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DEVELOPMENT OF INSULIN RESISTANCE IN OBESE ADOLESCENTS INTRODUCES GENOME REPROGRAMMING AND CHANGES THE EXPRESSION OF NUMEROUS ENDOPLASMIC RETICULUM STRESS RESPONSIVE GENES

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The development of obesity and its metabolic complications is associated with dysregulation of various intrinsic mechanisms, which control basic metabolic processes through changes in the expression of numerous regulatory genes. Endoplasmic reticulum stress is an impotent component of obesity related metabolic dysregulation as well as the development of insulin resistance and other complications of obesity.

The expression level of different genes as well as microRNA was measured in the blood of obese adolescents without signs of resistance to insulin and with insulin resistance in comparison with the group of relative healthy control individuals without signs of obesity. It was shown that in the blood of obese adolescents with normal insulin sensitivity the expression level of *IGFBP4*, *IGFBP5* and *HTRA1* genes was down-regulated, but *IGFBP2* and *IGFBP7* genes up-regulated as compared to control (normal)

group. At the same time, no significant changes in *IGF1* and *IGF2* gene expressions in this group of obese adolescents were found. Insulin resistance in obese adolescents led to up-regulation of *IGF2*, *IGFBP2*, and *IGFBP7* gene expressions as well as to down-regulation of the expression of *IGF1*, *IGFBP5* and *HTRA1* genes in the blood in comparison with the obese patients, which have normal insulin sensitivity. Furthermore, the level of *IGFBP4* gene expression was similar in both groups of obese adolescents.

Previously was shown that the expression of genes encoding IGF factors and IGF binding proteins as well as IRS1 are endoplasmic reticulum stress responsible and play important roles in the control of variable metabolic processes [1 – 4, p.3]. It was also shown that obesity is associated with up-regulation of the expression level of gene encoding polyfunctional protein insulinase (insulin degrading enzyme, IDE) and down-regulation of pitrilysin metallopeptidase 1 (PITRM1) independently from insulin resistance. Furthermore, suppression of ERN1 signaling pathway of endoplasmic reticulum stress down-regulates the expression of both these genes [5, p. 3]. It was also shown that obesity is associated with up-regulation of the expression level of genes encoding *HLA-DRA* and *HLA-DRB1*, which responsible for immune response, in the blood as compared to control group of relative healthy adolescents. At the same time, significant down-regulation was observed in the expression level of *HLA-G* gene in the blood of this group of obese adolescents. Furthermore, development of insulin resistance in obese individuals leads to significant down-regulation of *HLA-DRA*, *HLA-DRB1*, *HLA-G*, and *HLA-F* gene expressions as well as to up-regulation of *NFX1* gene as well as microRNA miR-190b in the blood as compared to obese patients without signs of insulin resistance.

Results of this study provide evidence that obesity affects the expression of the subset of genes related to glucose metabolism, cell proliferation and immune response in the blood and that development of insulin resistance in obese adolescents is associated with gene specific changes in the expression of *IGF1*, *IGF2*, *IGFBP2*, *IGFBP5*, *IGFBP7*, and *HTRA1* genes as well as with strong down-regulation of the expressions of *HLA-DRA*, *HLA-DRB1*, *HLA-F*, and *HLA-G* genes, which may be contribute to the development of obesity complications. It is possible that transcription factor *NFX1* and miR-190b participate in down-regulation of *HLA-DRA* gene expression in the blood of obese adolescents with insulin resistance.

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СУЧАСНИЙ ПЕРЕБІГ ЕНТЕРОВІРУСНОЇ ІНФЕКЦІЇ У ДІТЕЙ

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В останні роки намітилася чітка тенденція активації ентеровірусної інфекції в світі, про що свідчать постійно зареєстровані в різних країнах світу епідеміологічні підйоми захворюваності й спалахи [1]. З одного боку, це пов’язано із зменшенням рівня захворюваності