cathepsin M precursor	CTSM	-	+
Q60994	Adiponectin precursor *	ADIPOQ	-	+
Q9Z1P8	Angiopoietin-related protein 4 precursor	ANGPTL4	-	+
P08226	Apolipoprotein E precursor	APOE	-	+
IMMUNE FACTORS				
P07151	Beta-2-microglobulin precursor	B2M	-	+
P02747	Complement C1q subcomponent, C chain precursor	C1QC	-	+
Q8CG16	Complement C1r-A subcomponent precursor	C1R	-	+
Q6P6T1	Complement C1s subcomponent precursor	C1S	-	+
Q811M5	Complement component C6 precursor	C6	-	+
P06682	Complement component C9	C9	-	+
P04186	Complement factor B precursor	CFB	-	+
P32038	Complement factor D precursor	CFD	-	+
P06909	Complement factor H precursor	CFH	-	+

Q9WUW3	Complement factor I precursor	CFI	-	+
INFLAMMATORY CYTOKINES				
Q61729	Interleukin-12 beta chain precursor		-	+
Q9H293	Interleukin-17E precursor	IL25	-	+
Q95141	Interferon-alpha/beta receptor beta chain precursor	IFNAR2	-	+
P34884	Macrophage migration inhibitory factor (MIF)	MIF	-	+
P19876	Macrophage inflammatory protein 2-beta precursor	CXCL3	-	+
P97885	Small inducible cytokine B5 precursor	CXCL6	-	+
COLLAGEN				
P02467	Collagen alpha 2(I) chain precursor	COL1A2	-	+
P01026	Complement C3 precursor	C3	-	+
P02463	Collagen alpha 1(IV) chain precursor	COL4A1	-	+
P08572	Collagen alpha 2(IV) chain precursor	COL4A2	-	+
P15989	Collagen alpha 3(VI) chain precursor	COL6A3	-	+
P25067	Collagen alpha 2(VIII) chain precursor	COL8A2	-	+
Q28902	Collagen alpha 1(XII) chain	COL12A1	-	+
O35206	Collagen alpha 1(XV) chain precursor	COL15A1	-	+
P39060	Collagen alpha 1(XVIII) chain precursor	COL18A1	-	+
P08253	72 kDa type IV collagenase precursor	MMP2	-	+
P08124	Cuticle collagen 1 precursor	COL1	-	+
O19092	Cystatin C precursor	CST3	-	+
EXTRACELLULAR MATRIX PROTEINS				
P48675	Desmin	DES	-	+
P04937	Fibronectin precursor	FN1	-	+
Q01129	Decorin precursor (Bone proteoglycan II)	DCN	-	+
Q00174	Laminin alpha chain precursor	LAMA	-	+
Q16787	Laminin alpha-3 chain precursor	LAMA3	-	+
Q16363	Laminin alpha-4 chain precursor	LAMA4	-	+
Q61001	Laminin alpha-5 chain precursor	LAMA5	-	+
P02469	Laminin beta-1 chain precursor	LAMB1	-	+
P02870	Lectin	LGALS9B	-	+

P36573	32 kDa beta-galactoside-binding lectin	GBP	-	+
P15838	Legumin A2 precursor		-	+
Q99538	Legumain precursor	LGMN	-	+
P30120	Metalloproteinase inhibitor 1 precursor (TIMP-1)	TIMP1	-	+
P24347	Matrix metalloproteinase-11	MMP11	-	+
GROWTH FACTORS				
O77681	Growth/differentiation factor 9 precursor		-	+
	Insulin-like growth factor binding protein 3 precursor	IGFBP3		
P17936	Insulin-like growth factor binding protein 7 precursor	IGFBP7	-	+
Q16270	Insulin-like growth factor IA precursor	IGF1	-	+
P01343				
OTHERS				
O08619	Coagulation factor XIII A chain precursor	F13A1	-	+
P19540	Coagulation factor IX precursor	F9	-	+
Q62959	Leptin receptor precursor	LEPR?	-	+
P11151	Lipoprotein lipase precursor	LPL	-	+
Q9BGI2	Peroxiredoxin 4	PRDX4	-	+
Q08761	Vitamin K-dependent protein S precursor	PROS1	-	+
P34740	Syndecan-1 precursor		-	+
P35441	Thrombospondin-1 precursor	THBS1	-	+
P49746	Thrombospondin-3 precursor	THBS3	-	+
Q9UBV4	Wnt-16 protein precursor	WNT16	-	+
P28133	Wnt-3a protein (Fragment)	WNT3A	-	+

Note: Proteins were identified from the medium conditioned with epididymal adipose tissue of Zucker obese rats with or without TZD treatment.

Figure S1. Glucose tolerant test in Zucker obese rats with rosiglitazone treatment. (A) Zucker obese rats with a 4 day treatment of rosiglitazone have no significant improvement in glucose tolerance. (B) Zucker obese rats with 12 day treatment of rosiglitazone have increased glucose tolerance.

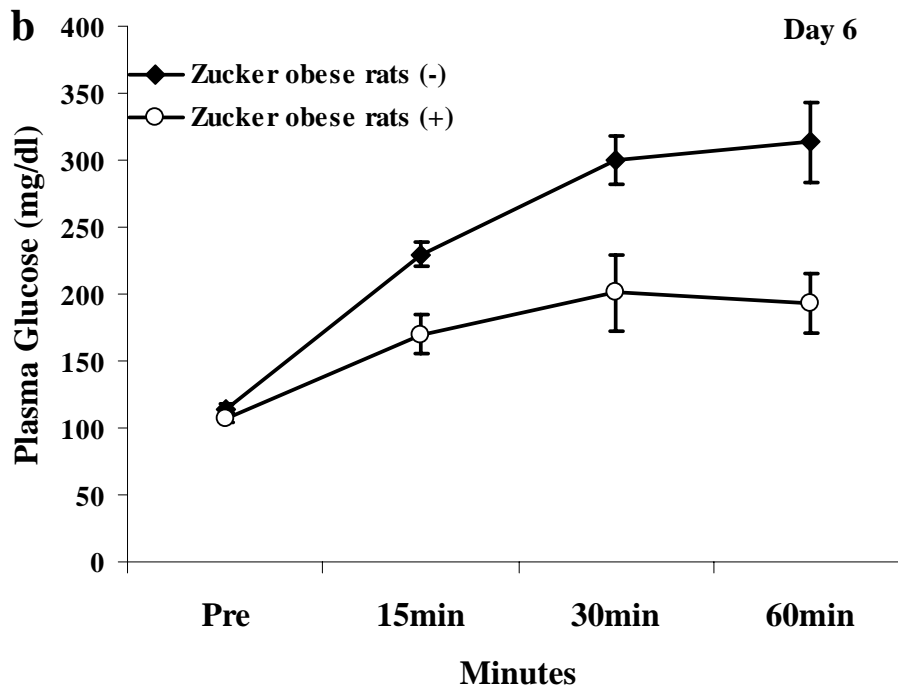
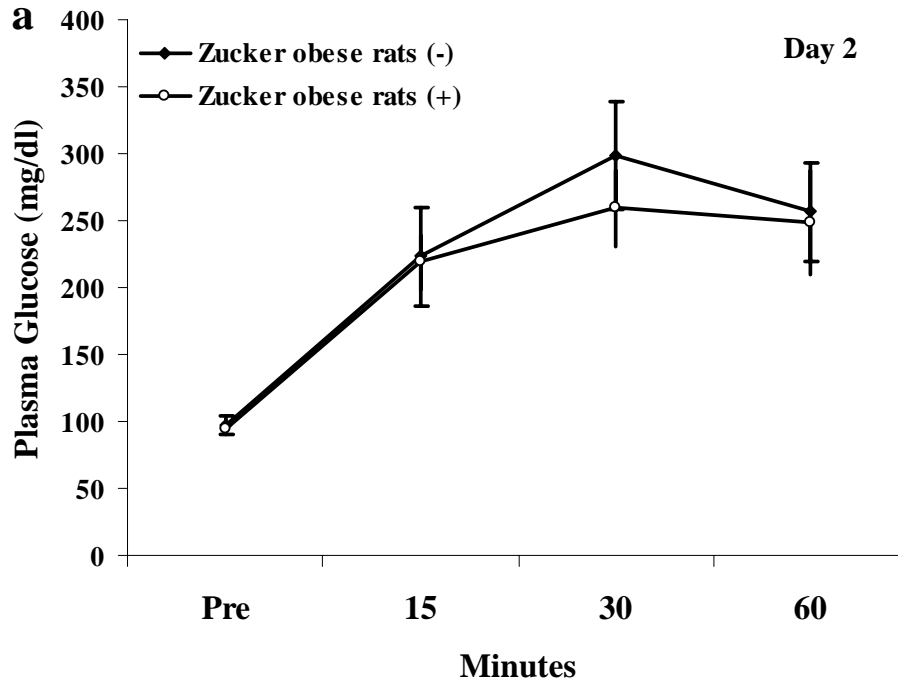


Table S2. Metabolic parameters in Zucker obese rats before and after Rosiglitazone treatment for 12 days

Treatment	NT	Rosi
Plasma glucose (mg/dl) (fasted)	150 ± 5.03	132 ± 15.82
Plasma TG (mg/dl)	300.78 ± 38.50	153.33 ± 19.42*
Plasma FFA (mM)	0.70 ± 0.12	0.39 ± 0.11*
Plasma adiponectin (µg/mL)	9.05 ± 0.73	11.71 ± 0.54*

Plasma levels of glucose, TG, FFA, and adiponectin were measured in Zucker obese rats (n = 8-12 rats from four experiments, 3 rats per group in each experiment) before and after treatment of Rosiglitazone for 12 days. Rats were fed a normal rodent diet, as described in material and methods section. Statistical analysis was performed by T-test. * p < 0.05 compared to non-treated rats (NT).

Table S3. Functional Analysis of TZD-Regulated Secretory Molecules From Obese Adipose Tissue

Functional Category	P-value	Molecules
Endocrine System Disorders	4.59E-13- 1.67E-04	B2M, APOE, SERPING1, COL4A1, FN1, LEPR, C1S, CLU, MMP2, IGFBP7, COL1A2, CTSD, IGF1, TIMP1, LPL, IGFBP3, SERPINE1, SERPINA3N, TIMP2, AGT
Metabolic Disease	4.59E-13- 1.77E-04	B2M, APOE, SERPING1, FN1, COL4A1, THBS1, LEPR, C1S, CLU, MMP2, IGFBP7, COL1A2, CTSD, ANGPTL4, IGF1, TIMP1, LPL, IGFBP3, SERPINE1, SERPINA3N, AGT
Immunological Disease	2.8E-12- 1.67E-04	B2M, APOE, SERPING1, FN1, LEPR, CLU, COL4A2, IGFBP7, IL25, C1R, COL1A2, CTSD, CXCL3, IGF1, TIMP1, CFH, TIMP2, AGT, MIF, THBS1, DCN, C1S, VIM, MMP2, CXCL6, IGFBP3, C4A, C6
Immune Response	1.36E-09- 1.5E-04	B2M, LAMA5, APOE, SERPING1, MIF, COL4A1, FN1, THBS1, CLU, CTSG, MMP2, IL25, CXCL6, CTSL2, CXCL3, IGF1, TIMP1, PROS1, CTSB, F9, C6, TIMP2, AGT

Inflammatory Disease	2.5E-09- 8.57E-06	B2M, APOE, MIF, FN1, THBS1, LEPR, CLU, VIM, MMP2, IGFBP7, COL4A2, IL25, CXCL6, C1R, CTSD, CXCL3, IGF1, TIMP1, POSTN, IGFBP3, C4A, CFH, AGT, TIMP2
Cellular Growth and Proliferation	2.75E-09- 3.02E-04	COL8A2, APOE, FN1, LEPR, PRDX4, CLU, COL4A2, IGFBP7, CTSL2, CTSD, CXCL3, LGMN, ANGPTL4, IGF1, TIMP1, POSTN, LAMB1, MMP11, SERPINE1, TIMP2, AGT, LAMA5, MIF, COL4A1, THBS1, DCN, VIM, MMP2, LAMA4, LAMA3, IGFBP3, CTSB, SPARC
Cardiovascular Disease	3.67E-09- 2.99E-04	B2M, APOE, ADAM17, FN1, LEPR, CLU, CTSG, CTSL2, CTSD, ANGPTL4, IGF1, TIMP1, PROS1, LPL, POSTN, MMP11, SERPINE1, AGT, TIMP2, COL4A1, THBS1, F13A1, MMP2, LAMA4, CTSB
Immune and Lymphatic System Development and Function	4.32E-08- 8.69E-05	B2M, LAMA5, APOE, MIF, FN1, LEPR, THBS1, IL25, CTSL2, CXCL3, IGF1, PROS1, LAMA3, CFH, C6, TIMP2, AGT
Connective Tissue Development and Function	5.68E-07- 2.99E-04	APOE, MIF, FN1, LEPR, MMP2, IGFBP7, CXCL3, IGF1, LPL, IGFBP3, SPARC, SERPINE1, AGT, TIMP2
Carbohydrate Metabolism	6.35E-07- 2.94E-04	APOE, LAMA5, MIF, SERPING1, FN1, THBS1, LEPR, CTSG, MMP2, CTSD, IGF1, LPL, CTSB, SERPINE1, AGT
Infectious Disease	1.34E-06- 2.18E-04	APOE, FN1, C1S, CLU, CXCL6, C1R, TIMP1, CFI, CTSB, F9, SPARC, SERPINE1, TIMP2
Amino Acid Metabolism	2.43E-06- 2.02E-04	IGF1, IGFBP3, AGT
Lipid Metabolism	3.25E-06- 1.5E-04	APOE, MIF, ANGPTL4, IGF1, LEPR, LPL, VIM, IGFBP7, AGT
Hepatic System Disease	1.44E-05- 1.44E-05	COL1A2, TIMP1, TIMP2
Endocrine System Development and Function	2.44E-05- 2.61E-04	FN1, IGF1, LEPR, IGFBP3, CLU, AGT
Cellular Function and Maintenance	7.51E-05- 7.51E-05	FN1, THBS1

Table S4. Pathway Analysis of TZD-Regulated Secretory Molecules From Obese Adipose Tissue

Pathway	-Log(P-value)	Ratio	Molecules
Complement System	1.34E+01	2.50E-01	C1R, CFD, SERPING1, C1S, C4A, CFI, C1QC, CFH, C6
Hepatic Fibrosis / Hepatic Stellate Cell Activation	7.95E+00	6.67E-02	COL1A2, FN1, IGF1, LEPR, TIMP1, IGFBP3, MMP2, TIMP2, AGT
Acute Phase Response Signaling	4.74E+00	3.98E-02	C1R, SERPING1, FN1, C1S, C4A, SERPINE1, AGT
Coagulation System	4.56E+00	1.08E-01	PROS1, F9, F13A1, SERPINE1
IGF-1 Signaling	2.03E+00	3.23E-02	IGF1, IGFBP3, IGFBP7
Leukocyte Extravasation Signaling	1.87E+00	2.07E-02	TIMP1, MMP2, MMP11, TIMP2
LXR/RXR Activation	1.33E+00	2.35E-02	APOE, LPL
Neuregulin Signaling	1.16E+00	2.15E-02	ADAM17, DCN
Axonal Guidance Signaling	9.78E-01	1.02E-02	ADAM17, ADAM22, IGF1, WNT16
Phenylalanine Metabolism	8.12E-01	9.35E-03	MIF
Antigen Presentation Pathway	7.77E-01	2.56E-02	B2M
Notch Signaling	7.56E-01	2.44E-02	ADAM17
Tyrosine Metabolism	5.87E-01	5.38E-03	MIF
IL-4 Signaling	5.51E-01	1.43E-02	B2M
Huntington's Disease Signaling	5.39E-01	8.62E-03	CTSD, IGF1
Ceramide Signaling	4.99E-01	1.22E-02	CTSD
VDR/RXR Activation	4.89E-01	1.25E-02	IGFBP3
Caveolar-mediated Endocytosis	4.89E-01	1.23E-02	B2M
TGF- β Signaling	4.89E-01	1.20E-02	SERPINE1
Role of Pattern Recognition Receptors in Recognition of Bacteria and Viruses	4.80E-01	1.18E-02	C1QC
FXR/RXR Activation	4.55E-01	1.00E-02	APOE
Glucocorticoid Receptor Signaling	4.53E-01	7.27E-03	SERPINE1, AGT
p53 Signaling	4.47E-01	1.15E-02	THBS1
Glycerolipid Metabolism	4.47E-01	6.90E-03	LPL
Amyotrophic Lateral Sclerosis Signaling	4.39E-01	9.26E-03	IGF1
Aryl Hydrocarbon Receptor Signaling	3.03E-01	6.58E-03	CTSD
Synaptic Long Term Depression	3.01E-01	6.21E-03	IGF1
14-3-3-mediated Signaling	2.68E-01	6.41E-03	VIM

Clatrin-mediated Endocytosis	2.66E-01	6.06E-03	IGF1
Wnt/ β -catenin Signaling	2.57E-01	6.06E-03	WNT16
RAR Activation	2.43E-01	5.49E-03	IGFBP3
IL-8 Signaling	2.43E-01	5.46E-03	MMP2
PPAR α /RXR α Activation	2.41E-01	5.49E-03	LPL
Protein Ubiquitination Pathway	2.21E-01	4.95E-03	B2M
LPS/IL-1 Mediated Inhibition of RXR Function	2.08E-01	5.05E-03	APOE
