



YOUR Weight Management genetic test Scientific Evidence Summary

FABP2 Ala54Thr (A54T) polymorphism

FABP2 protein is found in small intestine epithelial cells where it strongly influences fat absorption.

The FABP2 gene encodes the intestinal form of fatty acid binding protein2 (FABP2). FABP2 protein is found in small intestine epithelial cells where it strongly influences fat absorption.

Variations in DNA or polymorphisms in the gene result in greater binding of the fatty acids (released in the intestine from dietary fat consumption) which in turn results in higher absorption of fat **(1, 2)**. One such polymorphism, Ala54Thr, has been found to be associated with obesity. Multiple clinical research studies have indicated that individuals with the Thr54 form of the protein show increased absorption and/or processing of dietary fatty acids by the intestine. The Thr54 variant has been associated with elevated BMI and body fat **(3)**, increased abdominal fat **(4)**, and obesity and higher leptin levels (protein hormone that plays a key role in regulating energy intake and energy expenditure, including appetite and metabolism) **(5)**. Multiple dietary intervention clinical research studies show that the Ala54Thr polymorphism affects the response to changes in dietary fat in test meals. It has been reported that individuals with two copies

of the 54Thr/Thr variant show increased levels of postprandial triglycerides **(6, 7)** and increased levels of 14-18-carbon fatty acids **(8, 9)** compared with the 54Ala/Ala form of the protein. A group of obese, non-diabetic patients analyzed before and three months after a lifestyle modification program, consisting of hypocaloric diet (1,520 kcal/day) and aerobic exercise three times per week, **(10)** showed that carriers of the Thr54 allele (compared to the wild-type 54Ala/Ala homozygotes) failed to have a significant reduction in fat mass, LDL-cholesterol levels, and leptin levels. Other studies have demonstrated an association between FABP2 genotype and dietary fat intake, with moderate carbohydrate intake **(11, 12)**.

PPARG Pro12Ala (P12A) polymorphism

Peroxisome proliferator-activated receptor-gamma (PPARG) protein is abundantly expressed in fat cells and plays a key role in the formation of fat cells. It is crucial to lipid (fat) metabolism. Polymorphisms in this gene that are responsible for expression of variant forms of the protein have been associated with the development of type 2 diabetes. The variant form of the protein (Ala12) is associated with a decreased binding affinity to its target genes and thus with a reduction in its ability to regulate the expression of these target genes **(13)**. According to the 2005 obesity gene map **(14)**, multiple studies show association between PPARG gene and obesity involving the Pro12Ala polymorphism. Multiple clinical studies showed that individuals with the 12Pro/Pro form of the protein were more affected by the amount of fat in the diet **(15)** and had a direct association between higher BMI and the amount of fat intake as opposed to the Ala12 carriers **(16)**. These findings clearly indicated that 12Pro/Ala (carriers of one copy of the allele) individuals are more sensitive to the amount of fat in the diet **(17)**. Similarly, in a 3-year dietary and exercise intervention study, 12Ala/Ala subjects showed higher weight loss than in Pro12/Ala or in 12Pro/Pro subjects. Clinical studies consistently show that Pro12 allele is the high-risk allele and 12Pro/Pro subjects are more sensitive to the amount of fat in the diet, more resistant to weight loss and at increased risk of diabetes. The evidence of gene-diet interaction is strong.

PPARG protein is abundantly expressed in fat cells and plays a key role in the formation of fat cells.

ADRB2 Arg16Gly (R16E) and Gln27Glu (Q27E) polymorphisms

The beta-2 adrenergic receptor (ADRB2) gene product ADRB2 protein is expressed in fat cells. This receptor protein is involved in the mobilization of fat from the fat cells for energy in response to hormones called catecholamines (adrenaline, noradrenaline and dopamine). Several polymorphisms of this gene that result in amino acid changes have been identified. The two main well-characterized polymorphisms Arg16Gly and Gln27Glu are the most common in Caucasians. Laboratory studies indicate that these polymorphisms affect the overall expression (production) of the receptor **(18)**. The recent obesity gene map **(14)** shows association between variants in the ADRB2 gene and obesity, with most of the positive findings involving the Arg16Gly or Gln27Glu polymorphisms. Multiple studies show association between Glu27 and Gly16 alleles carriers and abdominal **(19, 20)** and central obesity **(21)**. A long-term clinical study showed that weight gain from childhood to adulthood **(22)** and weight gain during adulthood **(23, 24)** are higher in individuals who carry the Gly16 allele. A clinical study involving women with high carbohydrate diet reported that women with 27Gln/Glu genetic makeup had increased risk of obesity, while no association of obesity was observed in 27Gln/Gln women **(25)**.

27Gln/Gln was found to be a risk genetic profile in studies involving overfeeding of identical twins where higher weight gain and subcutaneous fat were observed compared to those with the Glu27 allele **(26)**. A study of overweight Japanese men enrolled in a 24-month weight loss program (1,600 kcal/day and aerobic exercise one hour daily) showed that men with the Gly16 allele were more resistant to weight loss and more likely to regain body weight after 6 months **(23)**. Women who were more active during their leisure time and were carriers of the Glu27 allele had higher BMI compared to similarly-active carriers, suggesting that these women may be more resistant to losing weight **(27)**. Results from intervention studies (exercise or diet) involving the Arg16Gly polymorphism indicate Gly16 allele is the high-risk allele, especially in studies involving exercise and endurance training. Long-term studies suggest that the Gly16 allele is associated with greater weight gain over time. Results from association studies suggest that the Glu27 allele is associated with an increased risk of obesity, abdominal obesity and obesity when adhering to a high carbohydrate diet.

ADRB2 receptor protein is involved in the mobilization of fat from the fat cells for energy in response to hormones called catecholamines (adrenaline, noradrenaline, and dopamine).

ADRB3 Trp64Arg (R64W) polymorphism

The beta-3 adrenergic receptor (ADRB3) protein is expressed in visceral adipose tissue and the fat depot where it is involved in the regulation of fat breakdown (lipolysis). Laboratory studies on isolated fat cells (adipocytes) show that the Trp64Arg polymorphism in the gene results in reduced lipolysis in response to a specific agonist in cells carrying the Arg64 allele **(28)**. Multiple clinical studies showed that Arg64 variant on the ADRB3 gene is strongly associated with increased BMI **(29-32)**. A case-control study (158 obese, 154 normal weight) showed an increased risk of obesity (OR = 2.98) in Arg64 carriers, but only in subjects who were sedentary **(33)**. A study of 61 obese women with type 2 diabetes enrolled in a 3-month intervention combining low-calorie diet and exercise showed that women with the Arg64 variant lost less weight (4.6 kg vs. 8.3 kg) and body mass (1.9 kg/m² vs. 3.4 kg/m²) than 64Trp/Trp women **(34)**. A study performed in 76 perimenopausal women enrolled in a 3-month intervention combining exercise and diet found that 48% of the women with the Arg64 variant lost weight compared to 69% of the women without the variant **(35)**. These two studies suggest that the variant is associated with difficulty in losing weight through diet and exercise. A study **(36)** performed on 29 men and 41 women showed that ADRB3 Arg64 carriers experienced greater loss of fat mass and trunk fat following 24 weeks of supervised aerobic exercise training compared to non-carriers.

The ADRB3 protein is involved in the regulation of fat breakdown (lipolysis).

ADRB2 Arg16Gly (R16E) and ADRB3 Trp64Arg (R64W) polymorphisms and Exercise

A number of studies have investigated the role of ADRB 2 and 3 polymorphisms on the risk of developing obesity and assessed the effect of physical activity on this risk. In a case-control study it was observed that the effect of the ADRB3 variant on obesity changes depending on the recreational physical activity levels **(37)**. Physical activity for each individual was evaluated based on a validated questionnaire about their leisure-time physical activities. Metabolic Equivalent Task (MET) value was assigned to each activity and a composite value of total weekly MET-hours per participant was computed. The ratio (M/S) between METs hours/week in physical activity (M) and the time spent sitting down during leisure time (S) was used to predict recreational energy expenditure. An increased obesity risk among carriers of the mutation (Arg64) was dramatically diminished when subjects had recreational energy expenditure levels higher than the median (M/S > 0.5). In the HERITAGE Family Study, it was observed that carriers of Arg16 and Arg64 alleles, respectively, for β 2- and β 3- adrenergic receptors showed a greater decrease in fat mass in response to endurance training (METs > 6) than subjects with other allelic combinations **(38)**. In a study conducted on 313 Spanish subjects, it was observed that carriers of Arg64 alleles in the ADRB3 gene could reduce the risk of developing obesity if their physical activity level was ≥ 20 MET hours/week **(37)**. Several observational studies have reported that women, who are overweight or obese at the time of diagnosis as well as who gain weight after diagnosis, are at greater risk for breast cancer recurrence and death than the non-overweight women **(39)**. To determine whether ADRB3 polymorphism (Trp64Arg) is associated with obesity and levels of subcutaneous or visceral fat in African-American breast cancer cases, a clinical study was conducted on 219 African-American breast cancer patients **(39)**. Each household or recreational activity was categorized as light (<3 METs), moderate (3-6 METs) or vigorous (>6 METs) intensity based on The Compendium of Physical Activities by Ainsworth et. al. **(40)**. The results from this study showed that physical activity modifies the effect of ADRB3 on obesity **(39)**. Consistent with the study of Spanish subjects **(33)**, these findings also indicated that the higher risk of obesity among carriers of the ADRB3 variant (Arg64) may be altered by moderate levels of physical activity (>13 MET hours/week).

ADRB2 and ADRB3 polymorphisms respond differently to differing amounts of physical activity.

References

1. **Baier LJ, Sacchettini JC, Knowler WC, Eads J, Paolisso G, Tataranni PA, Mochizuki H, Bennett PH, Bogardus C, and Prochazka M.** An amino acid substitution in the human intestinal fatty acid binding protein is associated with increased fatty acid binding, increased fat oxidation, and insulin resistance. *J Clin Invest* 95: 1281-1287, 1995.
2. **Levy E, Menard D, Delvin E, Stan S, Mitchell G, Lambert M, Ziv E, Feoli-Fonseca JC, and Seidman E.** The polymorphism at codon 54 of the FABP2 gene increases fat absorption in human intestinal explants. *J Biol Chem* 276: 39679-39684, 2001.
3. **Hegele RA, Harris SB, Hanley AJ, Sadikian S, Connelly PW, and Zinman B.** Genetic variation of intestinal fatty acid-binding protein associated with variation in body mass in aboriginal Canadians. *J Clin Endocrinol Metab* 81: 4334-4337, 1996.
4. **Yamada K, Yuan X, Ishiyama S, Koyama K, Ichikawa F, Koyanagi A, Koyama W, and Nonaka K.** Association between Ala54Thr substitution of the fatty acid-binding protein 2 gene with insulin resistance and intra-abdominal fat thickness in Japanese men. *Diabetologia* 40: 706-710, 1997.
5. **Albala C, Santos JL, Cifuentes M, Villarroel AC, Lera L, Liberman C, Angel B, and Perez-Bravo F.** Intestinal FABP2 A54T polymorphism: association with insulin resistance and obesity in women. *Obes Res* 12: 340-345, 2004.
6. **Pratley RE, Baier L, Pan DA, Salbe AD, Storlien L, Ravussin E, and Bogardus C.** Effects of an Ala54Thr polymorphism in the intestinal fatty acid-binding protein on responses to dietary fat in humans. *J Lipid Res* 41: 2002-2008, 2000.
7. **Agren JJ, Valve R, Vidgren H, Laakso M, and Uusitupa M.** Postprandial lipemic response is modified by the polymorphism at codon 54 of the fatty acid-binding protein 2 gene. *Arterioscler Thromb Vasc Biol* 18: 1606-1610, 1998.
8. **Agren JJ, Vidgren HM, Valve RS, Laakso M, and Uusitupa MI.** Postprandial responses of individual fatty acids in subjects homozygous for the threonine- or alanine-encoding allele in codon 54 of the intestinal fatty acid binding protein 2 gene. *Am J Clin Nutr* 73: 31-35, 2001.
9. **Lefevre M, Lovejoy JC, Smith SR, Delany JP, Champagne C, Most MM, Denkins Y, de Jonge L, Rood J, and Bray GA.** Comparison of the acute response to meals enriched with cis- or trans-fatty acids on glucose and lipids in overweight individuals with differing FABP2 genotypes. *Metabolism* 54: 1652-1658, 2005.
10. **de Luis DA, Aller R, Izaola O, Gonzalez Sagrado M, and Conde R.** Influence of ALA54THR Polymorphism of Fatty Acid Binding Protein 2 on Lifestyle Modification Response in Obese Subjects. *Ann Nutr Metab* 50: 354-360, 2006.
11. **Marin C, Perez-Jimenez F, Gomez P, Delgado J, Paniagua A, Lozano A, Cortes B, Jimenez-Gomez Y, Gomez M, Lopez-Miranda J.** The ala54 polymorphism of the fatty acid-binding protein 2 gene is associated with a change in insulin sensitivity after a change in the type of dietary fat. *Am J Clin Nutr* 82: 196-200, 2005.
12. **Takakura Y, Yohsioka K, Umekawa T, Kogure A, Toda H, Yoshikawa T, Yoshida T.** Thr54 allele of the FABP2 gene affects resting metabolic rate and visceral obesity. *Diab Res Clin Pract* 67: 36-42, 2005.
13. **Deeb SS, Fajas L, Nemoto M, Pihlajamaki J, Mykkanen L, Kuusisto J, Laakso M, Fujimoto W, and Auwerx J.** A Pro12Ala substitution in PPARgamma2 associated with decreased receptor activity, lower body mass index and improved insulin sensitivity. *Nat Genet* 20: 284-287, 1998.
14. **Rankinen T, Zuberi A, Chagnon YC, Weisnagel J, Argyropoulos G, et al.** The human obesity gene map: The 2005 update. *Obesity* 14: 529-644, 2005.
15. **Robitaille J, Despres JP, Perusse L, and Vohl MC.** The PPAR-gamma P12A polymorphism modulates the relationship between dietary fat intake and components of the metabolic syndrome: results from the Quebec Family Study. *Clin Genet* 63: 109-116, 2003.
16. **Memisoglu A, Hu PJ, Hankinson SE, Manson JE, De Vivo I, Willet WC, and Hunter DJ.** Interaction between a peroxisome proliferator-activated receptor gamma gene polymorphism and dietary fat intake in relation to body mass. *Hum Mole Genet* 12: 2923-2929, 2001.
17. **Lindi VI, Uusitupa MI, Lindstrom J, Louheranta A, Eriksson JG, Valle TT, Hamalainen H, Ilanne-Parikka P, Keinänen-Kiukaanniemi S, Laakso M, and Tuomilehto J.** Association of the Pro12Ala polymorphism in the PPAR-gamma2 gene with 3-year incidence of type 2 diabetes and body weight change in the Finnish Diabetes Prevention Study. *Diabetes* 51: 2581-2586, 2002.
18. **Green SA, Turki J, Innis M, and Liggett SB.** Amino-terminal polymorphisms of the human beta 2-adrenergic receptor impart distinct agonist-promoted regulatory properties. *Biochemistry* 33: 9414-9419, 1994.
19. **Lange LA, Norris JM, Langefeld CD, Nicklas BJ, Wagenknecht LE, Saad MF, and Bowden DW.** Association of adipose tissue deposition and beta-2 adrenergic receptor variants: the IRAS family study. *Int J Obes (Lond)* 29: 449-457, 2005.
20. **Gonzalez Sanchez JL, Proenza AM, Martinez Larrad MT, Ramis JM, Fernandez Perez C, Palou A, and Serrano Rios M.** The glutamine 27 glutamic acid polymorphism of the beta2-adrenoceptor gene is associated with abdominal obesity and greater risk of impaired glucose tolerance in men but not in women: a population-based study in Spain. *Clin Endocrinol (Oxf)* 59: 476-481, 2003.
21. **Masuo K, Katsuya T, Kawaguchi H, Fu Y, Rakuga H, et al.** B2-adrenoreceptor polymorphisms relate to obesity through blunted leptin-mediated sympathetic activation. *Am J Hypertens*, 19: 1084-91, 2006.
22. **Ellsworth DL, Coady SA, Chen W, Srinivasan SR, Elkasabany A, Gustat J, Boerwinkle E, and Berenson GS.** Influence of the beta2-adrenergic receptor Arg16Gly polymorphism on longitudinal changes in obesity from childhood through young adulthood in a biracial cohort: the Bogalusa Heart Study. *Int J Obes Relat Metab Disord* 26: 928-937, 2002.

23. **Masuo K, Katsuya T, Fu Y, Rakugi H, Ogiwara T, and Tuck ML.** Beta2- and beta3-adrenergic receptor polymorphisms are related to the onset of weight gain and blood pressure elevation over 5 years. *Circulation* 111: 3429-3434, 2005.
24. **van Rossum CT, Hoebee B, Seidell JC, Bouchard C, van Baak MA, de Groot CP, Chagnon M, de Graaf C, and Saris WH.** Genetic factors as predictors of weight gain in young adult Dutch men and women. *Int J Obes Relat Metab Disord* 26:517-528, 2002.
25. **Martinez JA, Corbalan MS, Sanchez-Villegas A, Forga L, Marti A, and Martinez-Gonzalez MA.** Obesity risk is associated with carbohydrate intake in women carrying the Gln27Glu beta2-adrenoceptor polymorphism. *J Nutr* 133: 2549-2554, 2003.
26. **Ukkola O, Tremblay A, and Bouchard C.** Beta-2 adrenergic receptor variants are associated with subcutaneous fat accumulation in response to long-term overfeeding. *Int J Obes Relat Metab Disord* 25: 1604-1608, 2001.
27. **Corbalan MS.** The 27Glu polymorphism of the beta2-adrenergic receptor gene interacts with physical activity influencing obesity risk among female subjects. *Clin Genet* 61: 305-307, 2002.
28. **Umekawa T, Yoshida T, Sakane N, Kogure A, Kondo M, and Honjo H.** Trp64Arg mutation of beta3-adrenoceptor gene deteriorates lipolysis induced by beta3-adrenoceptor agonist in human omental adipocytes. *Diabetes* 48: 117-120, 1999.
29. **Hoffstedt J, Poirier O, Thorne A, Lonnqvist F, Herrmann SM, Cambien F, and Arner P.** Polymorphism of the human beta3-adrenoceptor gene forms a well-conserved haplotype that is associated with moderate obesity and altered receptor function. *Diabetes* 48: 203-205, 1999.
30. **Allison DB, Heo M, Faith MS, and Pietrobelli A.** Meta-analysis of the association of the Trp64Arg polymorphism in the beta3 adrenergic receptor with body mass index. *Int J Obes Relat Metab Disord* 22: 559-566, 1998.
31. **Fujisawa T, Ikegami H, Kawaguchi Y, and Ogiwara T.** Meta-analysis of the association of Trp64Arg polymorphism of beta 3-adrenergic receptor gene with body mass index. *J Clin Endocrinol Metab* 83: 2441-2444, 1998.
32. **Kurokawa N, Nakai K, Kameo S, Liu ZM, and Satoh H.** Association of BMI with the beta3-adrenergic receptor gene polymorphism in Japanese: meta-analysis. *Obes Res* 9: 741-745, 2001.
33. **Marti A, Corbalan MS, Martinez-Gonzalez MA, and Martinez JA.** TRP64ARG polymorphism of the beta 3-adrenergic receptor gene and obesity risk: effect modification by a sedentary lifestyle. *Diabetes Obes Metab* 4: 428-430, 2002.
34. **Sakane N, Yoshida T, Umekawa T, Kogure A, Takakura Y, and Kondo M.** Effects of Trp64Arg mutation in the beta 3-adrenergic receptor gene on weight loss, body fat distribution, glycemic control, and insulin resistance in obese type 2 diabetic patients. *Diabetes Care* 20: 1887-1890, 1997.
35. **Shiwaku K, Nogi A, Anuurad E, Kitajima K, Enkhmaa B, Shimono K, and Yamane Y.** Difficulty in losing weight by behavioral intervention for women with Trp64Arg polymorphism of the beta3-adrenergic receptor gene. *Int J Obes Relat Metab Disord* 27: 1028-1036, 2003.
36. **Phares DA, Halverstadt AA, Shuldiner AR, Ferrell RE, Douglass LW, Ryan AS, Goldberg AP, and Hagberg JM.** Association between body fat response to exercise training and multilocus ADR genotypes. *Obes Res* 12: 807-815, 2004.
37. **Corbalan MS, Marti A, Forga L, Martinez-Gonzalez MA, and Martinez JA.** The risk of obesity and the Trp64Arg polymorphism of the beta3-adrenergic receptor: effect of modification by age. *Ann Nutr Metab* 46: 152-158, 2002.
38. **Ukkola O, Rankinen T, Rice T, Gagnon J, Leon AS, Skinner JS, Wilmore JH, Rao DC, and Bouchard C.** Interactions among the beta2- and beta3- adrenergic receptor genes and total body fat and abdominal fat levels in the HERITAGE Family Study. *Int J Obes* 27: 389-393, 2003.
39. **McKean-Cowdin R, Li X, Bernstein L, McTiernan A, Ballard-Barbash R, Gauderman WJ, and Gilliland F.** The ADRB3 Trp64Arg variant and obesity in African-American breast cancer cases. *Int J Obes* 31: 1110-1118, 2008.
40. **Ainsworth BE, Haskell WL, Whitt MC, Irwin ML, Swartz AM, Strath SJ, O'Brien WL, Bassett DR, Schmitz KH, Emplaincourt PO, Jacobs DR, and Leon AS.** Compendium of physical activities: an update of activity codes and MET intensities. *Med Sci Sports Exerc* 32 (Suppl 9): S498-S504, 2000.

Additional Sources:

- Tchernof A, Starling RD, Walston JD, Shuldiner AR, et al.** Obesity-related phenotypes and the β 3-adrenoreceptor gene variant in postmenopausal women. *Diabetes* 48: 1425-1428, 1999.
- Deeb SS, Fajas L, Nemoto M, Pihlajamaki J, Mykkanen L, Kuusisto J, Laakso M, Fujimoto W, and Auwerx J.** A Pro12Ala substitution in PPAR γ 2 associated with decreased receptor activity, lower body mass index and improved insulin sensitivity. *Nat Genet* 20: 284-287, 1998.
- Masugi J, Tamori Y, Mori H, Koike T, and Kasuga M.** Inhibitory effect of a proline-to-alanine substitution at codon 12 of peroxisome proliferator-activated receptor- γ 2 on thiazolidinedione-induced adipogenesis. *Biochem Biophys Res Commun* 268: 178-182, 2000.
- Kahara T, Takamura T, Hayakawa T, Nagai Y, Yamaguchi H, Katsuki T, Katsuki K, Katsuki M, and Kobayashi K.** PPAR γ gene polymorphism is associated with exercise-mediated changes of insulin resistance in healthy men. *Metabolism* 52: 209-212, 2003.
- Adamo KB, Sigal RJ, Williams K, Kenny G, Prud'homme D, and Tesson F.** Influence of Pro12Ala peroxisome proliferator-activated receptor γ 2 polymorphism on glucose response to exercise training in type 2 diabetes. *Diabetologia* 48: 1503-1509, 2005.
- Weiss EP, Kulaputana O, Ghiu IA, Brandauer J, Wohn CR, Phares DA, Shuldiner AR, and Hagberg JM.** Endurance training-induced changes in the insulin response to oral glucose are associated with the peroxisome proliferator-activated receptor- γ 2 Pro12Ala genotype in men but not in women. *Metabolism* 54: 97-102, 2005.
- Guettier J, Georgopoulos A, Tsai M, Radha V, Shanthrani S, Deepa R, Gross M, Rao G, Mohan V.** Polymorphisms in the fatty acid-binding protein 2 and apolipoprotein c-III genes are associated with the metabolic syndrome and dyslipidemia in a south Indian population. *J Clin Endocrinol Metab* 90: 1705-1711, 2004.
- Pollex R, Hanley A, Zinman B, Harris S, Khan H, Hegele R.** Metabolic syndrome in aboriginal Canadians: prevalence and genetic associations. *Atherosclerosis* 184: 121-129, 2006.
- Karani S, Radha V, Mohan V.** Thr54 allele carriers of the Ala54Thr variant of FABP2 gene have associations with metabolic syndrome and hypertriglyceridemia in urban South Indians. *Metabolism Clinical and Experimental* 55: 1222-12226, 2006.
- Pereira M, Swain J, Goldfine A, Rifai N, Ludwig D.** Effects of a low-glycemic load diet on resting energy expenditure and heart disease risk factors during weight loss. *JAMA* 292(20): 2482-2490, 2004.
- Hallikainen M, Toppinen L, Mykkanen H, Agren J, Laaksonen D, Miettinen T, Niskanen L, Poutanen K, Gylling H.** Interaction between cholesterol and glucose metabolism during dietary carbohydrate modification in subjects with the metabolic syndrome. *Am J Clin Nutr* 84: 1385-1392, 2006.
- Kallio P, Kolehmainen M, Laaksonen D, Kekalainen J, Salopuro T, Sivenius K, Pulkkinen L, Mykkanen H, Niskanen L, Uusitupa M, Poutanen K.** Dietary carbohydrate modification induces alterations in gene expression in abdominal subcutaneous adipose tissue in persons with the metabolic syndrome: the FUNGENUT study. *Am J Clin Nutr* 85: 1417-1427, 2007.
- Paradis A-M, Fontaine-Bisson B, Bosse Y, Robitaille J, Lemieux S, Jaques H, Lamarche B, Tchernof A, Couture P, Vohl M-C.** The peroxisome proliferator-activated receptor α Leu162Val polymorphism influences the metabolic response to a dietary intervention altering fatty acid proportions in healthy men. *Am J Clin Nutr* 81: 523-30, 2005.
- Macho-Azcarate T, Marti A, Gonzalez A, Martinez JA, Ibanez J.** Gln27Glu polymorphism in the beta2 adrenergic receptor gene and lipid metabolism during exercise in obese women. *Int J Obesity* 26: 1434-41, 2002.
- Kahara T, Hayakawa T, Nagai Y, Shimizu A, Takamura T.** Gln27Glu polymorphism of the β 2 adrenergic receptor gene in healthy Japanese men is associated with the change of fructosamine level caused by exercise. *Diabet Res Clin Practice* 64: 207-12, 2004.
- Marti A, Corbalan MS, Martinez-Gonzalez MA.** CHO intake alters obesity risk associated with Pro12Ala polymorphism of PPARG gene. *J. Physiol. Biochem.*, 58(4): 219-220, 2002.
- Frosch D, Mello P, Lerman C.** Behavioral consequences of testing for obesity risk. *Cancer Epidemiol Biomarkers Prev* 14: 1485-1489, 2005.