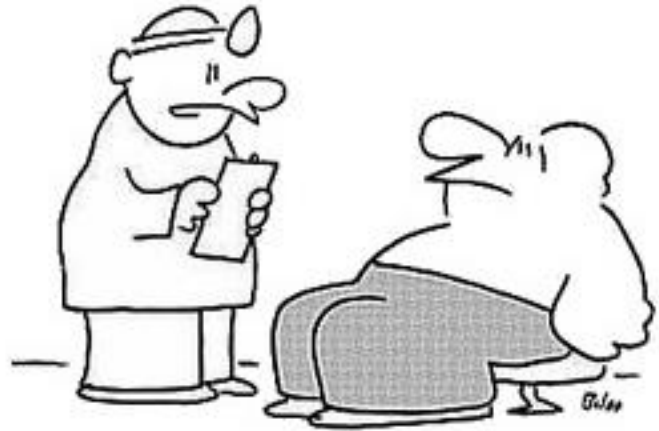


Fasting and Dietary Interventions for Cancer Treatment

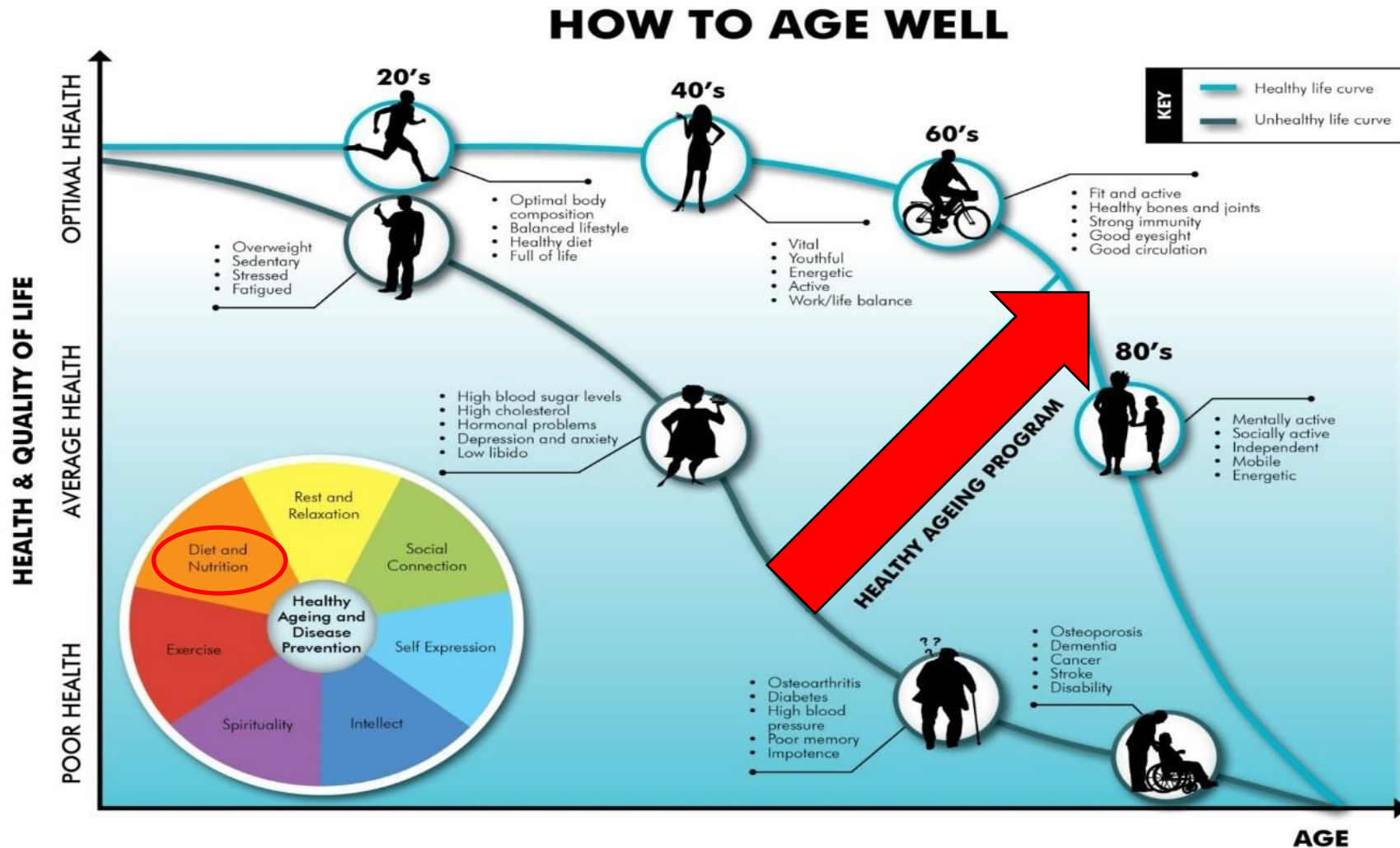


"LET'S EASE INTO THIS--I WANT YOU TO TRY FASTING BETWEEN MEALS."

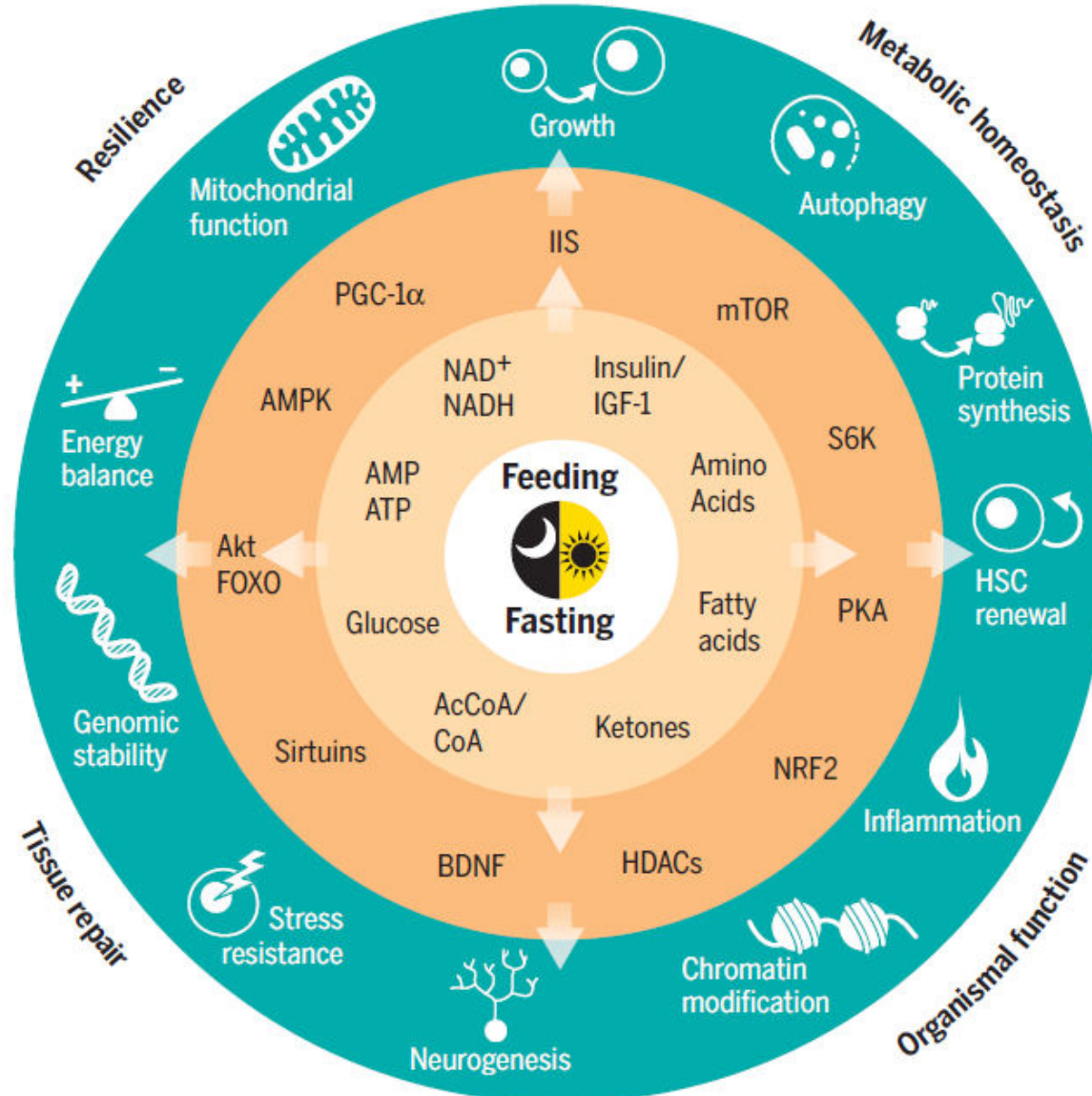
Sebastian Brandhorst, PhD
Longevity Institute
University of Southern California

Aging is a Catalyst of Chronic Diseases

- If we understand how we age and optimize the **pace and quality**, this could be one of the most powerful interventions to increase **healthspan**.

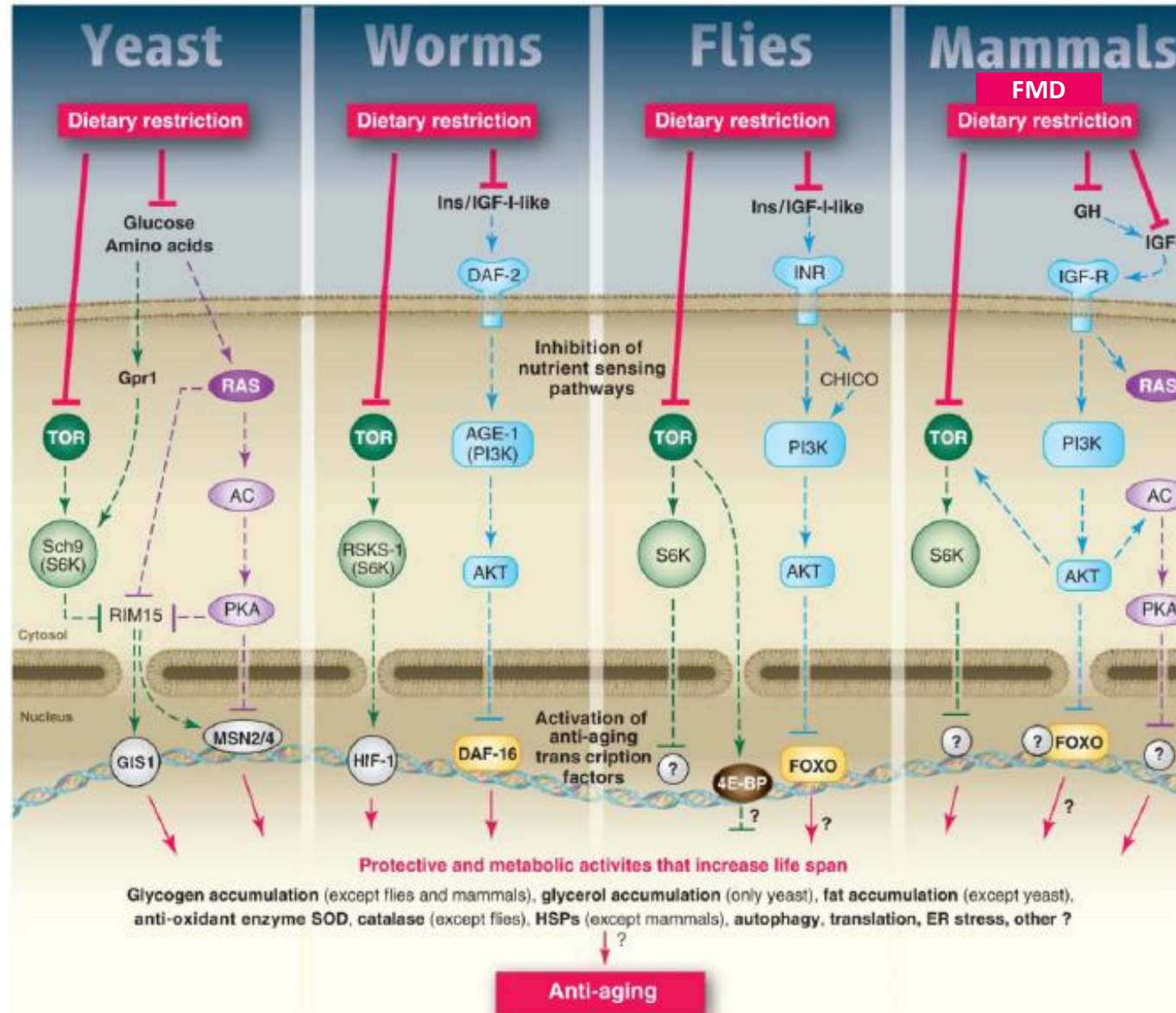


Biological Responses Implicated in Metabolite-Controlled Longevity Pathways

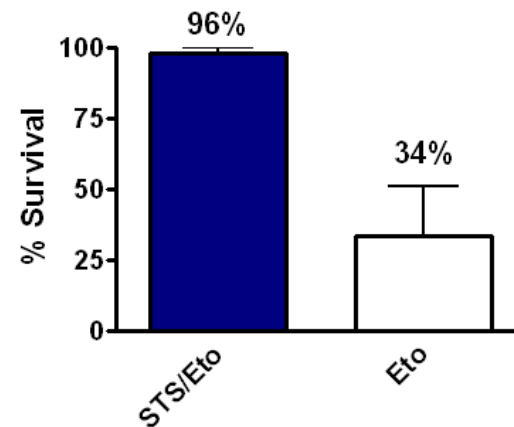
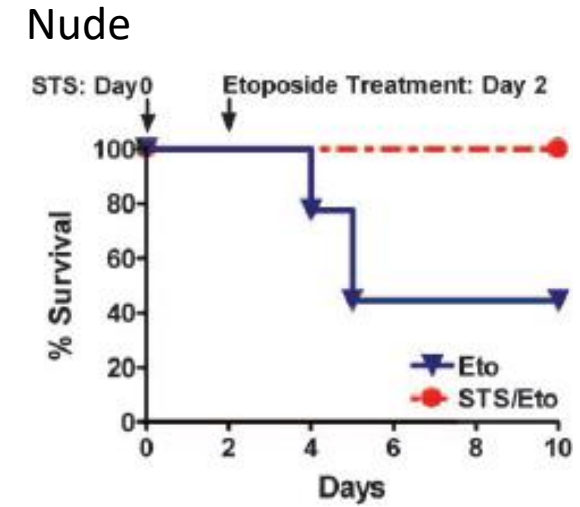
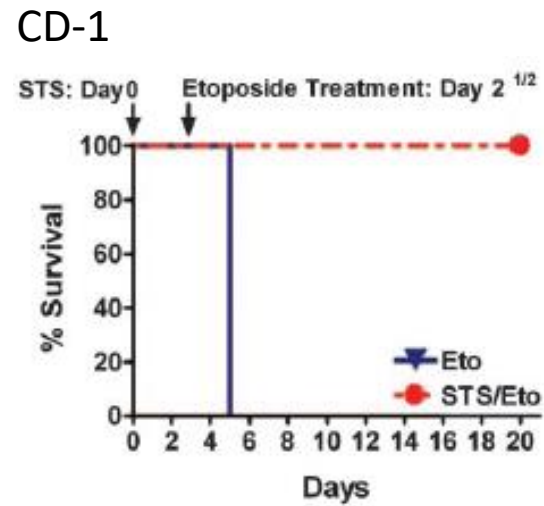
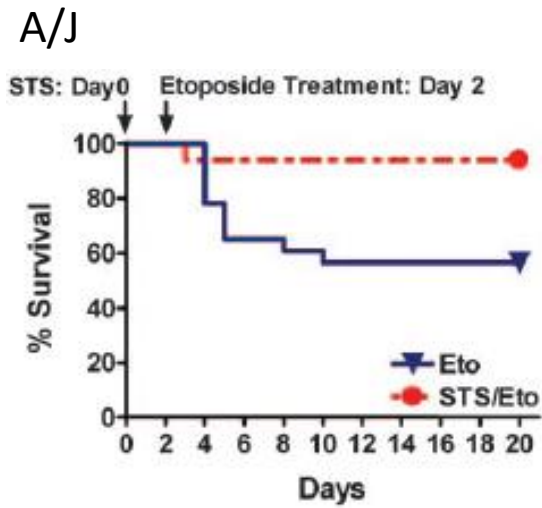


Can we use “Anti-Aging” Dietary Approaches to Treat Diseases?

Example: **Cancer**

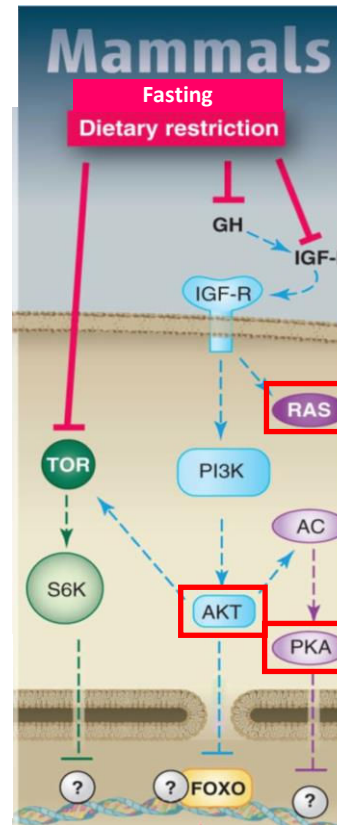
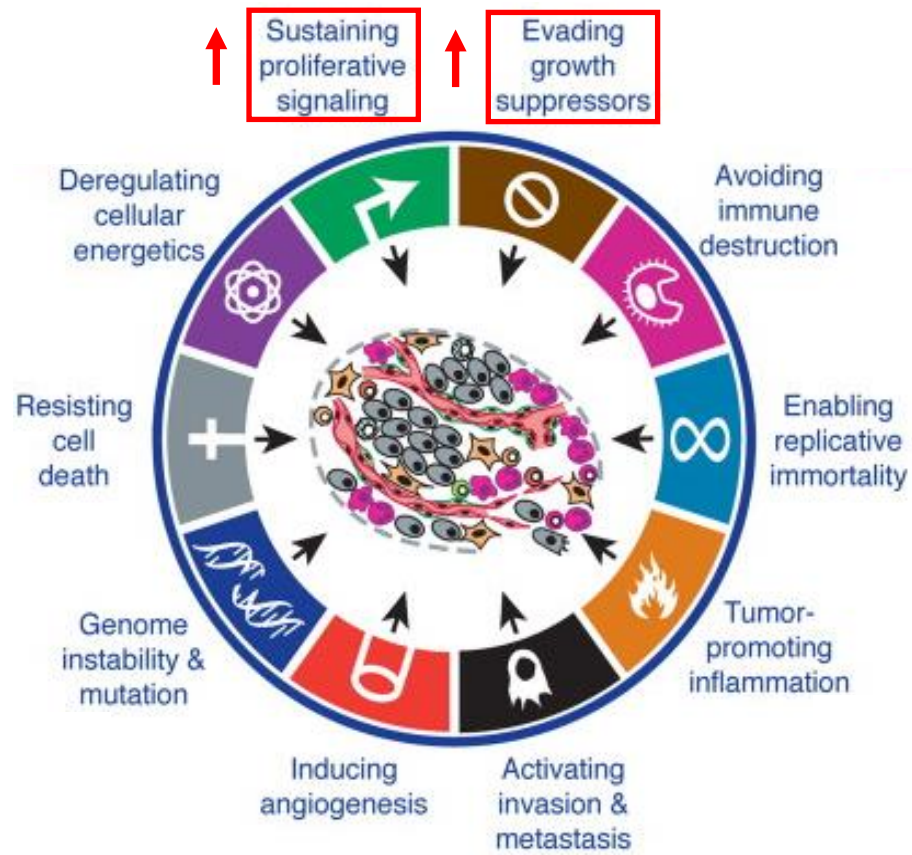


Fasting-induced Differential Stress Resistance

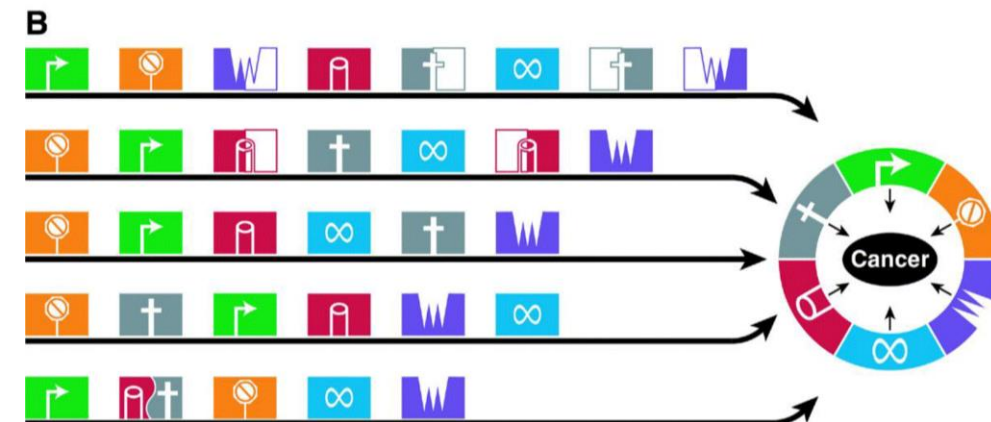


→ Detrimental if fasting induces similar protection in cancer cells!!!

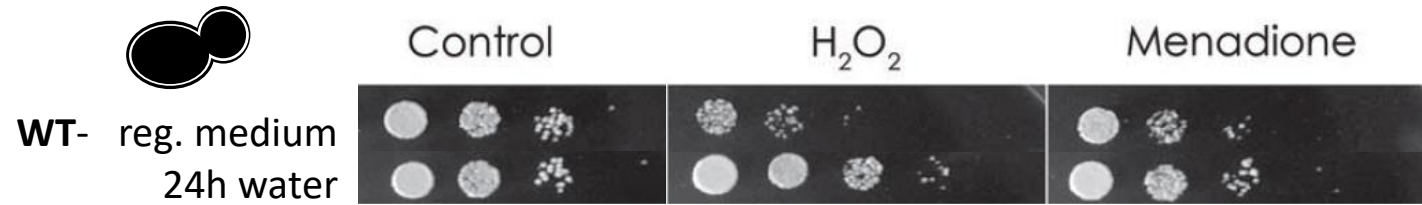
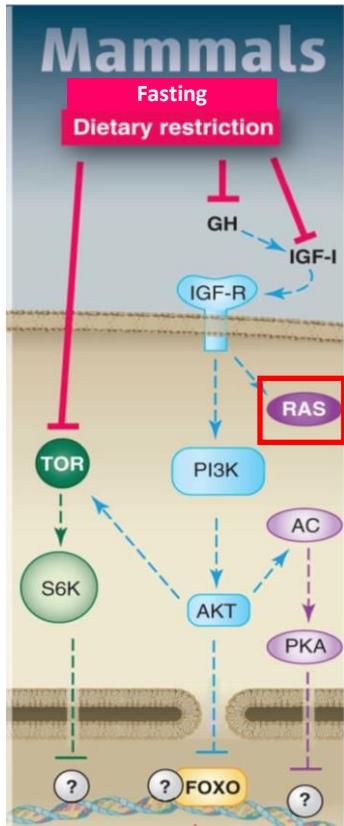
The Hallmarks of Cancer: Oncogenes in Pro-aging Pathways



Component	Acquired Capability	Example of Mechanism
	Self-sufficiency in growth signals	Activate H-Ras oncogene
	Insensitivity to anti-growth signals	Lose retinoblastoma suppressor
	Evading apoptosis	Produce IGF survival factors
	Limitless replicative potential	Turn on telomerase
	Sustained angiogenesis	Produce VEGF inducer
	Tissue invasion & metastasis	Inactivate E-cadherin

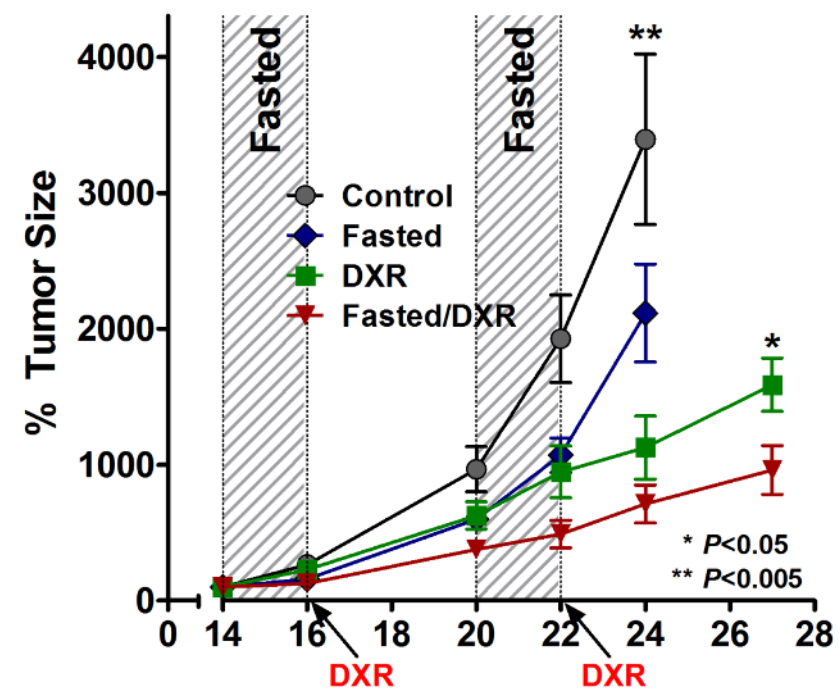
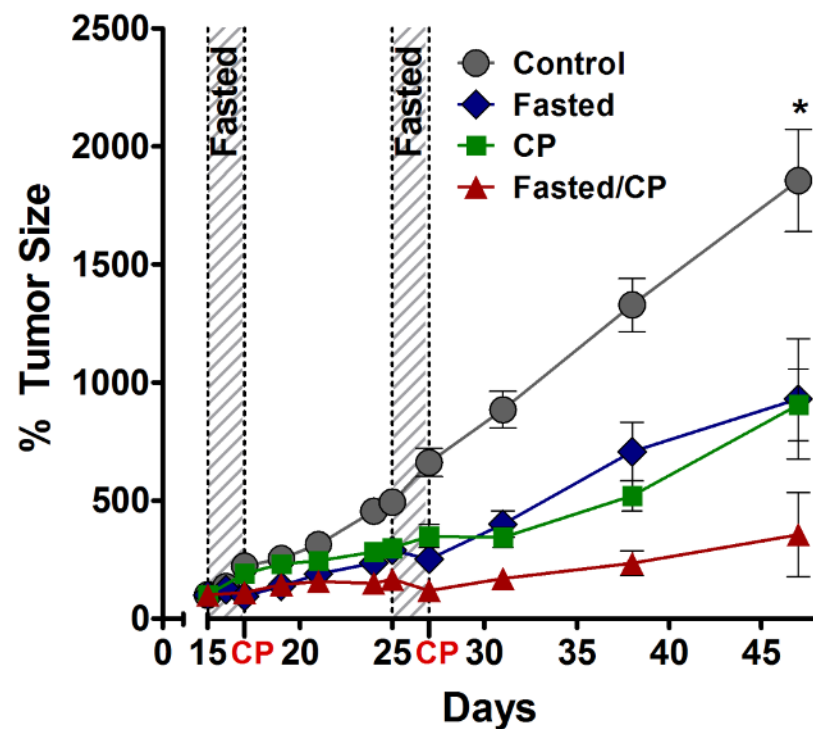


Fasting-induced Differential Stress Resistance & Sensitization



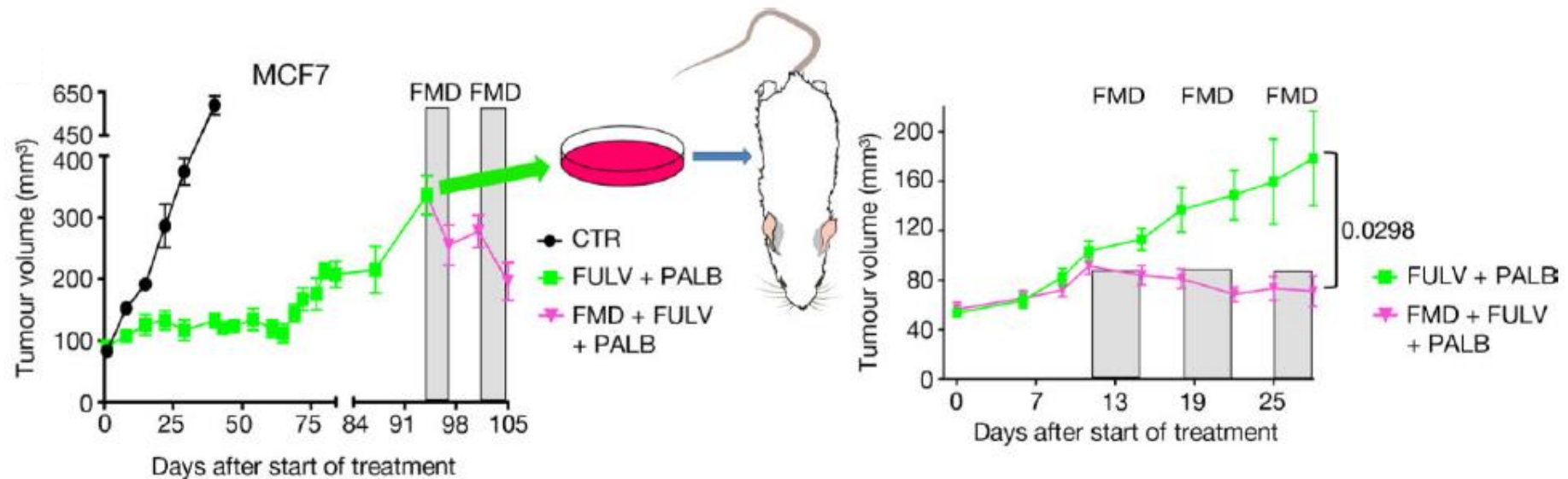
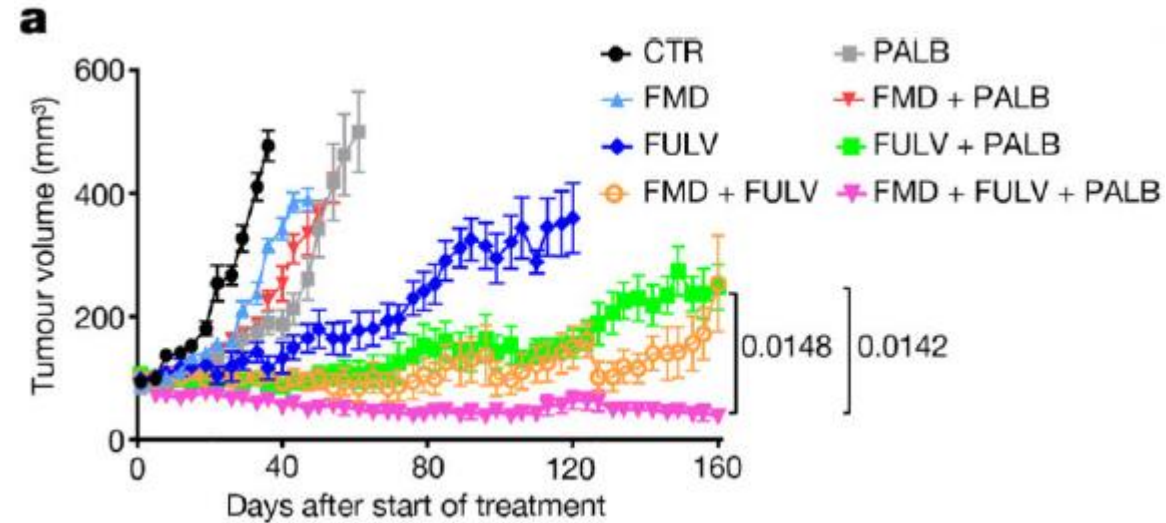
Fasting-induced Differential Stress Sensitization

Multiple fasting cycles are as effective as chemotherapy and improve the efficacy against breast and melanoma cancer cells in mice.



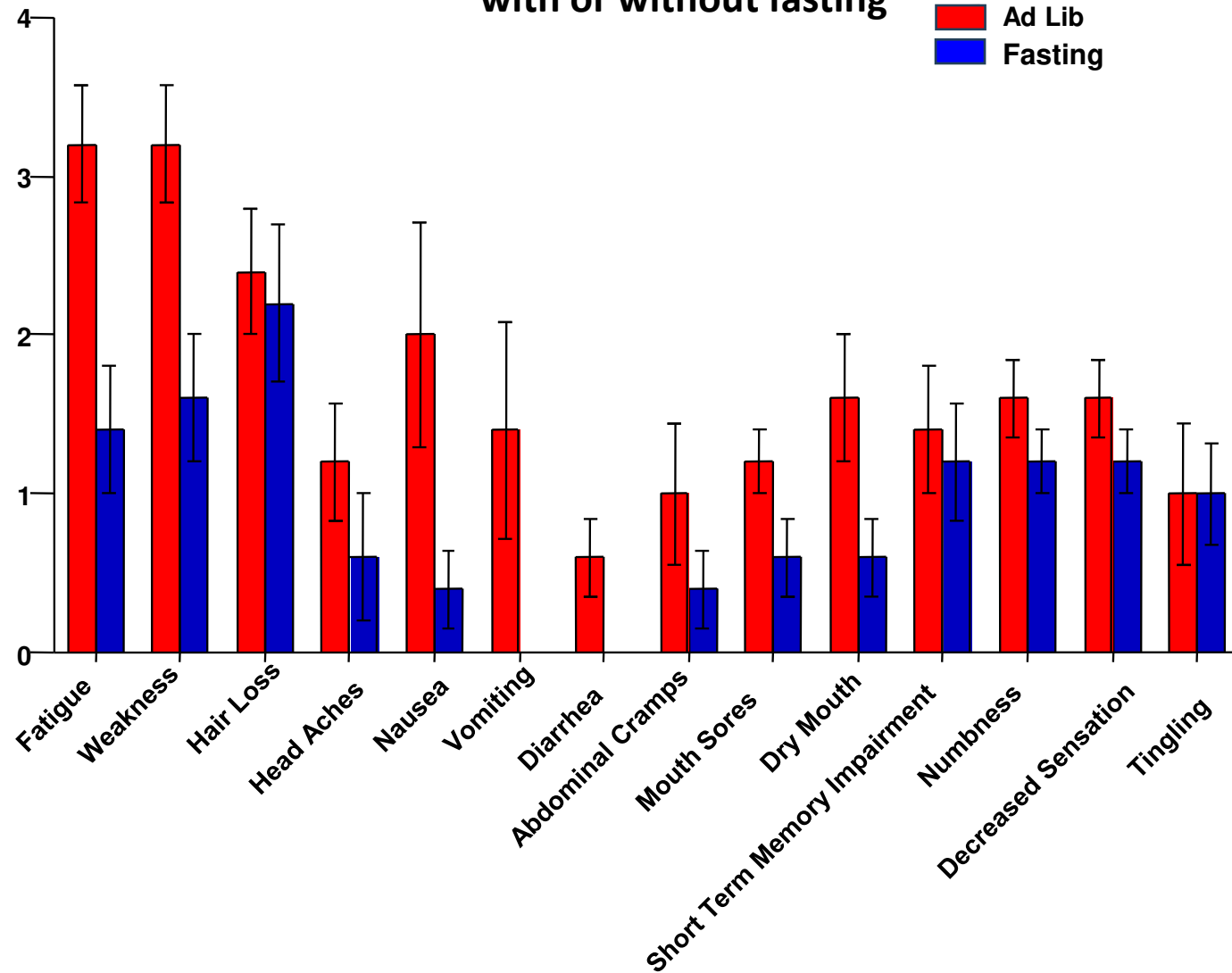
Fasting-induced Differential Stress Sensitization

Fasting-Mimicking Diet (FMD) Prevents Resistance to Combined Fulvestrant and Palbociclib



Fasting-induced Differential Stress Sensitization: Relevance for Cancer Patients?

Average self-reported severity of symptoms in patients that have received chemotherapy
with or without fasting



Fasting-induced Differential Stress Sensitization: Relevance for Cancer Patients?

FMD shows promising results as an adjunct to Neoadjuvant Chemotherapy for Breast Cancer

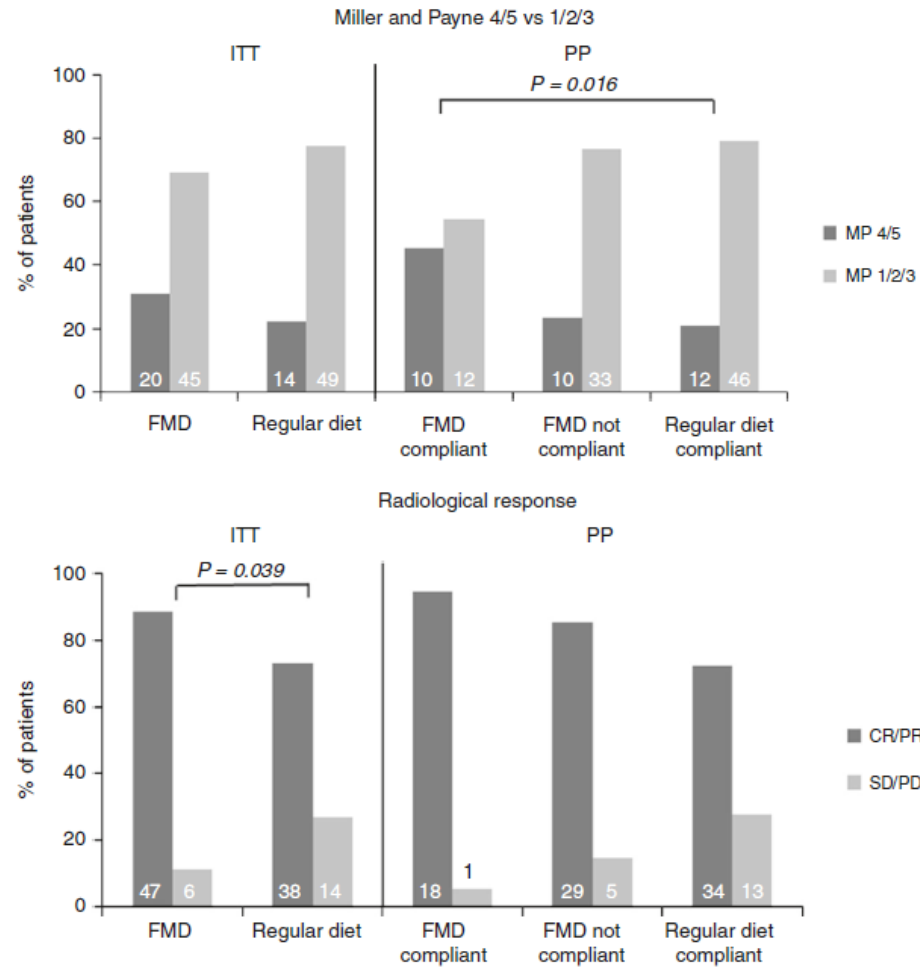
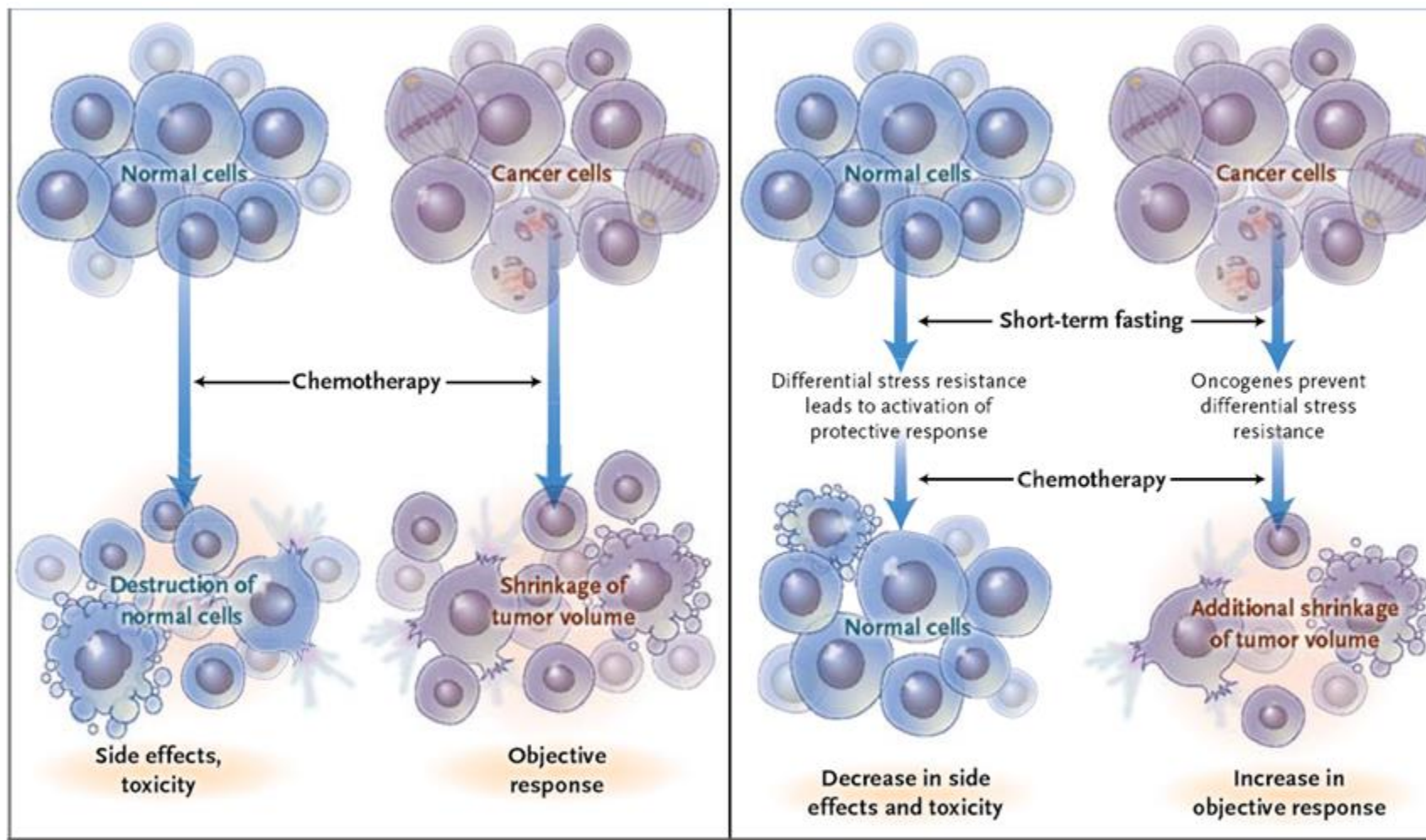


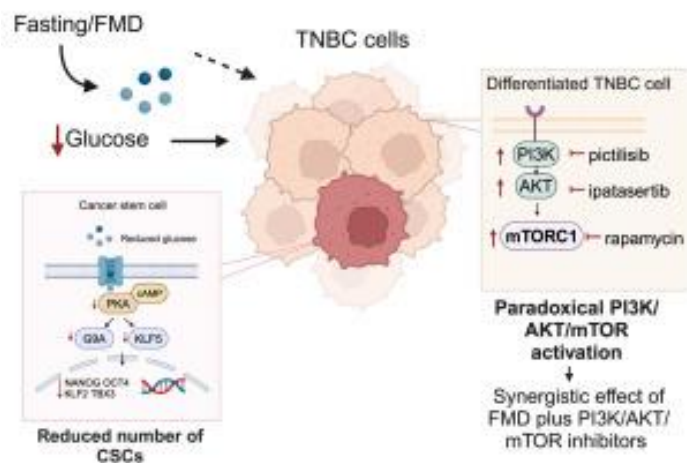
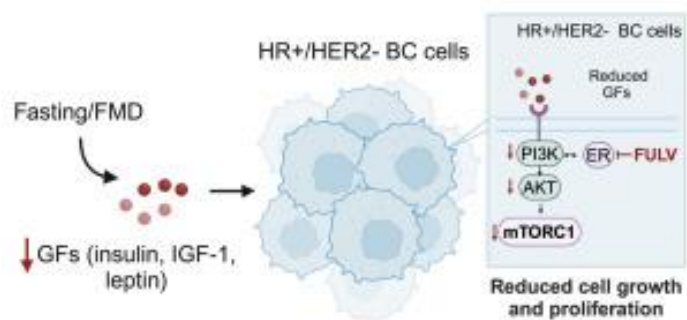
Fig. 2 Tumor response data for the ITT and PP analysis. The pathological response was given for Miller and Payne pathological response score 4/5 (90-100% tumor cell loss) vs. 1/2/3 (less than 90% tumor cell loss). The radiological response was scored according RECIST 1.1 and given for complete response + partial response vs. stable disease + progression disease. Abbreviations: FMD: fasting mimicking diet, ITT: Intention to treat, PP: Per protocol, MP: Miller and Payne, CR: complete response, PR: partial response, SD: stable disease, PD: progression disease. Logistic regression was used (2-sided).

Fasting to Optimize Cancer Management: **a simplified view*

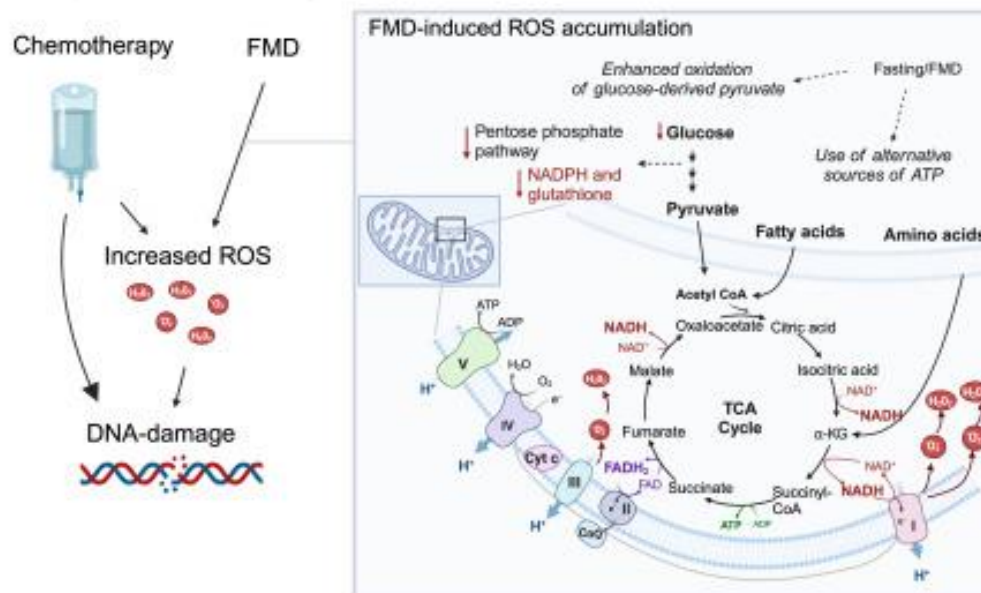


Mechanisms of Antitumor Fasting/FMD

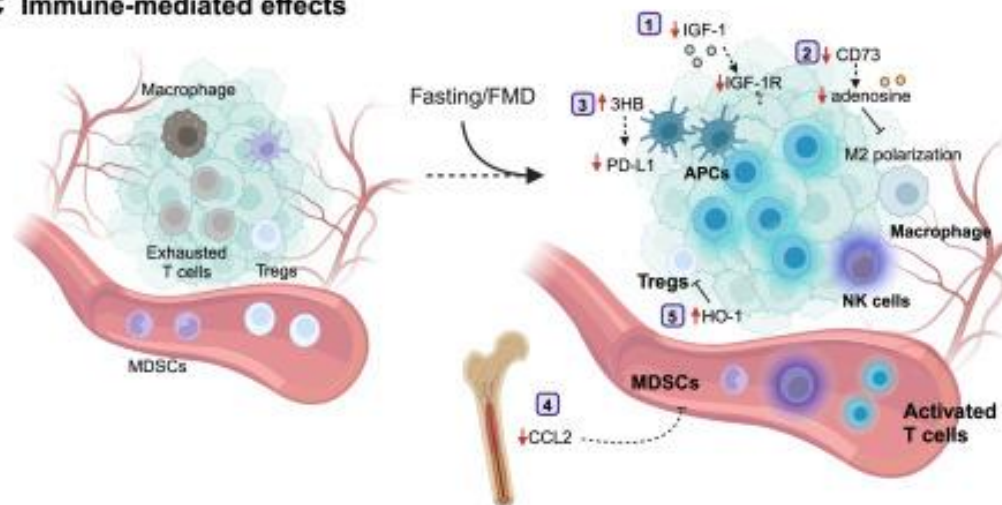
A Impact on proliferation and oncogenic pathways



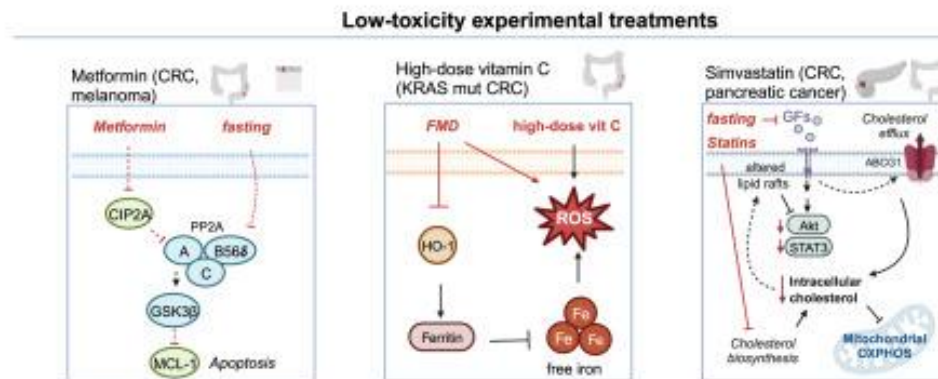
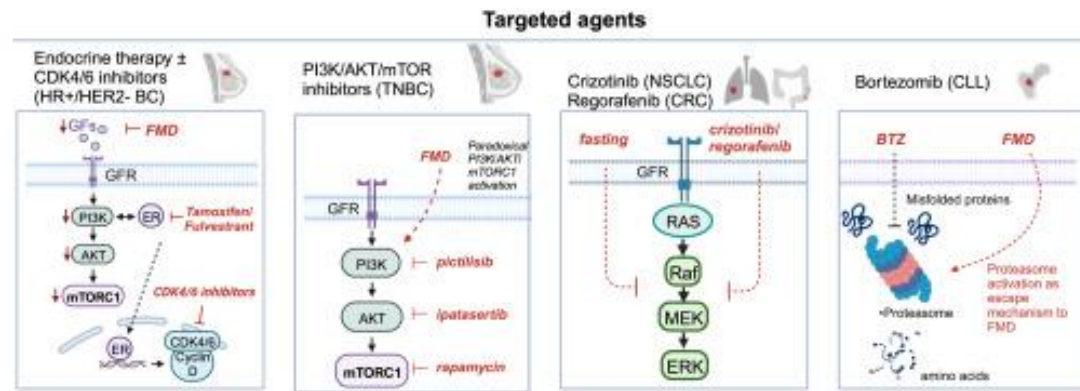
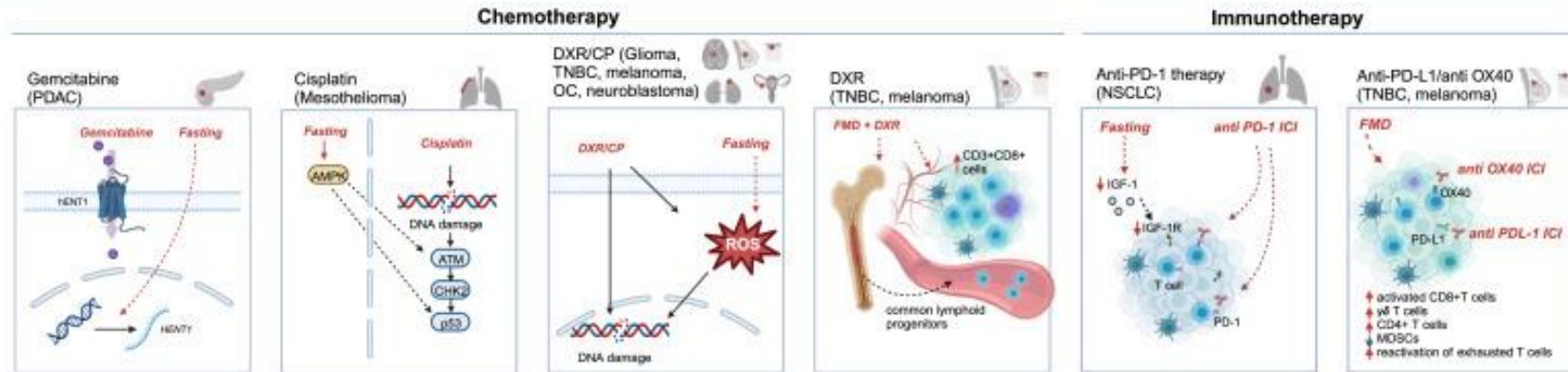
B Impact on DNA damage response and oxidative stress



C Immune-mediated effects



Fasting/FMD-based Strategies to Boost Cancer Treatment



Conclusions & Outlook

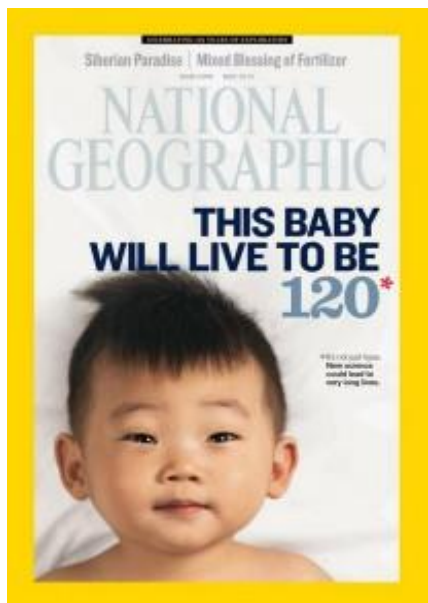
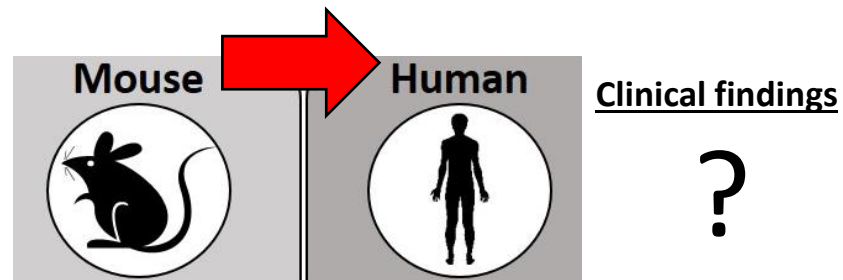


- Diets (*among other lifestyle factors*) present a powerful tool to prevent, or at least delay the onset of many chronic, age-related diseases.
- Fasting cycles can improve the efficacy of cancer treatment.

FMDs in the treatment of aging-related diseases

Preclinical findings:

- Reverses Type 1, Type 2 diabetes
- Reduces symptoms of MS
- Protects against chemo-toxicity
- Sensitizes cancers to chemotherapy



Thank you!

