The role of oxidative stress in Type 2 diabetes

Type 2 diabetes is a major health concern that affects people no matter their gender, race, or socio-economic background is. In type 2 diabetes, a person's body stops responding efficiently to insulin after a meal. This desensitization occurs at the cellular level.

Normally in response to insulin, the cell will move more glucose transporters (GLUT4) to cell membranes to pull glucose from the bloodstream. This mechanism ensures the cells get the sugar the person eats instead of leaving it in the blood.

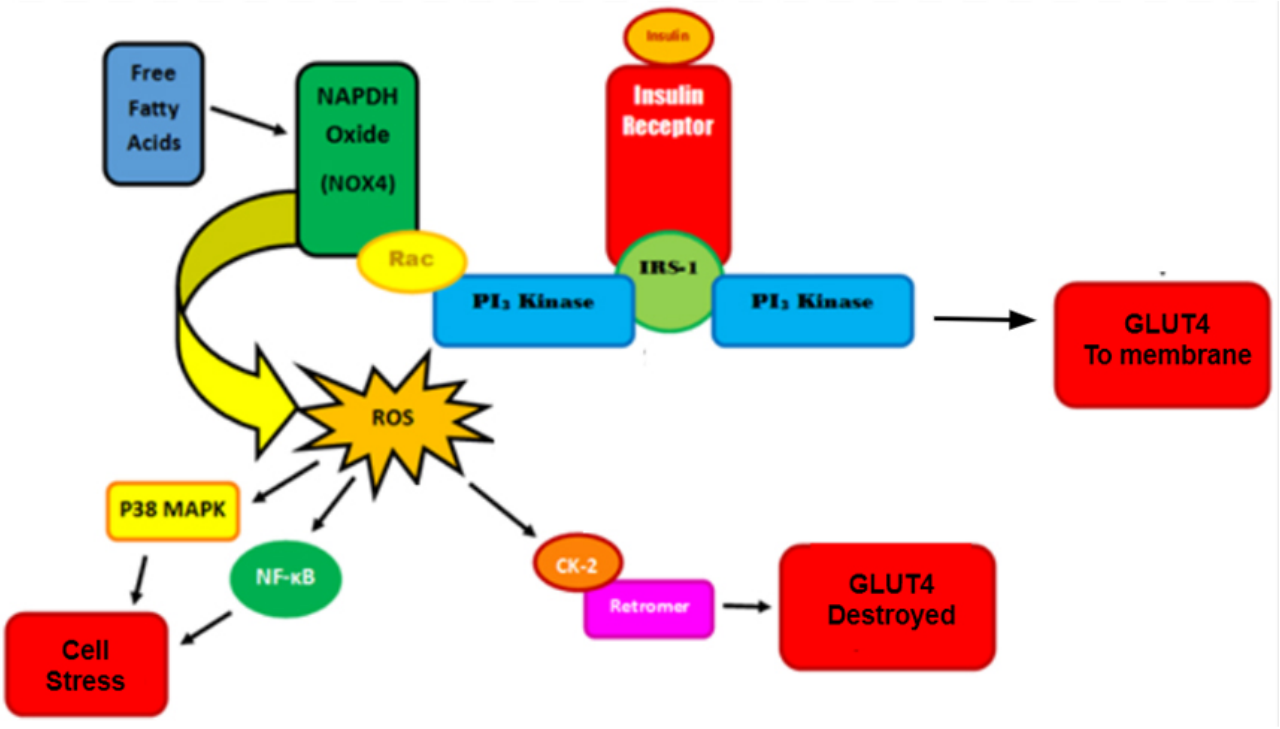

Fig. 1. Insulin receptor signaling pathway including ROS influence. The normal pathway begins with insulin binding to and activating the insulin receptor. The receptor then activates insulin receptor substrate-1 (IRS-1) which in turn activates phosphoinositide kinase (PI3 kinase), turning on a signaling pathway that increases GLUT4 in the cell membrane thus decreasing blood glucose levels. Conversely, overstimulation of the insulin receptor induces PI3 kinase to activate NADPH oxide (NOX4) through Rac GTPase. Free fatty acids also activate NOX4. NOX4 produces oxidants – reactive oxygen species (ROS) which stimulate two major pathways. One is the cellular stress pathway mediated by P38 MAP kinase (p38 MAPK) and nuclear factor kB (NF-kB). The other pathway induces destruction of GLUT4 transporters through the action of the retromer complex that is activated by casein kinase 2 (CK-2).

When glucose in the blood is excessive, more insulin is produced to bring blood sugar levels back to normal. Repeated increased insulin response turns on a second mechanism that produces oxidants and free radicals – reactive oxygen species (ROS). These molecules are damaging to the cell, but they also function as cellular messengers. In response to repeated excess insulin, the oxidants tell the cell to reduce the amount of GLUT4 in the cell membrane. Thus, the cells lose sensitivity to insulin.

Obesity compounds this problem. Excess fat causes inflammation throughout the body and increases oxidative stress. Free fatty acids also get released from fat and participate in ROS production. Interestingly, fat also secretes an anti-inflammatory compound called adiponectin when total body fat is low. Proper body weight maintenance is thus important for insulin sensitivity, partly because of high adiponectin levels.

Antioxidants, e.g., vitamins C & E have shown promise in improving insulin sensitivity and even reversing Type 2 diabetes. They directly combat the oxidants produced in the cells. Vitamins C & E have shown great performance in recent studies in improving insulin sensitivity. Flavonoids, plant pigment compounds, also function as antioxidants. These antioxidants including vitamins C & E are found abundantly in fruits and vegetables. Thus, a healthy and varied diet that is low in sugar with abundant antioxidants could provide exceptional protection against oxidation in conjunction with maintaining proper body weight.

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