

The Use of Anti-Inflammatory Nutrition To Slow The Aging Process

Dr. Barry Sears
President
Inflammation Research Foundation



**Anti-Aging Is Best
Defined As
Slowing The Development
Of Chronic Disease**



Chronic Disease Burden Kills

- 70% of 65-yr olds have at least two chronic diseases
- Most chronic diseases have common metabolic origins
- The more chronic diseases you have the faster you die

Fontana et al Nature 511:405 (2014)

**All Chronic Diseases Lead
Back To Inflammation**



FEBRUARY 23, 2004

BUSH'S
MILITARY RECORDS
IS DISNEY MOUSETRAPPED?

TIME

THE SECRET KILLER

- The surprising link between **INFLAMMATION** and **HEART ATTACKS, CANCER, ALZHEIMER'S** and other diseases
- What you can do to fight it



www.time.com AOL Keyword: TIME

Chronic Diseases Associated With Excess Inflammation

- Obesity
- Metabolic Syndrome
- Type 2 Diabetes
- Heart Disease
- Cancer
- Neurological
 - Alzheimer's, Depression, ADHD, Parkinson's
- Auto-immune
 - Type 1 Diabetes, RA, Multiple Sclerosis
- Asthma
- Allergies
- Other inflammatory conditions (“itis”)

What Is Inflammation?

- **Ancient Greeks**
 - Internal Fire
- **Ancient Romans**
 - Heat
 - Pain
 - Swelling
 - Redness


What Is Inflammation?

- Complex orchestration of pro-inflammatory and anti-inflammatory events
- Usually associated with pain
- Mediated by eicosanoids
- Treated by drugs that alter eicosanoids
 - Aspirin
 - NSAID' s
 - COX-2 inhibitors
 - Steroids

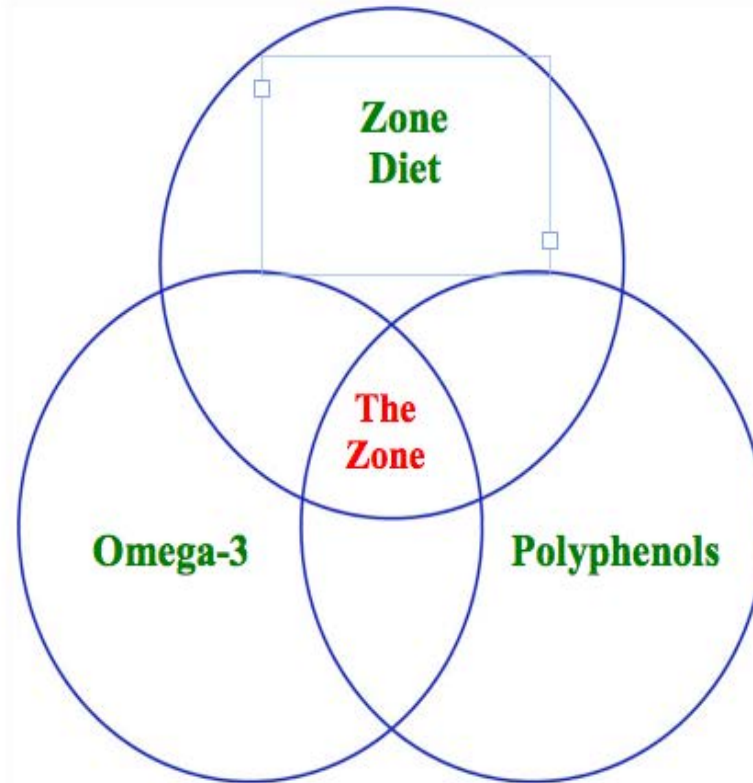
But You Need A Zone

- Too little of an inflammatory response
 - Sitting target for microbes
 - Injuries never heal
- Too much of an inflammatory response
 - The body attacks itself


Events That Turn On Inflammatory Responses

- Microbial invasion
 - Injuries
 - Diet
- 

Overview Of Anti-Inflammatory Nutrition




The Science Of The Zone

- Improved hormonal control
 - Resolution of inflammation
 - Control of gene expression
- 

Unique Roles For Each Dietary Intervention

- *Zone Diet*
 - Improved hormonal balance
 - Reduction of inflammation
 - Increase in satiety
- *Omega-3 Fatty Acids*
 - Acceleration of the resolution of inflammation
- *Polyphenols*
 - Activation of anti-oxidant, anti-inflammatory, and anti-aging genes

Benefits Of Being In The Zone

- Reduce the likelihood of chronic disease
 - Slow the rate of aging
 - Defines the evidence-based wellness
- 

Clinical Markers of the Zone

- **AA/EPA ratio**

- Marker of cellular inflammation
- Maintain between 1.5 and 3

- **TG/HDL ratio**

- Marker of insulin resistance in the liver
- <0.4 (mmol/l) or <1 (mg/dl)

- **HbA₁C**

- Marker of long-term glycemic control
- 5%

Phases Of Inflammation

Initiating Event




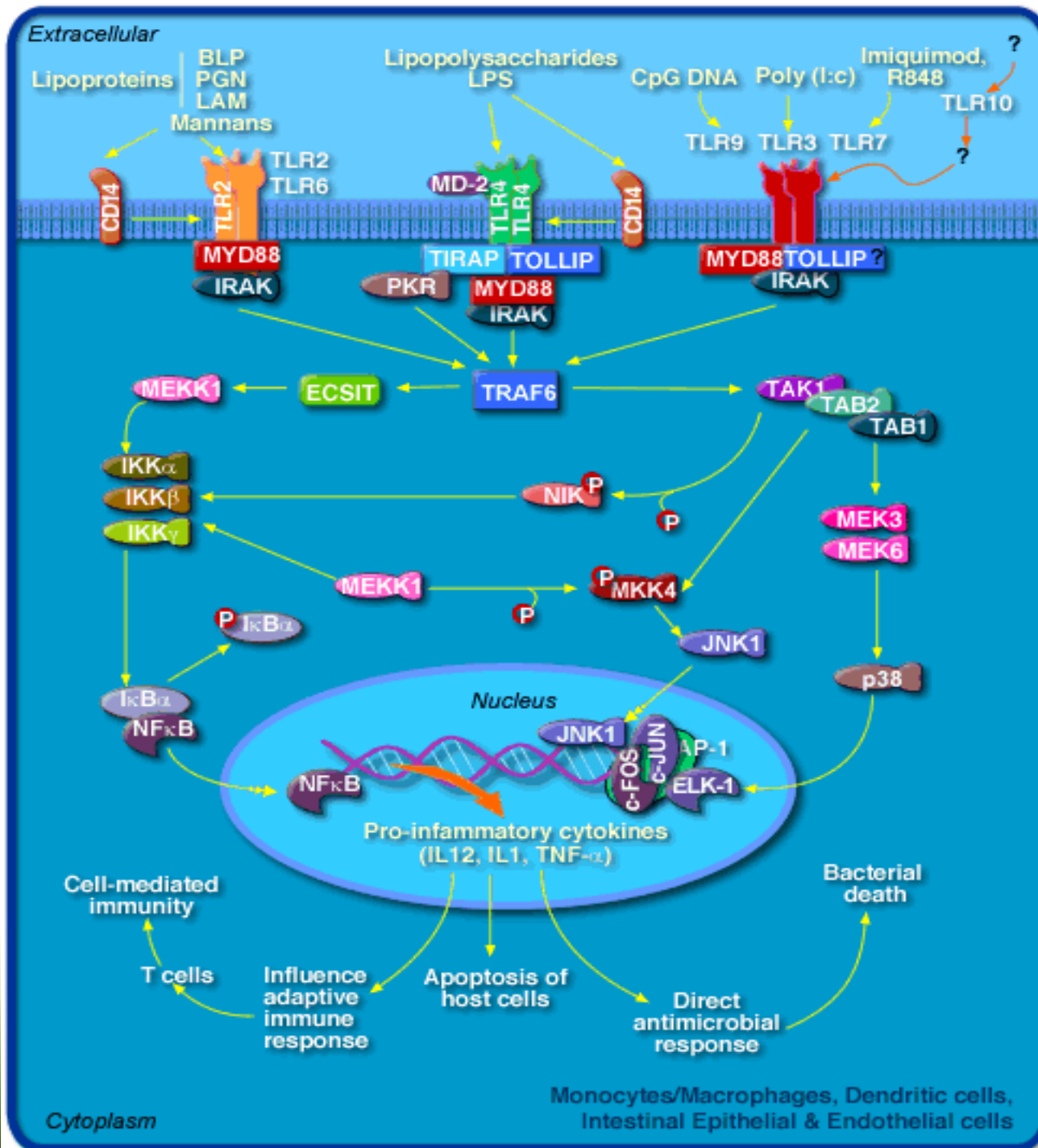
Pro-inflammatory Initiation Response
Cellular Destruction



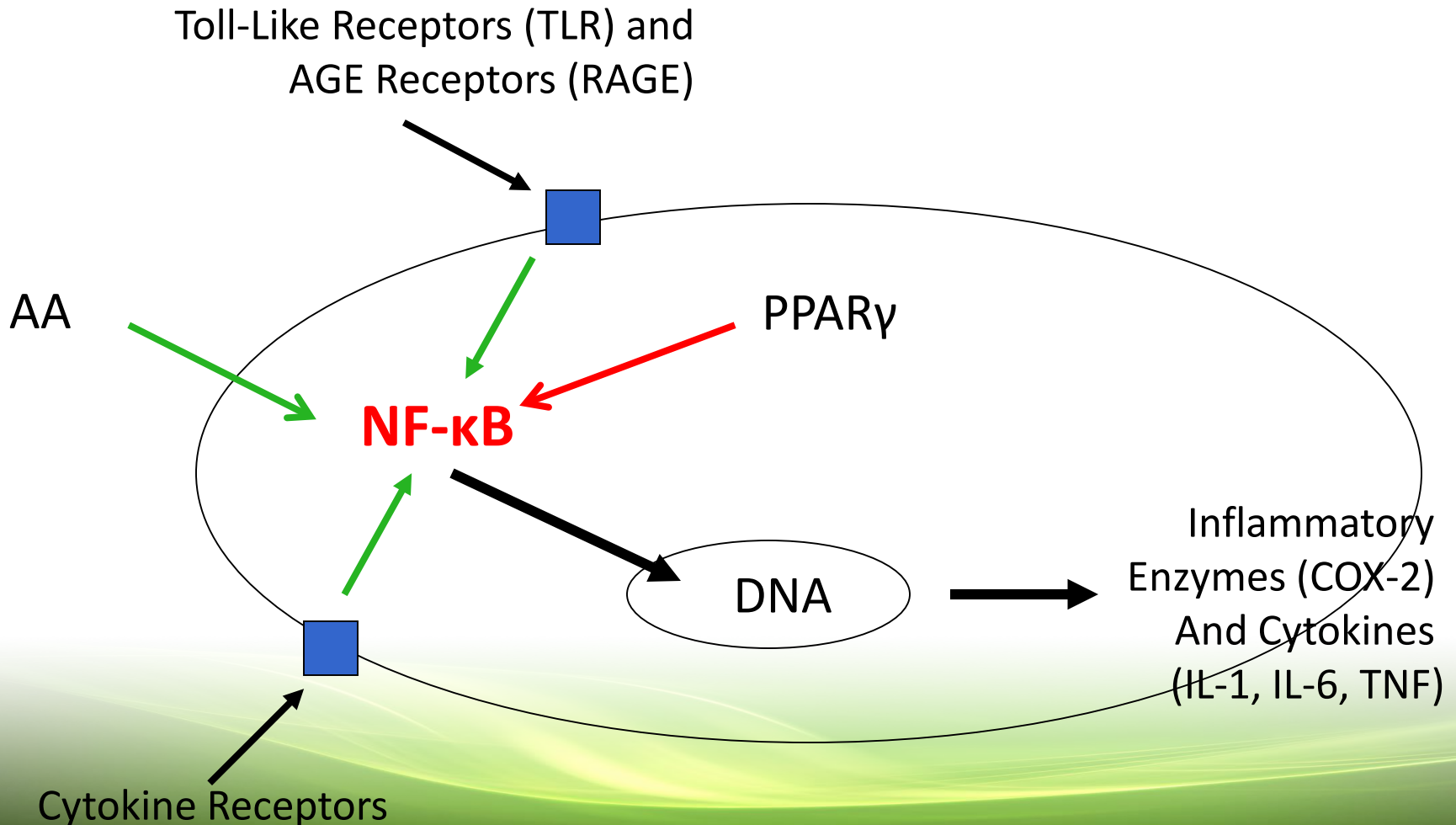
Anti-Inflammatory Resolution Response
Cellular Rejuvenation

What Is Cellular Inflammation?

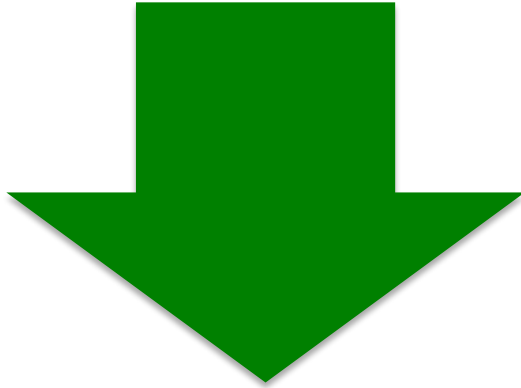
- Mismatch between the initiation and resolution of inflammation
 - Chronic activation of innate immune system
 - Inflammation below the perception of pain
- 



Innate Immune System Made Simple



Dietary Controls on NF- κ B Activity



Omega-6 Fatty
Acids, Saturated
Fatty Acids,
Excess Carbs, and
Excess Calories




Zone Diet,
Omega-3 Fatty
Acids, and
Polyphenols



What Causes Cellular Inflammation?



The Perfect Nutritional Storm

- Increased Omega-6 Consumption
 - Increased Refined Carbohydrate Consumption
 - Decreased Omega-3 Consumption
 - Decreased Polyphenol Consumption
- 

How It Happens

Omega-6 Fatty Acids



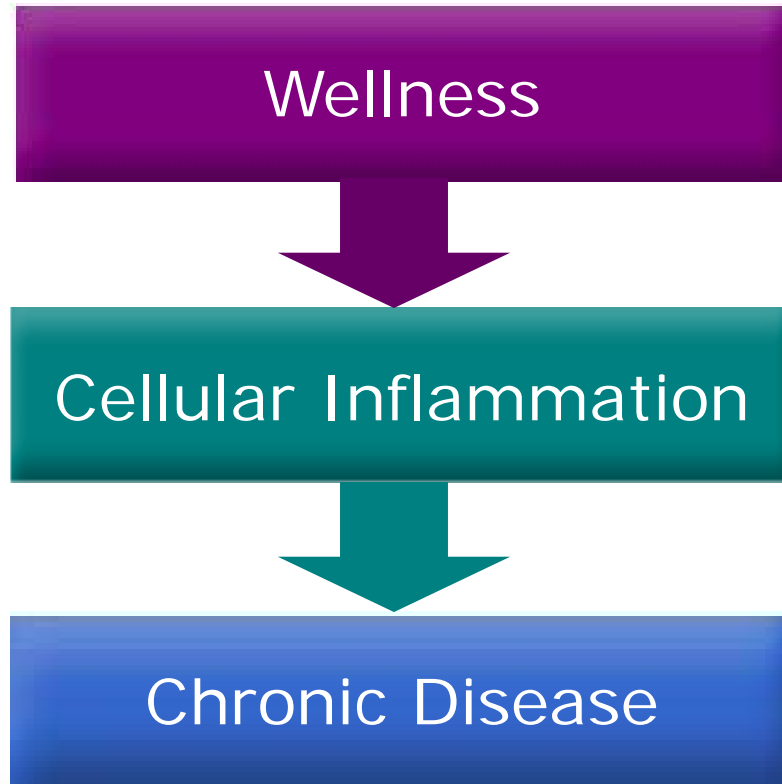
Activated by Insulin
Inhibited by Omega-3 Fats

Arachidonic Acid



Cellular
Inflammation

Three Stages Of Disease

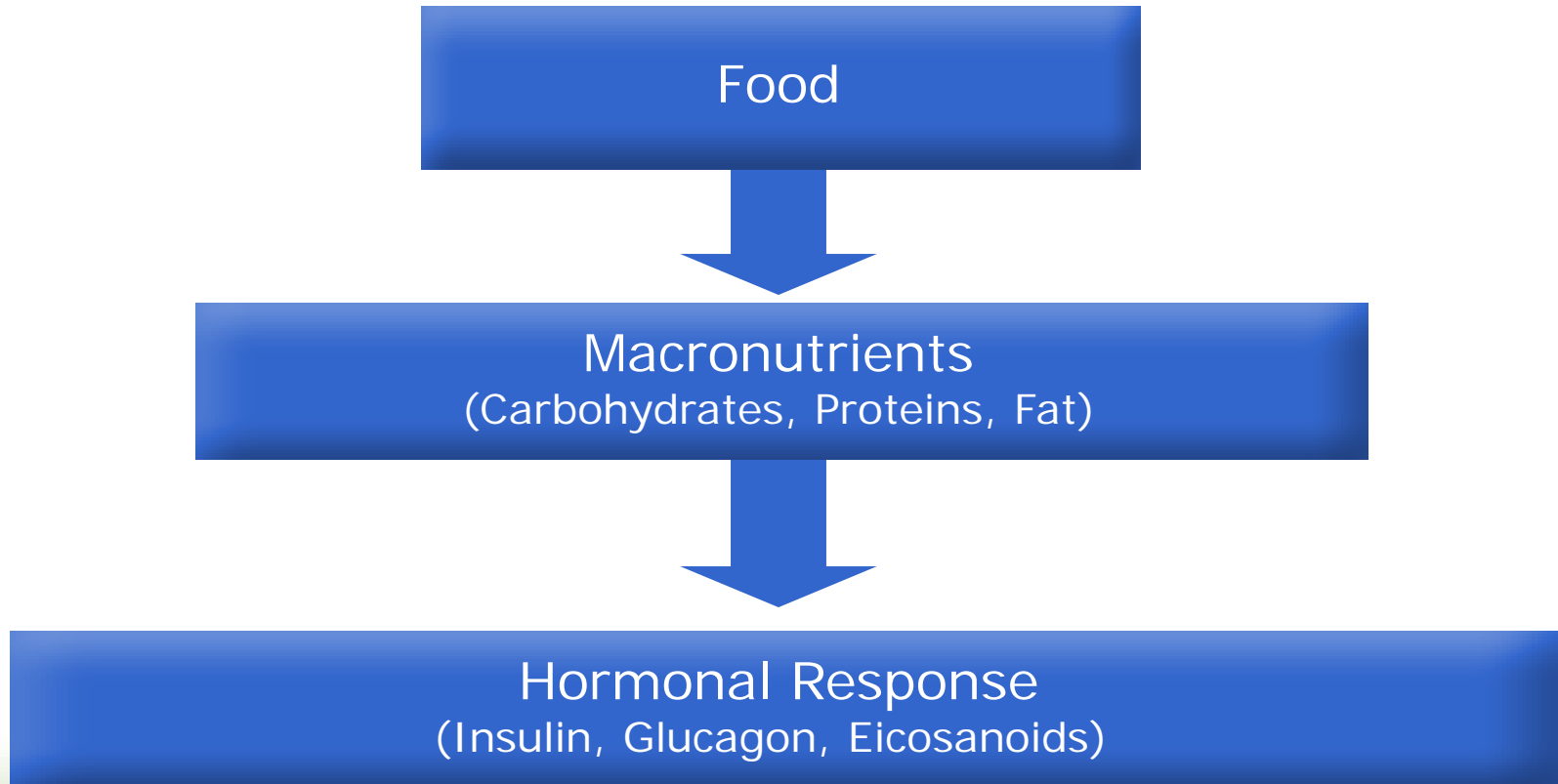


The Zone Diet:

Improved Hormonal Control



Food As A Drug



Insulin

Storage Hormone



Eicosanoids

Master Hormone

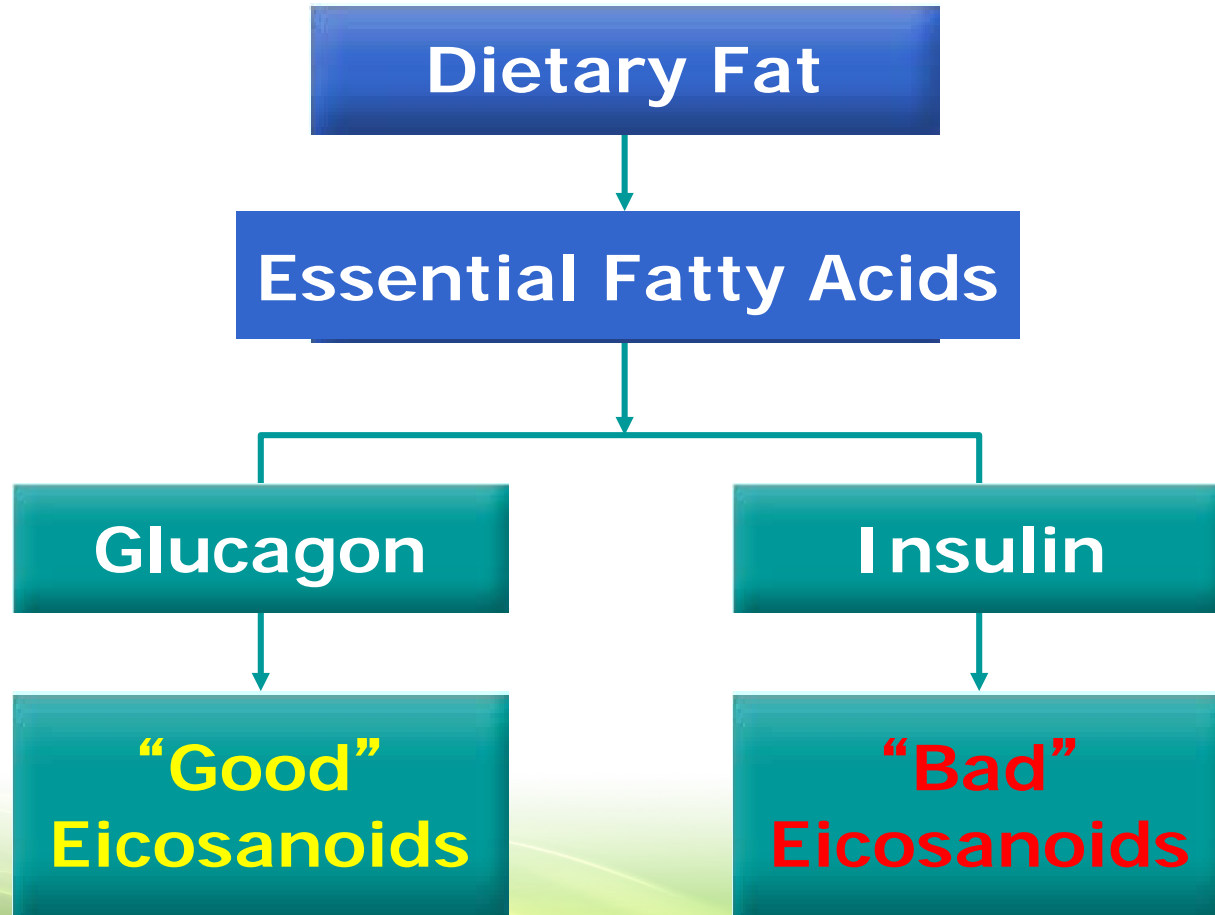


Glucagon

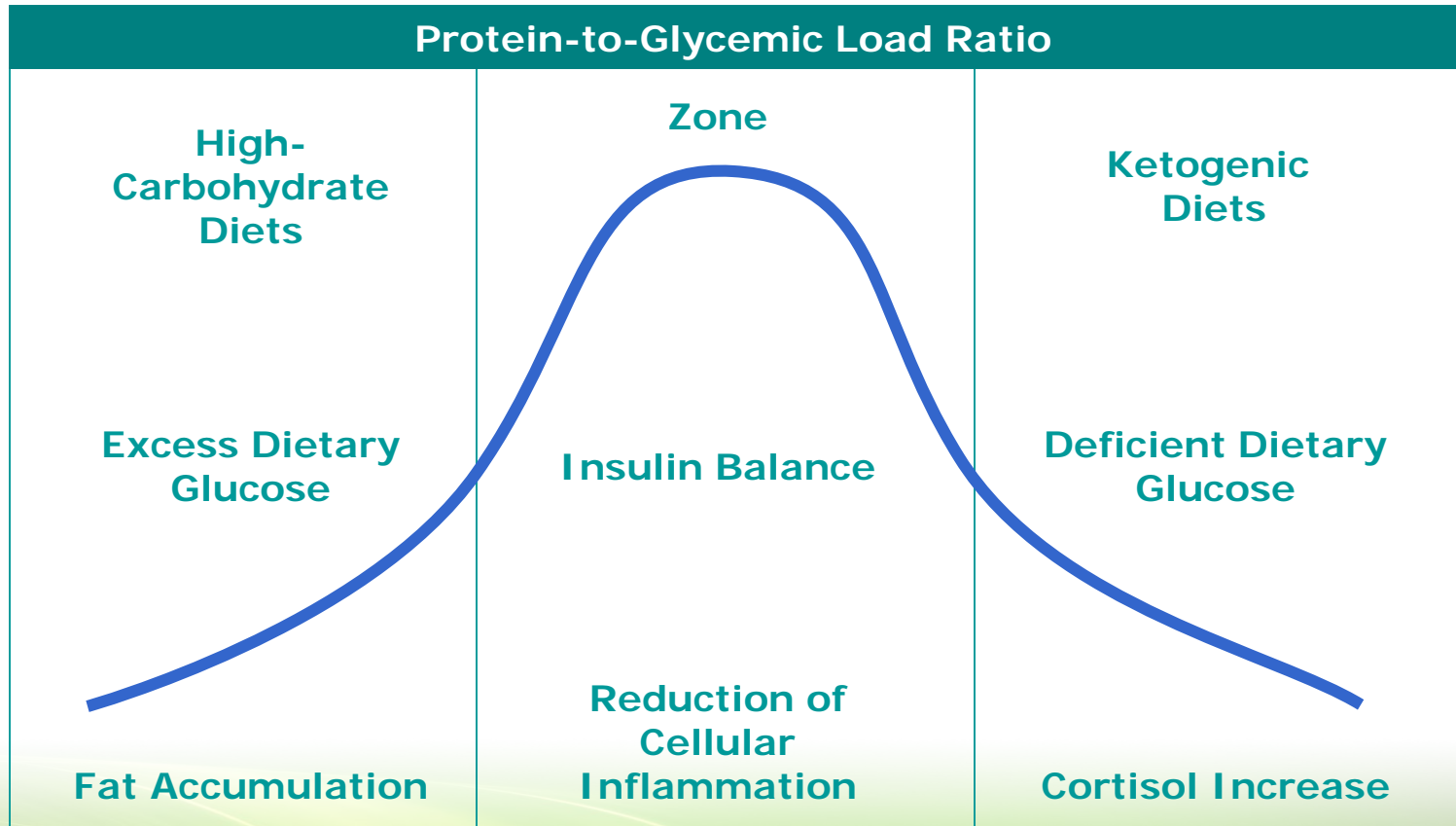
Mobilization Hormone



Eicosanoids Are Controlled By Dietary Fat And Insulin



The Zone Diet is Based Upon On Hormonal Control




Zone Diet

Recommendations (1995)

- 40% low-glycemic load carbs
- 30% low-fat protein
- 30% monounsaturated fat, but low in omega-6 and saturated fats
- 1,200 to 1,500 calories per day

Dietary Guidelines From The Joslin Diabetes Research Center At Harvard (2007)

- 40% low glycemic load carbs
 - 20-30% low-fat protein
 - 30-40% monounsaturated fat
 - 1,200 to 1,500 calories per day
- 

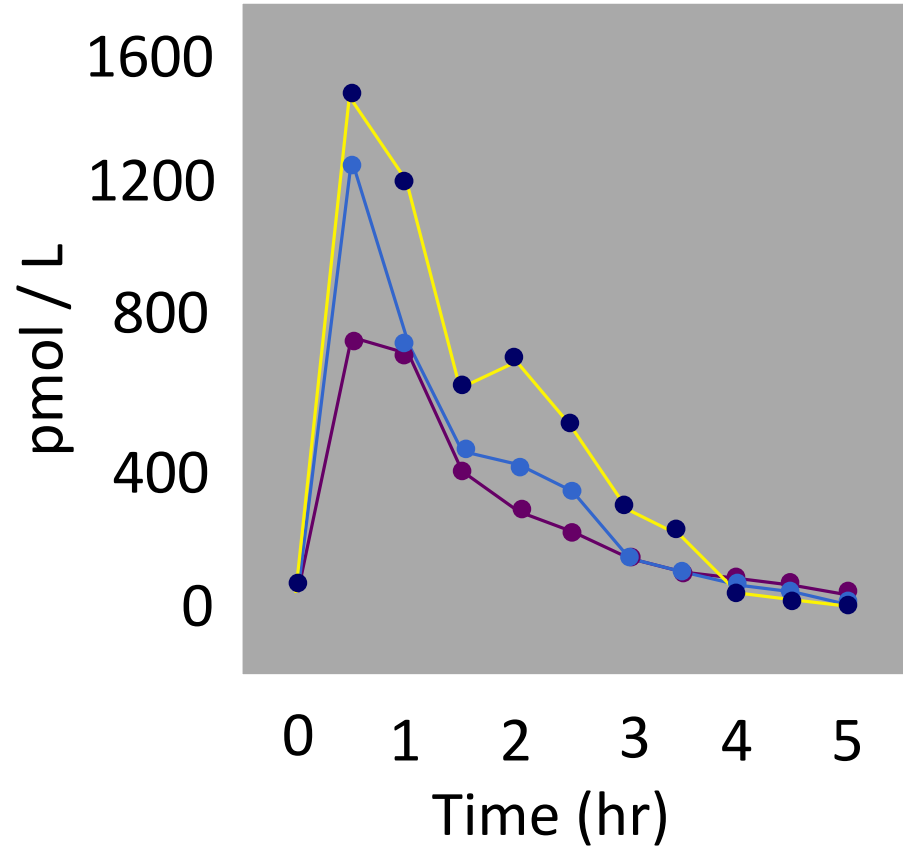
Per Cent Calories On A 40-30-30 Dietary Balance Can Be Deceiving

Macronutrient	1,200 calories/day	1,500 calories/day
Carbohydrate	120 g/day	150 g/day
Protein	90 g/day	112 g/day
Fat	40 g/day	50 g/day

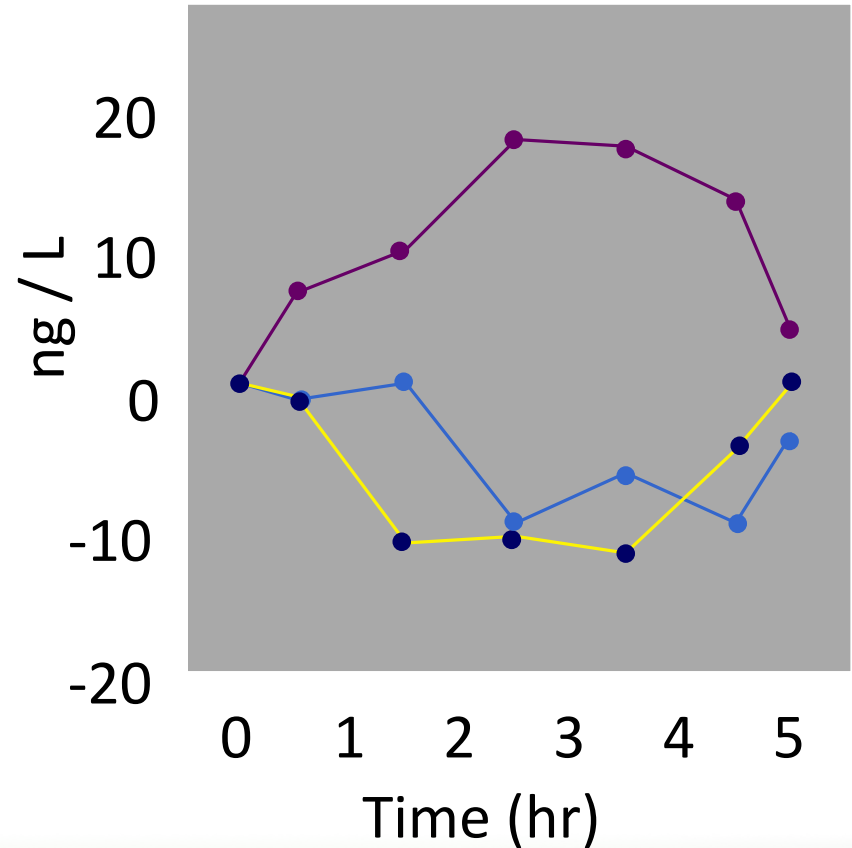
Zone Diet Induces Rapid

Changes in Hormonal Responses

Serum Insulin (change)

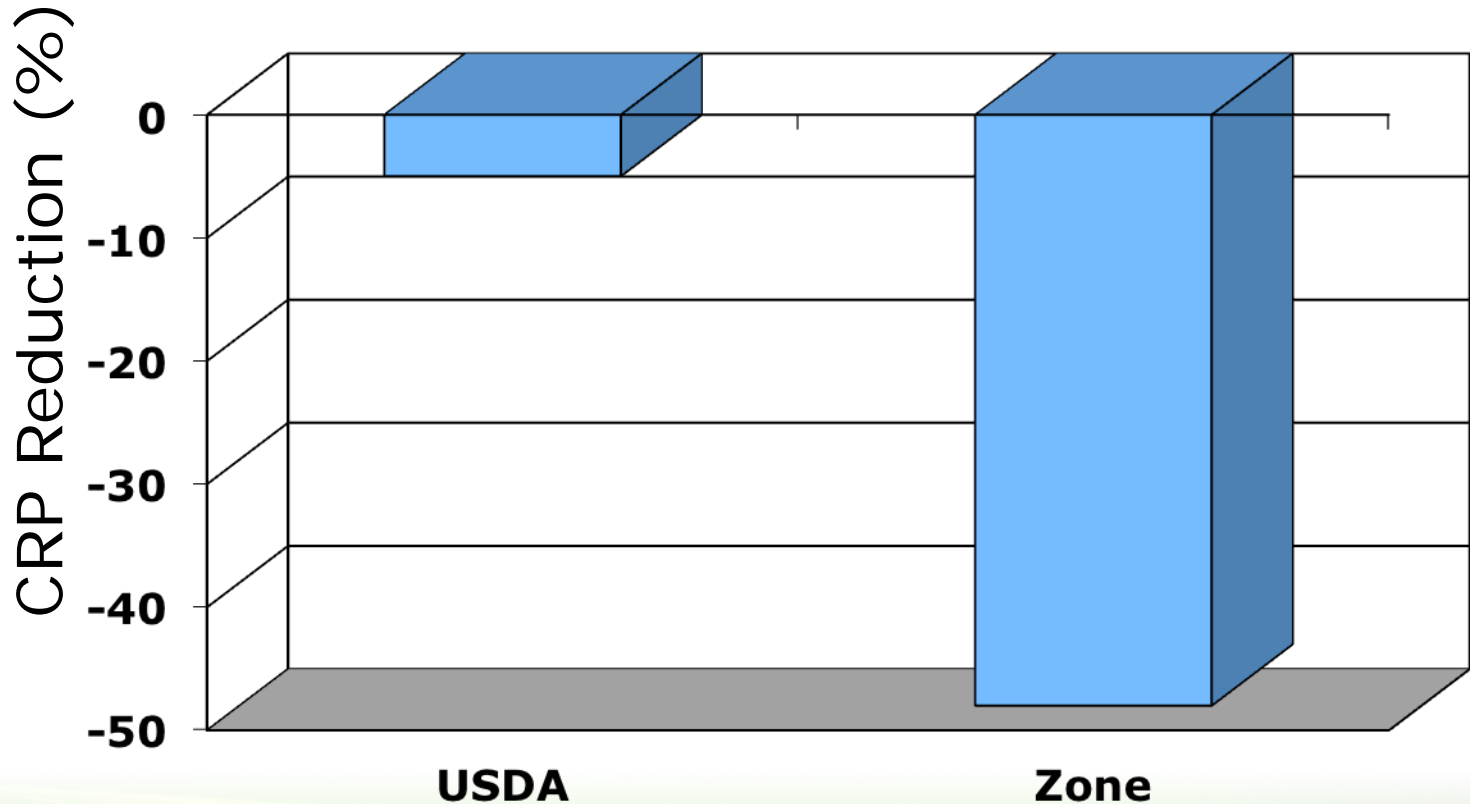


Plasma Glucagon (change)



- High Carbohydrate, High Glycemic Load Meal
- High Carbohydrate, Lower Glycemic Load Meal
- Zone Meal

The Zone Diet Reduces Cellular Inflammation

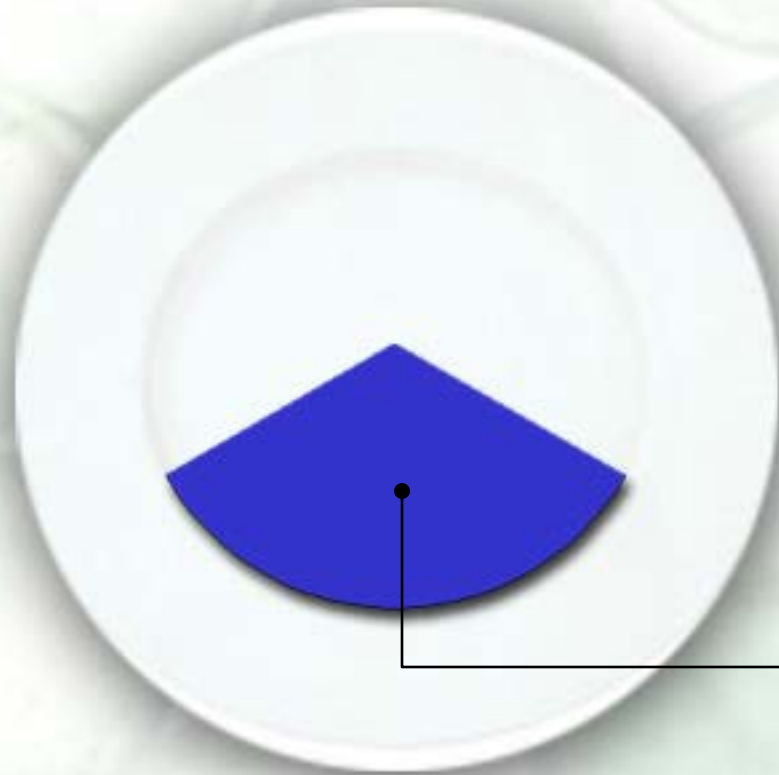


Pereira et al. JAMA 292: 2482 (2004)

How Difficult Is To Follow The Zone Diet?

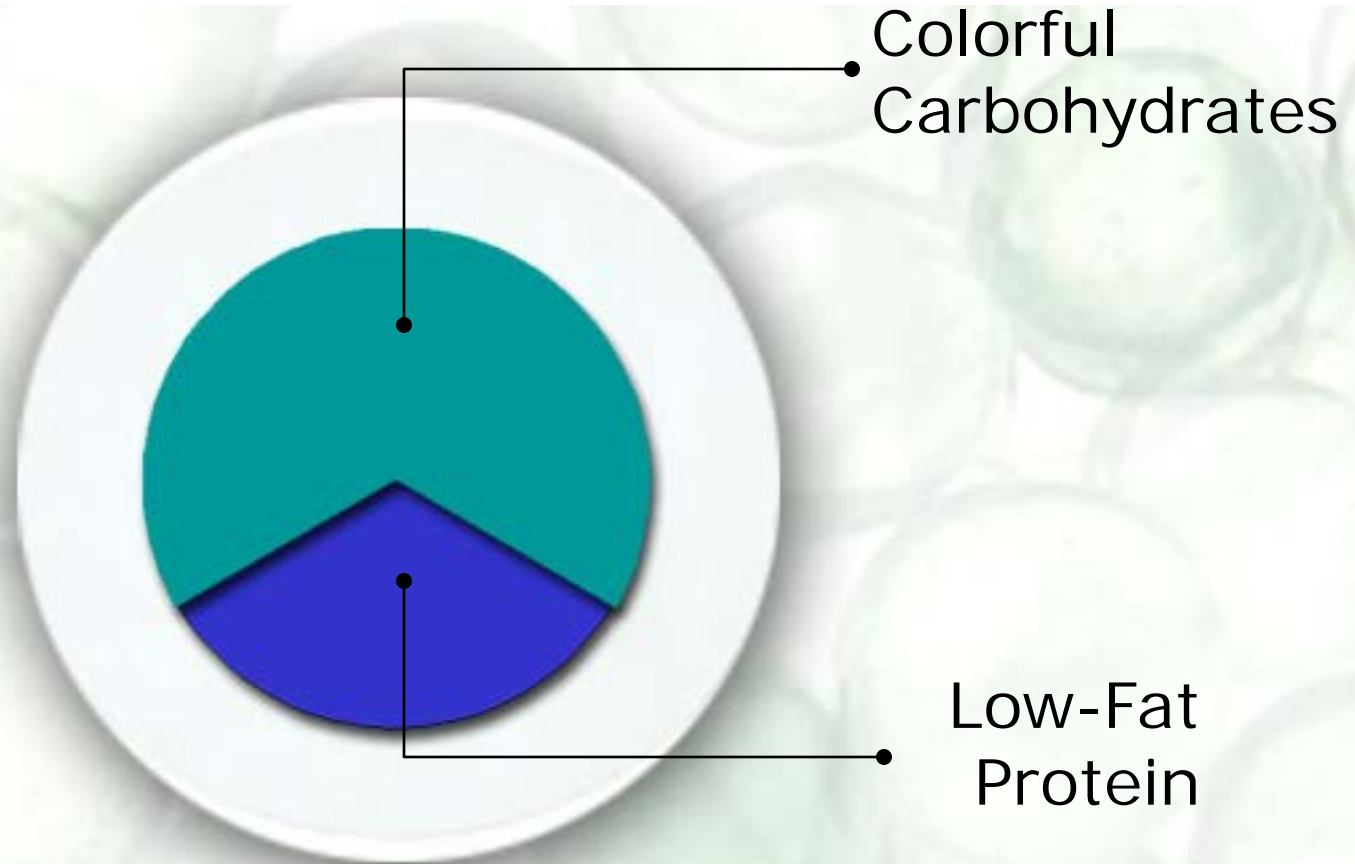


Start With:



Low-Fat
Protein

Balance With:



Finally Add Fat!

Good
Choices

- **High in Monounsaturated Fats**

Bad
Choices

- **High in Omega-6 and Saturated Fats**

Grains and Starches
(Use in Moderation)



Monounsaturated Fat



Low-fat Protein



Fruits



Vegetables



Zone Food Pyramid

The Zone Diet Is The Evolution Of The Mediterranean Diet

- It's Mediterranean ingredients with the Zone blueprint for hormonal balance
- The more white you put on the plate, the more inflammation you create

The Zone Diet Paradox:


*Calorie Restriction Without Hunger Or
Fatigue*



What 1,200 Calories Per Day Represents On The Zone Diet


- *Carbohydrates (120 grams)*
 - 8 servings (500 g) of cooked vegetables
 - 2 servings (200 g) of fresh fruit
 - 1 serving each of lentils (100 g) and oatmeal (100 g)
 - Provides >40 grams of total fiber
- *Protein (90 grams)*
 - Low-fat protein sources
- *Fat (40 grams)*
 - 2 tablespoons of extra virgin olive oil

The Zone Diet Is A Blueprint, Not A Philosophy

- *Vegan Zone*
 - No animal protein, no dairy or egg protein
 - *Lacto-ovo Vegetarian Zone*
 - No animal protein
 - *Paleo Zone*
 - No legumes, no dairy protein
 - *Omnivore Zone*
 - No restrictions on protein sources
- 

Anti-Inflammatory Supplements To The Zone Diet:

*Omega-3 Fatty Acids
and
Polyphenols*



Omega-3 Fatty Acids:

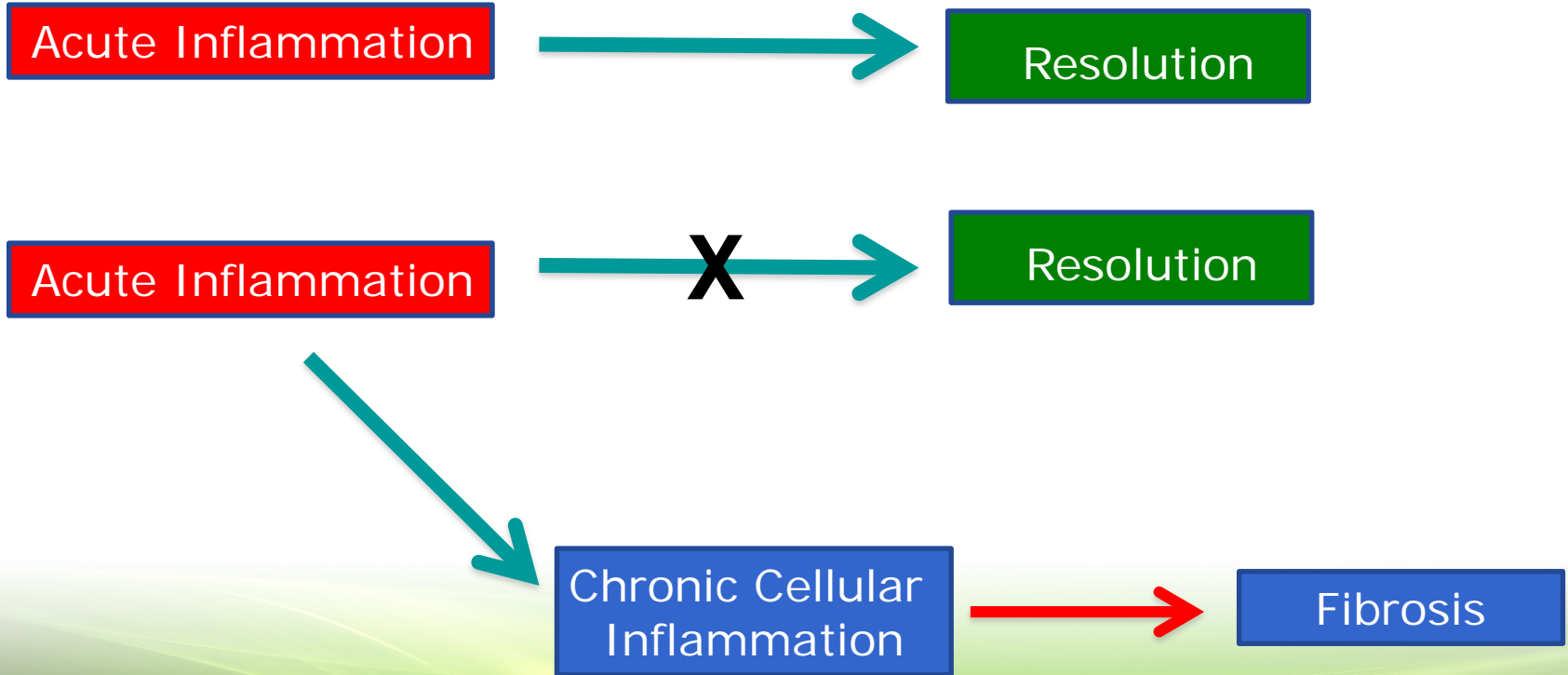
The Resolution of Inflammation




Inflammation Does Not Burn Out On Its Own



What Happens When Inflammation Is Not Resolved?

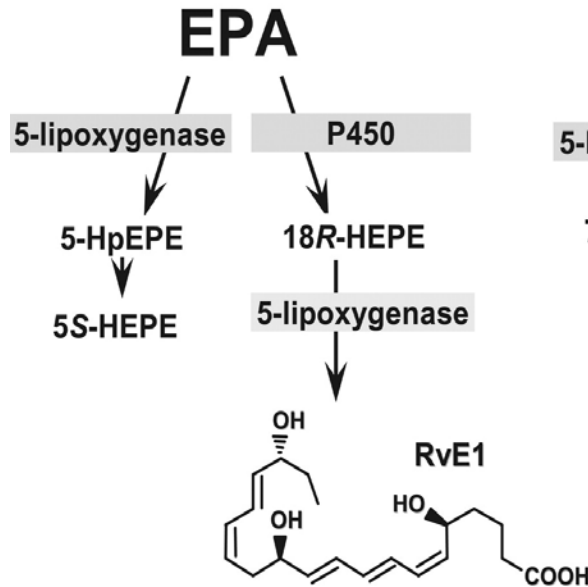


Chronic Diseases Characterized By Fibrosis

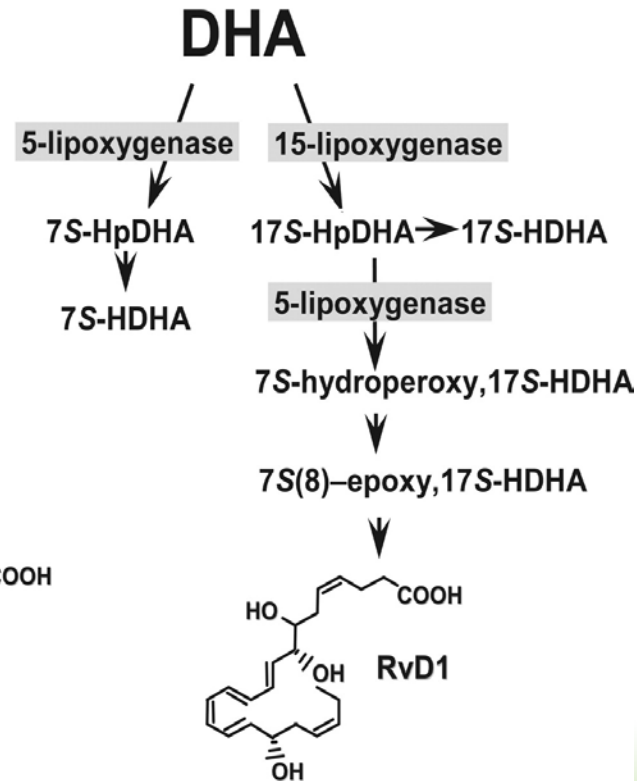
- Heart disease
 - Kidney disease
 - Lung disease
 - Liver disease
- 

Resolvins: Hormones of Rejuvenation

A



B



AA/EPA Ratio Indicates Extent of Cellular Inflammation

AA/EPA	Comments
< 1	Potential bleeding increase
1-3	Ideal for resolution of inflammation
3-6	Good
6-10	Beginning to move out of range
10-15	Cellular inflammation beginning to rise
> 15	Cellular inflammation is systemic

How Many Omega-3 Fatty Acids Do You Need For Resolution?


Maintain Wellness	2.5 g/day
Treat Obesity, Diabetes, and CHD	5 g/day
Treat Chronic Pain	7.5 g/day
Treat Neurological Disease	>10 g/day

Polyphenols:

The Color of the Zone



Polyphenols

- Provide plants with color
 - Little known before 1995
 - 8,000 known polyphenols
- 

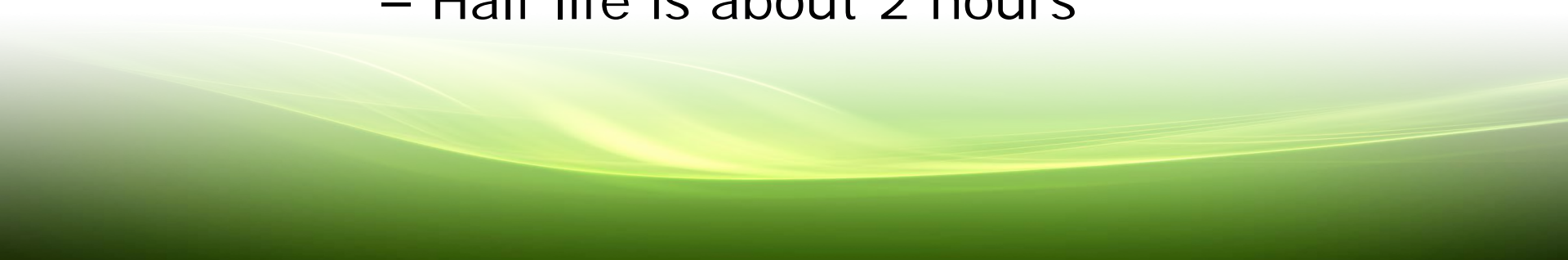
Polyphenols Modify Gene Transcription

- Anti-oxidants
 - Activation of Nrf2
- Anti-inflammatory
 - Inhibition of NF- κ B
- Anti-aging
 - Activation of SIRT-1

How Many Polyphenols Do You Need?

Reduce oxidation	0.5 g/day
Reduce cellular inflammation	1 g/day
Reduce the rate of aging	1.5 g/day

Problems with Polyphenols

- Low concentration
 - 0.2% in fruits
 - 0.1% in vegetables
 - Poor absorption
 - 2-20%
 - Limited lifetime in the blood
 - Half life is about 2 hours
- 

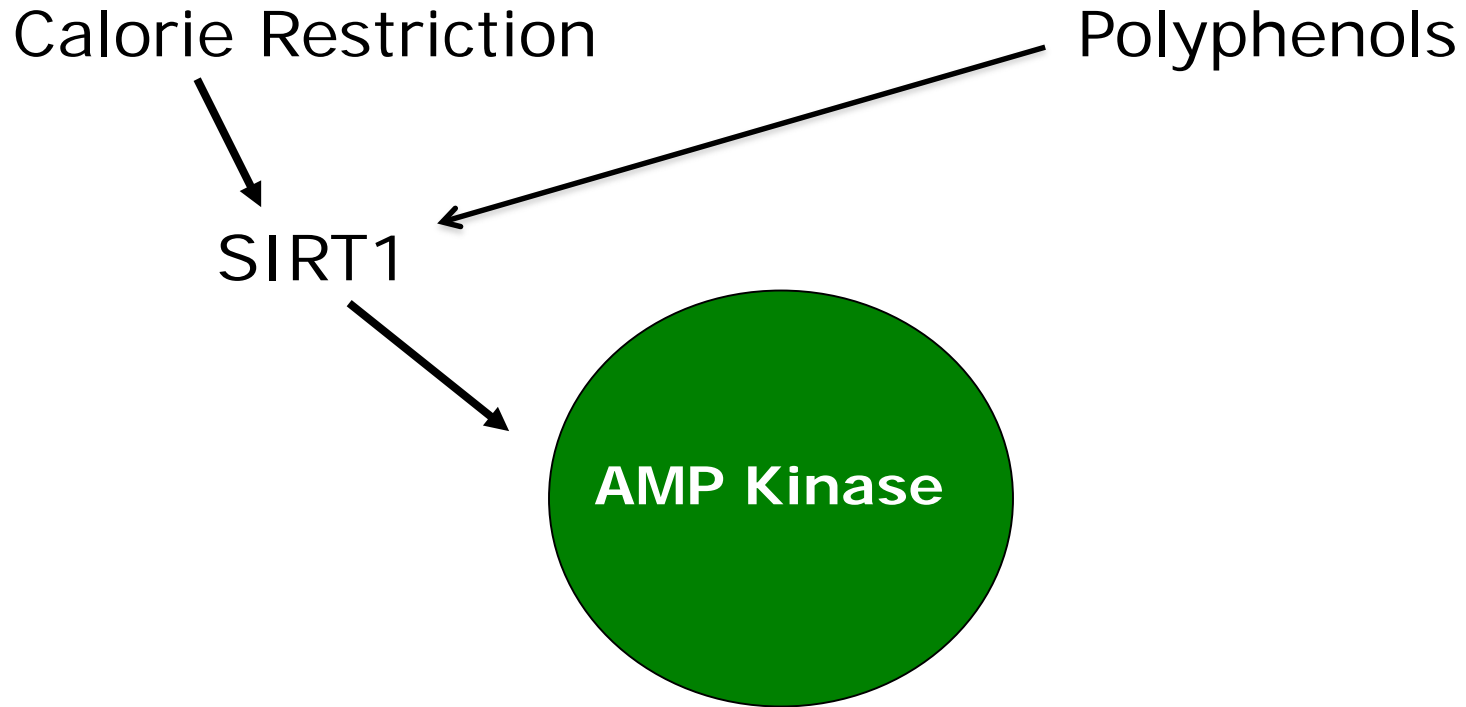
Polyphenol Concentrations

Polyphenol Source	Polyphenol content (g)/100 g
Polyphenol extracts	40-50
Cocoa powder	5
Blueberries	0.5
Red wine	0.09
Spinach	0.07
Extra virgin olive oil	0.03

Polyphenol Anti-Aging Actions

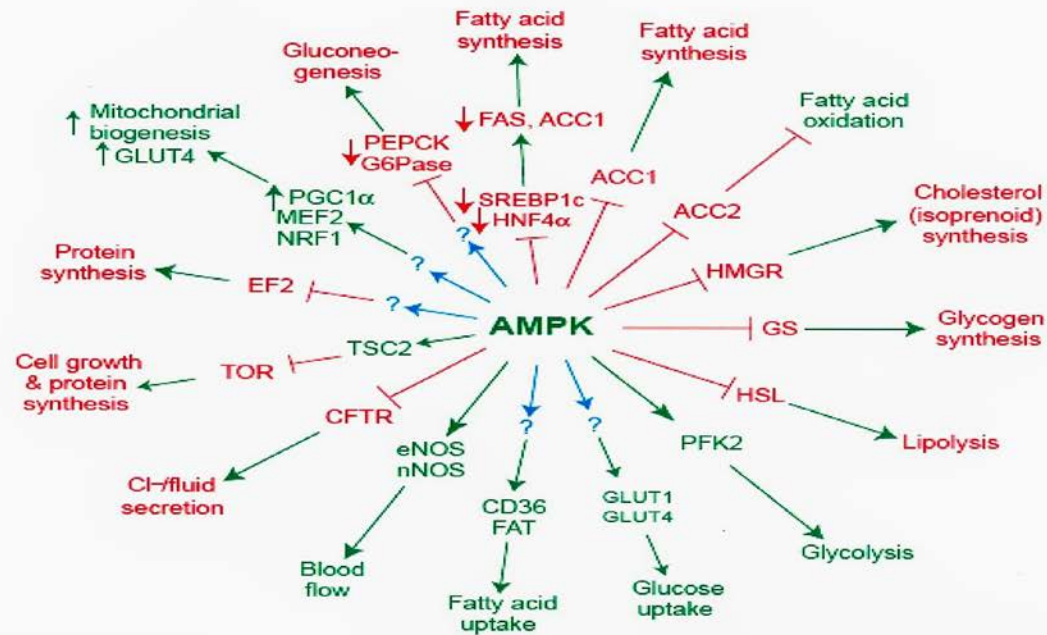
- Activation of AMP kinase
- Master switch for metabolism
- Mechanism of calorie restriction

AMP Kinase: The Enzyme of Life




Actions of AMP Kinase

Targets for AMPK.



Target proteins and processes activated by AMPK activation are shown in green, and those inhibited by AMPK activation are shown in red.

Reaching The Zone

- *Zone Diet*
 - Promotes hormonal balance
 - Reduces insulin resistance
 - Increases satiety
 - *Omega-3 fatty acids*
 - Decreases initiation of cellular inflammation
 - Increases resolution at therapeutic levels
 - *Polyphenols*
 - Anti-oxidant at low levels
 - Anti-inflammatory at moderate levels
 - Activates AMP kinase at therapeutic levels
- 

The Gut and Aging



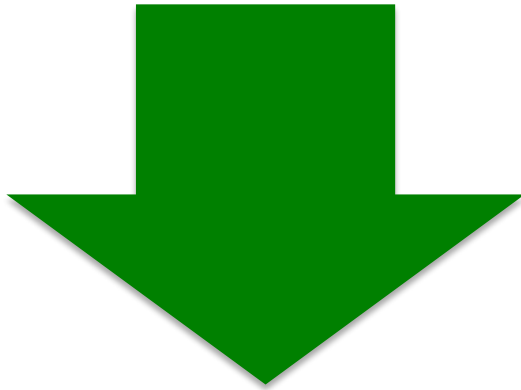
Our Bacterial “Organ”

- More complex than we thought
- Diet can determine overall microbe composition
- Composition can change within five days with dietary changes
- Can be source of chronic inflammation via TLR activation

Our Inner Skin That Allows Us To Live Longer

- Interface at a gigantic immunological load
 - Barbarians at the gate
 - Most dense ecological system in the world
- Mucus
 - First line of defense
- Epithelial cells
 - Primary barrier with tight junctions
- Immune cells
 - 70% of body's immune cells are in the gut
 - Final line of defense against microbial invasion

Dietary Controls On Gut Permeability




High-fat diets,
Alcohol, Drugs,
Antibiotics, and
Stress




Omega-3 Fatty
Acids,
Polyphenols,
and Prebiotics



3 Ps of Gut Health

- Probiotics
 - Flowers
 - Prebiotics
 - Fertilizer
 - Polyphenols
 - Landscaper
- 


Probiotics

- Target practice for the gut immune system
 - Most come from strains in fermented foods
 - Do not establish themselves in the gut
 - Have limited viability
- 

Prebiotics

- Fermentable fiber
- Provide energy for the microbes
- Promote probiotic bacteria growth
- Anaerobic fermentation of fiber into short chain fatty acids (SCFA)
 - Nutrition for microbes
 - Prevent degradation of mucus layer
 - Improve gut permeability
 - Reduce inflammation


Polyphenols

- How plants protect themselves
 - Promote good microbe growth
 - Inhibit pathogens
- 

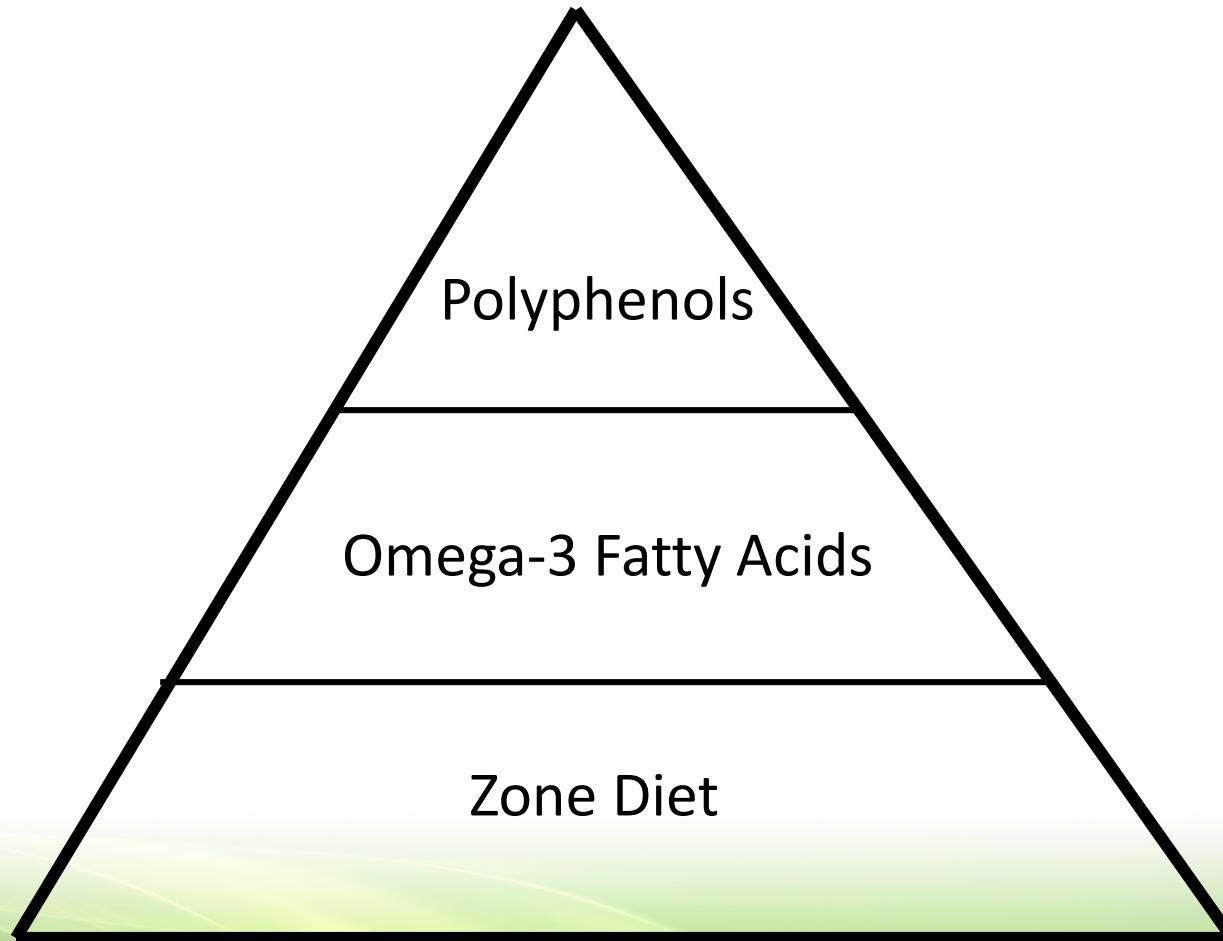
Role of Anti-Inflammatory Nutrition In Gut Health

- *Zone Diet*
 - Low-fat and calorie-restricted diet
 - Rich in fermentable fiber
 - Low in saturated and omega-6 fatty acids
- *Omega-3 fatty acids*
 - Improve gut barrier
 - Reduce inflammation
- *Polyphenols*
 - Landscapers of the microbiota

A New Powerful Message

- Diet can *turn on* inflammatory genes
 - Diet can *turn off* inflammatory genes
- 

Anti-Inflammatory Nutrition As Gene Therapy



INFLAMMATORY GENES

Why Anti-Inflammatory Nutrition Is Important

Cellular
Inflammation

Obesity

Diabetes

Alzheimer's



Anti-Inflammatory Nutrition As 21st Century Medicine

- Reduction of cellular inflammation
- Hormonal and genetic control
- Diet will be the primary drug
- High-dose fish oil and high-dose polyphenols will be key supplements
- Return to Hippocrates
 - “Let food be your medicine and let medicine be your food”