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BIOCHEMICAL MECHANISMS OF INSULIN RESISTANCE

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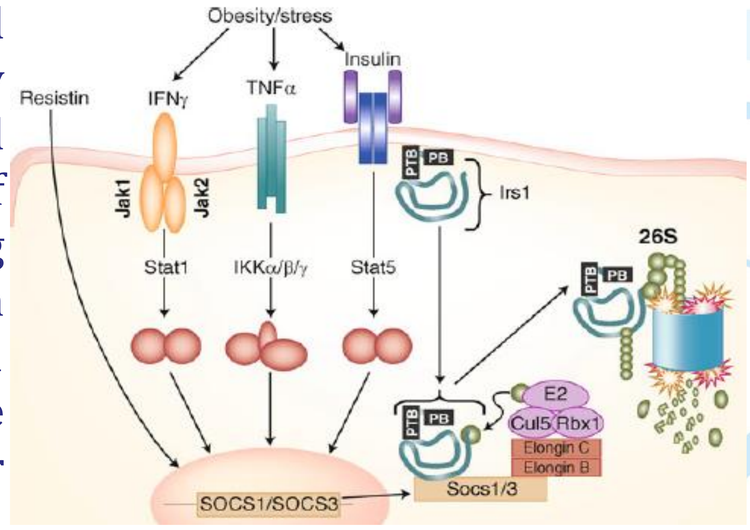
Introduction: The mutation of the Insulin Receptor Substrate-1 gene is a cause for insulin resistance. The mutations is due to the replacement of Gly with Arg at codon 972, which leads to the formation of a defective protein and that causes the translocation of the GLUT-4 protein.

Keywords: insulin resistance, GLUT-4, proinflammatory cytokines, IR-1.

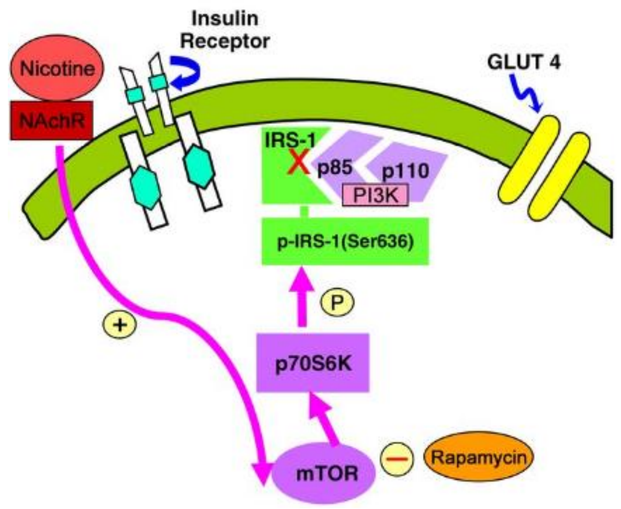
Material and methods: This is the synthesis of 20 medical research articles published in the period of 2010-2020, found with the research motors PubMed, Medscape, American Physiological Society Journal.

Purpose: To elucidate and describe the biochemical mechanisms behind insulin resistance (IR) that are at the core of the creation of an effective treatment for type 2 diabetes

Results: In obesity hypertrophied adipocytes are the source of proinflamatory cytokines, such TNFα, IL-6, resistin and IFNγ, that increase overexpression of suppressor of cytokine signaling (SOCS1/SOCS3), which influences insulin receptor-mediated phosphorylation of IRS1 and IRS2, there is a interruption of enzyme cascade of reactions that are necessary for the GLUT-4 translocation.



Interestingly, the core protein of hepatitis C virus upregulates SOCS3, which might explain why infected patients have increased fasting insulin levels compared with patients with other chronic liver diseases.



Nicotine binds to NAchR (nicotinic acetylcholine α1 receptors, that increases mechanistic target of rapamycin (mTOR)/p70S6K activity, which leads to increased IRS-1 Ser 636 phosphorylation, and reduce insulin-stimulated glucose uptake. Rapamycin is an mTOR inhibitor, that blocks these effects of nicotine on insuline resistance.

Conclusions: With the exception of the mutation in the Insulin Receptor Substrate-1 gene, all other pathogenic mechanisms of IR are essential for the development of effective medication in the treatment of patients with type 2 diabetes.