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Supplementary Table 1: Human studies investigating the association of irisin with obesity, insulin resistance, diabetes mellitus and metabolic syndrome

Study	Study groups	Study Type	Subject of study	Irisin levels associated with			N	Irisin levels also associated with
				Obesity (BMI)	IR (HOMA-IR)	Diabetes		
Schlogl (1)	Healthy	CS	Nutrition	NR	NR	NR	66	Higher ad libitum 24 h energy intake associated with lower fasting irisin concentrations the following morning. Fasting irisin concentrations not related to subsequent energy intake.
Ko (2)	Healthy	CS	Nutrition	NR	NR	NR	185	Fruit consumption (positive)/ Meat consumption (negative)
Anastasilakis (3)	Healthy	CS	Nutrition	**No**	**No**	**NR**	36	No association with standardized meal, caloric intake or diet quality
Loffler (4)	Children and young adults	CS	Nutrition	**positive**	NR	NR	189	No changes after meal or OGTT Fat free mass, muscle mass and WHR (positive)
Pekkala (5)	Healthy	CS	Exercise	NR	NR	NR	56	No association with glucose tolerance
Crujeiras (6)	Obese following diet vs normal weight	PC	Obesity	**positive**	NR	NR	142	Waist circumference, fat mass (positive) Reduction in irisin levels after weight loss Return to baseline irisin after regaining the lost weight
Huh (7)	Healthy vs obese	CS	Obesity	**positive**	NR	NR	29/ 117	Muscle mass, glucose, ghrelin, IGF1 (positive) Age, insulin, cholesterol, adiponectin (negative) Irisin levels were reduced 6 months after bariatric surgery
Stengel (8)	Anorectic vs normal vs obese	CC	Obesity	**positive**	NR	NR	40	Fat mass, body cell mass, fat free mass, insulin (positive)
Pardo (9)	Anorexic vs	CC	Obesity	**positive**	**positive**	NR	145	Irisin higher in obese vs anorexic or normal weight

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	normal vs obese							Fat mass, resting energy expenditure (positive)
Gutierrez-Repiso (10)	Morbidly obese vs nonobese	CC	Obesity	**positive**	NR	NR	45	% change in waist to hip ratio after bariatric surgery (positive)
Huerta (11)	Overweight/ obese women	RCT	Obesity	**positive**	**positive**	NR	73	Glucose, insulin (positive). No change in irisin levels during OGTT Irisin reduction after weight loss
Li M (12)	PCOS vs healthy	CS	PCOS	**positive**	**positive**	NR	301	WHR, % FAT, TG, TC, LDLC, AUC Insulin, free androgen index (FAI) (positive)
Pukajlo (13)	PCOS vs healthy	CC	PCOS	NR	NR	NR	301	MetS in PCOS and in controls, body fat (positive)
Bostanci (14)	PCOS vs. matched healthy	CC	PCOS	**positive**	NR	NR	70	Higher in PCOS women compared to controls Fasting insulin, total cholesterol (positive)
Bluher (15)	Obese Children	PC	Obesity	NR	NR	NR	65	Irisin increase after one year physical activity and diet
Polyzos (16)	NAFL,NASH, obese, lean	CC	Obesity Liver	**negative**	**No**	NR	68	Lower irisin in obese, or with NASH/NAFLD vs lean No correlation with cardiometabolic risk factors
Choi (17)	NAFLD vs healthy	CC	Obesity Liver	**No**	**positive**	NR	355	Higher irisin levels in NAFLD compared with healthy No association with obesity
Huth (18)	Healthy trained /untrained, obese, obese with IGT	CC	Obesity insulin resistance	**positive**	**positive (M/I index)**	NR	53	Fat mass (positive) Muscle citrate synthase, fitness (negative)
Crujeiras (19)	Obese after 8 week diet	PC	Insulin resistance	NR	**positive**	NR	136	Irisin levels paralleled body weight reduction after the dietary treatment (week 8) and returned to the baseline levels at 24 weeks in patients regaining the lost weight.
Sesti (20)	White	CS	Insulin	**positive**	**positive**	NR	192	Fasting and 2h post-load insulin (positive)

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	nondiabetic adults		resistance	**Fat mass**	**Matsuda index**			Intima media thickness (positive) Insulin stimulated glucose disposal, Matsuda index, insulin clearance (negative)
Reinehr (21)	Obese, normal weight children	PC	Insulin resistance	**No**	**positive**	NR	60	Irisin in obese/IFG > as in obese/NGT or normal weight HDL, fasting glucose, 2h Glucose in OGTT (positive)
Chen (22)	Healthy, obese, obese with acanthosis nigricans	CC	Insulin resistance	**positive**	**(positive) Higher fasting insulin**	NR	80	Higher irisin in obese with acanthosis nigricans vs obese without acanthosis nigricans or healthy
Qiu (23)	Nondiabetic adults	MA	Insulin resistance	NR	**positive**	NR	1912	The positive association between irisin and insulin resistance was small, but independent of BMI
Norheim (24)	Prediabetic vs healthy	PC	Obesity prediabetes	NR	NR	**positive**	26	Higher irisin level in prediabetes vs normal controls No association of irisin with chronic exercise
Sanchis-Gomar (25)	T2DM vs obese vs healthy	CS	Obesity prediabetes	**No**	NR	NR	153	Similar irisin levels between morbidly obese patients with atherogenic dyslipidemia vs without, as well as between obese diabetic patients vs nonobese diabetics. Urea, insulin in the nonobese diabetic group (negative) Homocystein, HbA1c in obese diabetic (negative)
Kurdiova (25)	T2DM, IGT,overweight/ obese, healthy	CS	prediabetes T2DM	**No**	**No Euglycemic hyperinsulinemic clamp**	**negative**	99	Lower irisin levels in T2DM subjects vs lean controls Waist circumference, fasting glucose, AUC glycemic curve, visceral obesity (negative)
Assyov (26)	NGT, prediabetes, T2DM	CC	prediabetes T2DM	**positive**	NR	**negative**	160	Lower irisin levels in T2DM< Prediabetes< NGT Fasting glucose, ALT, AST, GGT (negative)

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Duran (27)	T2DM vs IFG vs IGT vs NGT	CS	prediabetes T2DM	**negative**	NR	**negative**	263	Lower irisin in IFG, IGT or T2DM subjects vs NGT HDLC (positive) / postprandial glucose, LDLC, triglyceride (negative)
Liu (28)	T2DM vs nondiabetic controls	CS	T2DM	**positive** **NonDM**	NR	**negative**	156	No association with metabolic phenotype in T2DM Total cholesterol, triglycerides, fasting glucose, diastolic pressure in nondiabetic controls (positive)
Yang (29)	Healthy without T2DM but with 1st degree relat. with T2DM	CS	T2DM	**No**	**No**	**No**	122	No association with metabolic parameters in T2DM group HbA1c, eGFR, HOMAβ in NGT (positive)
Xiang (30)	Newly diagnos. T2DM, healthy	CS	T2DM	NR	NR	**negative**	222	Flow mediated dilatation(positive)
Zhang (31)	T2DM with vs without MVD vs healthy	CS	T2DM	NR	NR	**negative**	94	Irisin levels in T2DM with MVD < T2DM without MVD < healthy controls
Wang (32)	NGT vs T2DM	CS	T2DM	NR	**negative**	**negative**	140	No association with beta cell function related variables
Choi (33)	NGT vs new onset T2DM	CS	T2DM	NR	NR	**negative**	208	Reduced odds of newly diagnosed T2DM (positive) 2 h plasma glucose (negative)
Al-Daghri (34)	T2DM vs controls	CS	T2DM	NR	NR	**positive**	164	Frequency intensity time index (only in control group) (positive) DBP (overall), lean body mass (T2DM group) (negative)
Hu (35)	T2DM with/ without retinopathy	CC	T2DM diabetic retinopathy	NR	**negative**	**negative**	240	Lower irisin levels in T2DM group compared with control Fasting glucose, blood urea nitrogen, creatinine, age (negative) Creatinine clearance, ACE/ATII blocker use (positive)

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Liu (36)	T2DM with wide range of renal function	CS	T2DM nephro-pathy	**positive**	NR	NR	365	Higher irisin levels in T2DM with chronic kidney disease compared to T2DM without CKD. Fat mass, % fat mass, eGFR (positive) Age, pulse pressure (in T2DM patients with normal renal function) (negative)
Wang (37)	T2DM vs healthy controls	CS	T2DM nephro-pathy	NR	NR	**negative**	200	Irisin in T2DM macroalbuminuria < microalbuminuria < normoalbuminuria. 2h blood glucose, urinary albumin excretion (negative) Flow mediated dilation (positive)
Zhang (38)	Meta-Analysis	MA	T2DM	NR	NR	**negative**	1110	Lower irisin levels in T2DM compared to healthy
Espes (39)	T1DM, healthy	CS	T1DM	NR	NR	NR	70	Higher in T1DM compared to healthy controls
Lopez-Legarrea (40)	Excessive obese with MetS after diet	RCT	Obesity MetS	**positive**	**(positive)**	NR	96	Fat mass, carbohydrate intake (positive) / Circulating glucose (negative) Higher irisin associated with greater reduction on glucose, insulin, HOMA-IR, triglycerides after diet.
Park (41)	Caucasian, African Americans without history of MI, stroke, or DM	CS	MetS	**positive**	**positive**		151	Increased risk of MetS (positive) Fasting blood glucose, high triglycerides, low HDL, SBP, DBP (positive) Adiponectin (negative)
Moreno (42)	Active vs sedentary	CC	MetS	**positive**	**positive**	NR	428	Fasting insulin, fasting triglycerides in sedentary individuals (positive)
Hwang (43)	Seoul Metro City Diabetes	CS	MetS	**negative**	**negative**	**negative**	424	Favorable metabolic income: less obese, lower blood pressure and glucose (positive)

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	Prevention Pr.							Skeletal muscle mass (positive)
Yan (44)	Chinese with central obesity	CS	MetS	**No**	**No**	NR	1115	Reduced risk of metabolic syndrome, glucose (positive) Fasting insulin, HbA1c, albumin/globulin ratio (negative) No associations with blood pressure, triglycerides, HDL
Hirsch (45)	Prader Willi vs healthy BMI matched	CC	MetS	NR	**negative**	NR	51	Salivary irisin was higher in Prader-Willi syndrome Total cholesterol, LDL-Cholesterol, leptin, triglycerides in PWS (positive) HDL-Cholesterol in Prader-Willi Syndrome (negative)
Huh (46)	MetS vs healthy	PC	MetS exercise	NR	NR	NR	20	Similar increase of irisin levels in subjects with vs without MetS after exercise
Aronis (47)	Patient with ACS/ established coronary artery disease vs controls	CC PC	CV	NR	NR	NR	349	No association between irisin levels and ACS Major adverse cardiovascular events in patients with established coronary artery disease after PCI (positive) Did not predict the development of ACS
Emanuele (48)	Centenarians, young healthy, young with MI	CC	CV	NR	NR	NR		Irisin in young patients with myocardial infarction < young healthy patients < centenarians
Aydin (49)	AMI, matched controls	CC	CV	NR	NR	NR	25	Troponin I, CKMB and CK in AMI- Irisin measured in saliva (positive) Gradual decrease of saliva/serum irisin over 48h after AMI
de la Iglesia (50)	Caucasian with MetS in an energy restricted	PC	Lipid profile	NR	NR	NR	93	Total cholesterol, LDL, Apolipoprotein B (positive)

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	programme							
Panagiotou (51)	Overweight/obese with diabetes or two other CV risk factors	CS	Lipid profile	NR	NR	NR	39	HDL, large HDL particles and omentin (negative)
Wen (52)	CKD vs healthy	CC	Renal metabolic	**No**	NR	NR	57	Blood urea nitrogen (negative) HDL (positive)
Brondani (53)	T2DM vs Nondiabetic	CC	SNPs	NR	NR	NR	1440	FNDC5 gene: SNP rs3480: HbA1c levels in T2DM patients (positive) SNP rs1746661:Increased systolic blood pressure, total cholesterol and LDL (positive)
Staiger (54)	German families at increased risk for T2DM	CS	SNPs / Insulin resistance	NR	**positive**	NR	1976	rs16835198 and rs726344 of *FNDC5* with measures of insulin sensitivity (positive)
Ebert (55)	General population	CS	SNPs	NR	NR	NR	> 1000	Fat mass, fasting glucose, dyslipidemia (negative) Irisin decreased during OGTT in subjects with NGT, IFG, IGT or T2DM No association of rs726344 FNDC5 with irisin levels
Tanisawa (56)	Japanese men	CS	SNPs	NR	**No**	NR	163	No association of rs3480 and rs16835198 of *FNDC5* with circulating irisin
Zhao (57)	GDM, healthy	CC	GDM	NR	NR	**negative**	122	DBP, fasting blood glucose (negative)
Yuksel (58)	GDM, pregnant	CC	GDM	NR	NR	**negative**	40	No association with maternal age, gestational week at birth, BMI at birth, birth weight, neonatal height, systolic and diastolic blood pressure.

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								BMI at birth, as well as with HOMA-IR (negative)
Kuzmicki (59)	GDM, BMImatched NGT	CC	GDM	NR	NR	**negative**	270	Irisin levels increase in gestation, but this increase is lower in GDM compared to NGT controls.
Erol (60)	GDM, pregnant	CC	GDM	NR	NR	**negative**	50	Irisin levels lower in GDM vs controls in the first trimester
Ebert (61)	GDM, pregnant	CC	GDM	NR	NR	**No**	148	Similar irisin levels between GDM and controls Increased irisin after delivery in GDM compared to normal Fasting insulin during pregnancy (positive)
Garces (62)	Pregnant vs preeclamptic vs eumenorrheic	CC	GDM	NR	**positive**	**negative**	70	Irisin was lower in preeclamptic vs pregnant controls in the 3rd trimester of gestation. HOMA IR in the first trimester of normal pregnancy (positive)

(positive) positive association, (negative) negative association; CC, casecontrol study; CS, crosssectional study; PC, prospective cohort study; RCT, randomized controlled trial; (A)MI, (acute) myocardial infarction; CV, cardiovascular; DBP, diastolic blood pressure; MVD, macrovascular disease; NGT, normal glucose tolerance; IGT, impaired glucose tolerance; IFG, impaired fasting glucose; GDM, gestational diabetes mellitus; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus; MetS, metabolic syndrome; SNPs, single nucleotide polymorphism

References

1. Schlogl M, Piaggi P, Votruba SB, Walter M, Krakoff J, Thearle MS. Increased 24-hour ad libitum food intake is associated with lower plasma irisin concentrations the following morning in adult humans. Appetite. 2015;90:154-9.
2. Ko BJ, Park KH, Shin S, Zaichenko L, Davis CR, Crowell JA, et al. Diet quality and diet patterns in relation to circulating cardiometabolic biomarkers. Clin Nutr. 2015.
3. Anastasilakis AD, Polyzos SA, Saridakis ZG, Kynigopoulos G, Skouvaklidou EC, Molyvas D, et al. Circulating irisin in healthy, young individuals: day-night rhythm, effects of food intake and exercise, and associations with gender, physical activity, diet, and body composition. J Clin Endocrinol Metab. 2014;99(9):3247-55.
4. Loffler D, Muller U, Scheuermann K, Friebe D, Gesing J, Bielitz J, et al. Serum irisin levels are regulated by acute strenuous exercise. J Clin Endocrinol Metab. 2015;100(4):1289-99.
5. Pekkala S, Wiklund PK, Hulmi JJ, Ahtiainen JP, Horttanainen M, Pollanen E, et al. Are skeletal muscle FNDC5 gene expression and irisin release regulated by exercise and related to health? J Physiol. 2013;591(21):5393-400.
6. Crujeiras AB, Zulet MA, Lopez-Legarrea P, de la Iglesia R, Pardo M, Carreira MC, et al. Association between circulating irisin levels and the promotion of insulin resistance during the weight maintenance period after a dietary weight-lowering program in obese patients. Metabolism. 2014;63(4):520-31.
7. Huh JY, Panagiotou G, Mougios V, Brinkoetter M, Vamvini MT, Schneider BE, et al. FNDC5 and irisin in humans: I. Predictors of circulating concentrations in serum and plasma and II. mRNA expression and circulating concentrations in response to weight loss and exercise. Metabolism. 2012;61(12):1725-38.
8. Stengel A, Hofmann T, Goebel-Stengel M, Elbelt U, Kobelt P, Klapp BF. Circulating levels of irisin in patients with anorexia nervosa and different stages of obesity--correlation with body mass index. Peptides. 2013;39:125-30.
9. Pardo M, Crujeiras AB, Amil M, Aguera Z, Jimenez-Murcia S, Banos R, et al. Association of irisin with fat mass, resting energy expenditure, and daily activity in conditions of extreme body mass index. Int J Endocrinol. 2014;2014:857270.
10. Gutierrez-Repiso C, Garcia-Serrano S, Rodriguez-Pacheco F, Garcia-Escobar E, Haro-Mora JJ, Garcia-Arnes J, et al. FNDC5 could be regulated by leptin in adipose tissue. Eur J Clin Invest. 2014;44(10):918-25.
11. Huerta AE, Prieto-Hontoria PL, Fernandez-Galilea M, Sainz N, Cuervo M, Martinez JA, et al. Circulating irisin and glucose metabolism in overweight/obese women: effects of alpha-lipoic acid and eicosapentaenoic acid. J Physiol Biochem. 2015;71(3):547-58.
12. Li M, Yang M, Zhou X, Fang X, Hu W, Zhu W, et al. Elevated circulating levels of irisin and the effect of metformin treatment in women with polycystic ovary syndrome. J Clin Endocrinol Metab. 2015;100(4):1485-93.
13. Pukajlo K, Laczmanski L, Kolackov K, Kuliczkowska-Plaksej J, Bolanowski M, Milewicz A, et al. Irisin plasma concentration in PCOS and healthy subjects is related to body fat content and android fat distribution. Gynecol Endocrinol. 2015;31(11):907-11.
14. Bostanci MS, Akdemir N, Cinemre B, Cevrioglu AS, Ozden S, Unal O. Serum irisin levels in patients with polycystic ovary syndrome. Eur Rev Med Pharmacol Sci. 2015;19(23):4462-8.
15. Bluher S, Panagiotou G, Petroff D, Markert J, Wagner A, Klemm T, et al. Effects of a 1-year exercise and lifestyle intervention on irisin, adipokines, and inflammatory markers in obese children. Obesity (Silver Spring). 2014;22(7):1701-8.
16. Polyzos SA, Kountouras J, Anastasilakis AD, Geladari EV, Mantzoros CS. Irisin in patients with nonalcoholic fatty liver disease. Metabolism. 2014;63(2):207-17.
17. Choi ES, Kim MK, Song MK, Kim JM, Kim ES, Chung WJ, et al. Association between serum irisin levels and non-alcoholic fatty liver disease in health screen examinees. PLoS One. 2014;9(10):e110680.

18. Huth C, Dubois MJ, Marette A, Tremblay A, Weisnagel SJ, Lacaille M, et al. Irisin is more strongly predicted by muscle oxidative potential than adiposity in non-diabetic men. J Physiol Biochem. 2015;71(3):559-68.
19. Crujeiras AB, Pardo M, Arturo RR, Navas-Carretero S, Zulet MA, Martinez JA, et al. Longitudinal variation of circulating irisin after an energy restriction-induced weight loss and following weight regain in obese men and women. Am J Hum Biol. 2014;26(2):198-207.
20. Sesti G, Andreozzi F, Fiorentino TV, Mannino GC, Sciacqua A, Marini MA, et al. High circulating irisin levels are associated with insulin resistance and vascular atherosclerosis in a cohort of nondiabetic adult subjects. Acta Diabetol. 2014;51(5):705-13.
21. Reinehr T, Elfers C, Lass N, Roth CL. Irisin and its relation to insulin resistance and puberty in obese children: a longitudinal analysis. J Clin Endocrinol Metab. 2015;100(5):2123-30.
22. Chen JQ, Fang LJ, Song KX, Wang XC, Huang YY, Chai SY, et al. Serum Irisin Level is Higher and Related with Insulin in Acanthosis Nigricans-related Obesity. Exp Clin Endocrinol Diabetes. 2015.
23. Qiu S, Cai X, Yin H, Zugel M, Sun Z, Steinacker JM, et al. Association between circulating irisin and insulin resistance in non-diabetic adults: A meta-analysis. Metabolism. 2016;65(6):825-34.
24. Norheim F, Langleite TM, Hjorth M, Holen T, Kielland A, Stadheim HK, et al. The effects of acute and chronic exercise on PGC-1alpha, irisin and browning of subcutaneous adipose tissue in humans. FEBS J. 2014;281(3):739-49.
25. Sanchis-Gomar F, Alis R, Pareja-Galeano H, Sola E, Victor VM, Rocha M, et al. Circulating irisin levels are not correlated with BMI, age, and other biological parameters in obese and diabetic patients. Endocrine. 2014;46(3):674-7.
26. Assyov Y, Gateva A, Tsakova A, Kamenov Z. Irisin in the Glucose Continuum. Exp Clin Endocrinol Diabetes. 2016;124(1):22-7.
27. Duran ID, Gulcelik NE, Unal M, Topcuoglu C, Sezer S, Tuna MM, et al. Irisin levels in the progression of diabetes in sedentary women. Clin Biochem. 2015;48(18):1268-72.
28. Liu JJ, Wong MD, Toy WC, Tan CS, Liu S, Ng XW, et al. Lower circulating irisin is associated with type 2 diabetes mellitus. J Diabetes Complications. 2013;27(4):365-9.
29. Yang M, Chen P, Jin H, Xie X, Gao T, Yang L, et al. Circulating levels of irisin in middle-aged first-degree relatives of type 2 diabetes mellitus - correlation with pancreatic beta-cell function. Diabetol Metab Syndr. 2014;6(1):133.
30. Xiang L, Xiang G, Yue L, Zhang J, Zhao L. Circulating irisin levels are positively associated with endothelium-dependent vasodilation in newly diagnosed type 2 diabetic patients without clinical angiopathy. Atherosclerosis. 2014;235(2):328-33.
31. Zhang M, Chen P, Chen S, Sun Q, Zeng QC, Chen JY, et al. The association of new inflammatory markers with type 2 diabetes mellitus and macrovascular complications: a preliminary study. Eur Rev Med Pharmacol Sci. 2014;18(11):1567-72.
32. Wang L, Song J, Wang C, Lin P, Liang K, Sun Y, et al. Circulating Levels of Betatrophin and Irisin Are Not Associated with Pancreatic beta-Cell Function in Previously Diagnosed Type 2 Diabetes Mellitus Patients. J Diabetes Res. 2016;2016:2616539.
33. Choi YK, Kim MK, Bae KH, Seo HA, Jeong JY, Lee WK, et al. Serum irisin levels in new-onset type 2 diabetes. Diabetes Res Clin Pract. 2013;100(1):96-101.
34. Al-Daghri NM, Alokail MS, Rahman S, Amer OE, Al-Attas OS, Alfawaz H, et al. Habitual physical activity is associated with circulating irisin in healthy controls but not in subjects with diabetes mellitus type 2. Eur J Clin Invest. 2015;45(8):775-81.
35. Hu W, Wang R, Li J, Zhang J, Wang W. Association of irisin concentrations with the presence of diabetic nephropathy and retinopathy. Ann Clin Biochem. 2016;53(Pt 1):67-74.
36. Liu JJ, Liu S, Wong MD, Tan CS, Tavintharan S, Sum CF, et al. Relationship between circulating irisin, renal function and body composition in type 2 diabetes. J Diabetes Complications. 2014;28(2):208-13.

37. Wang HH, Zhang XW, Chen WK, Huang QX, Chen QQ. Relationship between serum irisin levels and urinary albumin excretion in patients with type 2 diabetes. J Diabetes Complications. 2015;29(3):384-9.
38. Zhang C, Ding Z, Lv G, Li J, Zhou P, Zhang J. Lower irisin level in patients with type 2 diabetes mellitus: A case-control study and meta-analysis. J Diabetes. 2016;8(1):56-62.
39. Espes D, Lau J, Carlsson PO. Increased levels of irisin in people with long-standing Type 1 diabetes. Diabet Med. 2015;32(9):1172-6.
40. Lopez-Legarrea P, de la Iglesia R, Crujeiras AB, Pardo M, Casanueva FF, Zulet MA, et al. Higher baseline irisin concentrations are associated with greater reductions in glycemia and insulinemia after weight loss in obese subjects. Nutr Diabetes. 2014;4:e110.
41. Park KH, Zaichenko L, Brinkoetter M, Thakkar B, Sahin-Efe A, Joung KE, et al. Circulating irisin in relation to insulin resistance and the metabolic syndrome. J Clin Endocrinol Metab. 2013;98(12):4899-907.
42. Moreno M, Moreno-Navarrete JM, Serrano M, Ortega F, Delgado E, Sanchez-Ragnarsson C, et al. Circulating irisin levels are positively associated with metabolic risk factors in sedentary subjects. PLoS One. 2015;10(4):e0124100.
43. Hwang YC, Jeon WS, Park CY, Youn BS. The ratio of skeletal muscle mass to visceral fat area is a main determinant linking circulating irisin to metabolic phenotype. Cardiovasc Diabetol. 2016;15:9.
44. Yan B, Shi X, Zhang H, Pan L, Ma Z, Liu S, et al. Association of serum irisin with metabolic syndrome in obese Chinese adults. PLoS One. 2014;9(4):e94235.
45. Hirsch HJ, Gross I, Pollak Y, Eldar-Geva T, Gross-Tsur V. Irisin and the Metabolic Phenotype of Adults with Prader-Willi Syndrome. PLoS One. 2015;10(9):e0136864.
46. Huh JY, Siopi A, Mougios V, Park KH, Mantzoros CS. Irisin in response to exercise in humans with and without metabolic syndrome. J Clin Endocrinol Metab. 2015;100(3):E453-7.
47. Aronis KN, Moreno M, Polyzos SA, Moreno-Navarrete JM, Ricart W, Delgado E, et al. Circulating irisin levels and coronary heart disease: association with future acute coronary syndrome and major adverse cardiovascular events. Int J Obes (Lond). 2015;39(1):156-61.
48. Emanuele E, Minoretti P, Pareja-Galeano H, Sanchis-Gomar F, Garatachea N, Lucia A. Serum irisin levels, precocious myocardial infarction, and healthy exceptional longevity. Am J Med. 2014;127(9):888-90.
49. Aydin S, Kobat MA, Kalayci M, Eren MN, Yilmaz M, Kuloglu T, et al. Decreased saliva/serum irisin concentrations in the acute myocardial infarction promising for being a new candidate biomarker for diagnosis of this pathology. Peptides. 2014;56:141-5.
50. de la Iglesia R, Lopez-Legarrea P, Crujeiras AB, Pardo M, Casanueva FF, Zulet MA, et al. Plasma irisin depletion under energy restriction is associated with improvements in lipid profile in metabolic syndrome patients. Clin Endocrinol (Oxf). 2014;81(2):306-11.
51. Panagiotou G, Mu L, Na B, Mukamal KJ, Mantzoros CS. Circulating irisin, omentin-1, and lipoprotein subparticles in adults at higher cardiovascular risk. Metabolism. 2014;63(10):1265-71.
52. Wen MS, Wang CY, Lin SL, Hung KC. Decrease in irisin in patients with chronic kidney disease. PLoS One. 2013;8(5):e64025.
53. Brondani LA, Boelter G, Assmann TS, Leitao CB, Canani LH, Crispim D. Irisin-encoding gene (FNDC5) variant is associated with changes in blood pressure and lipid profile in type 2 diabetic women but not in men. Metabolism. 2015;64(9):952-7.
54. Staiger H, Bohm A, Scheler M, Berti L, Machann J, Schick F, et al. Common genetic variation in the human FNDC5 locus, encoding the novel muscle-derived 'browning' factor irisin, determines insulin sensitivity. PLoS One. 2013;8(4):e61903.
55. Ebert T, Kralisch S, Wurst U, Scholz M, Stumvoll M, Kovacs P, et al. Association of metabolic parameters and rs726344 in FNDC5 with serum irisin concentrations. Int J Obes (Lond). 2016;40(2):260-5.

56. Tanisawa K, Taniguchi H, Sun X, Ito T, Cao ZB, Sakamoto S, et al. Common single nucleotide polymorphisms in the FNDC5 gene are associated with glucose metabolism but do not affect serum irisin levels in Japanese men with low fitness levels. Metabolism. 2014;63(4):574-83.
57. Zhao L, Li J, Li ZL, Yang J, Li ML, Wang GL**.** Circulating irisin is lower in gestational diabetes mellitus. Endocr J. 2015;62(10):921-6.
58. Yuksel MA, Oncul M, Tuten A, Imamoglu M, Acikgoz AS, Kucur M, et al. Maternal serum and fetal cord blood irisin levels in gestational diabetes mellitus. Diabetes Res Clin Pract. 2014;104(1):171-5.
59. Kuzmicki M, Telejko B, Lipinska D, Pliszka J, Szamatowicz M, Wilk J, et al. Serum irisin concentration in women with gestational diabetes. Gynecol Endocrinol. 2014;30(9):636-9.
60. Erol O, Erkal N, Ellidag HY, Isenlik BS, Aydin O, Derbent AU, et al. Irisin as an early marker for predicting gestational diabetes mellitus: a prospective study. J Matern Fetal Neonatal Med. 2016;29(22):3590-5.
61. Ebert T, Stepan H, Schrey S, Kralisch S, Hindricks J, Hopf L, et al. Serum levels of irisin in gestational diabetes mellitus during pregnancy and after delivery. Cytokine. 2014;65(2):153-8.
62. Garces MF, Peralta JJ, Ruiz-Linares CE, Lozano AR, Poveda NE, Torres-Sierra AL, et al. Irisin levels during pregnancy and changes associated with the development of preeclampsia. J Clin Endocrinol Metab. 2014;99(6):2113-9.