

Dietary Protein and Healthy Aging: Controversies and Mechanisms

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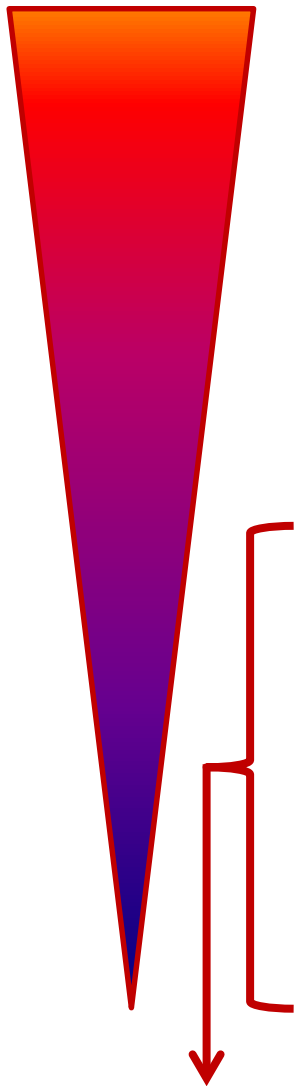


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School of Environmental
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States of Amino Acid Nutrition



➤ Toxicity

➤ Balanced

➤ Supplementation



➤ Adequacy

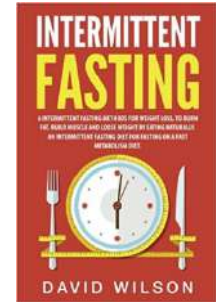
➤ Limitation

➤ Imbalanced

➤ Deprivation/
depletion

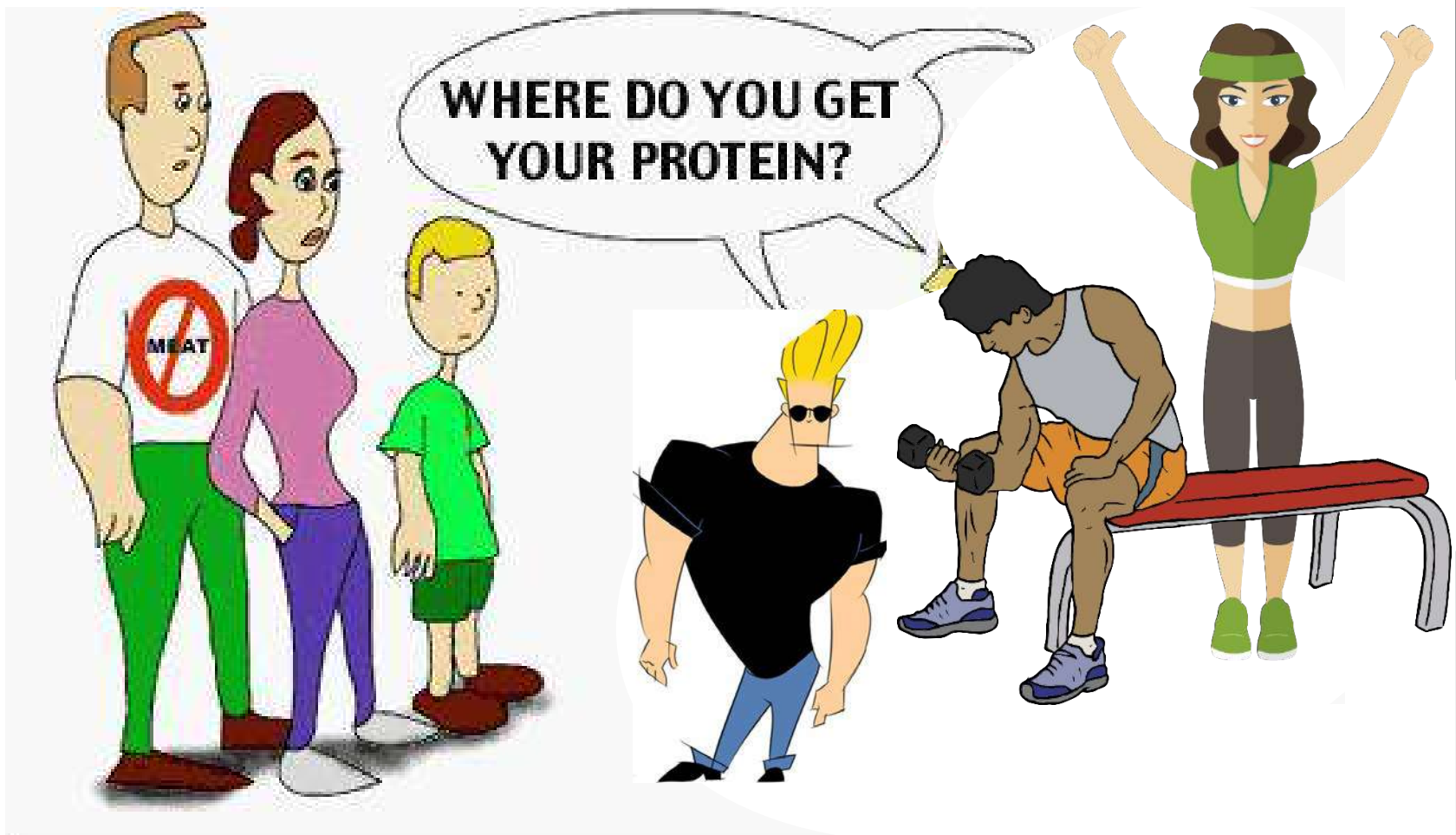


➤ Devoid



Insufficient for growth; *but is this unhealthy?*

Dietary protein: obsession and controversy



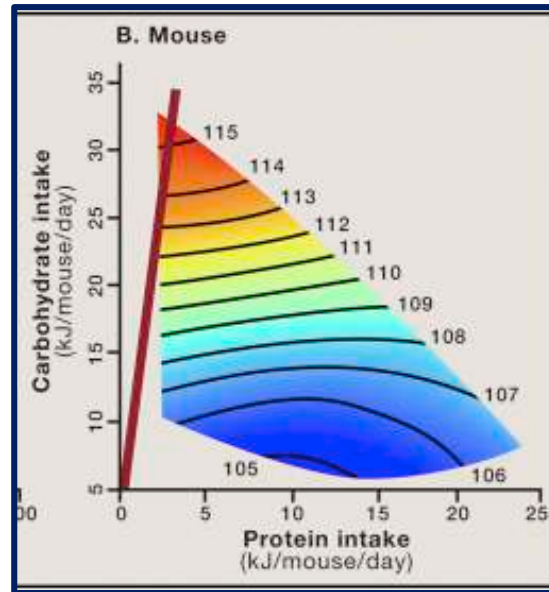
Adapted from:

<http://detox-fit.com/fighting-worlds-protein-obsession/>

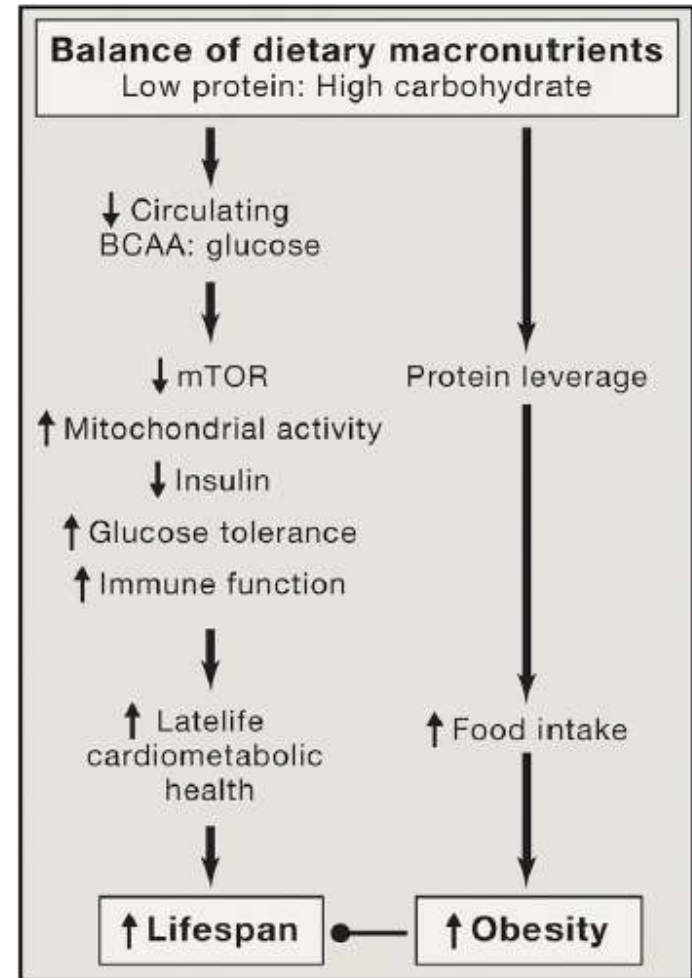
<https://hpjmh.com/2011/03/14/where-do-you-get-your-protein/>

<https://thevegandatabase.com/incomplete-plant-proteins-myth/>

Dietary restriction: do macronutrients matter?



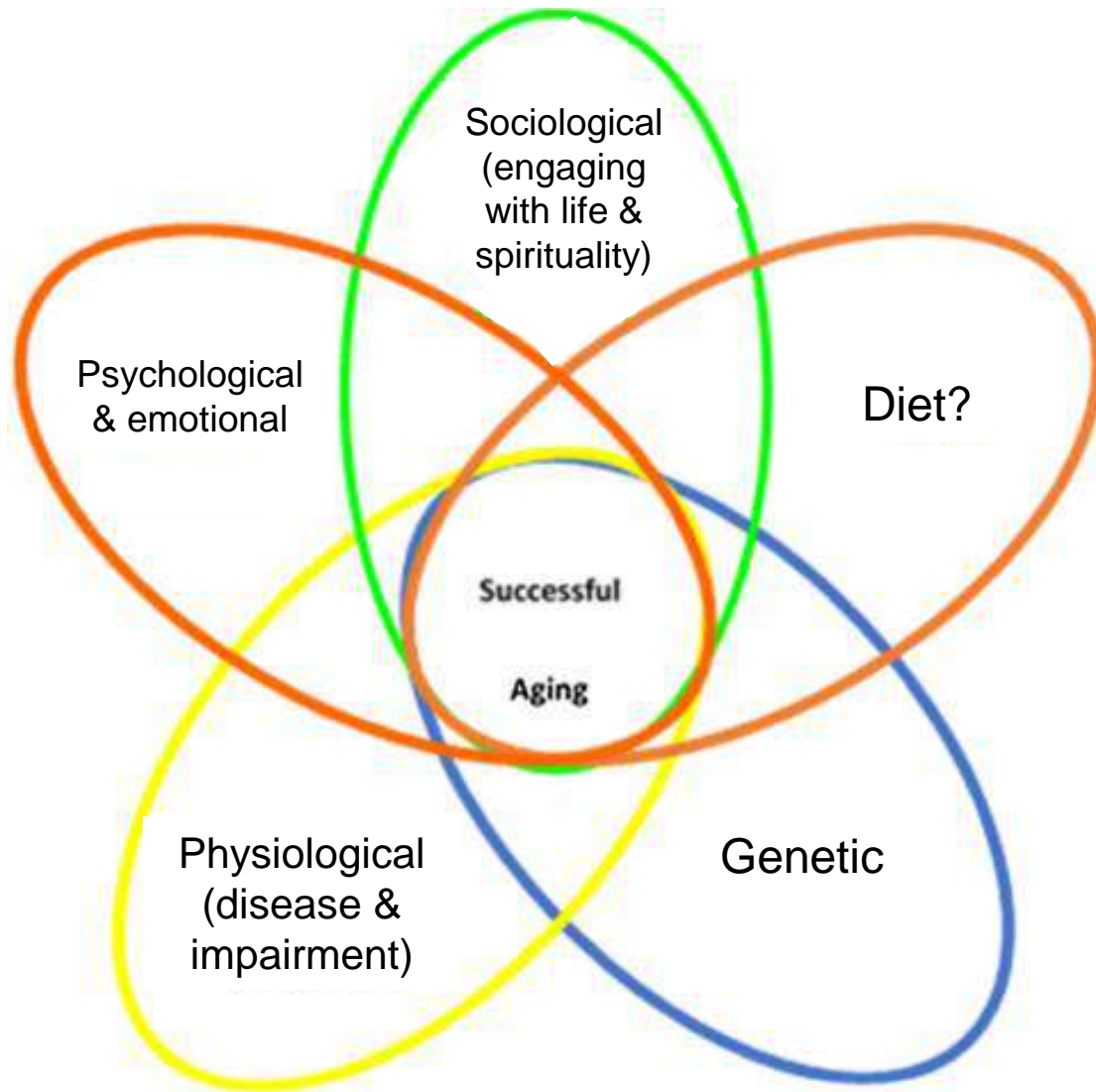
Protein Leverage Hypothesis



Cell 161, March 26, 2015

doi: 10.3390/nu8060370

Dietary Paradigms for Metabolic Health and Longevity

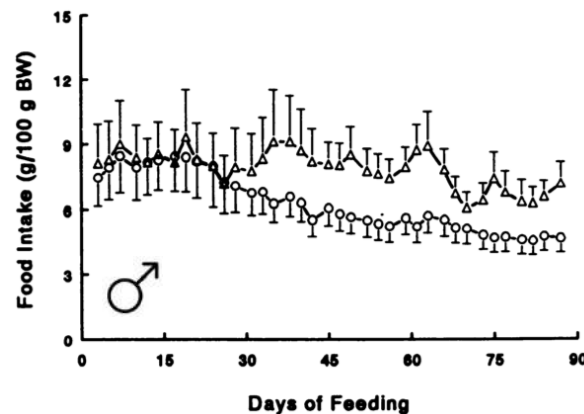
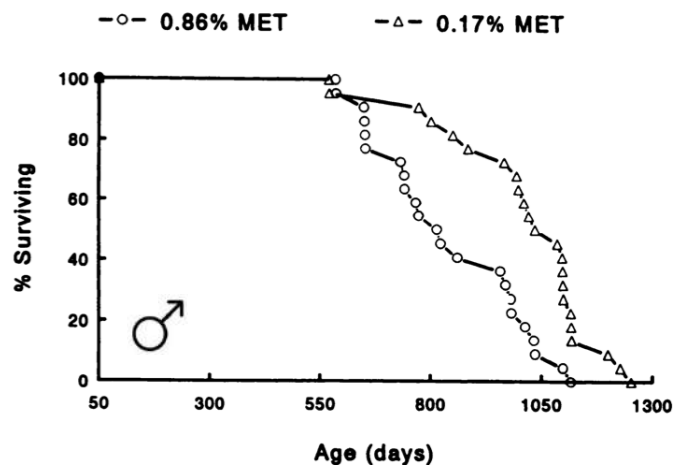


- Calorie restriction
- Protein restriction
- Less animal protein, replace with plant protein
- Essential amino acid restriction
- Sulfur amino acid restriction

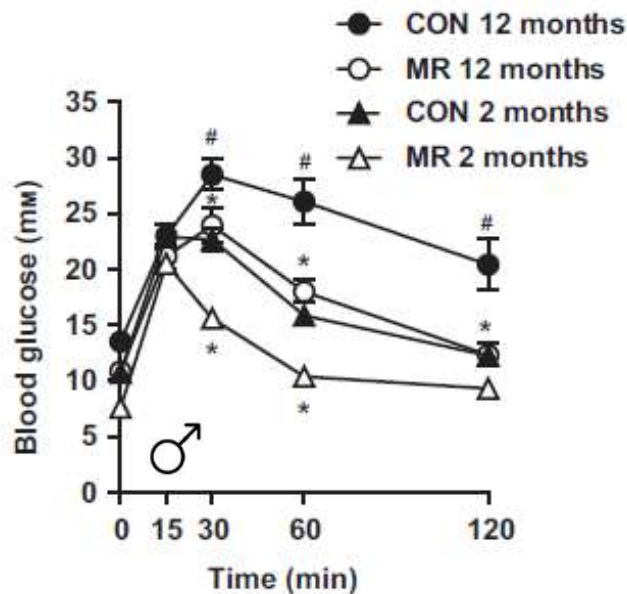
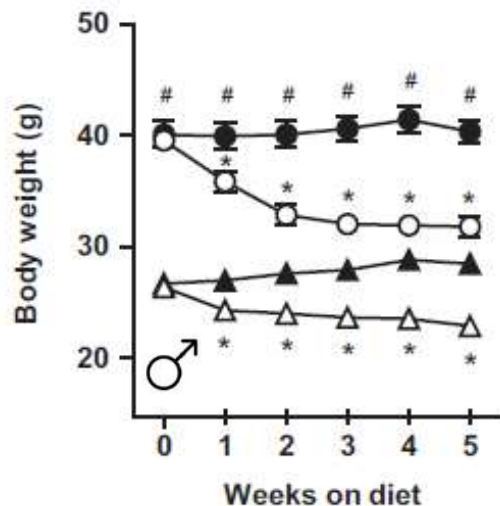
Ageing Research Reviews 39 (2017) 78–86

European Journal of Nutrition (2018) 57 (Suppl 2):S15–S34

Sulfur Amino Acid Restriction (SAAR) extends lifespan and is associated with a lean, metabolically younger phenotype

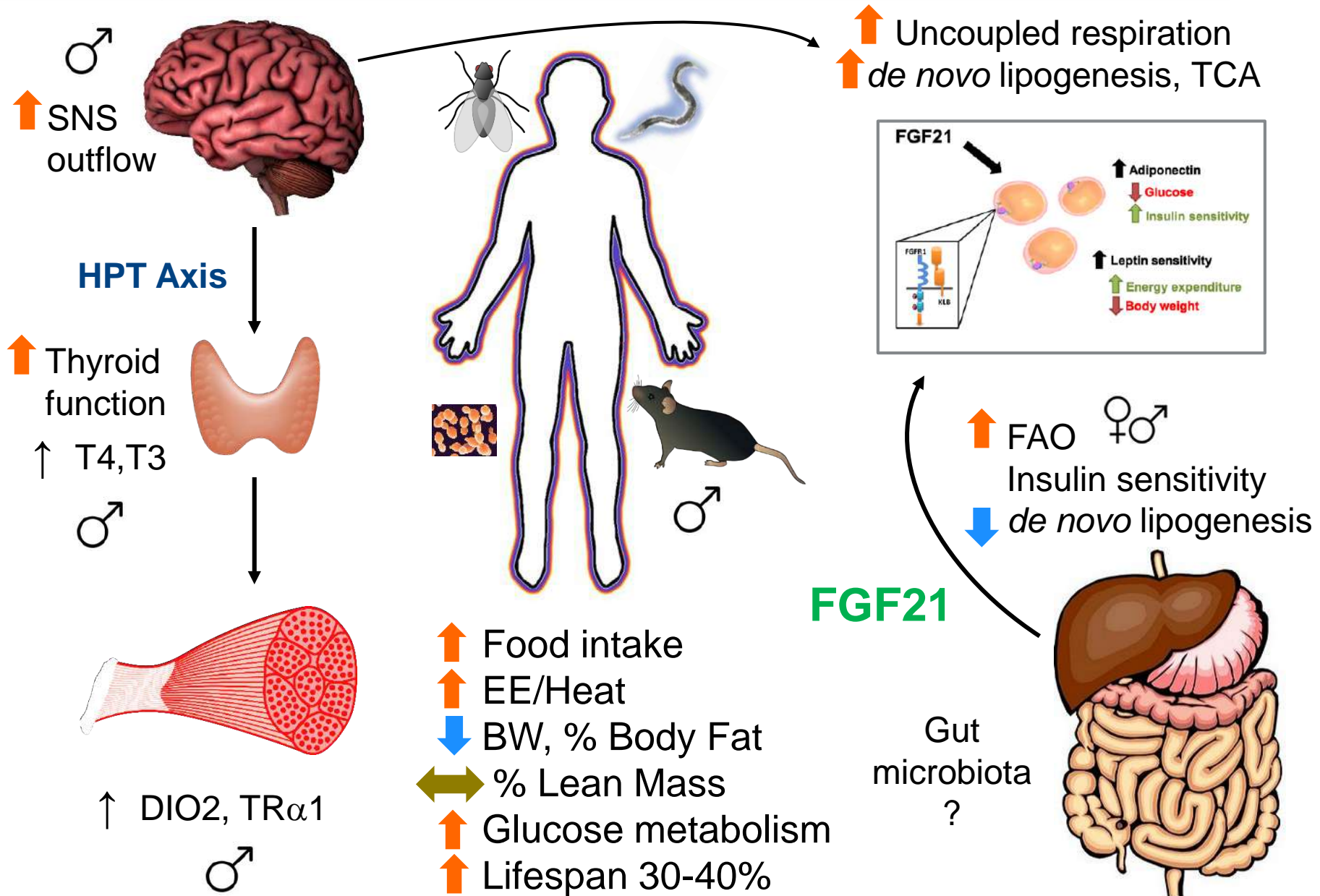


Orentreich et al. **Low methionine ingestion by rats extends life span.** *J Nutr.* (1993) 123(2):269-74.



Lees et al. **Methionine restriction restores a younger metabolic phenotype in adult mice with alterations in fibroblast growth factor 21.** *Aging Cell* (2014) 13:817-827. doi: 10.1111/accel.12238

Sulfur Amino Acid Restriction: Mechanisms



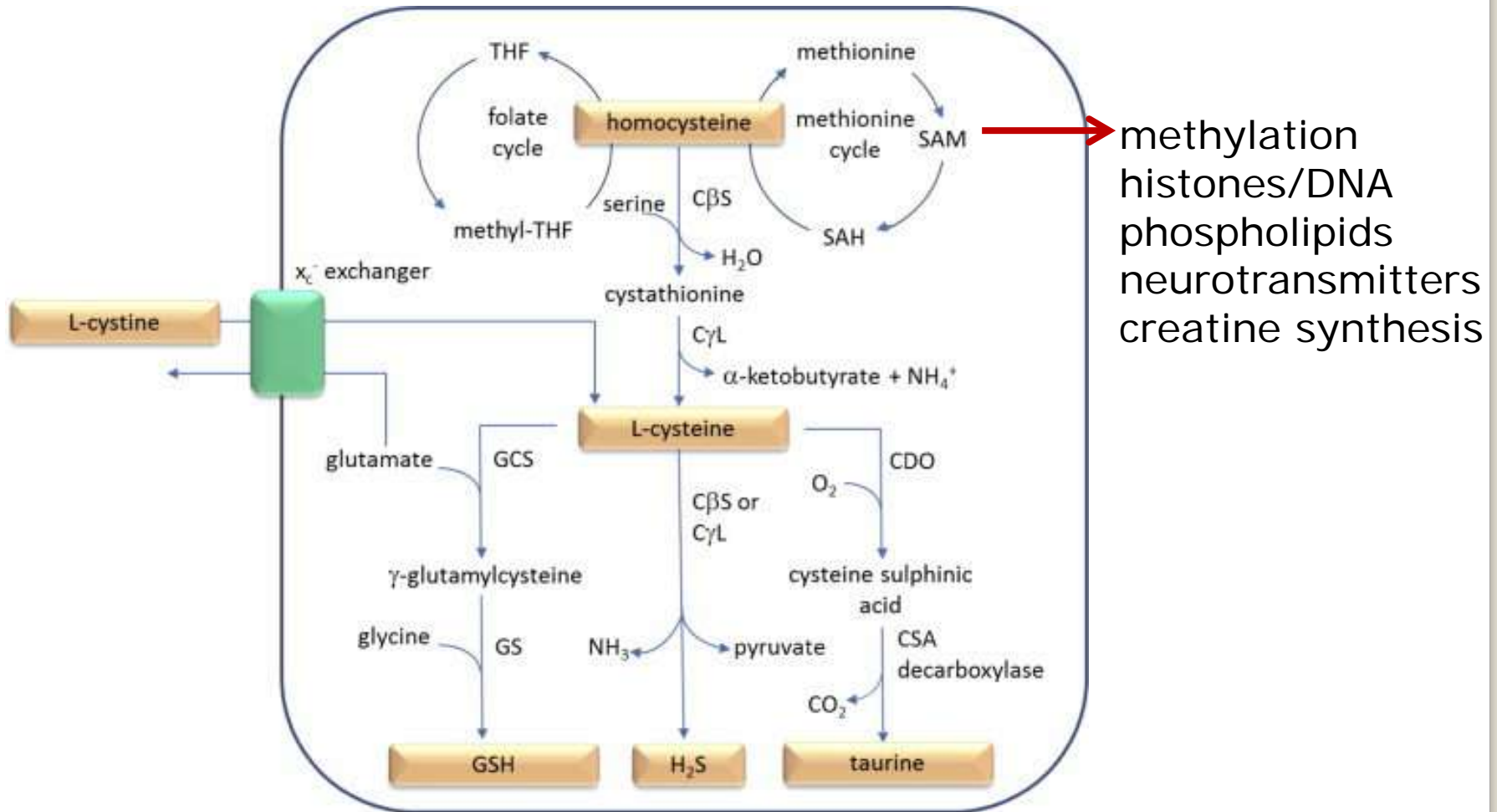
What's so special about SAAR?

- ◆ SAAR has stronger metabolic effects versus leucine restriction (LR).

Measured after 8 wk:	Compared to Control diet:	
	<u>SAAR</u>	<u>LR</u>
Food intake	↑↑ (+38%)	↑ (+22%)
Body weight	↓↓ (-25%)	↓ (-16%)
% body fat mass	↓↓ (-30%)	↓ (-22%)
Fasting insulin	↓↓ (-81%)	↓ (-48%)
Fasting glucose	↓	↔
Glucose clearance	↑↑	↑
Circulating FGF21	↑↑↑	↔
Liver triglyceride content	↓	↔
Liver lipogenic genes	↓	↔



Potential ways sulfur amino acid restriction improves health span



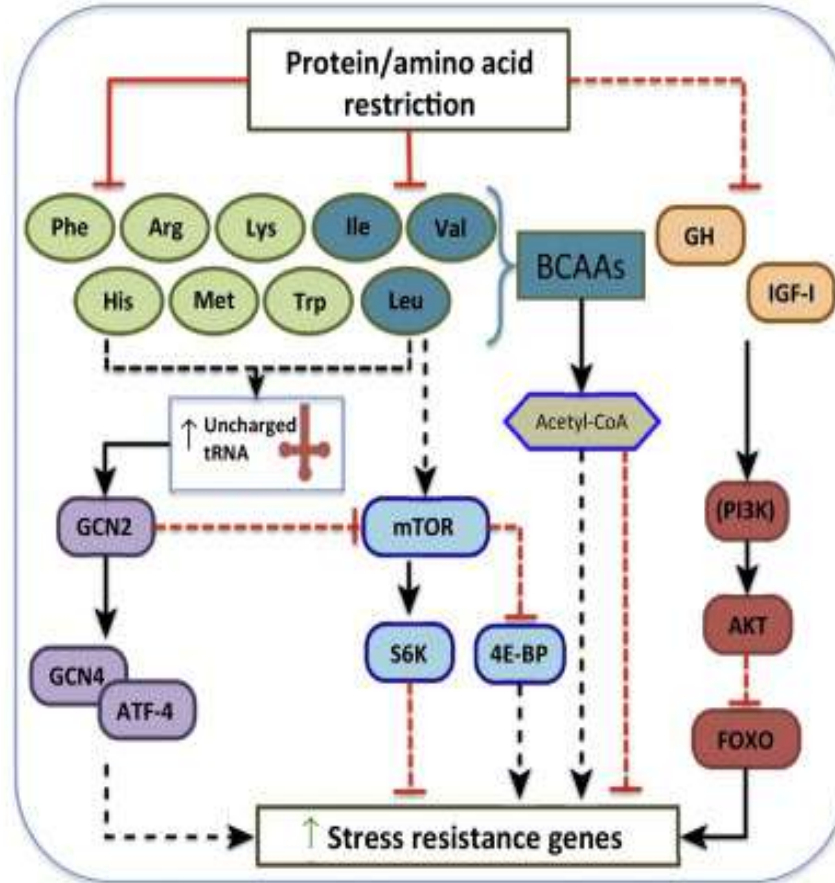
↑ antioxidant defenses, mitochondrial function

Proposed Mechanisms for how Dietary Restriction Promotes Healthspan

↓ Protein
↓ Fat



Increased longevity
reduce risk of CVD,
diabetes, and cancer



↑ Protein homeostasis

↑ Protein
↑ Fat



Reduced longevity
increase risk of CVD,
diabetes, and cancer

TRENDS in Endocrinology & Metabolism

Integrated Stress Response

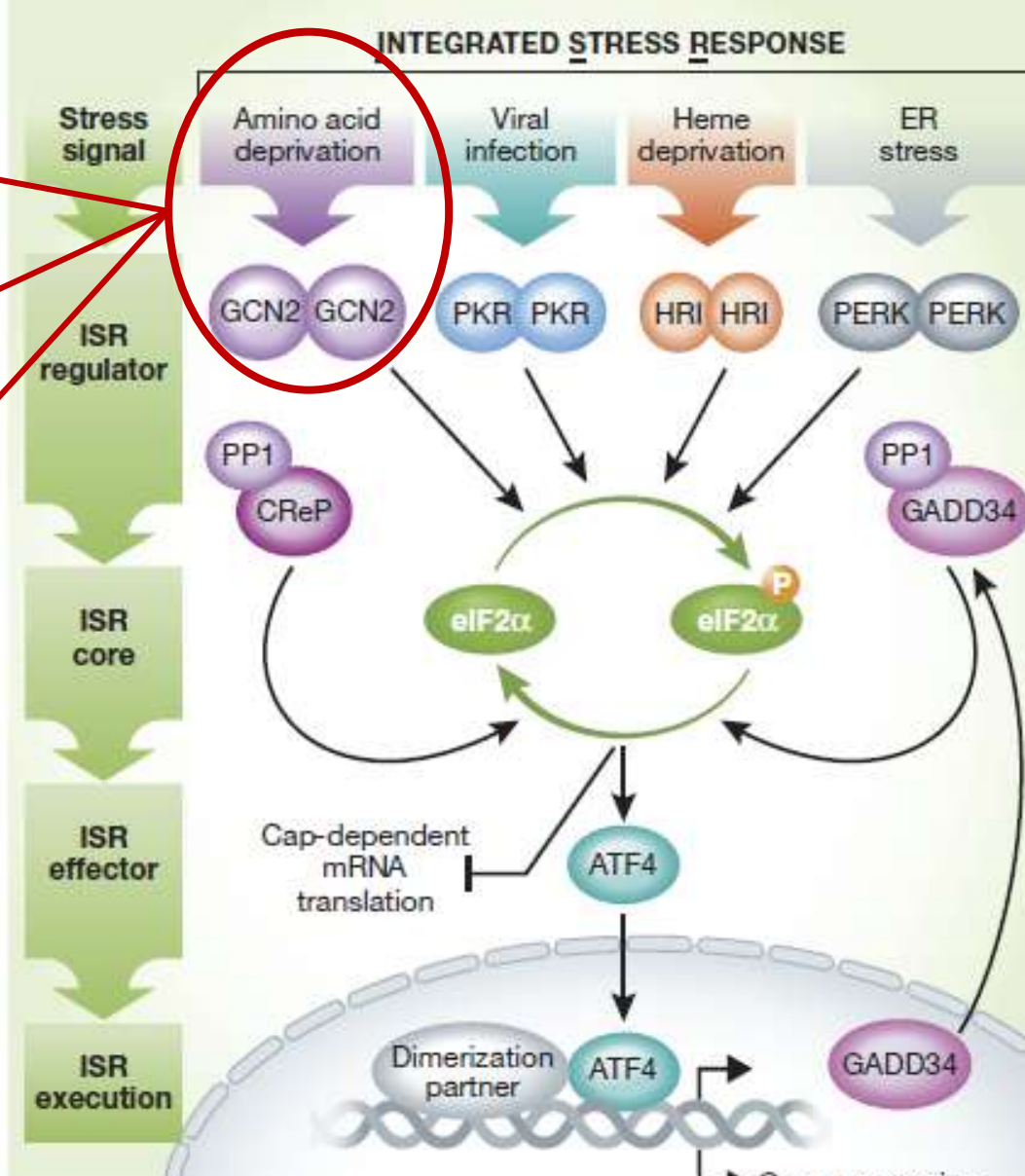
Diet



Drugs



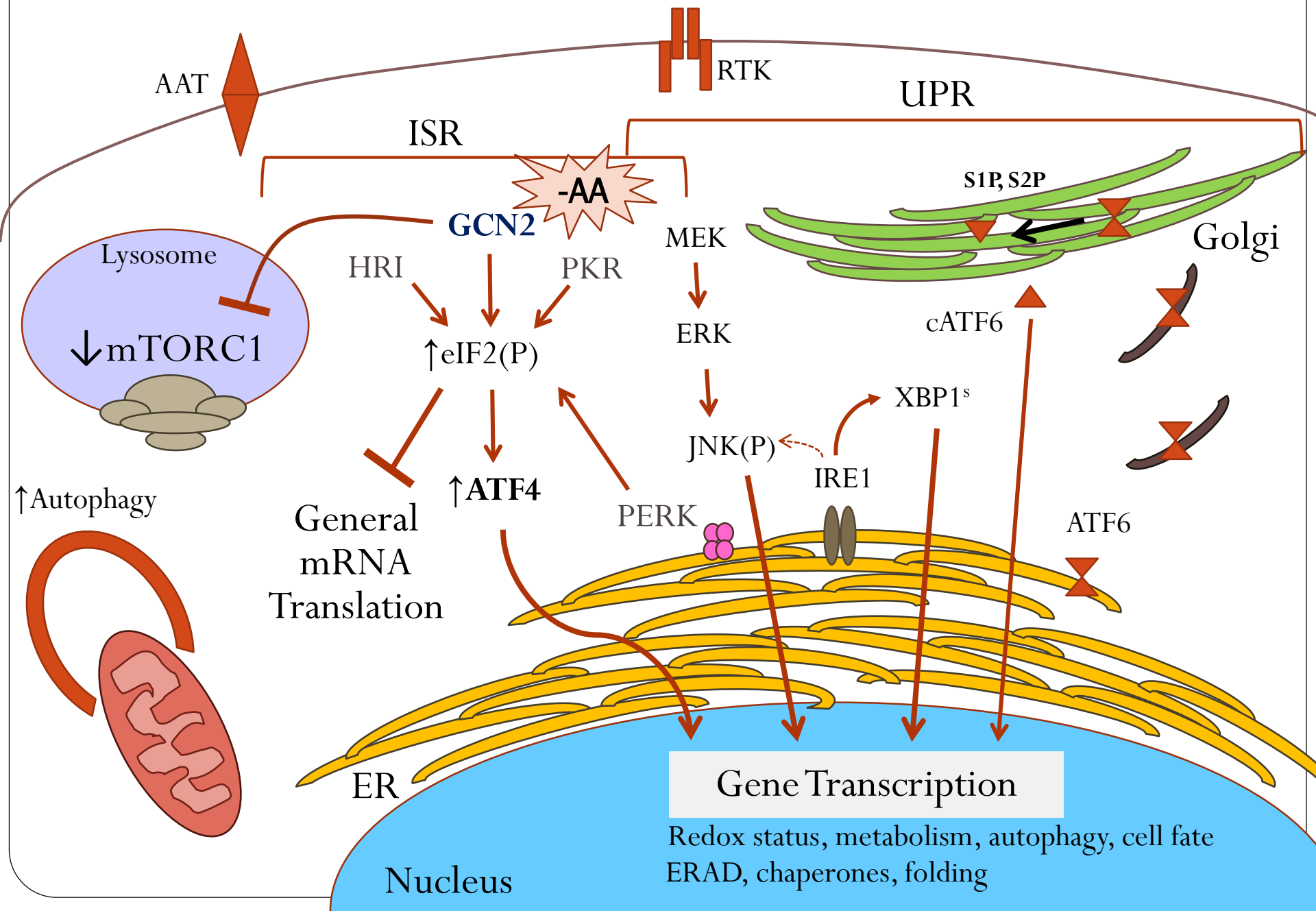
Genetics



EMBO Reports (2016) 17: 1374–1395

ISR Functions
 Adaptation
 Hormesis
 Preconditioning

The ISR Meets the UPR at the ER



Potential Areas for Collaboration:

Mechanisms linking dietary restriction with aging biology.

- Nutrient sensing pathways (ISR, mTOR)
- Proteostasis control (UPR, autophagy)
- Environmental factors (temperature, light, physical activity/exercise as medicine)

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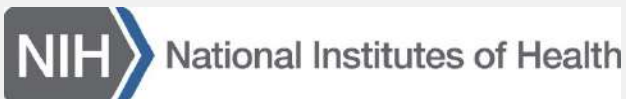
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Thank you! Questions?