

SINdem4Juniors

6th Winter Seminar on Dementia and Neurodegenerative Disorders

Recent Advances in Clinical and Experimental Research on Dementia and Neurodegenerative Disorders

Organized by SINdem4Juniors Young Members Executive Committee of The Italian Neurological Dementia Association

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The Fast Mimicking Diet - Wanda Rizza, PhD in Human Nutrition

Forewords

Calorie Restriction - CR: chronic reduction (20-40%) of the caloric intake without malnutrition.

Intermittent Fasting - IF: dietary approach based on switching between *fasting states* and *feeding states*; any fasting state can last 16 to 48 hrs and IF can be combined with any dietary protocol.

Prolonged Fasting - PF: form of fasting which lasts more than 72 h. Typically, a PF lasts 4-7 days, and it can be periodically repeated.

Fast Mimicking Diet - FMD: prolonged and periodic fasting protocol which does not consider the whole abstinence from food.

All these forms are examples of “Dietary Restriction”

Fast Mimicking Diet

Fast Mimicking Diet

- Form of Prolonged & Periodic Fasting
- 5-days Protocol
- Animal studies and human clinical trials (ongoing)
- Nutrient composition: low-protein, low-carb, high-fat
- Metabolic shift → ketosis



Fast Mimicking Diet

Aims

Activation of the anti-aging pathways

Cells and tissues regeneration, promotion of autophagy

Strong boost for the immune system

Visceral fat reduction, preservation of the FFM

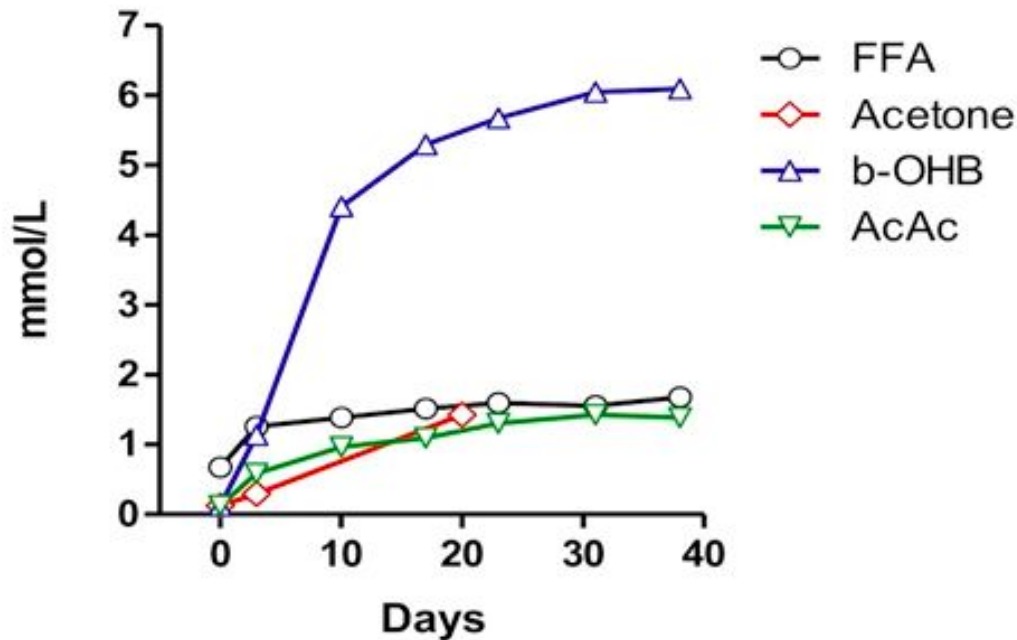
Decrease in the systemic low-grade and high-grade inflammation

Fast Mimicking Diet

Day	Calorie intake	Composition
1	1000-1100 kcal	10% protein 34% carbs 56% fats
2-5	750-800 kcal	9% protein 47% carbs 44% fats
6 (transition day)	Progressive caloric re-increase	Gradual reintroduction: <ul style="list-style-type: none">- Whole unrefined carbs- Proteins (first vegetables, than fish, eggs, meat, etc.)

After a Few Days of Fasting, the Human Body Switches From a Sugar to a Fat Burning Mode

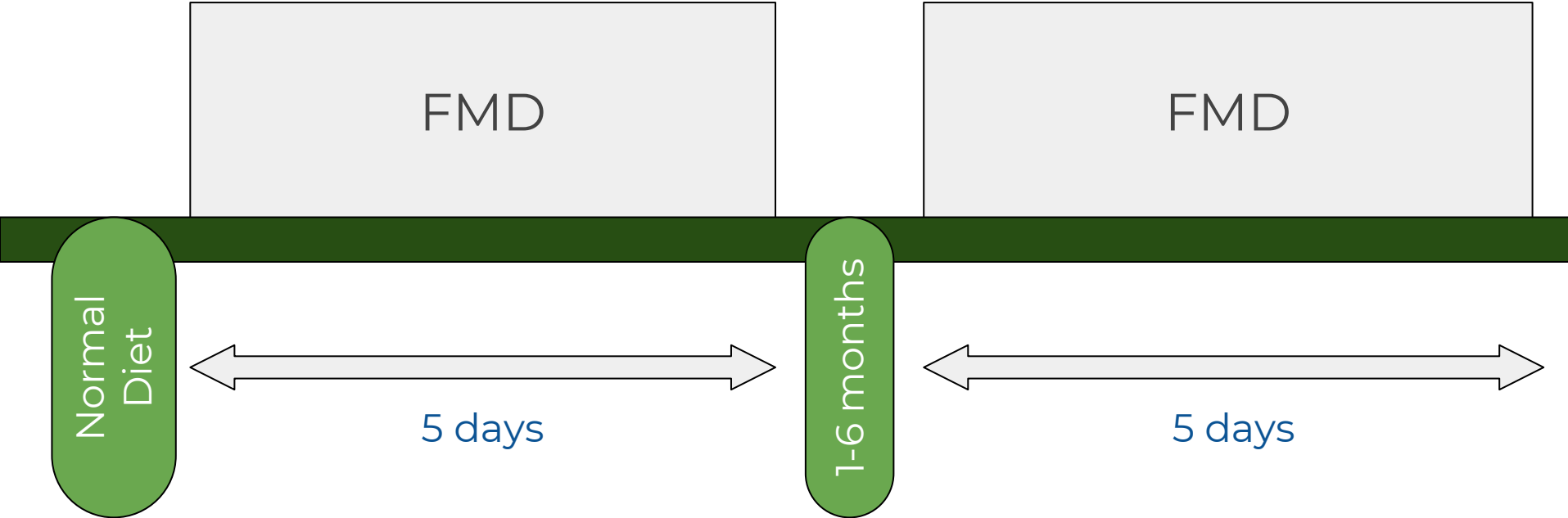
Fatty acids and ketone bodies in the blood of patients who are fasting



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Fast Mimicking Diet



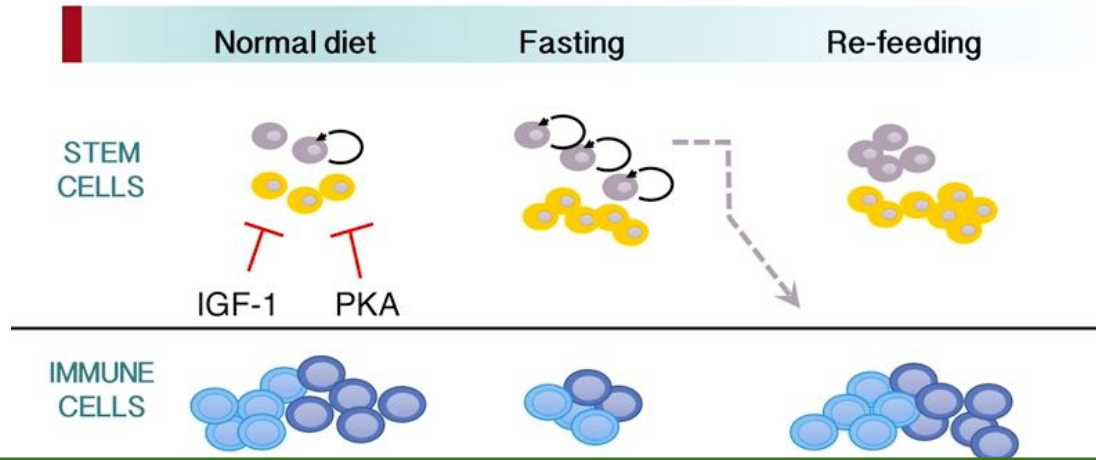
Fast Mimicking Diet

Action against multifactorial diseases
(tumors, MS, neurodegenerative diseases, CVD, etc.).

Awakening the rejuvenation from within.

Fasting is at the foundation of the body's ability to protect, repair and rejuvenate itself.

Regeneration From Within



*“The cellular and molecular mechanisms by which IF and FMD improve health and counteracts disease processes involve **activation of adaptive cellular stress response signaling pathways** that enhance mitochondrial health, DNA repair and autophagy.*

PF also promotes stem cell-based regeneration as well as long-lasting metabolic effects.”

How can Fasting work against Neurodegeneration?

Neuroprotection

1990s general hypothesis:

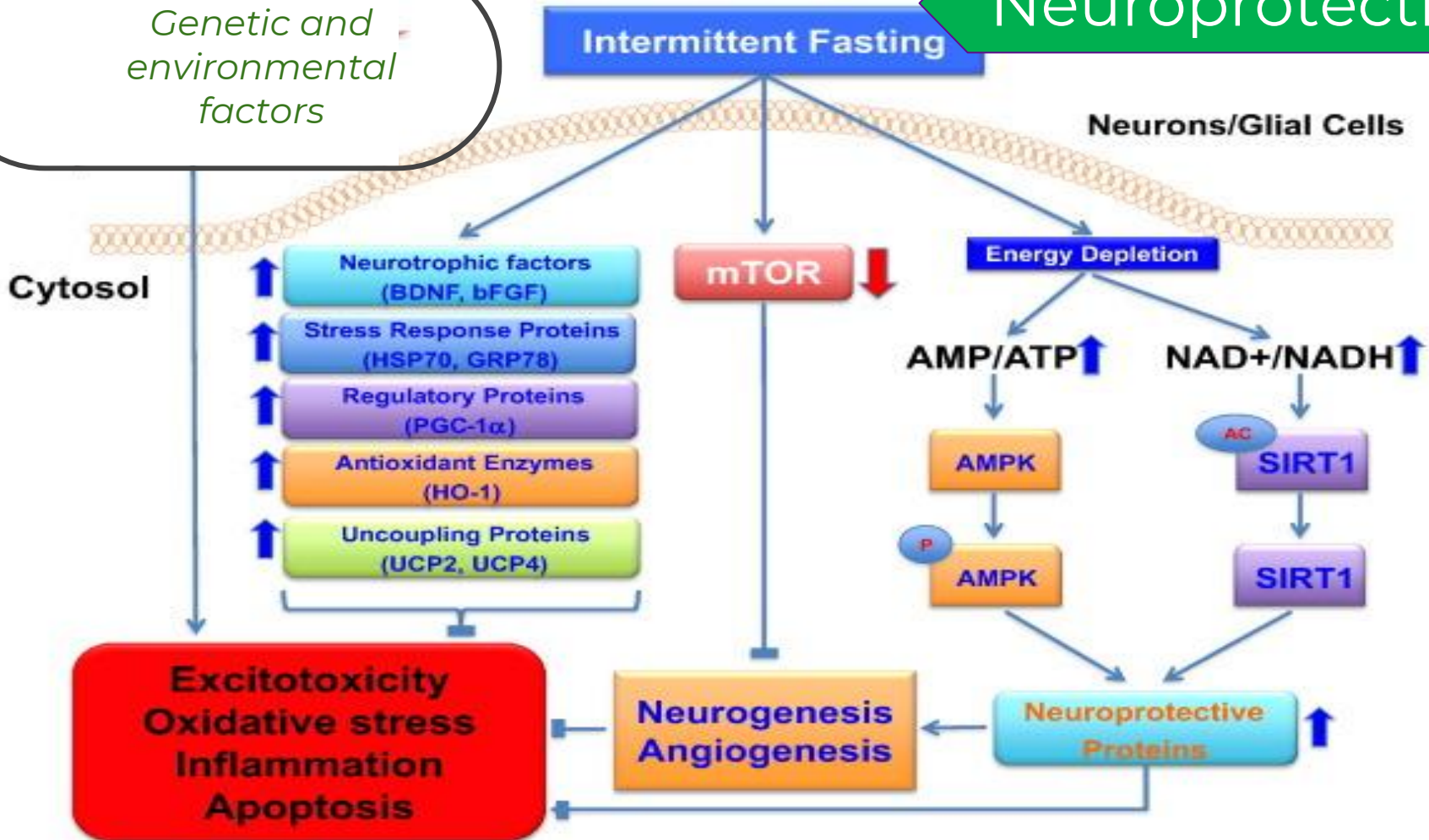
Ageing is a major risk factor for neurodegenerative disorders.



Fasting may protect neurons from
Genetic factors & Environmental factors.

Fasting can counteract ageing processes.

Neuroprotection



The mechanism(s) by which IF protects against synaptic dysfunction and cognitive deficits (*in mouse models and thus in humans*) is unknown, but may include:

- ***reduction in oxidative stress and inflammation;***
- ***preservation of mitochondrial function;***
- ***increased neurotrophic factor signaling and autophagy.***

Neuroprotection - BDNF

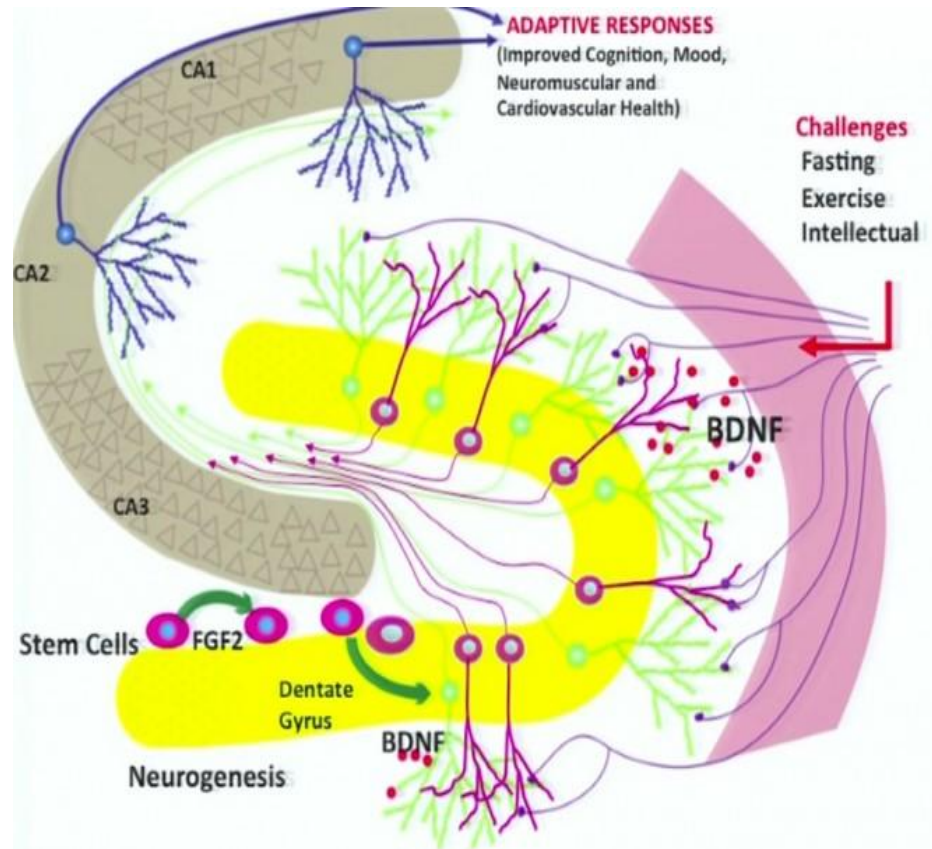
Benefits of BDNF

- Supports survival of existing neurons;
- Encourages growth and differentiation of new neurons and synapses through neurogenesis;
- Stimulates mitochondrial biogenesis;
- Contributes positively toward memory, learning and thinking;
- Exhibits anti-depressant activity.

Conversely, BDNF deficiencies have been linked to developmental disorders and depression.

How to increase BDNF levels

1. Low sugar intake
2. Intermittent Fasting
3. Periodic Fasting (FMD)
4. Sprinting
5. High Intensity Resistance Training



Neuroprotection - Insulin

The process of ageing is closely related to insulin.

Fasting

- Acts on the insulin/IGF-1 pathway
 - Improves insulin sensitivity and lower circulating insulin levels (20-31%)
 - Leads to a significant reduction in blood sugar levels (3-6%)
- Can positively affects the insulin-mediated effects on ageing and neurodegenerative diseases.

Summing Up

Benefits of Fasting

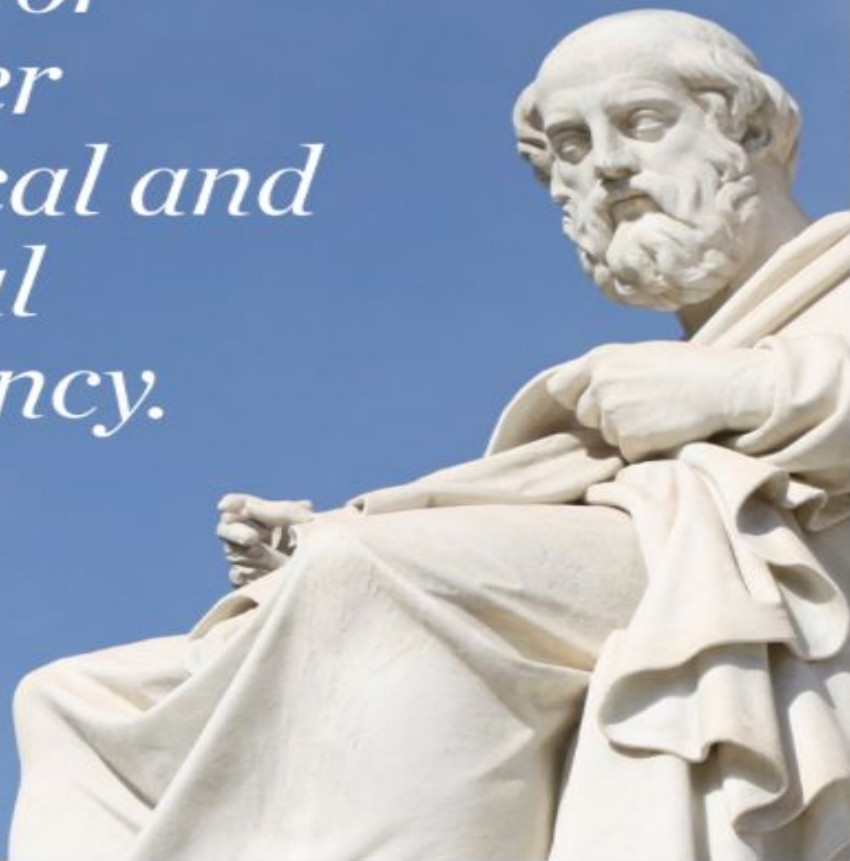
- It stimulates the reduction of both visceral fat and metabolic risk factors
- It activates and up-regulates of the anti-aging pathways
- It increases the autophagy
- It gives support and strength to the immune system
- It decreases inflammatory- and oxidative molecules expression
- It enhances cognitive functions and memory
- ***It protects the nervous system from degeneration both directly and***

*Fasting is at the foundation of the body's ability
to protect, repair and rejuvenate itself.*

*If fast for
greater
physical and
mental
efficiency.*

PLATO

DAVID
PERLMUTTER
MD



References

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[Fasting: Molecular Mechanisms and Clinical Applications](#) - 2014

[Intermittent Fasting and Human Metabolic Health](#) - 2015

[Interventions to Slow Aging in Humans: Are We Ready?](#) - 2015

[Health effects of intermittent fasting: hormesis or harm? A systematic review](#) - 2015

[Impact of intermittent fasting on health and disease processes](#) - 2016

[Potential Benefits and Harms of Intermittent Energy Restriction and Intermittent Fasting Amongst Obese, Overweight and Normal Weight Subjects—A Narrative Review of Human and Animal Evidence](#) - 2017

[BDNF and 5-HT: a dynamic duo in age-related neuronal plasticity and neurodegenerative disorders](#) - 2004

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[Fasting, Circadian Rhythms, and Time-Restricted Feeding in Healthy Lifespan](#) - 2016

[Fasting-mimicking diet and markers/risk factors for aging, diabetes, cancer, and cardiovascular disease](#) - 2017

[Fasting-induced differential stress sensitization in cancer treatment](#) - 2015

[Caloric restriction and intermittent fasting: Two potential diets for successful brain aging](#) - 2006

[Diet mimicking fasting promotes regeneration and reduces autoimmunity and multiple sclerosis symptoms](#) - 2016

[Beneficial effects of intermittent fasting and caloric restriction on the cardiovascular and cerebrovascular systems](#) - 2005

[Nutrition and fasting mimicking diets in the prevention and treatment of autoimmune diseases and immunosenescence](#)
- 2017

[Effects of intermittent fasting on glucose and lipid metabolism](#) - 2017

Fast Mimicking Diet

- Significant reduction in C-Reactive Protein;
- 72 hours+ within optimal ketosis (ketones of 1.5+ mmol/L);
- Reduction in body fat by 0.5%+ sustained for at least 1 week following FMD - i.e. no immediate bounce-back;
- Significant reduction in IGF-1;
- Absence of significant increases in measures of stress, adrenal stress, heart rate variability or sleep quality.

DR-IF mediated changes for healthy aging of Man

Gross Physiology

CNS

Neuroprotection

Circulation

Euglycemia

Reduced Ins/IGF-1

Increased cortisol

Increased trophic factors

Increased ketones

Visceral organs

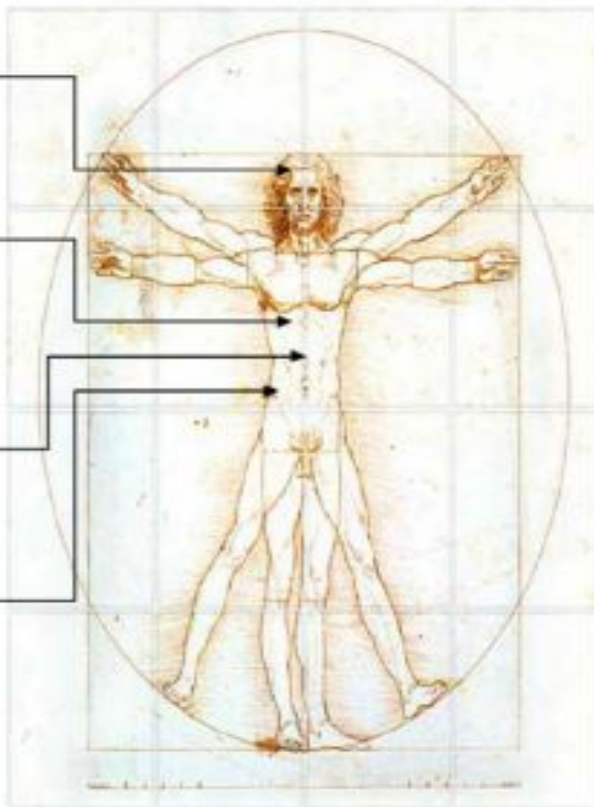
Hepatic stress protection

Adipose

Reduced mass

Stress

Increased resistance



Cellular Physiology

Energy Metabolism

Increased Ins sensitivity

Fat mobilization

PPAR activation

Protein Stability

Hsp upregulation

DNA stability

Sirtuin upregulation

Cell survival

FoxO activation

BDNF upregulation

Synaptogenesis

IFN- γ upregulation

Molecular pathways

*Modulation of ROS
and AGEs
production*

**IGF-1/
insulin
pathway**

**Sirtuin
pathway**

*Neuro-
protection*

**mTOR
pathway**

**AMPK
pathway**

**PPAR and
co-factors**

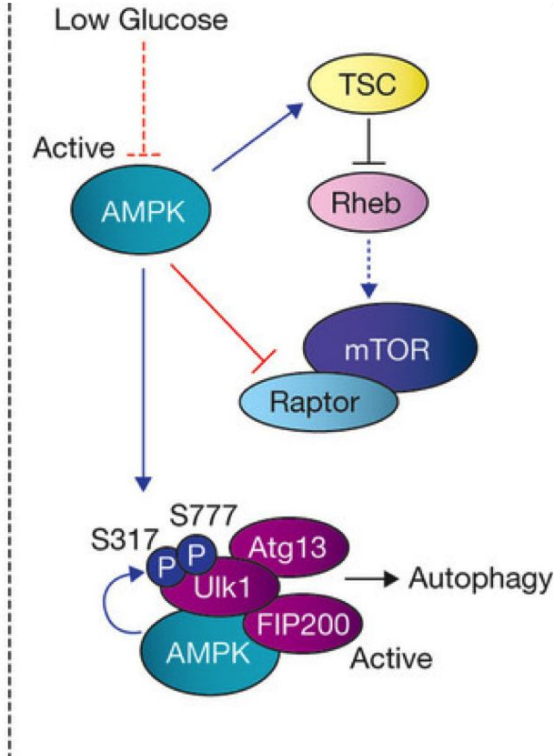
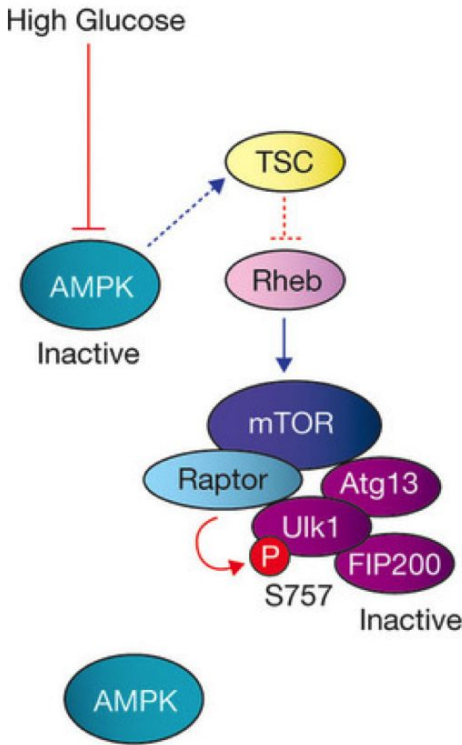
*Regulation of
autophagy*

**FoxO
transcription
factors**

Hormesis?

AMPK vs mTOR

- Metabolic diseases
- Lypogenesis
- Cancer
- Aging



- DNA repair
- Autophagy
- Mitochondrion genesis
- Longevity

P — : Inhibitor
P — : Activation