

# Immune System Trigger of Type 2 Diabetes

Ryan Patch – Visualization in Bioinformatics

## Type 2 Diabetes Defined:

(Dye-uh-BEET-eez) Previously known as “noninsulin-dependent diabetes mellitus” (NIDDM) or “adult-onset diabetes.” Type 2 diabetes is the most common form of diabetes mellitus. About 90 to 95 percent of people who have diabetes have type 2 diabetes. People with type 2 diabetes produce insulin, but either do not make enough insulin or their bodies do not use the insulin they make. Most of the people who have this type of diabetes are overweight.

[win.uiddk.nih.gov/publications/glossary/V1/1hruZ.htm](http://win.uiddk.nih.gov/publications/glossary/V1/1hruZ.htm)

Insulin is present but doesn't work adequately. Usually occurs over the age of 30 and is controlled by diet and medication or diet and insulin. Also known as non insulin dependent and maturity onset diabetes.

[www.diabetes.org.au/glossary.htm](http://www.diabetes.org.au/glossary.htm)

## Obesity And Diabetes

“Although there are some genetic causes for insulin resistance, the most common cause is an excess of nutrition a condition called ‘Nutrient Toxicity’. Both excess glucose and excess fat can cause insulin resistance in muscle and fat tissues and excess fat can cause insulin resistance in the liver. High fat feeding and fat infusion rapidly lead to the development of insulin resistance caused by impairment in glucose transport.”

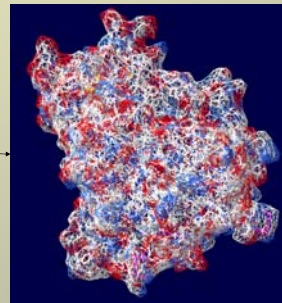
“Obesity resulting from excess nutrient intake can also cause insulin resistance by an increase in the production of agents that impair insulin action such as TNF $\alpha$  and resistin and a decrease in the production of an insulin sensitizing compound adiponectin.”

<http://www.innmls.elsevierhealth.com/periodicals/hope/article/PIIS186631605002074/abstract>

### TNF (Tumor Necrosis Factor) Alpha

“TNF-alpha is a soluble cytokine (A hormone-like molecule, produced by one cell, that has an effect on another cell) with a wide variety of functions: it causes damage to tumour cells but has no effect on normal cells; it is involved in the induction of cachexia; it is a potent pyrogen, causing fever by direct action or by stimulation of interleukin-1 secretion; and it can stimulate cell proliferation and induce cell differentiation under certain conditions.”

<http://www.infobiogen.fr/db/index-emboss/prints/PR01235>



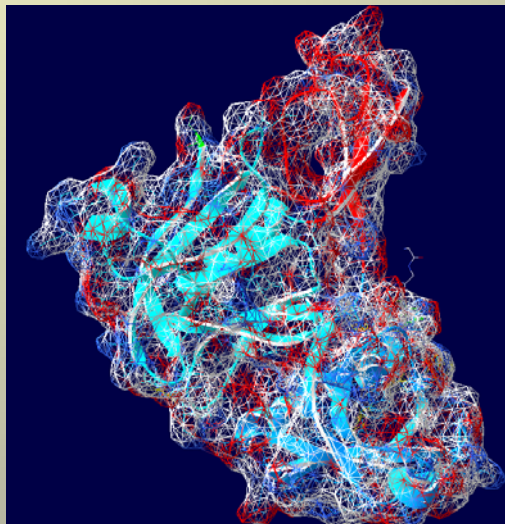
Studies have proven that TNF- $\alpha$  interferes with the activities of a protein structure named Insulin Receptor Substrate-1 (IRS-1).

“Insulin receptor substrate (IRS) molecules are key mediators in insulin signaling and play a central role in maintaining basic cellular functions such as growth, survival, and metabolism. They act as docking proteins between the insulin receptor and a complex network of intracellular signaling molecules”

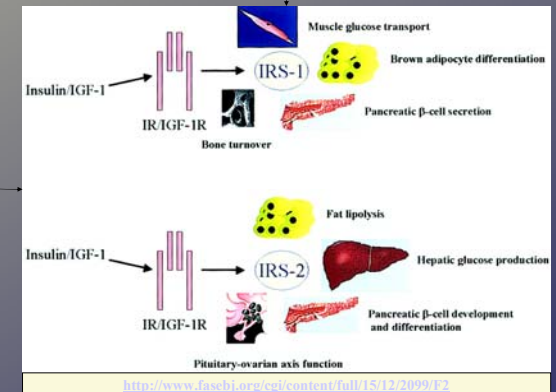
<http://www.fasebj.org/cgi/content/full/15/12/2099#AB5>

Research conducted to pinpoint the activities of TNF- $\alpha$  interaction with IRS-1 receptors shows that the presence of TNF- $\alpha$  during the early maturation of IRS-1 cells interrupts the normal processing of glucose into glycogen. Glycogen is a complex carbohydrate molecule made up of glucose and stored in the liver and muscle cells. When carbohydrate energy is needed, glycogen is converted into glucose for use by the muscle cells. This process is slightly improved when the body tries to produce extra insulin to counteract the lack of glycogen, but does not return levels to normal. TNF- $\alpha$  has been shown to affect the uptake of glucose into muscle cells and can alter the growth of muscle tissue.

<http://diabetes.diabetesjournals.org/cgi/content/full/50/5/1102>



Theoretical Model of IRS-1



<http://www.fasebj.org/cgi/content/full/15/12/2099#F2>

Obesity is targeted as the primary factor in Type-2 Diabetes. The excess fats and sugars, from diet, contribute to the body's own production of the tumor disintegrating compound TNF-Alpha. When over produced this compound interferes with the normal insulin processing activities of muscle, skeletal, pancreatic, and liver systems.

Some studies have suggested that regular salicylics, like those found in aspirin, can hinder TNF- $\alpha$  interference with Insulin Receptor Substrate-1, and curb some of these side effects.

<http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=209353>

However research has definitively shown that when excess TNF- $\alpha$  is removed from the IRS-1 structure, insulin processes return to normalized levels, and muscle cell maturation can take place normally.

<http://diabetes.diabetesjournals.org/cgi/content/full/50/5/1102>