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Adipose Tissue Integrated Stress Response (ISR) Activation: Implications for Obesity and Diabetes

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Description

Obesity has become a global epidemic, affecting about one-third of the world's population. This condition significantly increases the risk of developing type 2 diabetes mellitus. Adipose tissue, once primarily viewed as an energy reservoir, plays a critical role in maintaining metabolic balance through the secretion of various signaling molecules known as adipokines. These adipokines, including leptin and adiponectin, influence insulin sensitivity, lipid metabolism, and overall energy regulation. A better understanding of the mechanisms governing adipose tissue function, especially regarding adipokine signaling and metabolic pathways, could pave the way for novel therapeutic approaches to address obesity and related metabolic disorders. The Integrated Stress Response (ISR) is a well-conserved pathway that is activated in response to cellular stressors, such as Endoplasmic Reticulum (ER) stress, amino acid deprivation, and hypoxia. This pathway is initiated by the phosphorylation of eIF2 α (eukaryotic translation initiation factor 2 alpha) at serine-51 [1]. Activation of eIF2α leads to a temporary reduction in global protein synthesis, allowing cells to conserve resources and adapt to stress conditions. Concurrently, translation of specific transcription factors, such as ATF4 (Activating Transcription Factor 4), is upregulated, which then stimulates the expression of genes involved in stress responses and metabolic adaptation. Research using genetically modified mice has highlighted the significant role of ISR in metabolic regulation. For example, mice with a homozygous mutation preventing eIF2 α phosphorylation (*S51A* mutation) [2] exhibit severe hypoglycemia and die shortly after birth due to impaired gluconeogenesis. Conversely, mice with a heterozygous S51A mutation show compromised glucose metabolism and a higher tendency towards obesity. These findings underscore the importance of ISR pathways in maintaining glucose and lipid homeostasis under normal physiological conditions [3]. Recent studies have explored the role of ISR activation within adipose tissue. Activation of eIF2 α kinases in adipocytes under metabolic stress conditions, such as obesity, suggests that the ISR might influence adipocyte function and overall energy balance [4]. For instance, a recent study using a transgenic mouse model with targeted ISR activation in adipose tissue demonstrated significant improvements in obesity and diabetes resulting from a high-fat diet. This indicates that ISR activation in adipose tissue can reduce food intake and impact metabolic outcomes, highlighting the potential of targeting ISR pathways in managing obesity and type 2 diabetes [5]. Understanding how ISR modulates adipose tissue function provides valuable insights into potential strategies for treating obesity and related metabolic conditions. Further research is needed to elucidate the detailed molecular mechanisms by which ISR signaling affects systemic metabolism, which could lead to new therapeutic targets for managing these diseases. In summary, the ISR is a fundamental mechanism that responds to cellular stress and has significant implications for metabolic regulation in adipose tissue and beyond. By influencing adipokine secretion and metabolic pathways, [6] ISR activation presents a promising target for developing new treatments for obesity and type 2 diabetes. Continued research into the molecular mechanisms of ISR-mediated metabolic regulation is crucial for advancing effective strategies and improving clinical outcomes for these conditions [7].

The Integrated Stress Response (ISR) plays a critical role in maintaining metabolic balance and responding to cellular stress, with profound implications for adipose tissue function and overall metabolic health. Through the phosphorylation of eIF2 α the ISR regulates protein synthesis and activates stress-responsive genes, which are essential for cellular adaptation to various stress conditions such as endoplasmic reticulum stress and nutrient deprivation [8].

Recent research underscores the significance of ISR pathways in adipose tissue, highlighting their impact on glucose metabolism and susceptibility to obesity. Evidence from studies using genetically modified mice indicates that both disruptions and activations of ISR can markedly influence metabolic outcomes. Specifically, ISR activation in adipocytes has shown potential in improving diet-induced obesity and diabetes, suggesting that targeting ISR pathways could be a promising strategy for managing these conditions [9].

Overall, a deeper understanding of ISR modulation in adipose tissue provides valuable insights into new therapeutic approaches for obesity and type 2 diabetes. Continued investigation into the molecular mechanisms underlying ISR's effects on metabolism is important for developing effective treatments and improving clinical outcomes for these widespread metabolic disorders. Future research should focus

on elucidating these mechanisms and translating findings into targeted therapeutic strategies to address the growing global health challenge posed by obesity and diabetes [10].

References

1. Vetreno RP, Qin L, Coleman LG, Crews FT (2021) Increased toll-like receptor-myd88-nfkappab-proinflammatory neuroimmune signaling in the orbitofrontal cortex of humans with alcohol use disorder. Alcohol Clin Exp Res 45: 1747-1761.
2. Coleman L G , Zou J, and Crews FT (2017) Microglial-derived miRNA let-7 and HMGB1 contribute to ethanol-induced neurotoxicity *via* TLR7. J Neuroinflammation 14: 22.
3. Oddo S, Caccamo A, Shepherd JD, Murphy MP, Golde TE, et al. (2003) Triple-transgenic model of Alzheimer's disease with plaques and tangles: intracellular abeta and synaptic dysfunction. Neuron 39: 409-421.
4. Li YD, Luo YJ, Xie L, Tart DS, Sheehy RN, et al. (2023) Activation of hypothalamic-enhanced adult-born neurons restores cognitive and affective function in Alzheimer's disease. Cell Stem Cell 30415-432.
5. Schmidt W, Popham RE, Israel Y (1987) Dose-specific effects of alcohol on the lifespan of mice and the possible relevance to man. Br J Addict 82: 775-788.
6. Coleman LG, He J, Lee J, Styner M, Crews FT (2011) Adolescent binge drinking alters adult brain neurotransmitter gene expression, behavior, brain regional volumes and neurochemistry in mice. Alcohol Clin Exp Res 35: 671-688.
7. Zou J, Walter TJ, Barnett A, Rohlman A, Crews FT, et al.(2022) Ethanol induces secretion of proinflammatory extracellular vesicles that inhibit adult hippocampal neurogenesis through g9a/glp-epigenetic signaling. Front Immunol 13: 866073.
8. Qin L, Zou J, Barnett A, Vetreno RP, Crews FT, et al. (2021) Trail mediates neuronal death in aud: A link between neuroinflammation and neurodegeneration. Int J Mol Sci 22: 2547.
9. Guaita AA, Melvin A, Rimmington D, Dattilo A, Miedzybrodz ka EL, et al. (2019) GDF15 provides an endocrine signal of nutritional stress in mice and humans. Cell Metab 29: 707-718.
10. Roden M, Shulman GI (2019) The integrative biology of type 2 diabetes. Nature 576: 51-60.