INSULIN RESISTANCE MECHANISMS

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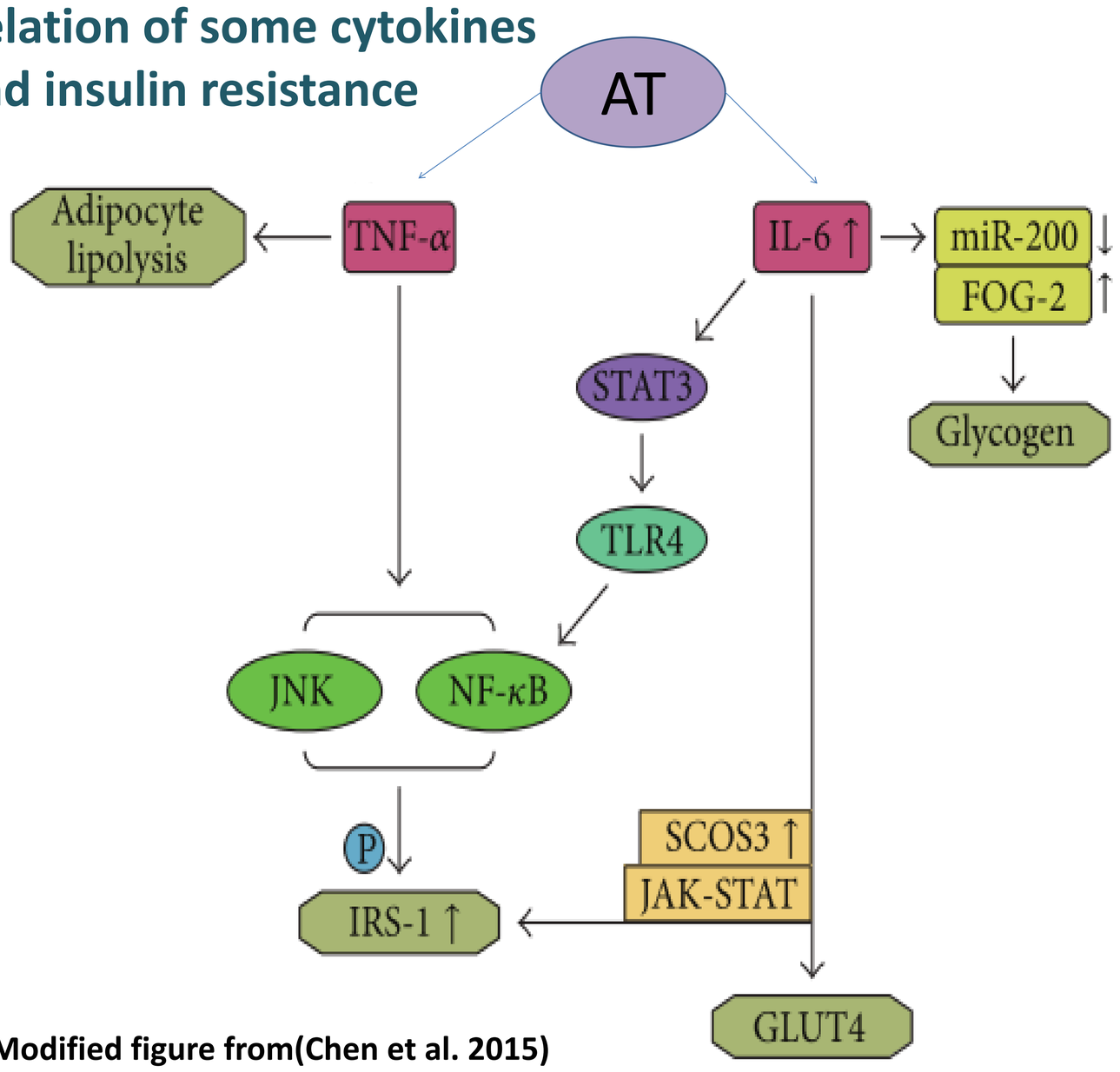
INTRODUCTION

Insulin is a hormone produced by the pancreatic Langerhans' β cells, which is essential for anabolic metabolism. There are several factors that may harm or prevent its action, being obesity the most common of them. Insulin resistance is a common problem and studies about its treatments are still being made.

OBJECTIVES

- Understanding the documented mechanisms that cause insulin resistance and its relation with obesity
- Knowing some of the habitual treatments and actual alternatives.

Relation of some cytokines and insulin resistance



Modified figure from(Chen et al. 2015)

OTHER INSULIN RESISTANCE MECHANISMS

Oxidative stress and ROS	↑JNK , Ikκβ , MAPK ↓ IRS-1, IRS-2, Insulin receptor
	prevents GLUT4 action
Hyperinsulinemia	↑MAPK, inflammatory cytokines ↓ IRS-1, IRS-2
Hyperglycemia	↑JNK, NF-κβ, ROS ↓ GLUT4
Mitochondrial dysfunction	↑ Fatty acids
Endoplasmatic reticulum stress	↑ JNK, Ikκβ, IKK Cell β destruction
Hipercortisolisme	Lead to IRS-1, PI3K and PKB defect

OBESITY AND INSULIN RESISTANCE

Direct relation

Obese individuals have a decreased GLUT4 expression in the adipocytes. The increase in levels of circulating fatty acids prevents the correct activation of PI3K. Resistance to insulin causes a decrease in lipolysis, causing accumulation of triglycerides and hyperlipidemia.

Obesity and inflammation

Obesity produces a chronic inflammation metabolic state, increasing the levels of several cytokines that end up having an essential role in the development of insulin resistance. This response is produced mainly by the Tlr4 stimulation caused by free fatty acids and eventually activating the NF-κβ pathway.

Inflammation and insulin resistance, responsible cytokines

- Tnf-α, IL-1β, IL-6, MCP-1, resistin: ↑ at inflammation. Activation of NF-κβ or JNK, inactivation of IRS-1, or GLUT-4 expression decrease
- Leptina and adiponectin: ↓ at la inflammation. Improvement of insulin sensitivity

SOME TREATMENTS

- **Metformin:** Mobilizes GLUT to cellular membrane
  Lactic acidosis
- **Sulphonylureas:** ↑Insulin secretion and glucose transport to cells
  Cardiovascular risk
- **GLP-1 analogues:** ↑Insulin secretion and weight loss
  Gastrointestinal problems

CONCLUSION: Insulin resistance is a complex syndrome that has many causes. The main factor that drives to it is obesity, in some way by itself but mainly by the inflammation state as a result of the resulting secreted cytokines. Other insulin resistance mechanisms may or may not be related with obesity and act on various pathways. There are treatments that palliate insulin resistance since time ago, but the improved actual knowledge may offer new and safer alternatives.