
MASTERING DIABETES
USING A LOW-FAT, PLANT-BASED
WHOLE-FOOD LIFESTYLE

What We'll Cover Today

1. What are the dietary causes of insulin resistance?
2. What is the ***biological mechanism*** of insulin resistance?
3. How to maximize insulin sensitivity using a low-fat, plant-based, whole-food lifestyle

Raise Your Hand if You are Currently Living with Any Form of Diabetes

Raise Your Hand if Diabetes Affects Someone in Your Family

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I Was Diagnosed with 3 Auoimmune Conditions in My Senior Year of College

- Hashimoto's thyroiditis
- Alopecia universalis
- Type 1 diabetes

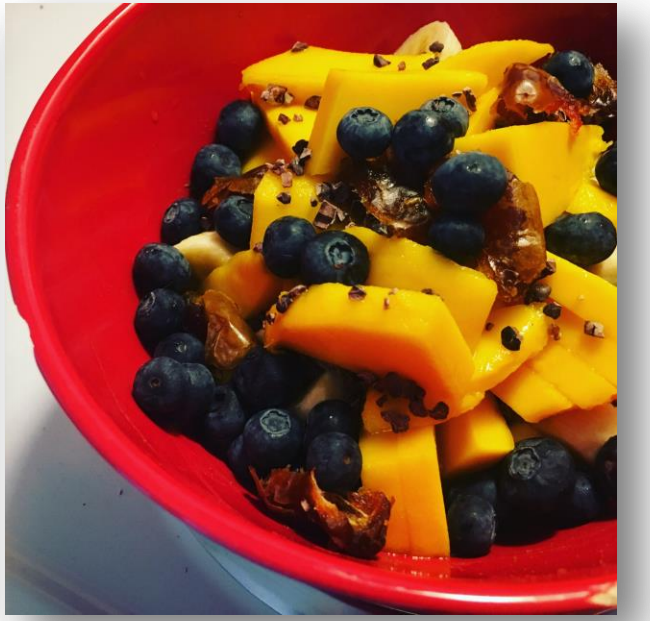
STANFORD UNIVERSITY

My Doctors Immediately Instructed Me To Eat a Low-Carbohydrate Diet

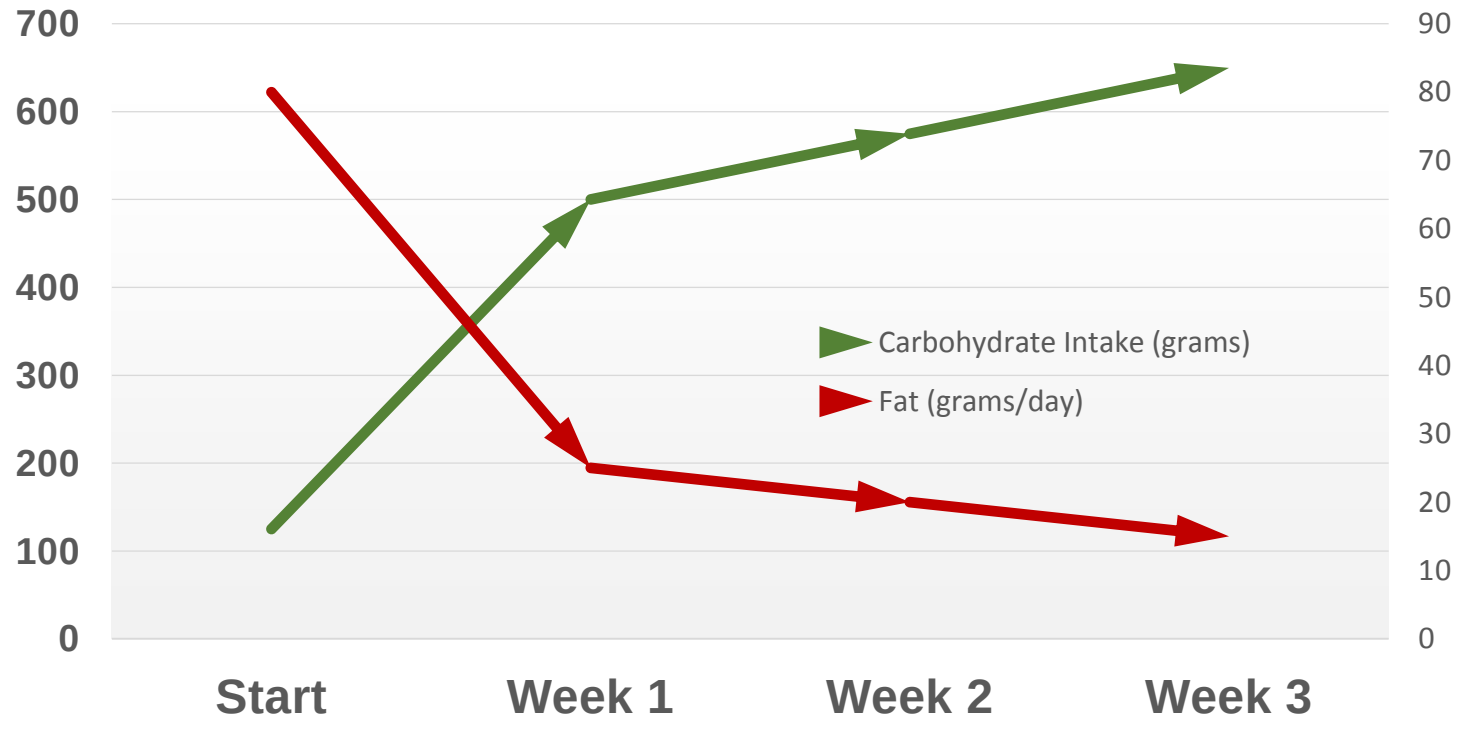
No Matter How Hard I Tried, My Blood Glucose Was Uncontrollable

- I suffered from very low energy
- I became depressed
- My blood glucose meter became a random number generator
- Exercise became extremely difficult

After 1 Year, I Transitioned to a Low-Fat, Plant-Based, Whole-Food Diet



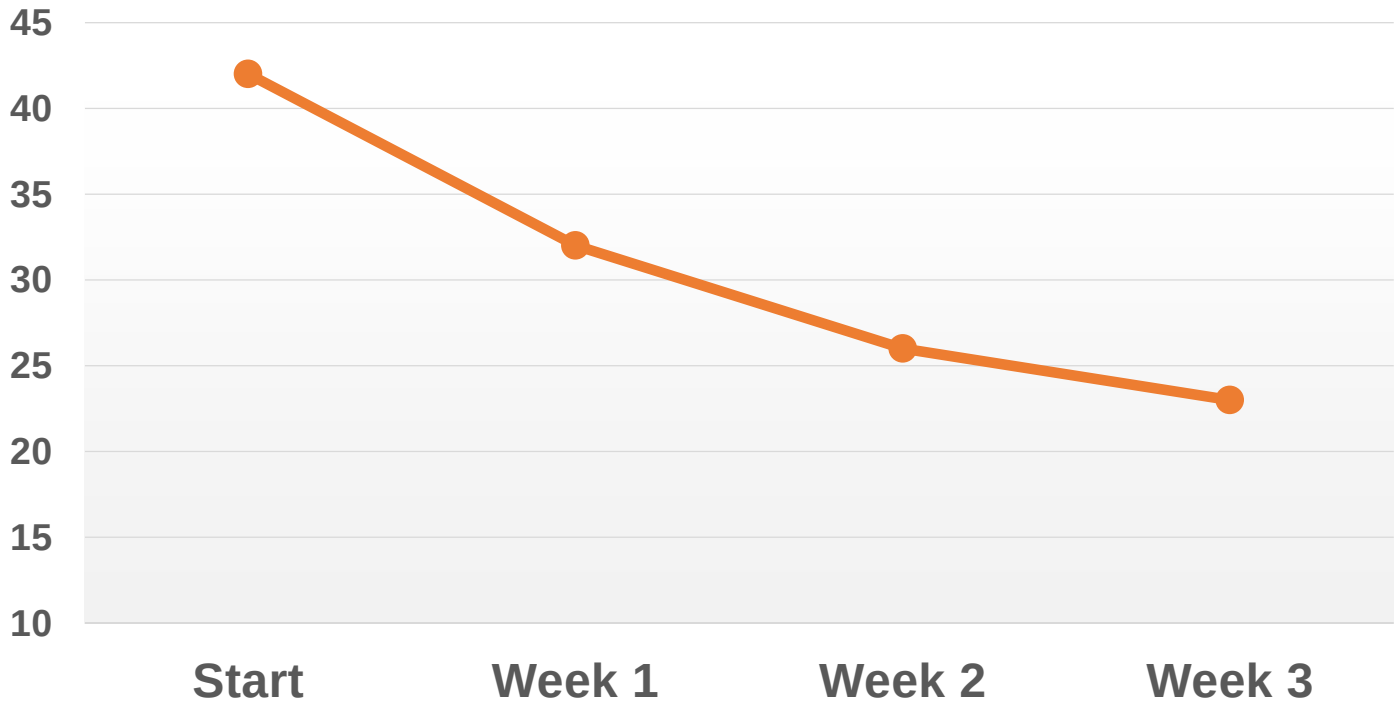
I Increased My Carbohydrate Intake by 420% and Reduced My Total Fat Intake Significantly



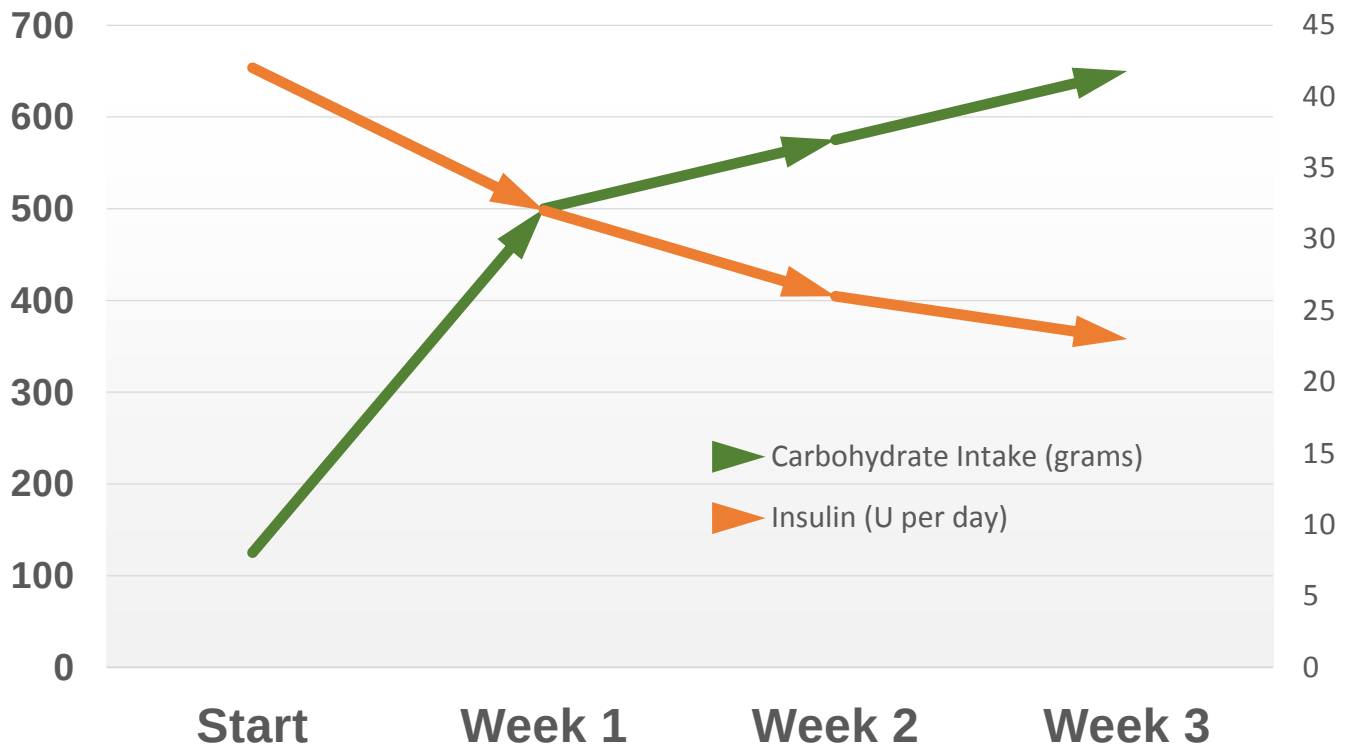
I Expected My Blood Glucose And Insulin Use to Skyrocket

Because more glucose means more insulin…

Instead, I Reduced My Insulin Use By *43% in 3 Weeks*



My Carbohydrate Intake and Insulin Use *Diverged*



I Earned a PhD in Nutritional Biochemistry

I studied insulin resistance for 5 years at UC Berkeley

I wrote a thesis on the causes of insulin resistance

"Am I a Freak of Nature?"

Berkeley
UNIVERSITY OF CALIFORNIA

17 Years Later…

- I have reduced my insulin use by 45%
- I eat 600-700 grams of carbohydrate energy per day
- I inject about 25U of insulin per day
- My A1c values consistently range between 5.4%-5.7%
- I exercise as much as I choose

Mew

Blu

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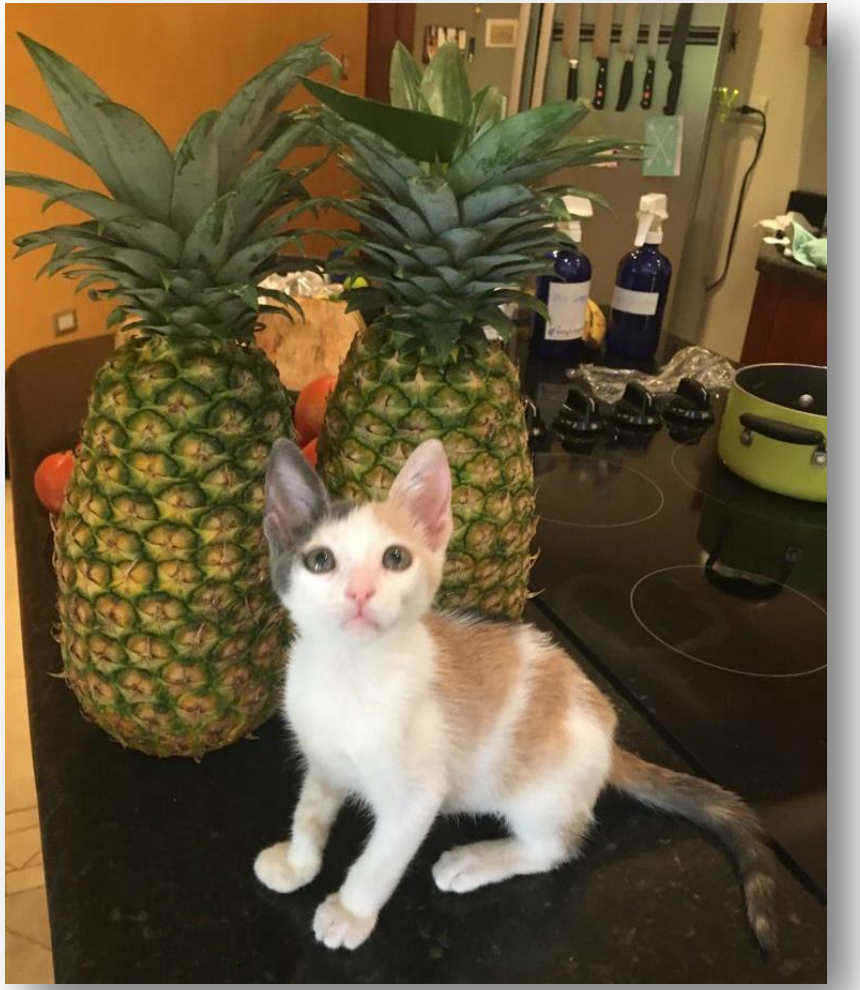

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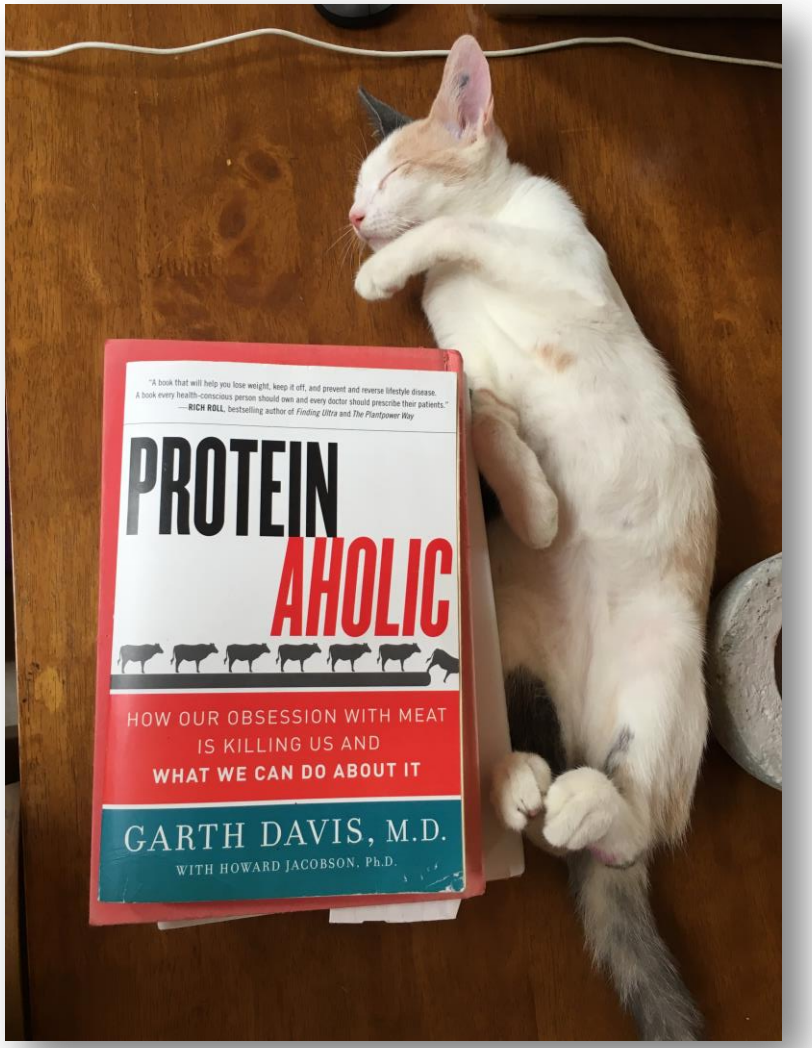
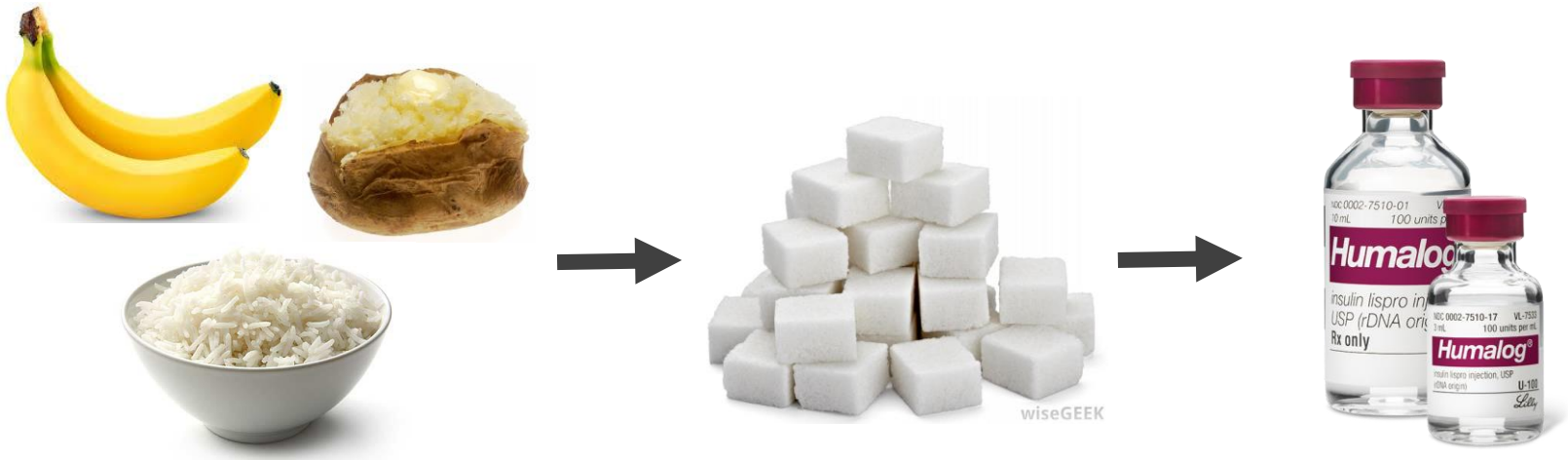
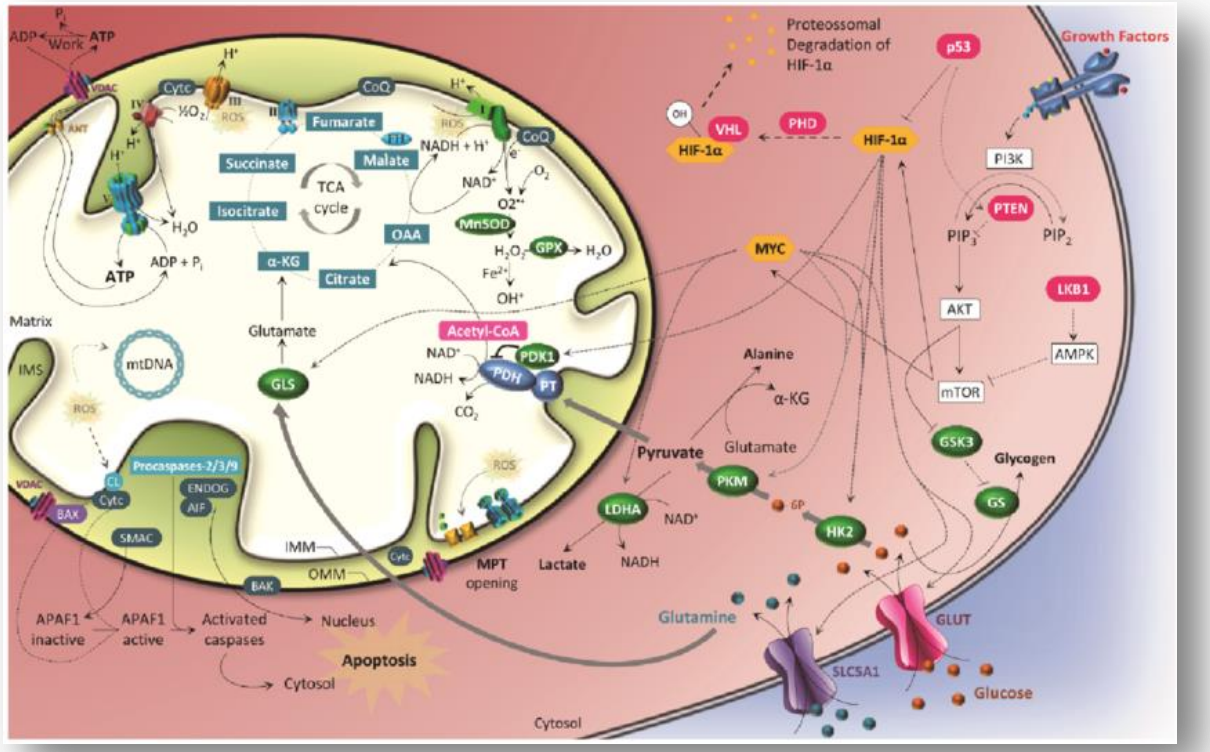
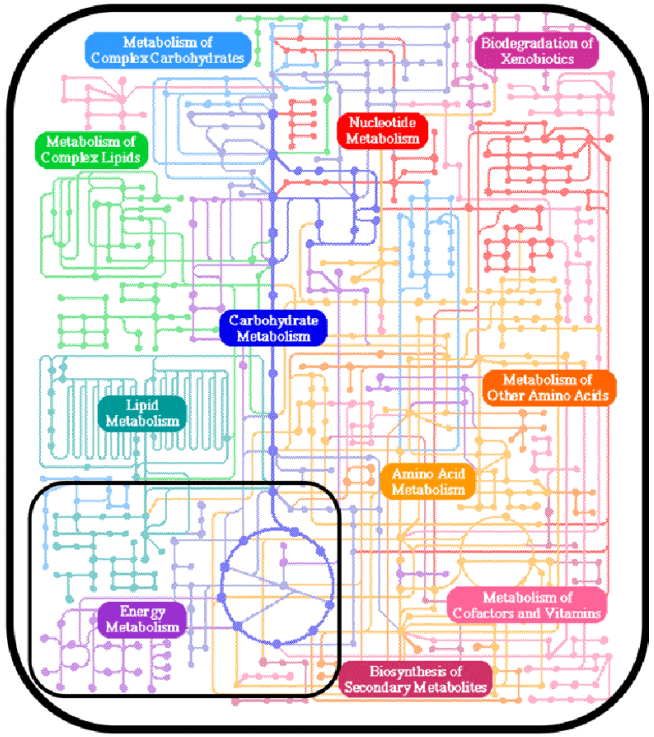


Traditional Carbohydrate Metabolism is a *Single Variable* Relationship



Biological Processes are Rarely (if ever) *Single Variable* Relationships





Type 1 Diabetes
Type 1.5 Diabetes

Prediabetes
Type 2 Diabetes

Insulin Resistance

Gestational Diabetes
Polycystic Ovarian Syndrome (PCOS)

What Causes Insulin Resistance?

Insulin Resistance is Caused By…

the accumulation of ***excess*** saturated fat in tissues that are not designed to store large quantities of fat

Disordered Lipid Metabolism and the Pathogenesis of Insulin Resistance

DAVID B. SAVAGE, KITT FALK PETERSEN, AND GERALD I. SHULMAN

Departments of Internal Medicine and Cellular and Molecular Physiology, Howard Hughes Medical Institute, Yale University School of Medicine, New Haven, Connecticut

Savage DB, Petersen KF, Shulman GI. Disordered Lipid Metabolism and the Pathogenesis of Insulin Resistance. *Physiol Rev* 87: 507–520, 2007; doi:10.1152/physrev.00024.2006.—Although abnormal glucose metabolism defines type 2 diabetes mellitus (T2DM) and accounts for many of its symptoms and complications, efforts to understand the pathogenesis of T2DM are increasingly focused on disordered lipid metabolism. Here we review recent human studies exploring the mechanistic links between disorders of fatty acid/lipid metabolism and insulin resistance. As "mouse models of insulin resistance" were comprehensively reviewed in *Physiological Reviews* by Nandi et al. in 2004, we will concentrate on human studies involving the use of isotopes and/or magnetic resonance spectroscopy, occasionally drawing on mouse models which provide additional mechanistic insight.

How Free Fatty Acids Inhibit Glucose Utilization in Human Skeletal Muscle

Michael Roden

First Medical Department, Hanusch Hospital, A-1140 Vienna, Austria

Rat muscle studies suggest competition between free fatty acids (FFA) and glucose for oxidation, resulting in glucose-6-phosphate accumulation. However, FFA decrease glucose-6-phosphate in human skeletal muscle, indicating direct inhibition of glucose transport/phosphorylation. This mechanism could redirect glucose from muscle to brain during fasting and explain the insulin resistance associated with high-lipid diets and obesity.

Perspectives in Diabetes

Role of Fatty Acids in the Pathogenesis of Insulin Resistance and NIDDM

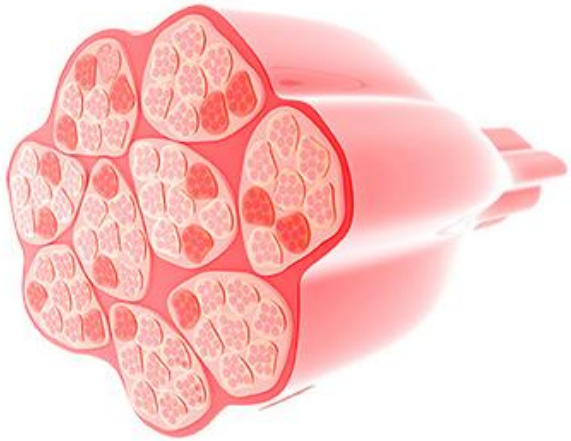
Guenther Boden

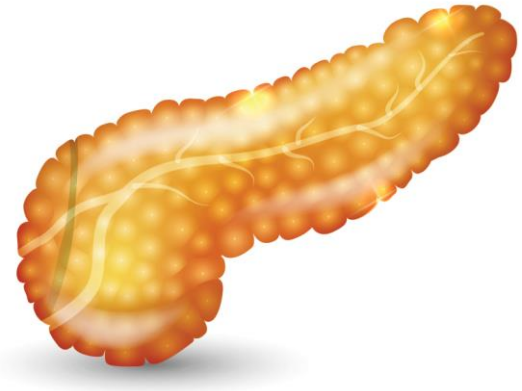
Mechanism of Free Fatty Acid–induced Insulin Resistance in Humans

Michael Roden, Thomas B. Price, Gianluca Perseghin, Kitt Falk Petersen, Douglas L. Rothman, Gary W. Cline, and Gerald I. Shulman

Department of Internal Medicine, Yale University School of Medicine, New Haven, Connecticut 06520

Insulin Resistance is Primarily a Dysfunction of Your *Muscle* and *Liver*





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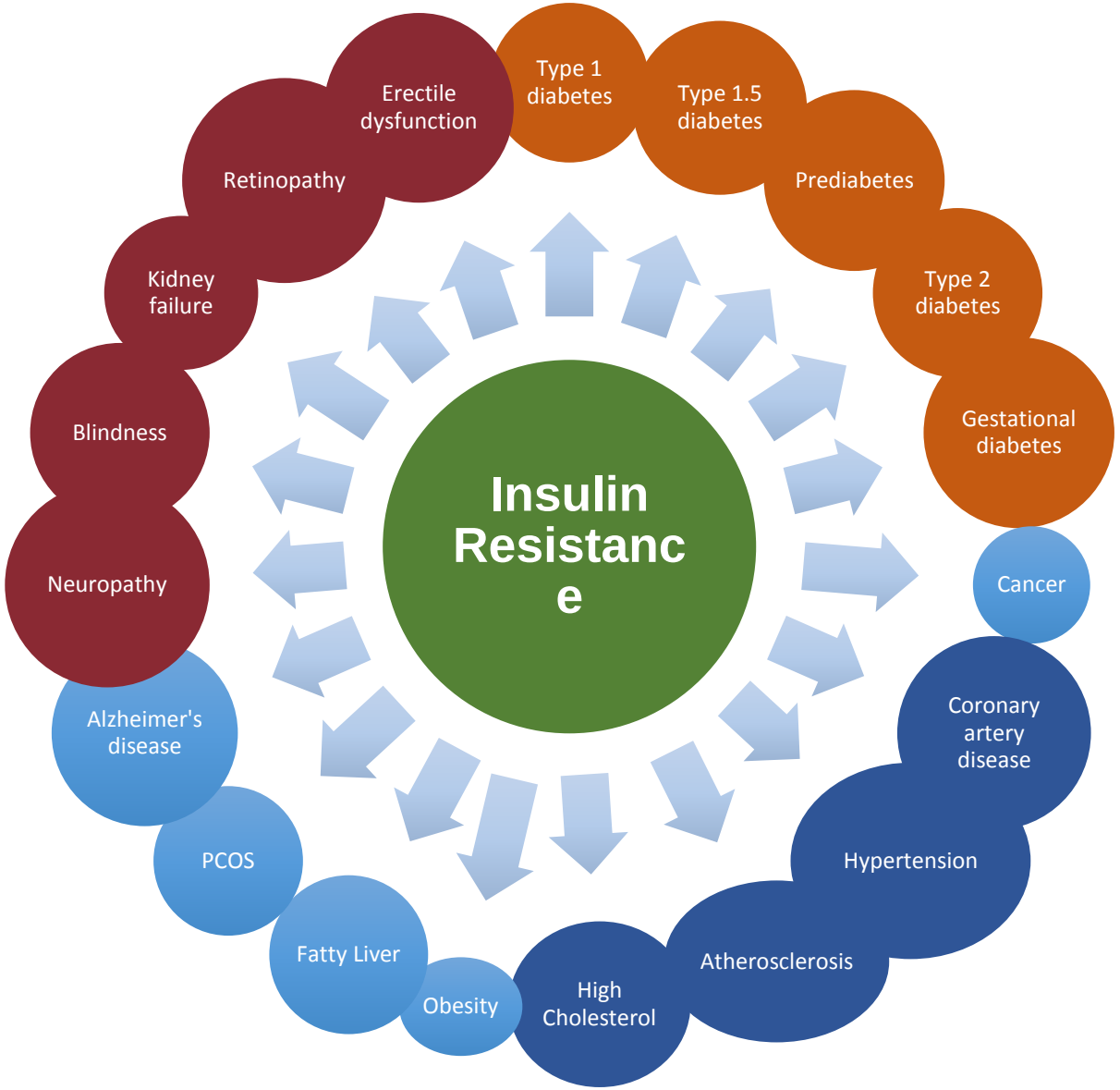

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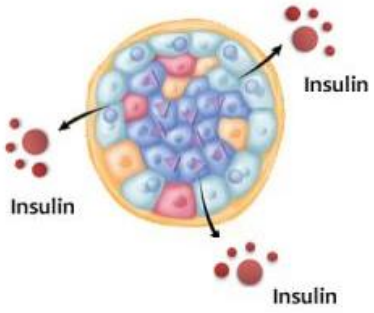
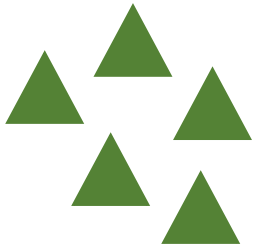
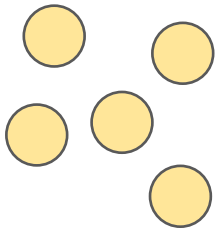


2 Beta Cells

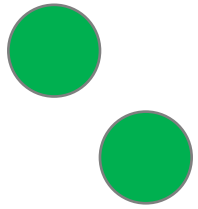
5 Glucose Molecules



5 Insulin Molecules

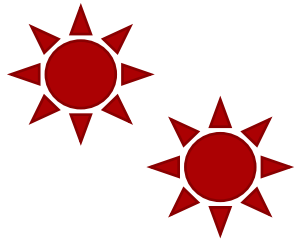


5 Saturated Fatty Acids



2 Insulin Receptors

2 IRS Molecules

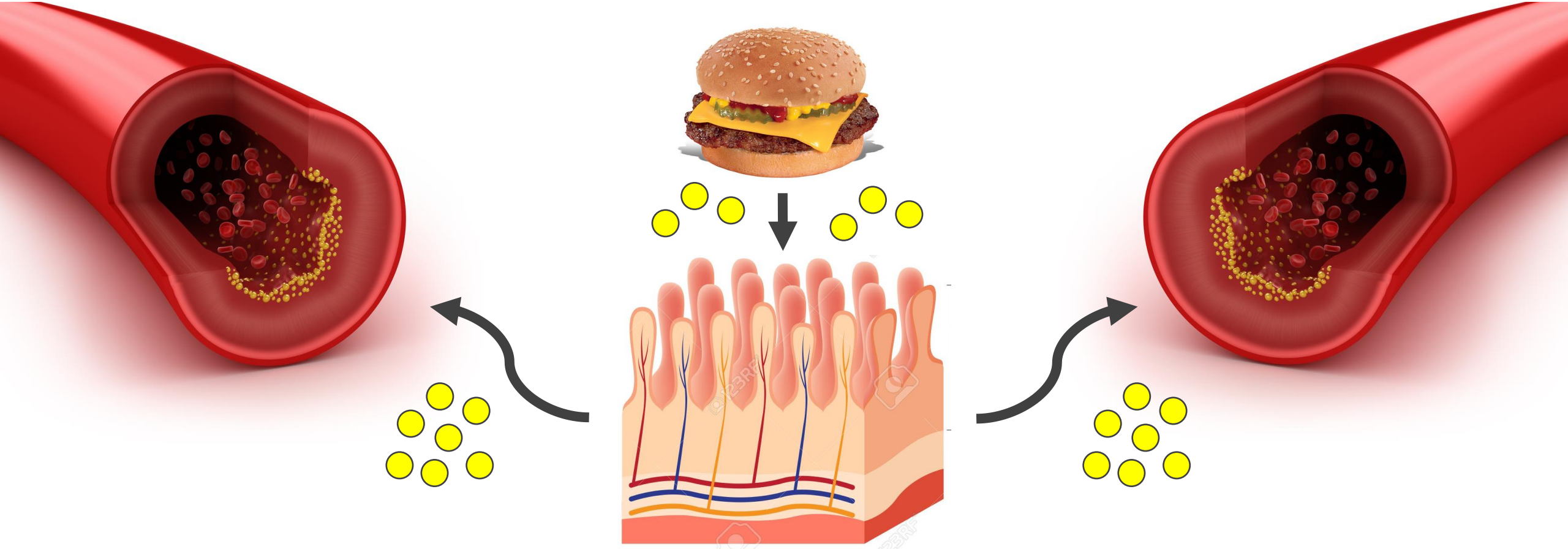


2 DAG Molecules

The Sequence of Events of Insulin Resistance

- **Step 1:** Lipids enter your blood before glucose
- **Step 2:** Fatty acids enter your liver and muscle
- **Step 3:** Fatty acids enter your adipose tissue
- **Step 4:** Your adipose tissue becomes inflamed
- **Step 5:** Your beta cells become lipotoxic

Step 1: Lipids Enter Your Blood *Before* Glucose



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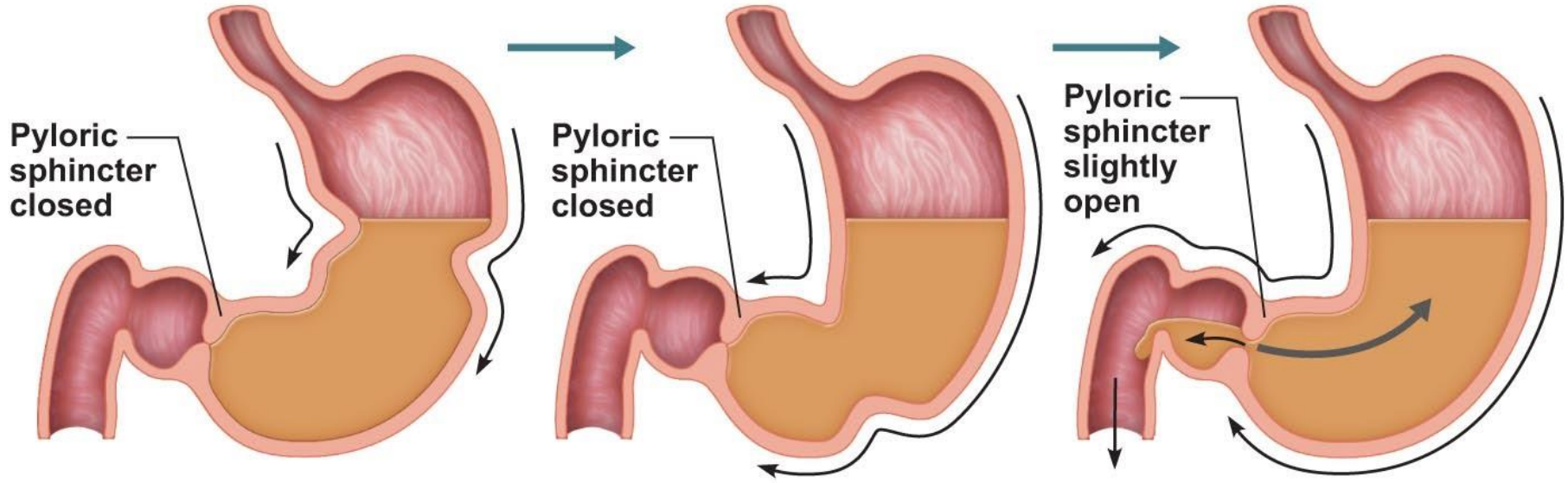
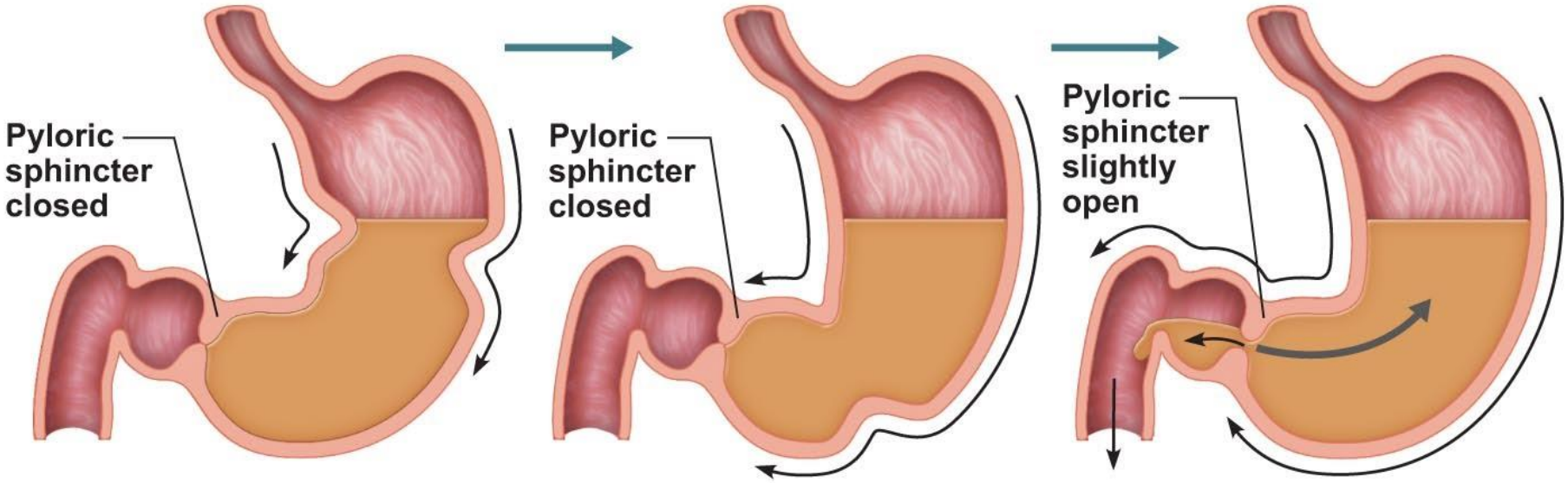


Fat-Rich Meals Slow Your Gastric Emptying Rate

Step 1: Lipids Enter Your Blood *Before* Glucose



Lipids are Absorbed Rapidly and CHO is Absorbed Slowly

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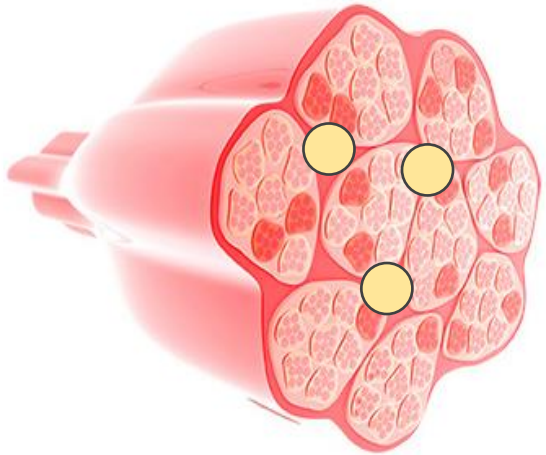
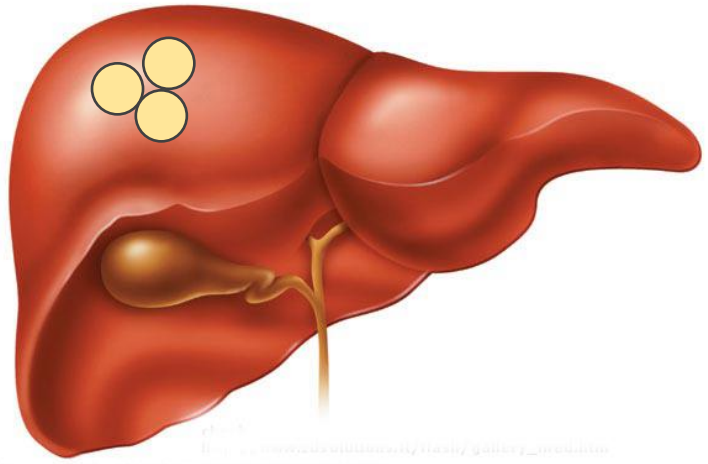
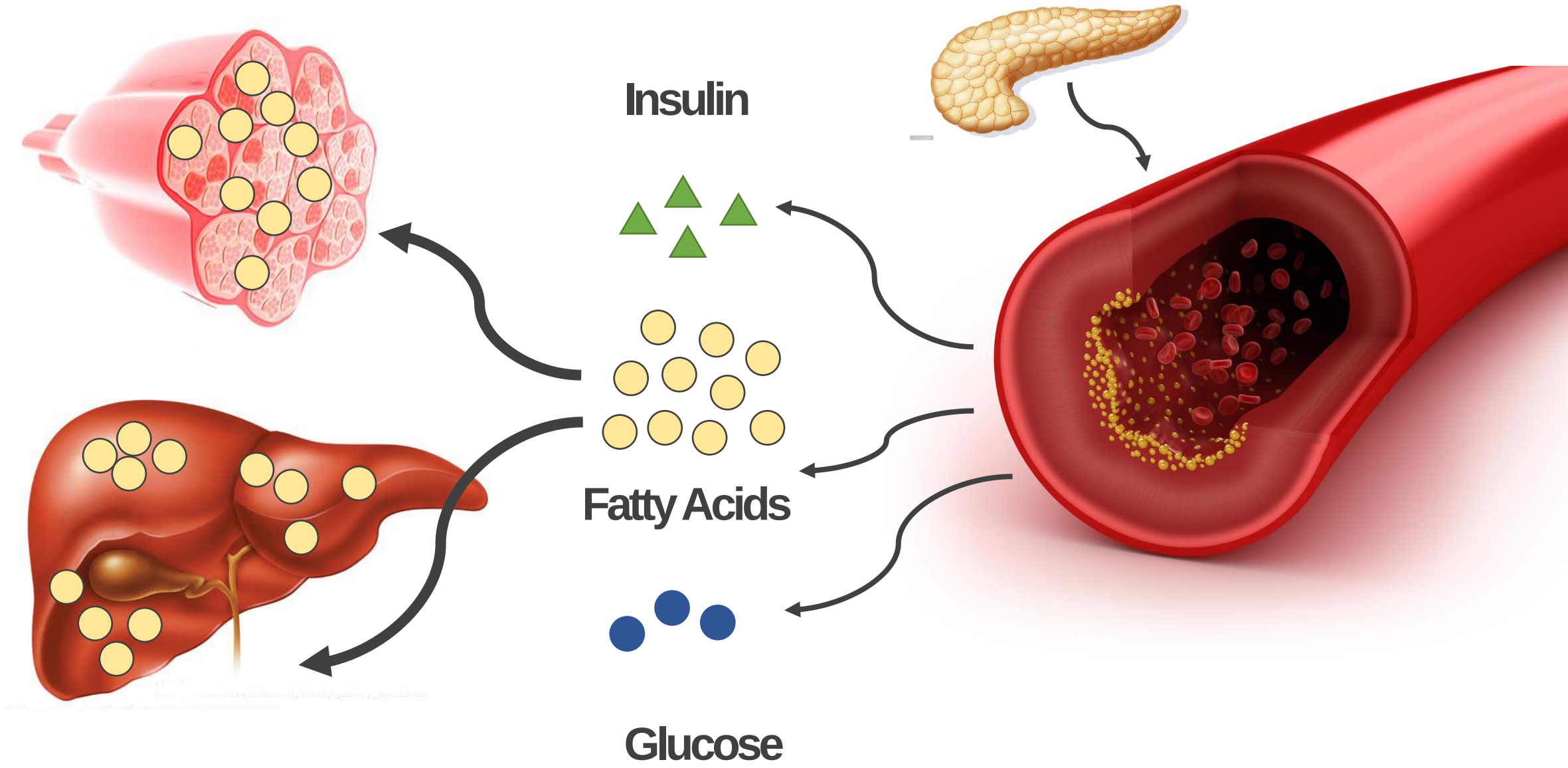


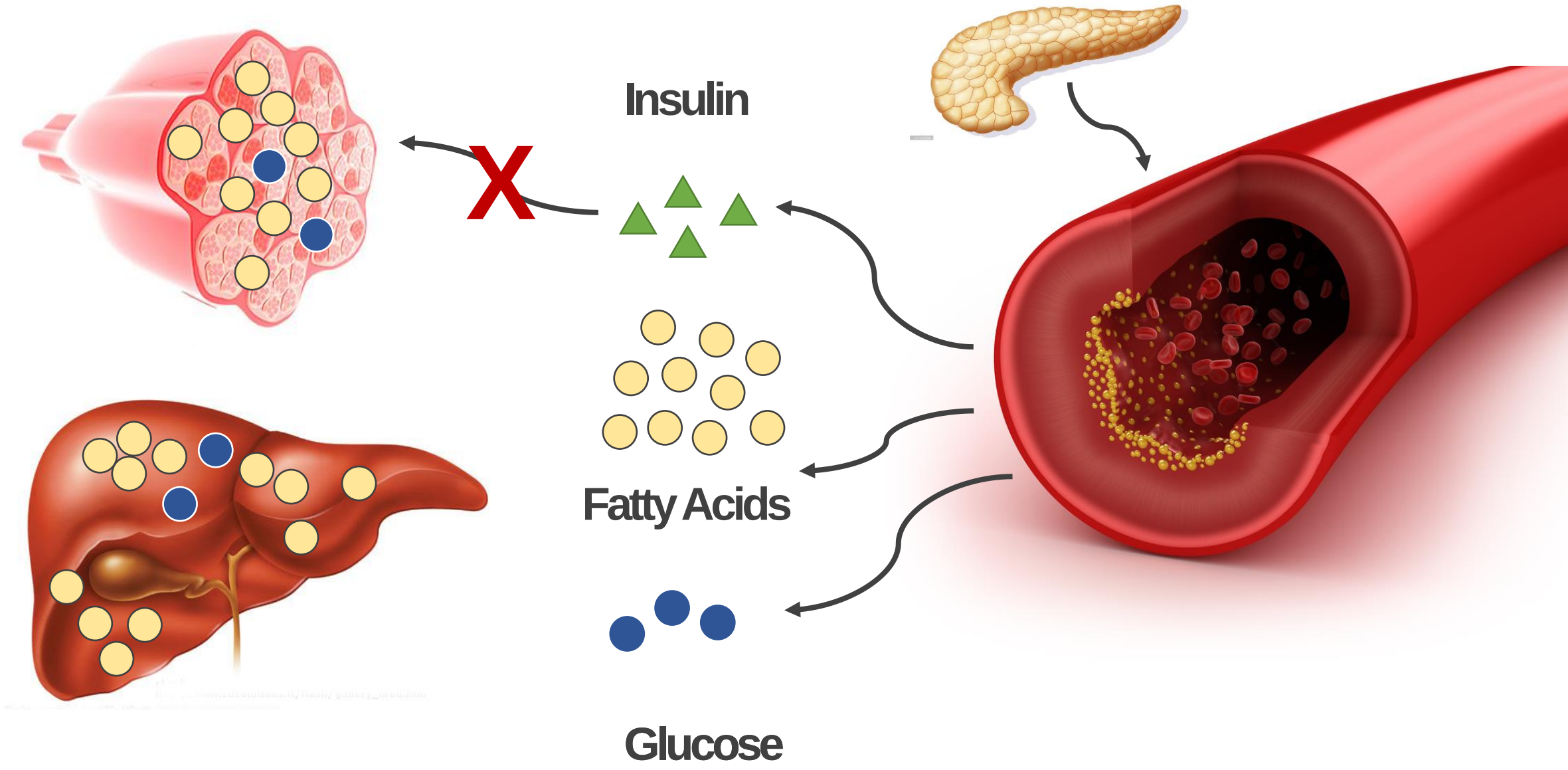


Insulin

Fatty Acids

Glucose


Insulin
Fatty Acids
Glucose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Fatty Acids
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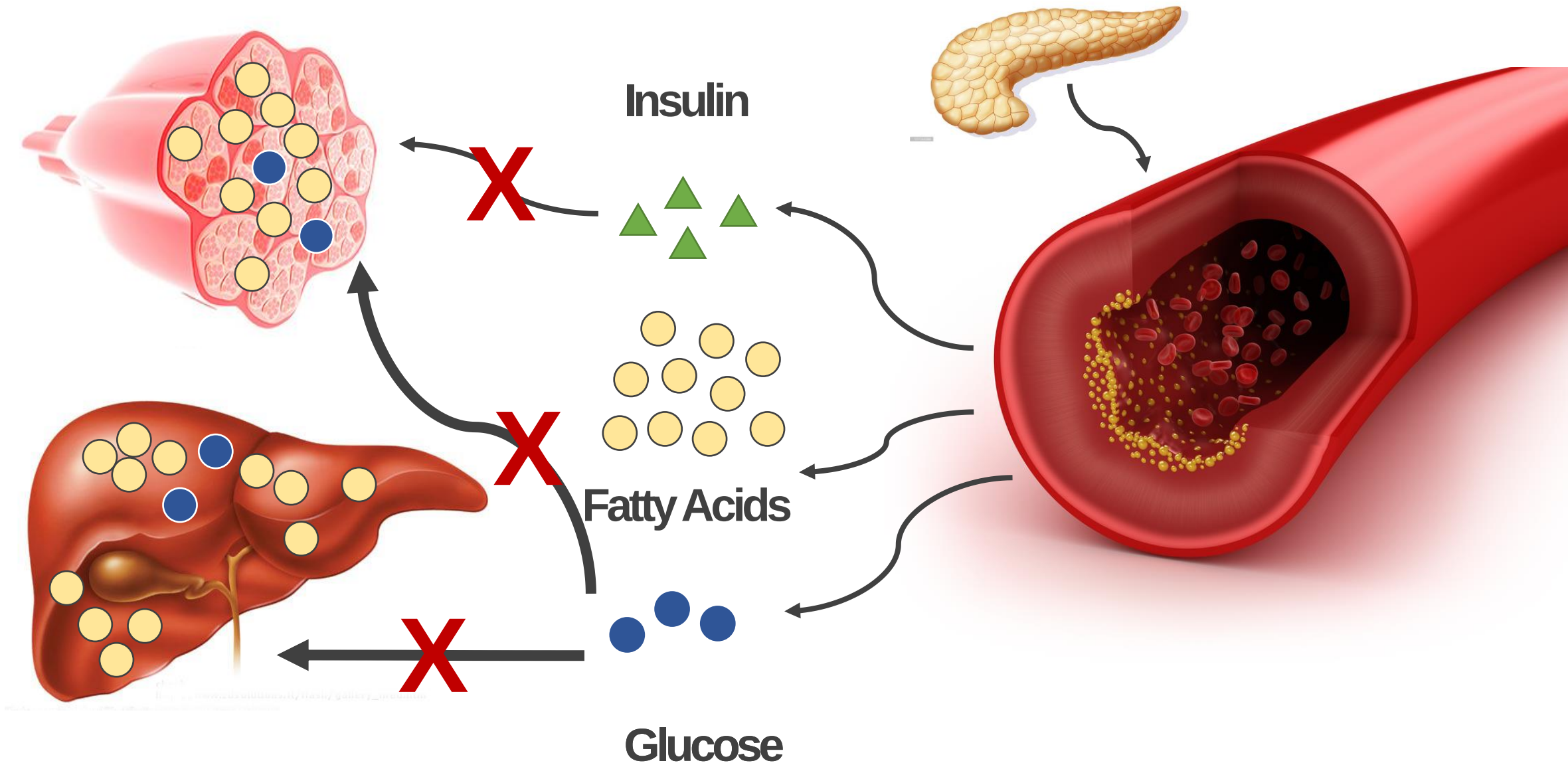
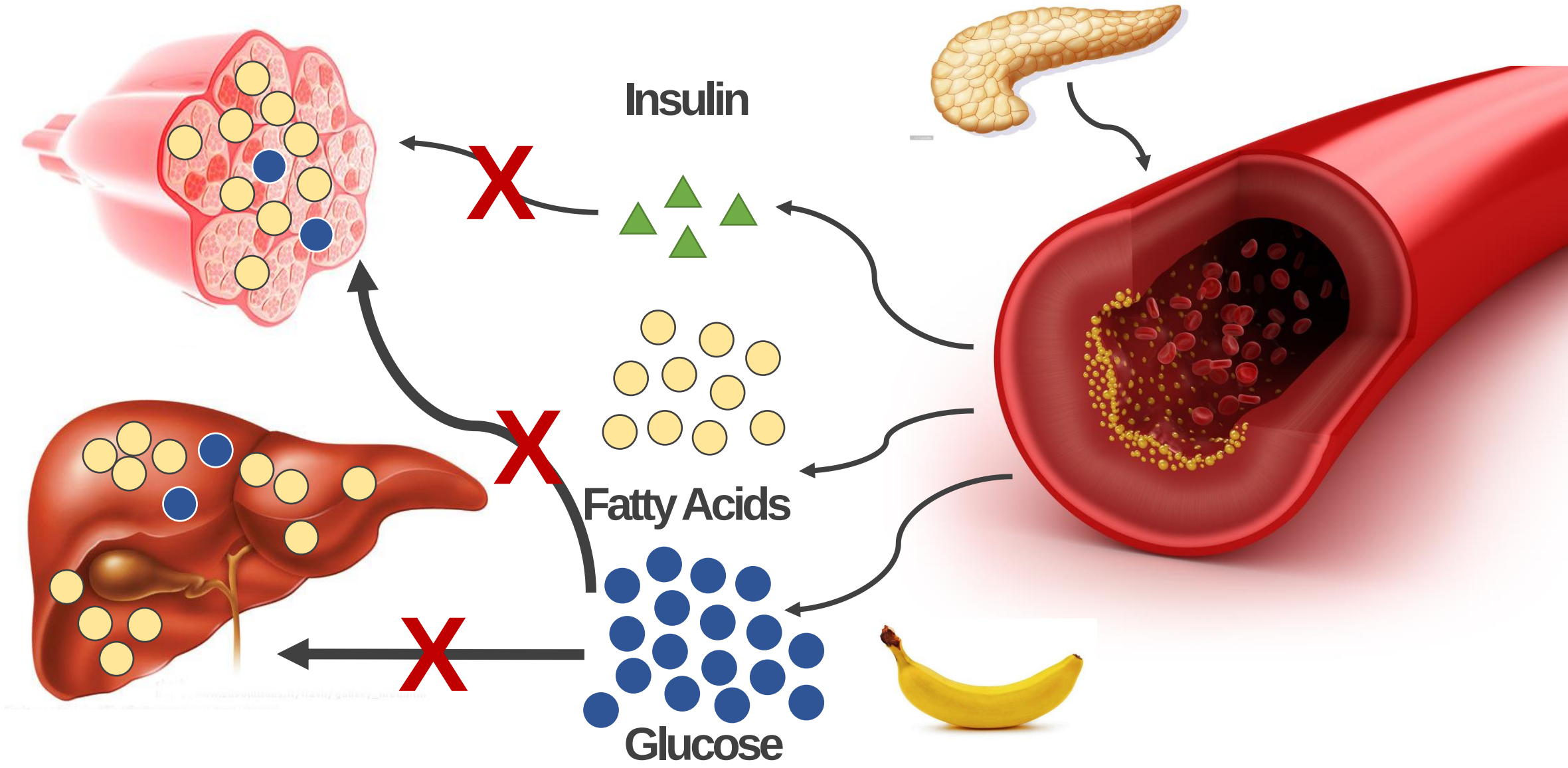

Insulin
Fatty Acids
Glucose


Insulin
Fatty Acids
Glucose

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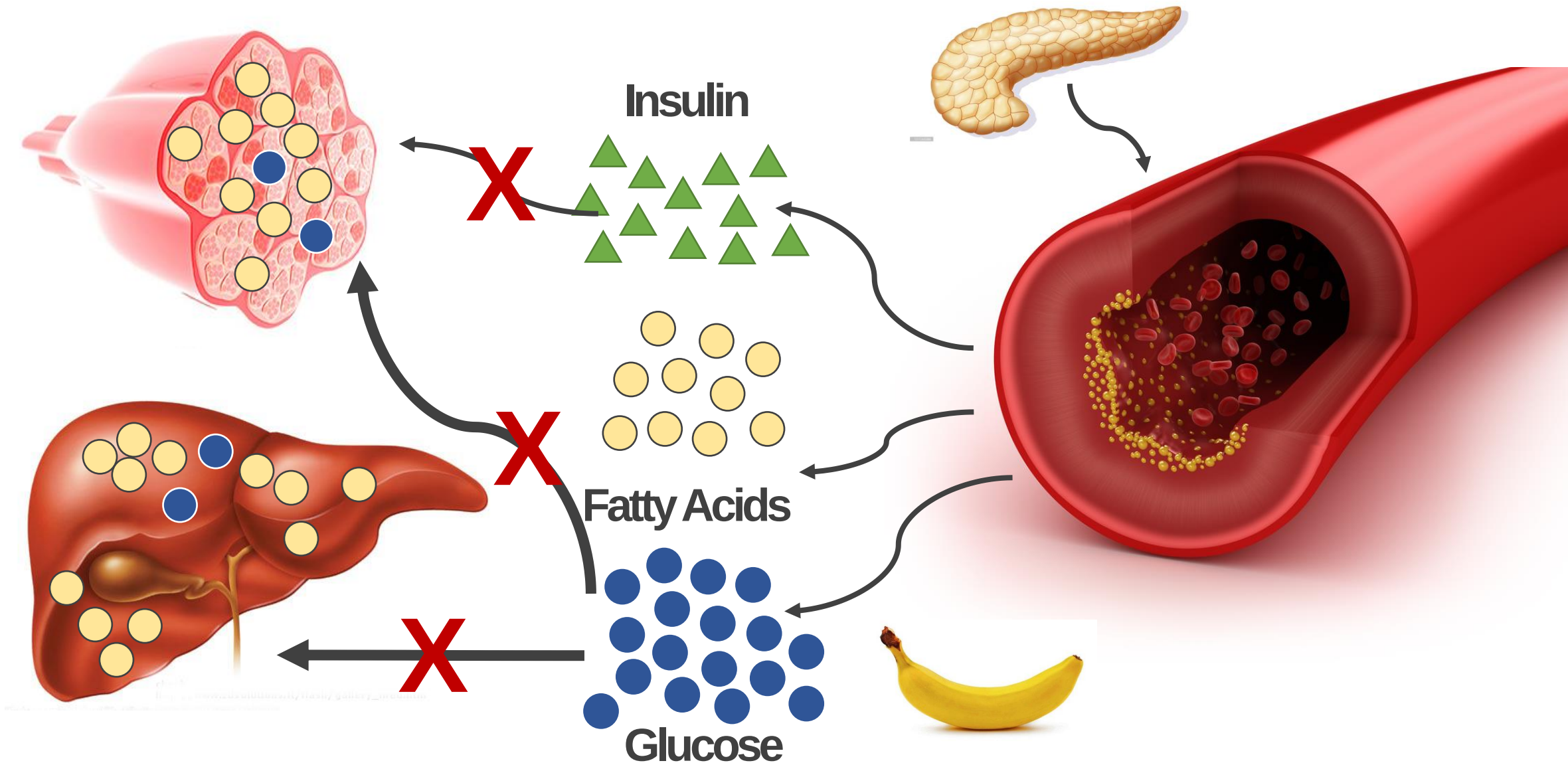

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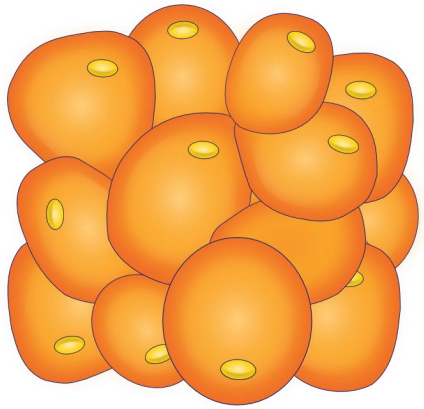
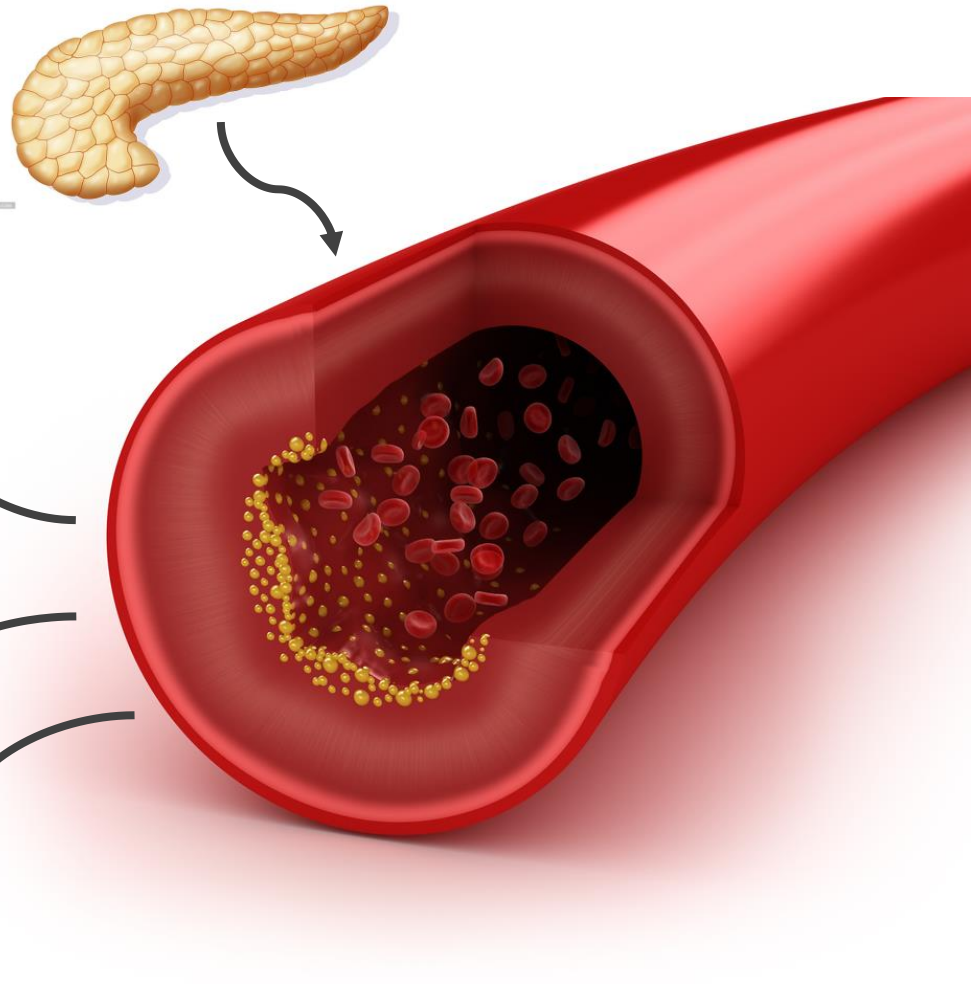
- **Step 5:** Your beta cells become lipotoxic

My job is to protect peripheral tissues from accumulating excess saturated fat





Insulin

Fatty Acids

Glucose

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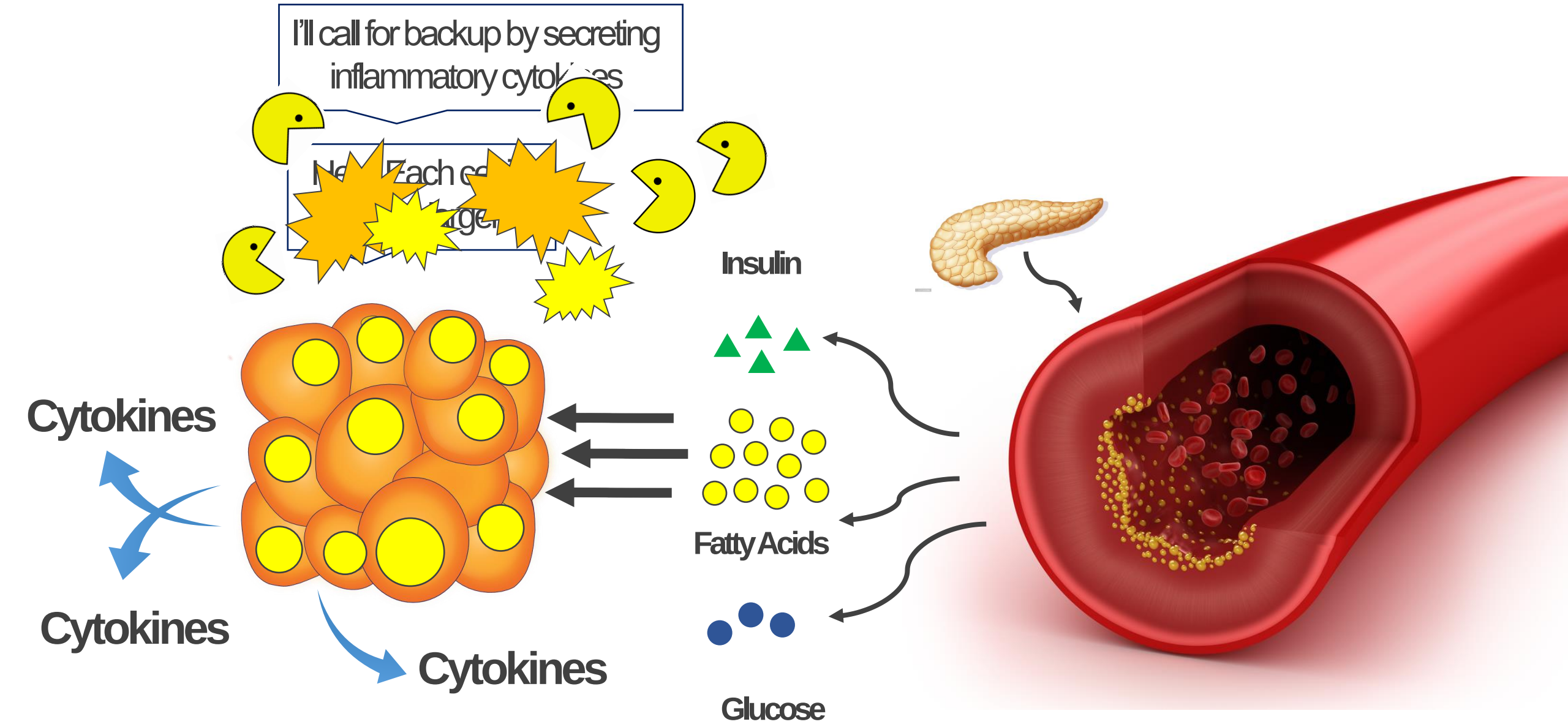
I'll call for backup by secreting inflammatory cytok
Insulin
Cytokines
Cytokines
Cytokines
Fatty Acids
Glucose

Endocr J. 2012;59(10):849-57. Epub 2012 Aug 9.

Adipose tissue inflammation and ectopic lipid accumulation.

Suganami T[1], Tanaka M, Ogawa Y.

Author information

Abstract

Obesity may be viewed as a chronic low-grade inflammatory disease as well as a metabolic disease. Indeed, unbalanced production of pro- and anti-inflammatory adipocytokines critically contributes to the obesity-induced insulin resistance. In addition to lipid-laden mature adipocytes, adipose tissue is composed of various stromal cells such as preadipocytes, endothelial cells, fibroblasts, and immune cells that may be involved in adipose tissue functions. Accumulating evidence has suggested that adipocytes and stromal cells in adipose tissue change dramatically in number and cell type during the course of obesity, which is referred to as "adipose tissue remodeling." Among stromal cells, infiltration of macrophages in obese adipose tissue precedes the development of insulin resistance in animal models, suggesting that they are crucial for adipose tissue inflammation. We have provided evidence suggesting that a paracrine loop involving saturated fatty acids and tumor necrosis factor-α derived from adipocytes and macrophages, respectively, aggravates obesity-induced adipose tissue inflammation. On the other hand, storing excessive energy as triglyceride is also a fundamental function of adipose tissue. Recent evidence suggests that reduced lipid storage in obese adipose tissue contributes to ectopic lipid accumulation in non-adipose tissues such as the liver, skeletal muscle, and pancreas, where lipotoxicity impairs their metabolic functions. Notably, chronic inflammation is capable of inducing insulin resistance, lipolysis, and interstitial fibrosis in adipose tissue, all of which may reduce the lipid-storing function. Understanding the molecular mechanism underlying adipose tissue remodeling may lead to the identification of novel therapeutic strategies to prevent or treat obesity-induced adipose tissue inflammation.

Review

From excess adiposity to insulin resistance: The role of free fatty acids

Cristiano Capurso [a], Antonio Capurso [b,*]

[a] University of Foggia, Department of Internal Medicine and Geriatrics, Foggia, Italy
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Obesity
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ABSTRACT

With a positive caloric balance, adipocytes undergo excessive hypertrophy, which causes adipocyte dysfunction, as well as adipose tissue endocrine and immune responses. A preferential site of fat accumulation is the abdominal-perivisceral region, due to peculiar factors of the adipose tissue in such sites, namely an excess of glucocorticoid activity, which promotes the accumulation of fat; and the greater metabolic activity and sensitivity to lipolysis, due to increased number and activity of β3-adrenoceptors and, partly, to reduced activity of α2-adrenoceptors. As a consequence, more free fatty acids (FFA) are released into the portal system. Hypertrophic adipocytes begin to secrete low levels of TNF-α, which stimulate preadipocytes and endothelial cells to produce MCP-1, in turn responsible for attracting macrophages to the adipose tissue, thus developing a state of chronic low-grade inflammation which is causally linked to insulin resistance.

Excess of circulating FFA, TNF-α and other factors induces insulin resistance. FFA cause insulin resistance by inhibiting insulin signaling through the activation of serin-kinases, i.e. protein kinase C-Θ, and the kinases JNK and IKK, which promote a mechanism of serine phosphorylation of Insulin Receptor Substrates (IRS), leading to interruption of the downstream insulin receptor (IR) signaling. TNF-α, secreted by hypertrophic adipocytes and adipose tissue macrophages, also inhibits IR signaling by a double mechanism of serine-phosphorylation and tyrosine-dephosphorylation of IRS-1, causing inactivation and degradation of IRS-1 and a consequent stop of IR signaling.

Such mechanisms explain the transition from excess adiposity to insulin resistance, key to the further development of type 2 diabetes.

Chronic inflammation in fat plays a crucial role in the development of obesity-related insulin resistance

Haiyan Xu, … , Louis A. Tartaglia, Hong Chen

J Clin Invest. 2003;112(12):1821-1830. https://doi.org/10.1172/JCI19451.

adipocyte lipolysis and formation of multinucleate giant cells. These data suggest that macrophages in WAT play an active role in morbid obesity and that macrophage-related inflammatory activities may contribute to the pathogenesis of obesity-induced insulin resistance. We propose that obesity-related insulin resistance is, at least in part, a chronic inflammatory disease initiated in adipose tissue.

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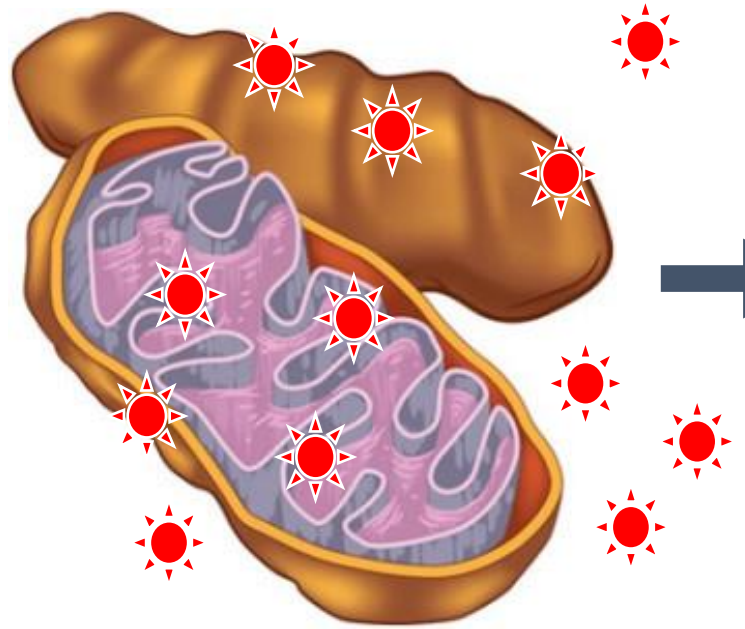
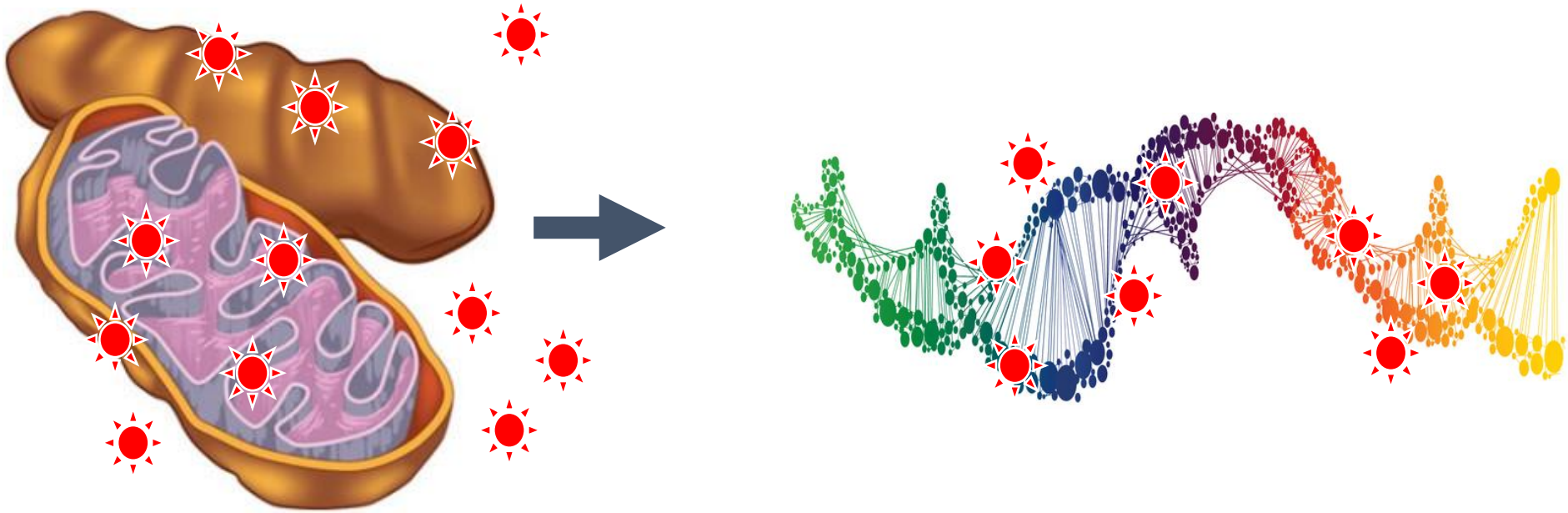
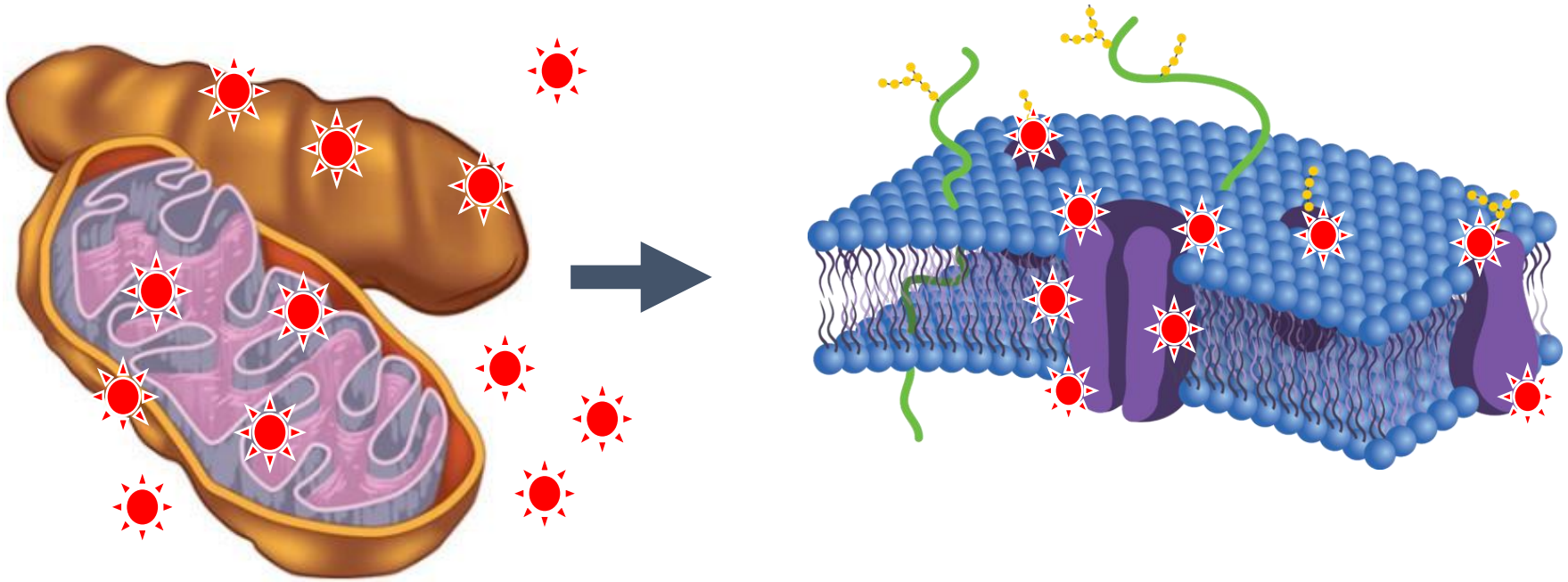
High Fat Diets Increase Free Radical Production in Beta Cell Mitochondria

High-Fat Diet →  → Free Radicals

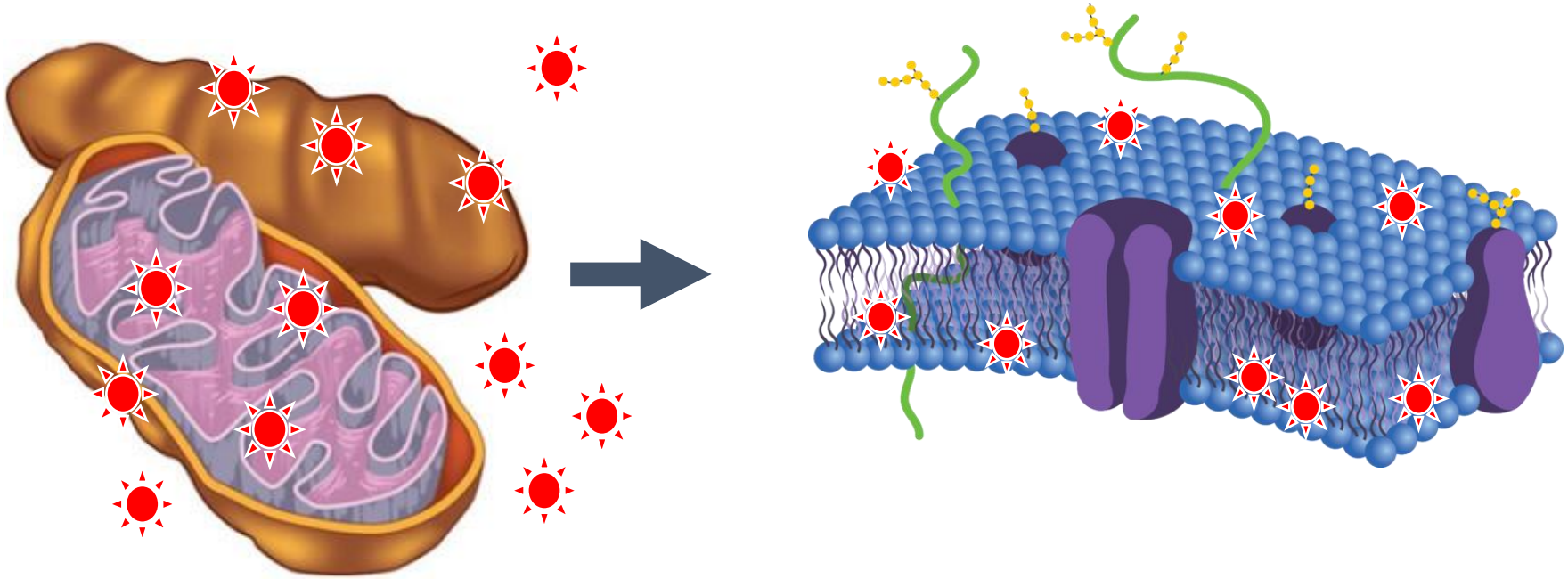
Free Radicals Cause *Direct* DNA Damage



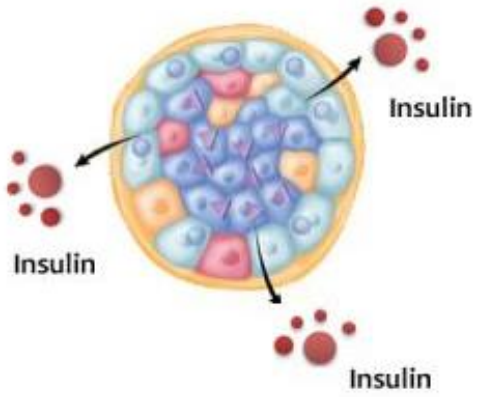
Free Radicals Cause Protein Oxidation



Free Radicals Cause Lipid Peroxidation



Step 1: Normal Islet Function



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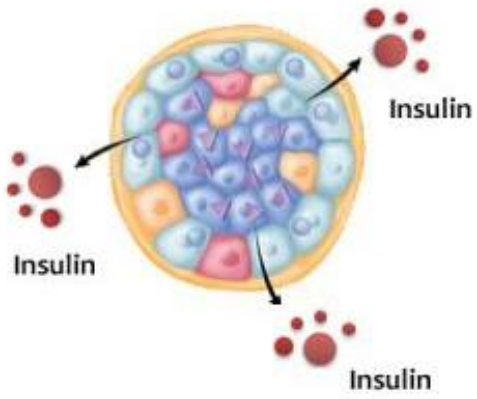
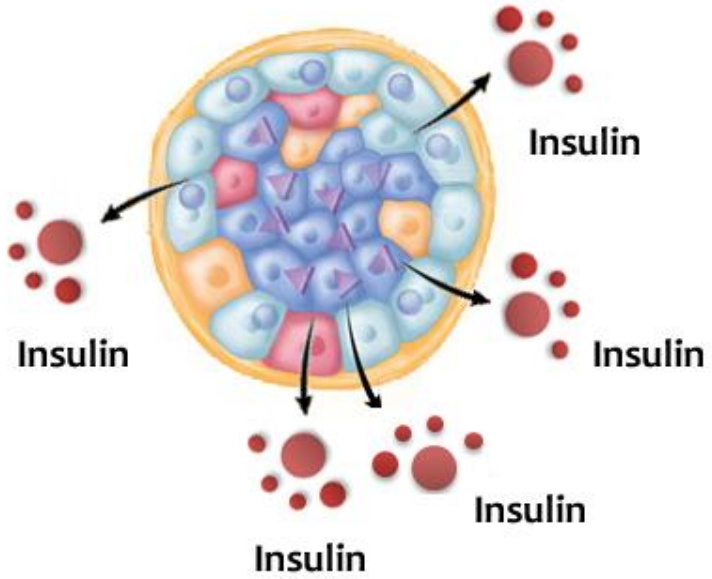


Step 2: Islet Hyperplasia and Hyperinsulinemia



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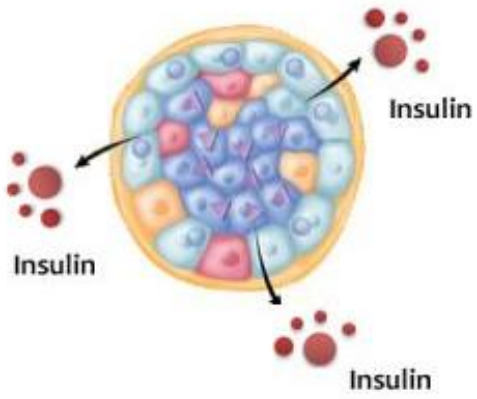

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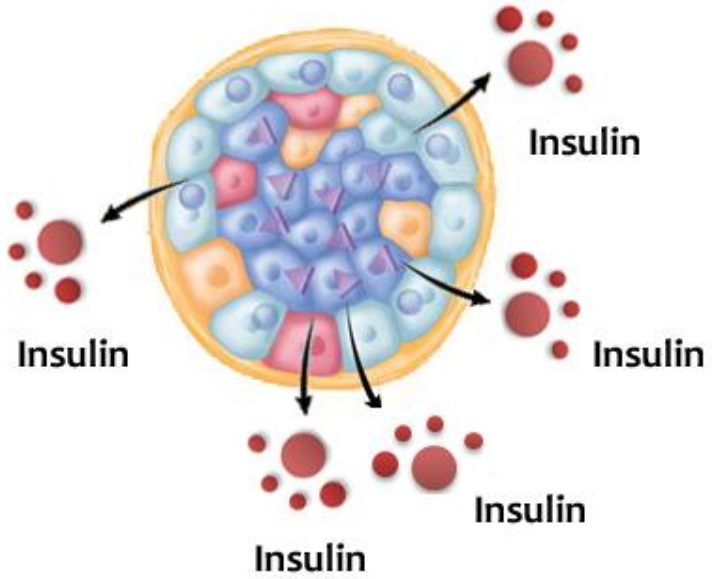

Step 3: Beta Cell Sucicide

The role of lipids in the pathogenesis of muscle insulin resistance and beta cell failure in type II diabetes and obesity

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Key words: Free fatty acids, triglyceride, long chain acyl CoAs, thiazolidinediones, high fat diet

Summary: This review considers evidence for, and putative mechanisms of, lipid-induced muscle insulin resistance. Acute free fatty acid elevation causes muscle insulin resistance in a few hours, with similar muscle lipid accumulation as accompanies more prolonged high fat diet-induced insulin resistance in rodents. Although causal relations are not as clearcut in chronic human insulin resistant states such as obesity and type 2 diabetes, it is now recognised that muscle lipids also accumulate in these states. The classic Randle glucose-fatty acid cycle is only one of a number of mechanisms by which fatty acids might influence muscle glucose metabolism and insulin action. A key factor is seen to be accumulation of muscle long chain acyl CoAs, which could alter insulin action via several mechanisms including chronic activation of protein kinase C isoforms or ceramide accumulation. These interactions are fundamental to understanding metabolic effects of new insulin "sensitizers", eg thiazolidinediones, which alter lipid metabolism and improve muscle insulin sensitivity in insulin resistant states. Recent work has also pointed to a possible role of lipids in beta cell deterioration ("lipotoxicity") associated with type 2 diabetes.

Lipotoxicity of β-Cells in Obesity and in Other Causes of Fatty Acid Spillover

Roger H. Unger and Yan-Ting Zhou

ways of nonoxidative metabolism leading to apoptosis of certain tissues. FA overload in skeletal muscle causes insulin resistance; in myocardium, it impairs cardiac function; and in pancreatic islets, it causes β-cell dysfunction, apoptosis, and diabetes. All abnormalities in these tissues can be blocked by troglitazone, an inhibitor of FA accumulation. *Diabetes* 50 (Suppl. 1):S118–S121, 2001

Target organ	Potential lipotoxic consequences
Pancreas	Reduced insulin secretion, pancreatic β-cell failure, islet dysfunction, impaired proliferative capacity, and lipoapoptosis
Heart	Myocardial insulin resistance, cardiac steatosis, cardiomyopathy, and heart failure
Liver	Fatty liver, nonalcoholic steatohepatitis, and cirrhosis
Muscle	Reduced insulin-stimulated glucose-uptake and insulin resistance

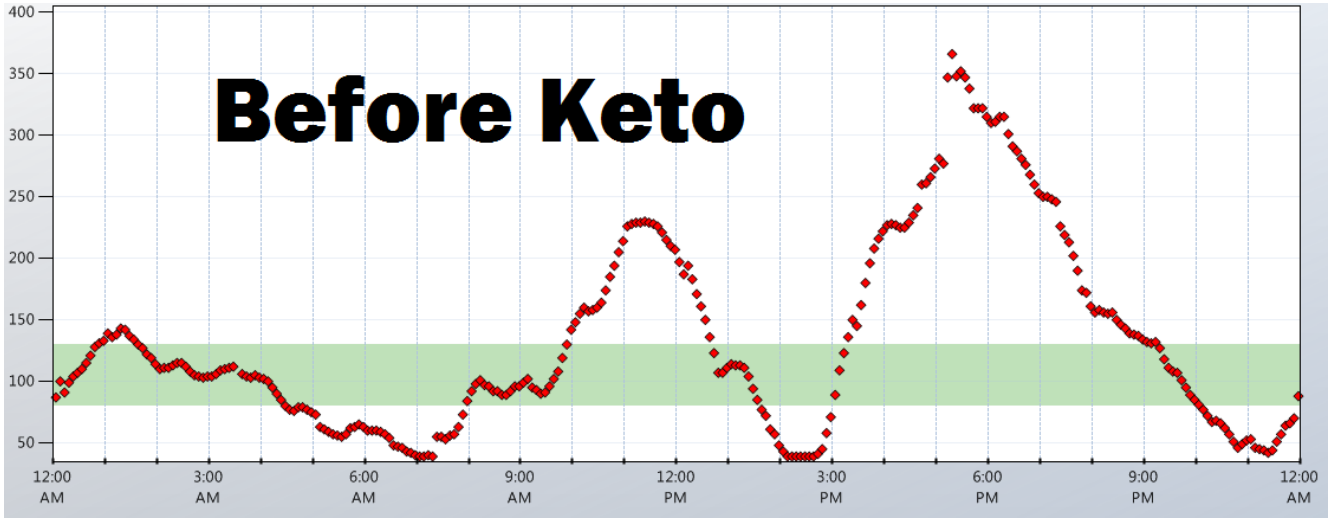
Mastering Diabetes Online Group Coaching

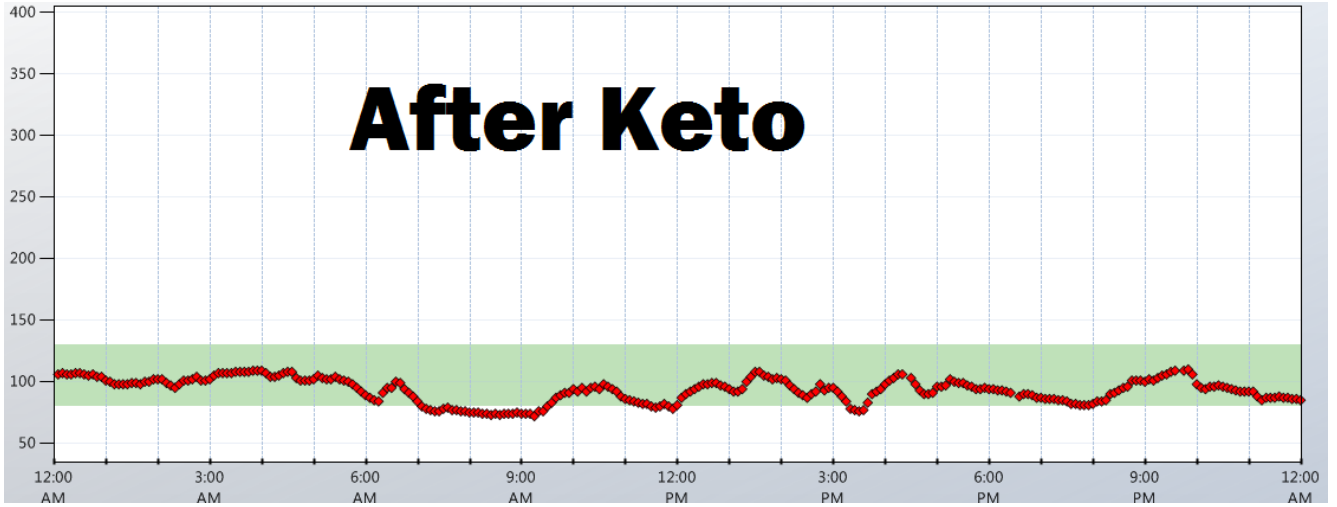
"My A1c is 4.7!"

"My blood glucose has never been lower!"

"My blood glucose is between 80-90 all day long!"

Mastering Diabetes Online Group Coaching





Low-Carbohydrate and Ketogenic Diets Reduce Your A1c…but *Increase Your Level of Insulin Resistance*

Low-Carbohydrate, High-Fat Diet

- **Improved BG Control**
- **Reduced A1c**
- **Weight Loss**
- Reduced Total Cholesterol
- Increased HDL Cholesterol
- Reduced Triglycerides
- Reduced Blood Pressure

Short-Term Improvements

- Muscle Insulin Resistance
- Liver Insulin Resistance
- Beta Cell Insulin Resistance
- Carbohydrate Intolerance
- Beta Cell Apoptosis
- High Cholesterol
- Hypertension

Long-Term Side Effects

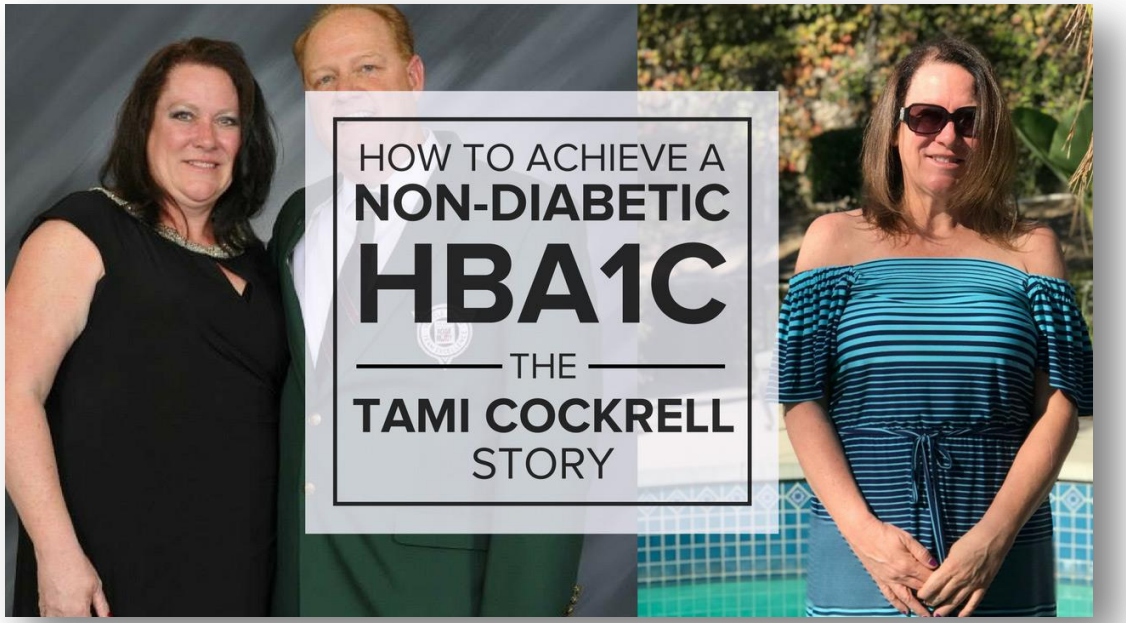
How Do You Maximize Insulin Sensitivity Using a Low-Fat, Plant-Based, Whole-Food Lifestyle?

The Mastering Diabetes Program

The world's first online coaching program designed to teach you how to MAXIMIZE Your insulin sensitivity using low-fat, plant-based, whole-food nutrition

Joaquin B.
Prediabetes

Weight: -35 pounds in 60 days
Fasting BG: 145 to 95 in 7 days
Carbohydrate Intake: 75 to 350 g/day
Energy Levels: Significantly Improved



Tami Cockrell
Type 2 Diabetes

Weight: -37 pounds in 4.5 months
Fasting BG: 123 to 93 mg/dL
A1c: 7.1% to 5.3%
Total Cholesterol: 266 to 200 mg/dL
LDL Cholesterol: 160 to 129 mg/dL
Metformin: 2000 mg/day to ZERO

Low-Fat, Plant-Based, Whole-Food Nutrition

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Fruits
Starchy vegetables
Non-starchy vegetables
Beans, lentils and peas
Green leafy vegetables
Intact whole grains
Herbs and spices

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Fruits
Starchy vegetables
Non-starchy vegetables
Beans, lentils and peas
Green leafy vegetables
Intact whole grains
Herbs and spices

Nuts
Seeds
Avocados
Coconuts
Olives
Pastas
Breads (also sprouted)

Mastering Diabetes Online Group Coaching

Fruits
Starchy vegetables
Non-starchy vegetables
Beans, lentils and peas
Green leafy vegetables
Intact whole grains
Herbs and spices

Nuts
Seeds
Avocados
Coconuts
Olives
Pastas
Breads (also sprouted)

Dairy products
Eggs
Red and white meat
Fish and shellfish
Oils of any kind
Refined sugars
Pastries and breads

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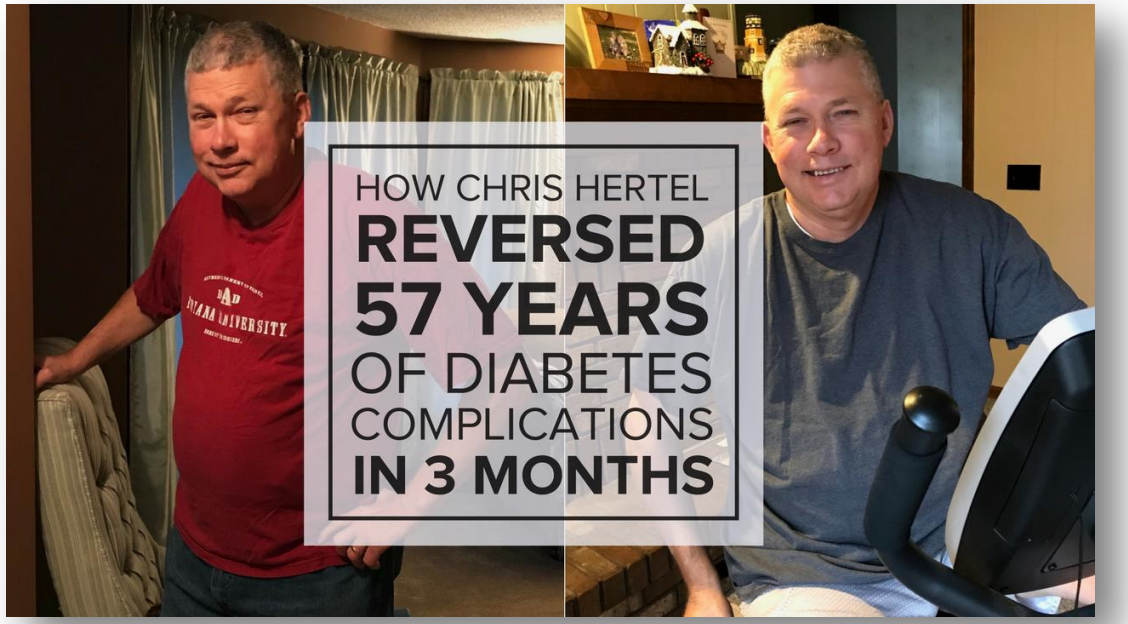
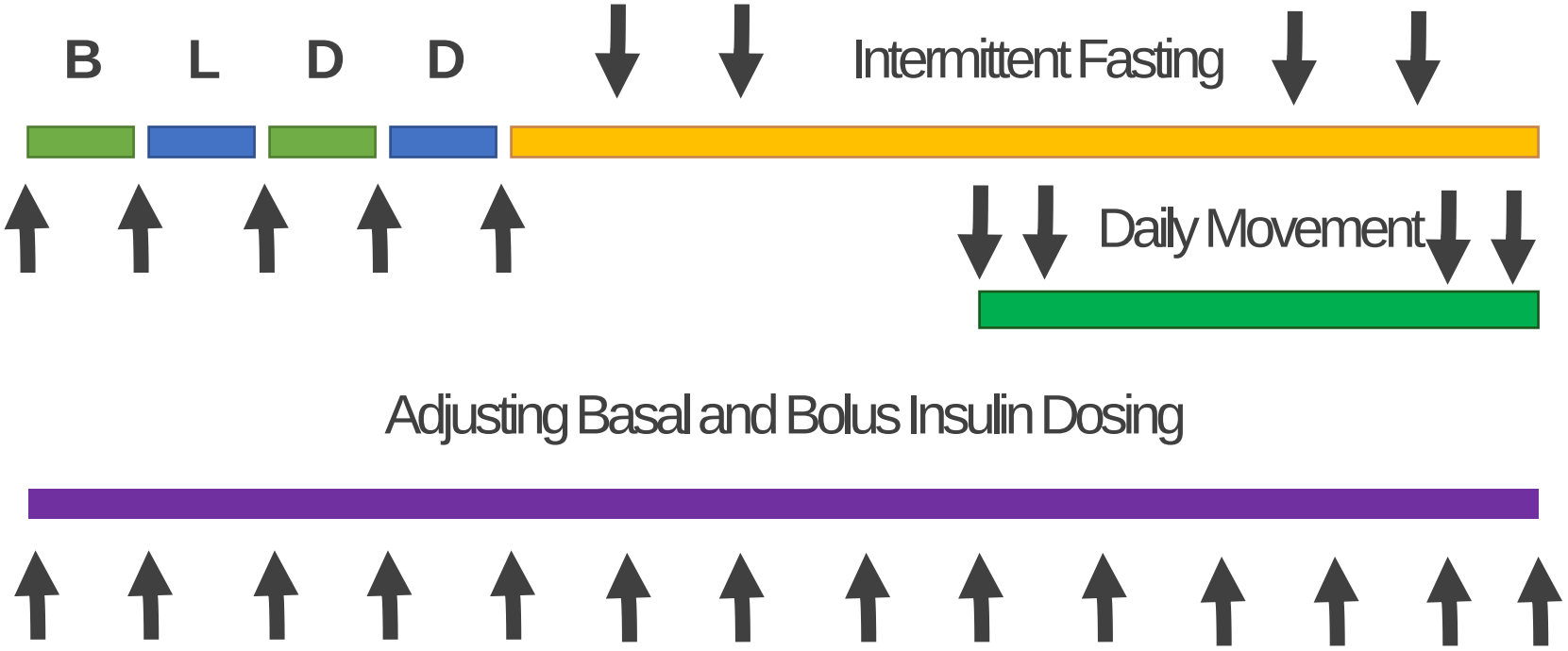


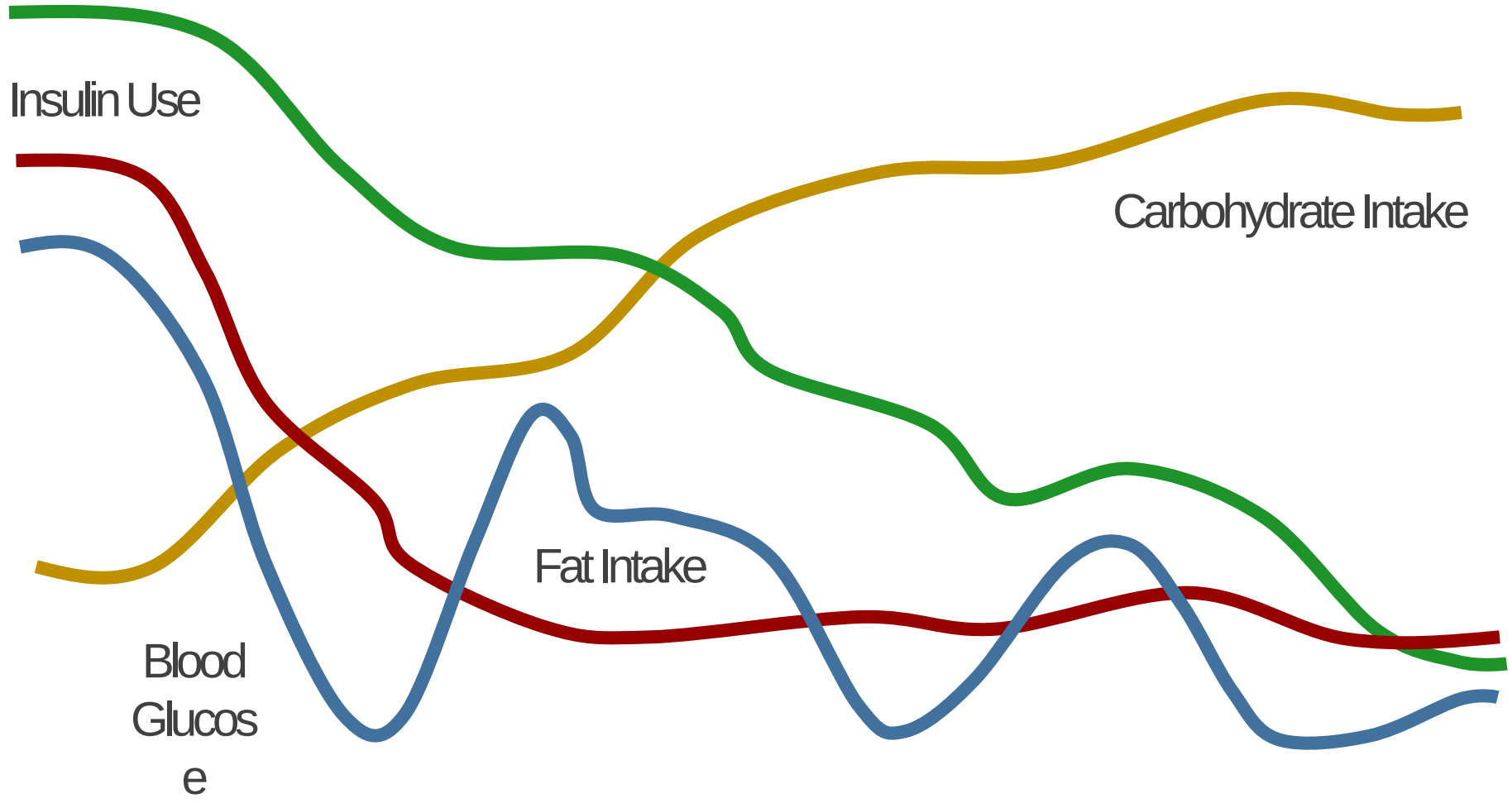
Chris Hertel
Type 1 Diabetes

Weight: -76 pounds in 11 months
Fasting BG: 160 to 85 mg/dL
A1c: 6.5% to 5.2%
Basal Insulin: -20U per day
Bolus Insulin: -15U per day

We Recommend a Step-by-Step Approach



We Recommend a Step-by-Step Approach



Low-Fat, Plant-Based, Whole-Food Diet Guidelines for Maximum Insulin Sensitivity

1. Eat a minimum of 70-80% carbohydrate from whole plant foods
2. Eat a maximum of 10-15% fat from whole plant foods
3. Eat a maximum of 10-15% protein from whole plant foods
4. Sweat for 30-60 minutes per day
5. Intermittent fast when necessary
6. Join a community of others for daily inspiration and commitment

Raj B.
Type 2 Diabetes

A1c: 7.4% to 5.2%
Metformin: 2,000mg to 0 mg
Fasting BG: 180 to 85 mg/dL
Total Cholesterol: 215 to 149
Weight: -64 pounds
Fatty Liver Disease: *Reversed*

Sanna S.
Type 1 Diabetes

Carbohydrates: 25 to 200 grams per day
Insulin: 22 to 11 U per day
24-hour urine protein: 4.7 to 0.5 grams
Cholesterol: 267 to 112 mg/dL
Blood pressure: 150/100 to 102/75 mmHg
Stage 3 Kidney Disease: Reversed

Meet Your Team of Dedicated Expert Coaches

Cyrus Khambatta, PhD
Type 1 Diabetes

Robby Barbaro
Type 1 Diabetes

Kylie Buckner, MSN, RN
Plant-Based Nurse

Adam Sud
Reversed Type 2 Diabetes

Marc Ramirez
Reversed Type 2 Diabetes