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EXPRESSION OF PROTEIN PHOSPHATASE DUSP GENES IN SUBCUTANEOUS ADIPOSE TISSUE OF OBESE MEN WITH NORMAL AND IMPAIRED GLUCOSE TOLERANCE

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We studied the expression of genes encodes the family of DUSP protein phosphatases in subcutaneous adipose tissue and isolated adipocytes of two groups of obese men: with normal and impaired glucose tolerance as compared to control group (lean men). It was shown that the expression level of DUSP1, DUSP4, DUSP6, DUSP22, and PTEN genes is decreased both in subcutaneous adipose tissue and in isolated adipocytes of obese men with normal glucose tolerance as compared to control group. Magnitude of obesity-mediated changes in expression levels of these genes was gene specific and more robust in the case of protein phosphatase DUSP4. In the group of obese men with glucose intolerance the level of DUSP1, DUSP4, DUSP6, and DUSP22 gene expressions in subcutaneous adipose tissue and isolated adipocytes was also decreased as compared to control group, but was significantly higher than in obese patients with normal glucose tolerance. Results of this study provide evidence that the expression of protein phosphatase family DUSP and PTEN genes is decreases in subcutaneous adipose tissue and isolated adipocytes of obese men with normal glucose tolerance and these changes possibly associated with developing of obesity and metabolic abnormalities. However, impaired glucose tolerance in obesity is associated with up-regulation of DUSP1, DUSP4, DUSP6, and DUSP22 gene expressions.

Key words: mRNA expression, DUSP1, DUSP4, DUSP6, DUSP22, PTEN, subcutaneous adipose tissue, adipocytes, obesity, glucose intolerance.

Introduction. The obesity and its metabolic complications are the most profound public health problems and associated with dysregulation of basic metabolic processes, including cell proliferation and sensitivity to insulin action (Bray and Young, 2009; Huang et al., 2011; Kovac et al., 2009; Scott et al., 2008). In obese individuals adipose tissue is at the center of metabolic complications and increased body weight. Moreover, obesity as well as metabolic syndrome results from tight interactions between genes and environmental factors. Several molecular and cellular studies have demonstrated relationships between the development of metabolic abnormalities and the disruption of circadian rhythms through dysregulation of circadian and numerous other gene expressions, including genes encoding protein kinases and protein phosphatases for phosphorylation and dephosphorylation of different regulatory factors (Green et al., 2008; Ramsey et al., 2007; Ando et al., 2011; Shimba et al., 2011; Duong et al., 2011; Lombardi et al., 2012; Shaw et al., 2009; Ozcan et al., 2004).

Protein phosphatases regulate a wide array of different physiological events, including cellular growth and proliferation, mitochondrial function and biogenesis, and activity of factors that have been linked to insulin resistance, obesity and its metabolic complications (Ruderman et al., 2013; Wang and Kaufman, 2012). Cell cycle progression is a key player in the cell proliferation and is very precisely controlled by a multitude of enzymatic reactions among which protein dephosphorylation, carried out by a family of dual specificity phosphatases (DUSP), plays an important role (Song et al., 2012; Groschl et al., 2013). The family of these protein phosphatases inactivates their target kinases by dephosphorylating both the phosphoserine/threonine and phosphotyrosine residues, controlling its activity during the meiotic cell cycle, especially kinases, which are tightly associated with cellular proliferation (Casteel et al., 2010; Cagnol et al., 2013; Degl'Innocenti et al., 2013; Piya et al., 2013; Li et al., 2010).

Thus, expression of the MAP kinase phosphatase DUSP4 is associated with increased cell proliferation (Groschl et al., 2013). Moreover, protein phosphatase DUSP1 is essential for the prevention of apoptosis induced by deoxynivalenol

in the epithelial cell line HepG2 (Casteel et al., 2010). It is interesting that DUSP6, as a novel transcriptional target of TP53, regulates TP53-mediated apoptosis by modulating expression levels of BCL2 family proteins (Piya et al., 2013). This protein phosphatase is overexpressed in thyroid carcinoma and contributes to neoplastic properties of thyroid cancer cells (Degl'Innocenti et al., 2013). Recently was shown that activation of the MEK/ERK signaling pathway promotes expression of dual-specificity phosphatase 4 resulting in nuclear ERK1/2 inhibition (Cagnol et al., 2013).

Moreover, JNK pathway-associated phosphatase (dual specificity phosphatase 22 also known as mitogen-activated protein kinase phosphatase X) activates the JNK signaling pathway by dephosphorylation of stress-activated protein kinase/c-Jun N-terminal kinase (SAPK/JNK) as well as focal adhesion kinase and suppresses cell migration (Li et al., 2010). Tumor suppressor gene *PTEN* (phosphatase and tensin homolog) represents dual-specificity protein phosphatase and phosphatidylinositol 3,4,5-trisphosphate 3-phosphatase. It contains a tensin like domain as well as a catalytic domain similar to that of the dual specificity protein tyrosine phosphatases. Unlike most of the protein tyrosine phosphatases, PTEN preferentially dephosphorylates phosphoinositide substrates and is involved in the regulation of the cell cycle, preventing cells from growing and dividing too rapidly as well as controls insulin signaling and glucose homeostasis (Kechagioglou et al., 2014; Dean et al., 2014). It was also shown that effect of PTEN mutations is an apparently divergent: increased risks of obesity and cancer but a decreased risk of type 2 diabetes (Hodakoski et al., 2014; Pal et al., 2012).

It is possible that identification of the mechanisms of metabolic abnormalities in obesity and its complications at molecular and cellular levels will be useful for better understanding the developing of obesity and associated with obesity metabolic complications. However, a detailed molecular mechanism of the involvement of DUSP protein phosphatase regulatory networks in the development of obesity and its metabolic complications are not clear yet and remains to be determined.

Because the function of some protein phosphatases is closely linked to metabolic homeostasis and these enzymes can modulate the intracellular signaling network and lead to development of obesity and its metabolic complications (insulin resistance and glucose intolerance), the main goal of this work was to study the role of the expressions of DUSP protein phosphatase genes in subcutaneous adipose tissue of obese individuals for evaluation of its possible significance to development of human obesity and glucose intolerance.

Material and Methods. The 18 male subjects participate in this study. They were divided into three equal groups (6 men in each group): lean individuals as control and patients with obesity and with or without glucose intolerance. Subjects studied were recruited from the patients' cohort at Institute of Experimental Endocrinology Slovak Academy of Sciences. All participants gave written informed consent and the studies were approved by the local research ethics committees of Institute of Experimental Endocrinology.

Clinical characteristics of the study participants were previously described (Ratushna O.O. et al., 2012). The lean (control) participants were individuals with mean age 45 ± 8 years and mean body mass index (BMI) 23 ± 1.4 kg/m^2. The obese participants with normal glucose tolerance as well as the patients with glucose intolerance were individuals with mean age (45 ± 8 and 44 ± 7 years, correspondingly) and mean BMI (32 ± 1.4 and 34 ± 1.4 kg/m^2, correspondingly). Thus, BMI, which is a main criteria of obesity, in these last two groups of patients was significantly higher (+39 and +48 %, correspondingly; $P<0.05$) as compared to the group of control individuals. Moreover, obese men with normal glucose tolerance have significantly lower insulin sensitivity index (-35 %; $P<0.05$). In obese individuals with impaired glucose tolerance, versus obese subjects with normal glucose tolerance, the 2h OGTT (oral glucose tolerance test) and fasting insulin level were significantly increased (+47 and +62 %, correspondingly; $P<0.05$). At the same time, insulin sensitivity index was decreased almost two fold; $P<0.05$. Thus, a group of obese patients with impaired glucose tolerance has insulin resistance.

RNasy Lipid Tissue Mini Kit (QIAGEN, Germany) was used for RNA extraction from subcutaneous adipose tissue or isolated adipocytes of lean and obese individuals with normal or impaired glucose tolerance according to manufacturer's protocol. Adipocytes were isolated from subcutaneous adipose tissue as described (Considine et al., 1997).

The expression levels of genes related to regulation of an angiogenesis (*DUSP1, DUSP4, DUSP6,* and *DUSP22*) were measured in subcutaneous fat tissue by real-time quantitative polymerase chain reaction of complementary DNA (cDNA). QuaniTect Reverse Transcription Kit (QIAGEN, Germany) was used for cDNA synthesis. The 7900 HT Fast Real-Time PCR System (Applied Biosystems), Absolute QPCR SYBRGreen Mix (Thermo Scientific, UK) and pair of primers specific

for each studied gene (Sigma, USA) were used for quantitative polymerase chain reaction.

For investigation of serine/threonine specific protein phosphatase DUSP1 (dual specificity phosphatase 1), also known as MKP2 (mitogen-activated protein kinase phosphatase 2), gene expression we used next forward and reverse primers: (5'–ctgccttgatcaacgtctca–3') and (5'–acccttcctccagcattctt–3'). The nucleotide sequences of these primers correspond to sequences 850-869 and 1009-990 of human DUSP1 cDNA (GenBank accession number NM_004417). The size of amplified fragment is 160 bp.

The amplification of DUSP4 (dual specificity phosphatase 4) also known as MKP2 (mitogen-activated protein kinase phosphatase 2) cDNA was performed using forward primer (5'–aggcggctatgagaggtttt –3') and reverse primer (5'–cactgccgaggtagaggaag –3'). These oligonucleotides correspond to sequences 904 – 923 and 1094 – 1075 of human DUSP4 cDNA (GenBank accession number NM_005923). The size of amplified fragment is 191 bp.

For amplification of serine/threonine specific protein phosphatase DUSP6 (dual specificity phosphatase 6), known as mitogen-activated protein kinase phosphatase 3 (MKP3) cDNA we used forward (5'–ccggctttacttctgtctcg–3') and reverse (5'–tgtgcgacgactcgtatagc–3') primers. The nucleotide sequences of these primers correspond to sequences 310-329 and 628-609 of human DUSP6 cDNA (GenBank accession number NM_001946). The size of amplified fragment is 319 bp.

The amplification of DUSP22 (dual specificity phosphatase 22), known as mitogen-activated protein kinase phosphatase X (MKPX) and JNK-stimulatory phosphatase-1 (JSP1), cDNA was performed using forward (5'–tcctcctccctgtaacatgc–3') and reverse (5'–gctgggatgcacaggtattt–3') primers. The nucleotide sequences of these primers correspond to sequences 366-385 and 603-584 of human DUSP22 cDNA (GenBank accession number NM_020185). The size of amplified fragment is 238 bp.

For amplification of PTEN (phosphatase and tensin homolog), known as dual-specificity protein phosphatase and phosphatidylinositol 3,4,5-trisphosphate 3-phosphatase PTEN, cDNA we used forward (5'–accaggaccagaggaaacct–3' and reverse (5'–gctagcctctggatttgacg–3') primers. The nucleotide sequences of these primers correspond to sequences 1871-1890 and 2111-2092 of human PTEN cDNA (GenBank accession number NM_000314). The size of amplified fragment is 241 bp.

The amplification of beta-actin (ACTB) cDNA was performed using forward - 5'–ggacttcgagcaagagatgg –3' and reverse - 5'–agcactgtgttggcgtacag –3' primers. These primers nucleotide sequences correspond to 747 – 766 and 980 – 961 of human *ACTB* cDNA (GenBank accession number NM_001101). The size of amplified fragment is 234 bp. The expression of beta-actin mRNA was used as control of analyzed RNA quantity. The primers were received from "Sigma" (USA).

The expression of beta-actin mRNA was used as control of analyzed RNA quantity. The amplified DNA fragments were analyzed on a 2 % agarose gel and that visualized by 5x Sight DNA Stain (EUROMEDEA). An analysis of quantitative PCR was performed using special computer program "Differential expression calculator".

Statistical analyses were performed according to Student's *t*-test using OriginPro 7.5 software. All values are expressed as mean ± SEM from six independent experiments; $P < 0.05$ was considered as significant difference.

Results and Discussion. The expression of genes encodes several dual specificity protein phosphatases was studied in subcutaneous adipose tissue and adipocytes, isolated from this tissue, of two groups of obese men (with normal and impaired glucose tolerance) and control group (lean individuals) for estimation of its possible significance in the development of obesity and metabolic complications, including glucose intolerance. As shown in fig. 1, the expression level of mRNA of dual specificity protein phosphatase DUSP1, also known as MKP1 (mitogen-activated protein kinase phosphatase 1), in subcutaneous adipose tissue of obese men with normal glucose tolerance is decreased (-28 %, $P < 0.05$) as compared to control group, but in adipocytes, isolated from this tissue, these changes were stronger (more than two fold, $P < 0.05$). At the same time, in the group of obese individuals with glucose intolerance the level of protein phosphatase DUSP1 gene expressions in subcutaneous adipose tissue and isolated adipocytes was significantly higher than in obese patients with normal glucose tolerance (+17 and +20 %, correspondingly; $P < 0.05$).

Investigation of the expression of protein phosphatase DUSP4, also known as MKP2 (mitogen-activated protein kinase phosphatase 2), clearly demonstrates that in subcutaneous adipose tissue of obese men with normal glucose tolerance this protein phosphatase mRNA expression level is decreased (close to three fold, $P < 0.05$) as compared to control group (Fig. 2). Moreover, in adipocytes, isolated from this adipose tissue, more robust changes were observed in the expression level of DUSP4 mRNA (four fold, $P < 0.05$). As shown in Fig. 2, both in subcutaneous adipose tissue and in isolated adipocytes we found an increased level of this protein phosphatase mRNA (+18 and +36 %, correspondingly; $P < 0.05$).

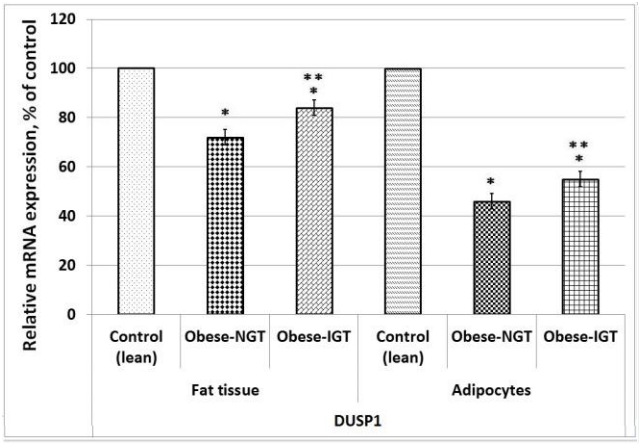

Fig. 1. The expression level of serine/threonine specific protein phosphatase DUSP1 (dual specificity phosphatase 1), also known as MKP1 (mitogen-activated protein kinase phosphatase 1), mRNA in subcutaneous adipose tissue and adipocytes, isolated from this tissue, of lean men (control) and obese individuals with and without impaired glucose tolerance (IGT).

*The values of DUSP1 mRNA expressions were normalized to the expression of beta-actin mRNA, are expressed as mean ± SEM and represented as a percent of control (Lean, 100 %); n = 6; * - P < 0.05 vs group of control individuals; ** - P < 0.05 vs group with obesity and normal glucose tolerance test (NGT).*

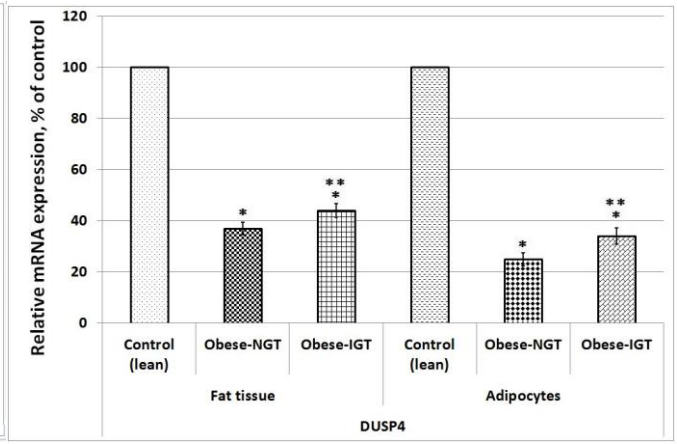

Fig. 2. The expression level of serine/threonine specific protein phosphatase DUSP4 (dual specificity phosphatase 4), also known as MKP2 (mitogen-activated protein kinase phosphatase 1), mRNA in subcutaneous adipose tissue and adipocytes, isolated from this tissue, of lean men (control) and obese individuals with and without impaired glucose tolerance (IGT).

*The values of DUSP4 mRNA expressions were normalized to the expression of beta-actin mRNA, are expressed as mean ± SEM and represented as a percent of control (Lean, 100 %); n = 6; * - P < 0.05 vs group of control individuals; ** - P < 0.05 vs group with obesity and normal glucose tolerance test (NGT).*

The expression level of genes, encoded the dual specificity protein phosphatases DUSP6 and DUSP22, also known as MKP3 (mitogen-activated protein kinase phosphatase 3) and MKPX (mitogen-activated protein kinase phosphatase X), correspondingly, is also decreased with similar magnitude both in subcutaneous adipose tissue and in adipocytes, isolated from this tissue, of obese individuals with normal glucose tolerance as compared to the group of men without obesity: -40 and -27 % for *DUSP6* and *DUSP22* genes in adipose tissue and -48 and -26 % for *DUSP6* and *DUSP22* genes in adipocytes, correspondingly; $P < 0.05$ (Fig. 3 and 4). At the same time, in obese men with impaired glucose tolerance the level of these two gene expressions is also increased in subcutaneous adipose tissue (+20 and +15 % for *DUSP6* and *DUSP22* genes, correspondingly; $P < 0.05$) and in adipocytes, isolated from adipose tissue (+42 and +22 % for *DUSP6* and *DUSP22* genes, correspondingly; $P < 0.05$).

It was shown that the expression level of gene, encoded the dual-specificity protein phosphatase and phosphatidylinositol 3,4,5-trisphosphate 3-phosphatase PTEN (phosphatase and tensin homolog), is also decreased both in subcutaneous adipose tissue (-30 %; $P < 0.05$) and in isolated adipocytes (-35 %; $P < 0.05$) of obese individuals with normal glucose tolerance as compared to the group of control men (Fig. 5).

Moreover, magnitude of obesity-mediated changes in the expression levels of *PTEN* gene was similar to that of *DUSP1*, *DUSP6*, and *DUSP22* genes and more robust only in the case of *DUSP4* gene. At the same time, in the group of obese individuals with impaired glucose tolerance the expression level of *PTEN* gene was also decreased in subcutaneous adipose tissue and isolated adipocytes as compared to control group, but did not changed in statistically significant manner as compared to obese patients with normal glucose tolerance (Fig. 5).

Protein phosphatases as well as protein kinases play an important role in different diseases associated with proliferative processes, including obesity and its metabolic complications, the most profound public health problems (Huang et al., 2011; Scott et al., 2008; Green et al., 2008; Ando et al., 2011). We investigated adipose tissue because in obese individuals this tissue is at the center of increased body weight and metabolic complications and shown that expression level of several dual specificity protein phosphatases is decreased in subcutaneous adipose tissue of obese individuals. These protein phosphatases regulate a cellular growth and proliferation, activity of regulatory factors that have been linked to insulin resistance, obesity and its metabolic complications (Ruderman et al., 2013; Wang and Kaufman, 2012).

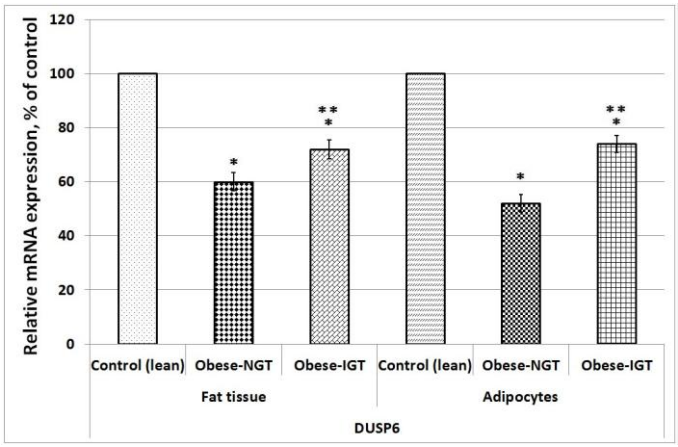

Fig. 3. The expression level of serine/threonine specific protein phosphatase DUSP6 (dual specificity phosphatase 6), also known as MKP3 (mitogen-activated protein kinase phosphatase 3), mRNA in subcutaneous adipose tissue and adipocytes, isolated from this tissue, of lean men (control) and obese individuals with and without impaired glucose tolerance (IGT).

*The values of DUSP6 mRNA expressions were normalized to the expression of beta-actin mRNA, are expressed as mean ± SEM and represented as a percent of control (Lean, 100 %); n = 6; * - P < 0.05 vs group of control individuals; ** - P < 0.05 vs group with obesity and normal glucose tolerance test (NGT).*

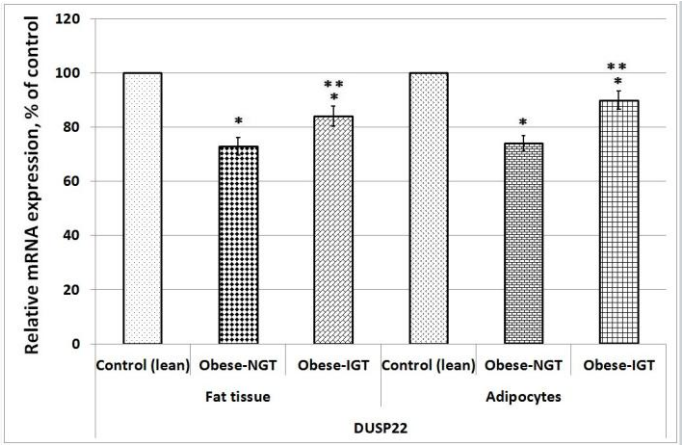

Fig. 4. The expression level of serine/threonine specific protein phosphatase DUSP22 (dual specificity phosphatase 22), also known as MKPX (mitogen-activated protein kinase phosphatase X) or JNK-stimulatory phosphatase-1 (JSP1), mRNA in subcutaneous adipose tissue and adipocytes, isolated from this tissue, of lean men (control) and obese individuals with and without impaired glucose tolerance (IGT).

*The values of DUSP22 mRNA expressions were normalized to the expression of beta-actin mRNA, are expressed as mean ± SEM and represented as a percent of control (Lean, 100 %); n = 6; * - P < 0.05 vs group of control individuals; ** - P < 0.05 vs group with obesity and normal glucose tolerance test (NGT).*

It is possible that decreased expression of DUSP1 and DUSP4 protein phosphatases has relation to development of obesity because it is a key player in the regulation of cell proliferation through protein dephosphorylation, because these protein phosphatases inactivates their target kinases by dephosphorylating both the phosphoserine/threonine and phosphotyrosine residues, controlling its activity during the meiotic cell cycle, especially kinases, which are tightly associated with cellular proliferation (Song et al., 2012; Groschl et al., 2013; Casteel et al., 2010; Cagnol et al., 2013; Degl'Innocenti et al., 2013; Piya et al., 2013; Li et al., 2010).

Moreover, the decreased expression of protein phosphatase DUSP4 in subcutaneous adipose tissue of obese individuals possibly contributes to adipose tissue growth, because recently was shown that increased expression of dual specificity phosphatase 4 resulting in nuclear ERK1/2 inhibition (Cagnol et al., 2013). Thus, our results concerning decreased expression of protein phosphatase DUSP4 in subcutaneous adipose tissue of obese individuals should result in nuclear ERK1/2 activation. It is interesting to note that protein phosphatase DUSP6 may participate in adipocyte proliferation in obesity through regulation of TP53-mediated apoptosis and changing the expression levels of BCL2 family proteins, because DUSP6 is a transcriptional target of tumor suppressor TP53 (Piya et al., 2013). Moreover, we have shown that the expression level of dual specificity phosphatase 22 is also decreased in subcutaneous adipose tissue of obese individuals and possibly induces cell migration, because this protein phosphatase activates the JNK signaling pathway by dephosphorylation of stress-activated protein kinase/c-Jun N-terminal kinase and suppresses cell migration (Li et al., 2010).

We have also shown that developing of glucose intolerance in obese individuals usually leads to slight but statistically significant increase of expression level of different dual specificity protein phosphatase genes in subcutaneous adipose tissue of obese individuals. It is possible that these changes in *DUSP* gene expressions are connected to the development of insulin resistance and metabolic complications, including glucose intolerance, but functional significance of this increased expression of *DUSP* genes is not clear yet and warrants further investigation.

Investigation of the expression of tumor suppressor gene *PTEN*, which represents two enzymatic activities: dual specificity protein phosphatase and phosphatidylinositol 3,4,5-trisphosphate 3-phosphatase, we have shown suppression of its expression in subcutaneous adipose tissue of obese individuals.

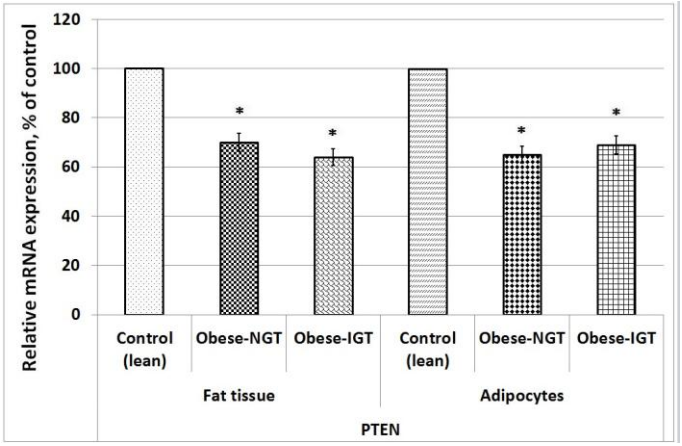

Fig. 5. The expression level of tumor suppressor PTEN (phosphatase and tensin homolog), also known as dual-specificity protein phosphatase and phosphatidylinositol 3,4,5-trisphosphate 3-phosphatase PTEN, mRNA in subcutaneous adipose tissue and adipocytes, isolated from this tissue, of lean men (control) and obese individuals with and without impaired glucose tolerance (IGT).

*The values of PTEN mRNA expressions were normalized to the expression of beta-actin mRNA, are expressed as mean ± SEM and represented as a percent of control (Lean, 100 %); n = 6; * - P < 0.05 vs group of control individuals.*

These changes in *PTEN* gene expression can also contribute to developing of obesity, because unlike most of the protein tyrosine phosphatases, PTEN preferentially dephosphorylates phosphoinositide substrates and is involved in the regulation of the cell cycle, preventing cells from growing and dividing too rapidly as well as controls insulin signaling and glucose homeostasis (Kechagioglou et al., 2014; Dean et al., 2014). With our results is consistent data that effect of PTEN mutations is an apparently divergent: increased risks of obesity and cancer but a decreased risk of type 2 diabetes (Hodakoski et al., 2014; Pal et al., 2012).

It is possible that our results clarifies some molecular mechanisms of adipose tissue growth in obesity and will be useful for better understanding the developing of obesity and associated with obesity metabolic complications, because protein phosphatases is closely linked to metabolic homeostasis, can modulate the intracellular signaling network and leads to development of obesity as well as its metabolic complications such as insulin resistance and glucose intolerance.

Results of this study provide evidence that the expression of protein phosphatase family DUSP and *PTEN* genes is decreases in subcutaneous adipose tissue and adipocytes, isolated from this tissue, of obese individuals with normal glucose tolerance; however, impaired glucose tolerance in obese men is associated with up-regulation of *DUSP1*, *DUSP4*, *DUSP6,* and *DUSP22* gene expressions.

Conclusions. 1. It was shown that the expression level of *DUSP1*, *DUSP4*, *DUSP6*, *DUSP22,* and *PTEN* genes is decreased both in subcutaneous adipose tissue and in isolated adipocytes of obese men with normal glucose tolerance as compared to control group.

2. In the group of obese men with glucose intolerance the level of *DUSP1*, *DUSP4*, *DUSP6,* and *DUSP22* gene expressions in subcutaneous adipose tissue and isolated adipocytes was also decreased as compared to control group, but was significantly higher than in obese patients with normal glucose tolerance.

3. Impaired glucose tolerance in obese individuals is associated with up-regulation of *DUSP1*, *DUSP4*, *DUSP6,* and *DUSP22* gene expressions.

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ЕКСПРЕСІЯ ГЕНІВ ПРОТЕЇНФОСФАТАЗ У ПІДШКІРНІЙ ЖИРОВІЙ ТКАНИНІ У ЧОЛОВІКІВ З ОЖИРІННЯМ ТА НОРМАЛЬНОЮ АБО ПОРУШЕНОЮ ТОЛЕРАНТНІСТЮ ДО ГЛЮКОЗИ

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Проведено вивчення експресії генів, що кодують протеїнфосфатази родини DUSP у підшкірній жировій тканині та ізольованих адіпоцитах двох груп чоловіків з ожирінням: з нормальною і порушеною толерантністю до глюкози у порівнянні з контрольною групою осіб без ознак ожиріння. Встановлено, що рівень експресії генів DUSP1, DUSP4, DUSP6 та DUSP 22 знижується як у підшкірній жировій тканині чоловіків, так і в ізольованих із неї адіпоцитах, за умов ожирінням і нормальної толерантності до глюкози у порівнянні з контрольною групою чоловіків, причому величина обумовлених ожирінням змін в рівні експресії генів є гено-специфічною і виражена більшою мірою для гена протеїнфосфатази DUSP4. За умов ожиріння, ускладненого порушеною толерантністю до глюкози, рівень експресії генів DUSP1, DUSP4, DUSP6 та DUSP22 у підшкірній жировій тканині та ізольованих адіпоцитах був також зниженим у порівнянні з контрольною групою, але був більшим від значень рівня експресії цих генів, виявлених у групі чоловіків з ожирінням і нормальною толерантністю до глюкози. Результати даної роботи вказують на те, що у підшкірній жировій тканині та ізольованих адіпоцитах чоловіків з ожирінням пригнічується експресія генів протеїнфосфатаз родини DUSP та PTEN і, ймовірно, ці зміни пов'язані з розвитком ожиріння та метаболічних порушень. Разом з тим, з порушенням толерантності до глюкози асоціюється підвищення рівня експресії лише генів DUSP1, DUSP4, DUSP6 та DUSP22.

Ключові слова: експресія мРНК, DUSP1, DUSP4, DUSP6, DUSP22, PTEN, підшкірна жирова тканина, адіпоцити, ожиріння, порушена толерантність до глюкози.

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