INTERMITTENT FASTING

AUTOPHAGY & SUMMATION

A DR. H MEDITATION ©2018

SAFETY 1ST ☺ - CONTRAINDICATIONS

Definite Concerns

- Kidney Disease (Renal Failure)
- Heart Arrhythmia
- Recurrent Syncope
- Type 1 Diabetes
- Poorly Controlled Blood Sugars
- Post-Surgical Recovery
- Children under 18
- Expectant &/or Lactating Mothers

Possible Contraindications

- Moderate to Advanced Hepatitis?
- Menstruation?
- Winter?

ADDITIONAL CONTRAINDICATIONS

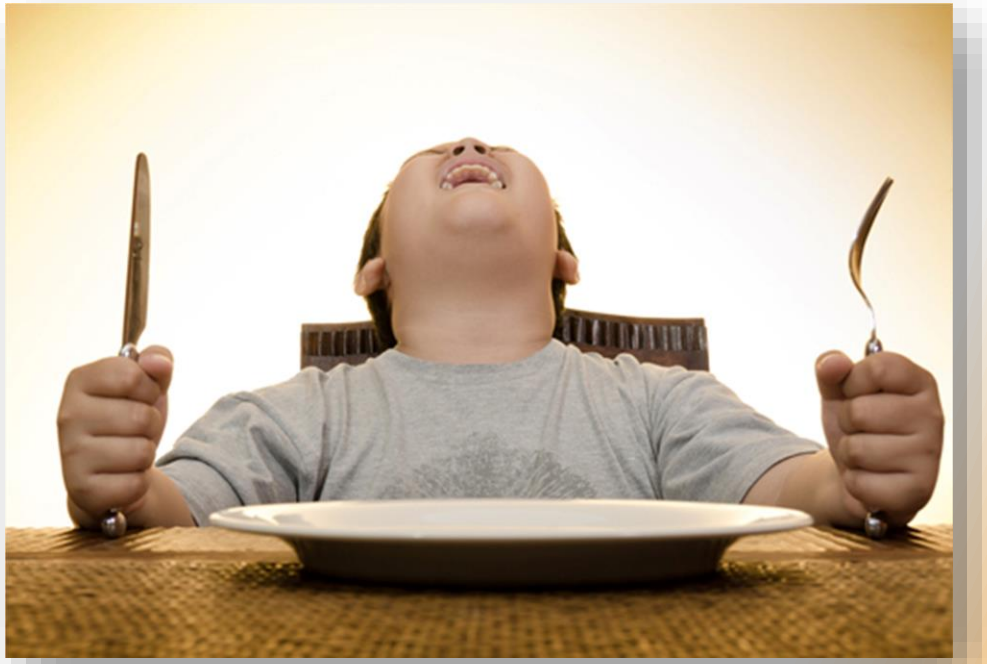
Clinical Observations
Specific To Intermittent Fasting

- Hashimoto's Thyroiditis
- Inflammatory Bowel Disease
- Graves' Disease
- Adrenal Fatigue?
- Other Autoimmune Conditions?

TYPES OF FASTING

What Makes a Fast…a Fast?

- **Hunger Pains** → Glucagon → Starts Autophagy
- Glycogen Depletion → Ketones → Peak Autophagy
- Intermittent Fasting → Glucagon
- Clinical Fasting → Ketones



All Fasting

- Zero Calorie - Water Only For Set Time Period
- Herbs & Nutrients (ok)

Juice Fasting

- Not Fasting…Really Feasting

Intermittent Fasting

- Not Technically Fasting but Activates Autophagy
- 16-Hours w/o Food (**Other Variations Too**)
- Basically Calorie Responsible (CR) Living

GLUCAGON – 6 TO 8 HOUR MARK

Stage 1 - Glycogen Mobilization

- Initial Goal - Activate Glucagon & use up Glycogen Reserves.

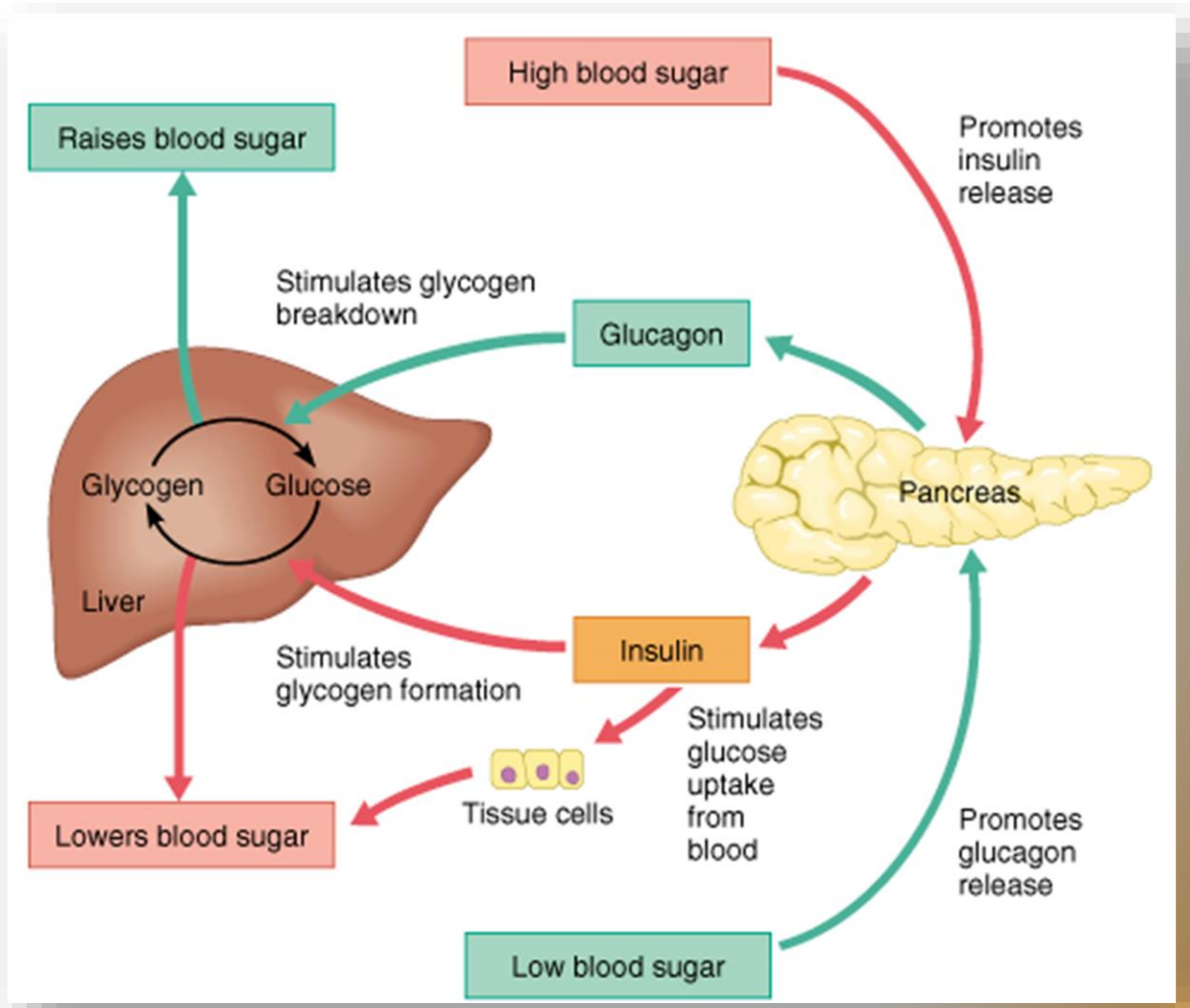
Why?

- Glucagon activates AMPK & inhibits mTOR…2 keys to Autophagy.
- **Autophagy doesn't peak until Glycogen is fully depleted.**

Recommendations

- Drink Water!!!!
- IR Sauna Sweating for 45 to 60 min.

  OR
- Glycogen Depletion Cardio 90 min max.



PRANAYAMA SLEEP & WATER

What are some Intermittent Fasting keys?

- **Hunger Pains**
- **16 Hours w/o Food**
- Sleep…this is when the magic happens
- Pranayama Breathing Meditation
- **Move/Sweat Before Eating**
- Yoga
- **Sauna Therapy**
- Drink Water &/or Tea
- Earthing In Nature

TECHNOLOGY FASTING

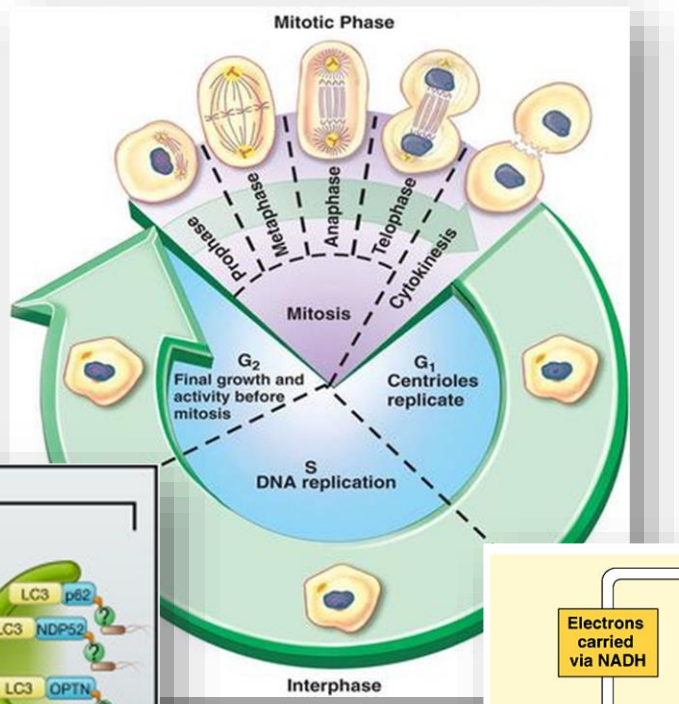
What is Technology Fasting?

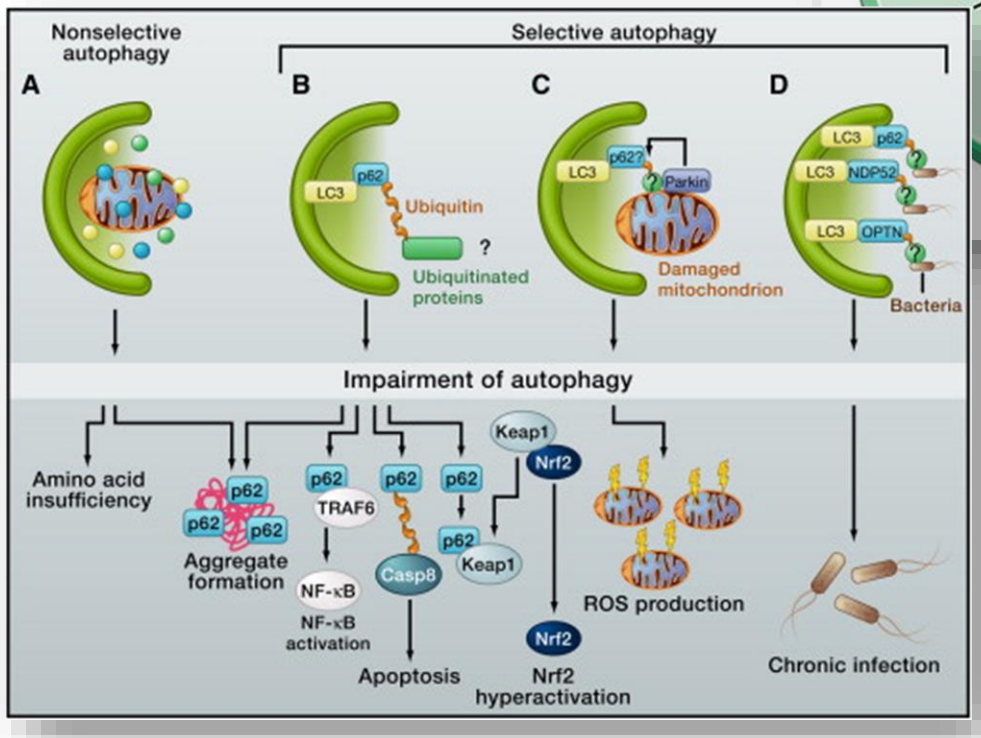
- The great irony of fasting is that it should be called ‘slowing’ because nothing will teach you how much of a hurry life has become for you like fasting will.

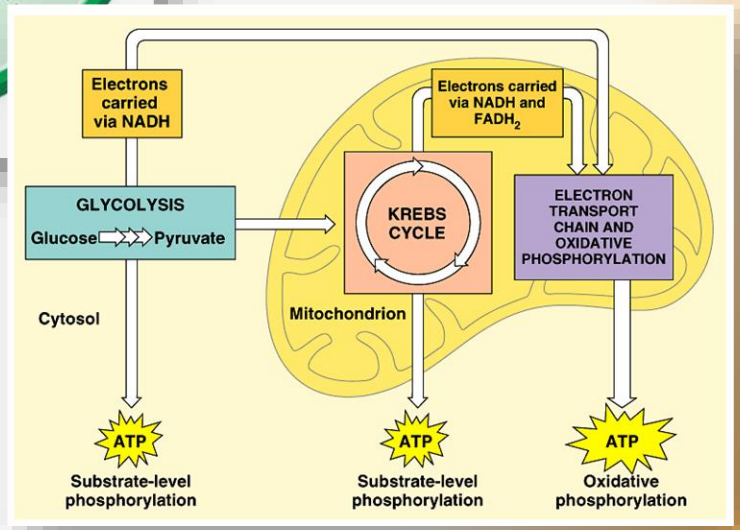
- Social Media, TV, 24 Hour Negative News Cycles, Computers, Running from One Errand to Another, Traffic…we’ve gotten ourselves in a great big hurry. **Give yourself a huge gift and turn all the external noise off so you can really listen to what’s going on inside**. 😊

CELLS CAN DO 1 THING AT A TIME

1. **Absorb/Metabolize/Detox** – Cellular Energy Production
2. **Autophagy** – Cellular Repair
3. **Mitosis** – Cellular Replication







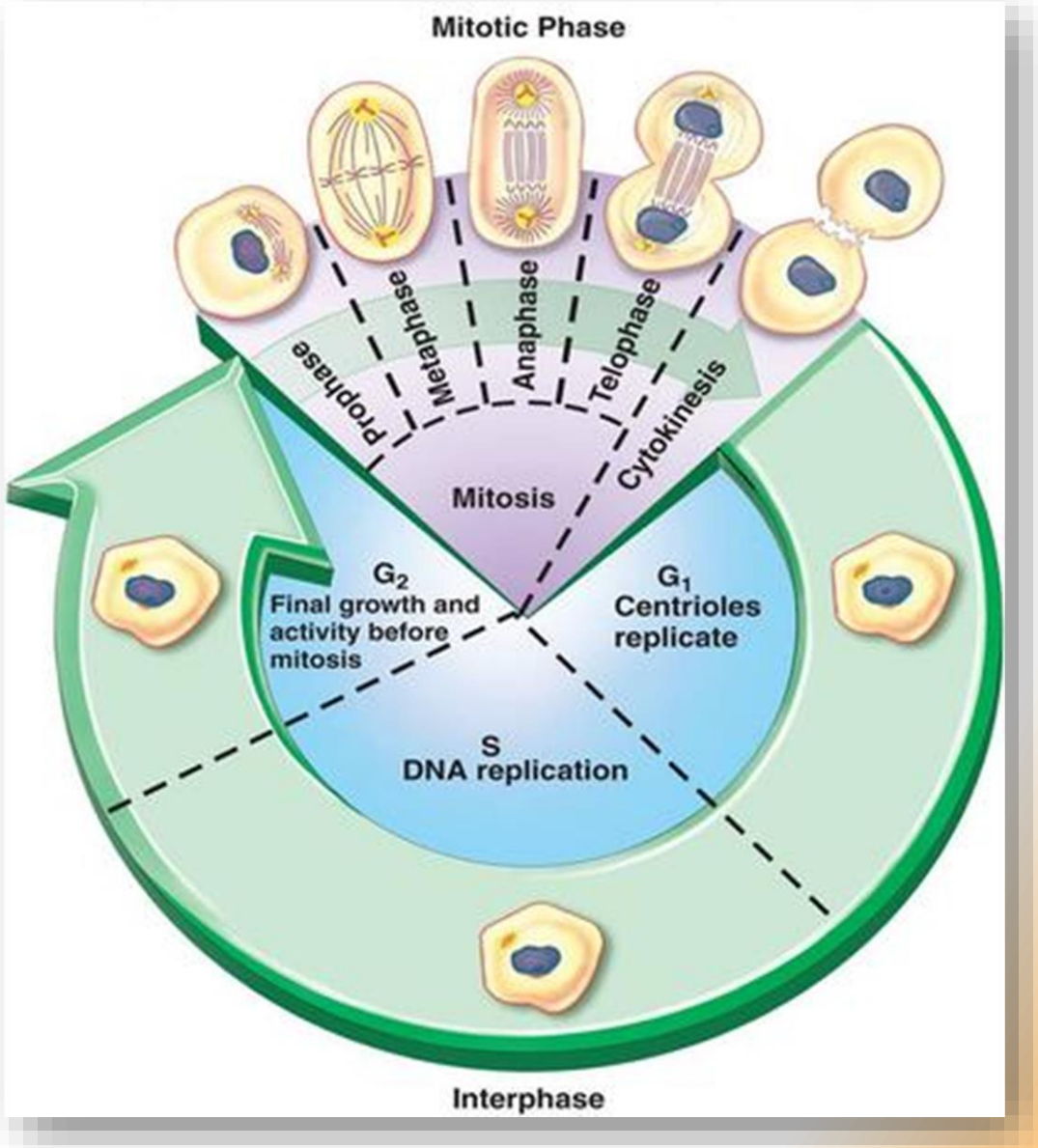
THE 6 RESPONSIBILITIES OF INTERPHASE

Metabolism Is Enhanced By Energetic Cleansing During Interphase

1. Nutrient Absorption
2. Enzymatic Metabolization
3. Mitochondrial Energy Production
4. Protein Assembly
5. Enzymatic Detoxification

Repair Is Enhanced By Intermittent Fasting During Interphase

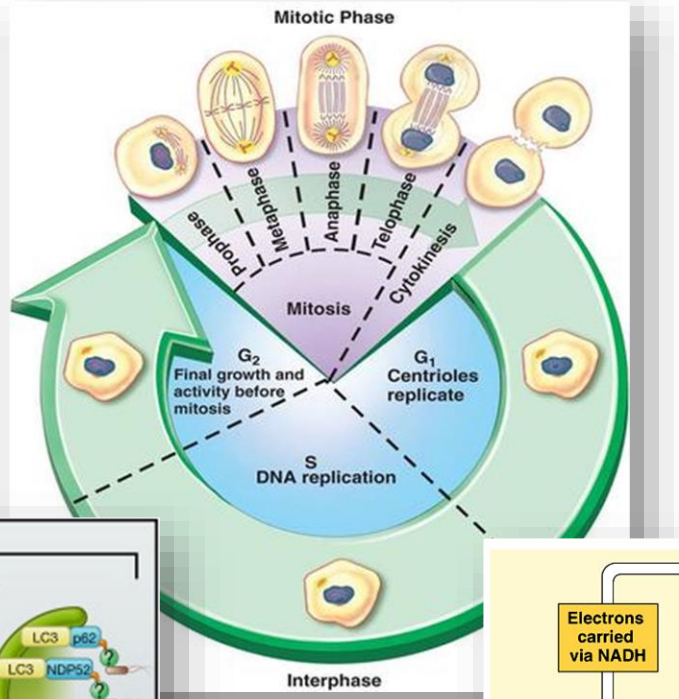
6. Autophagy – Repairs DNA & Organelles to Prepare Cell for Healthy Replication.

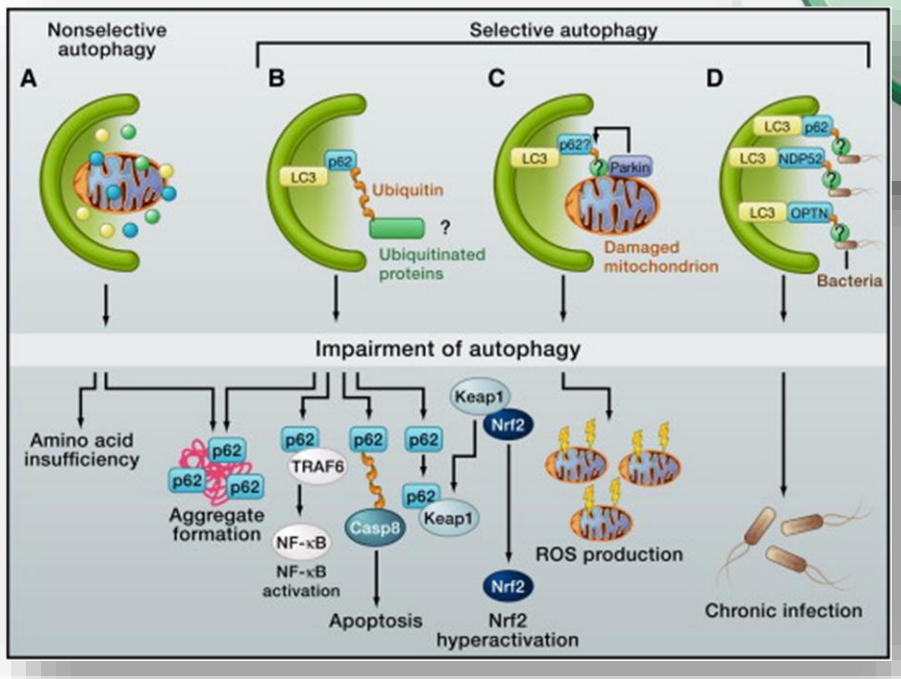


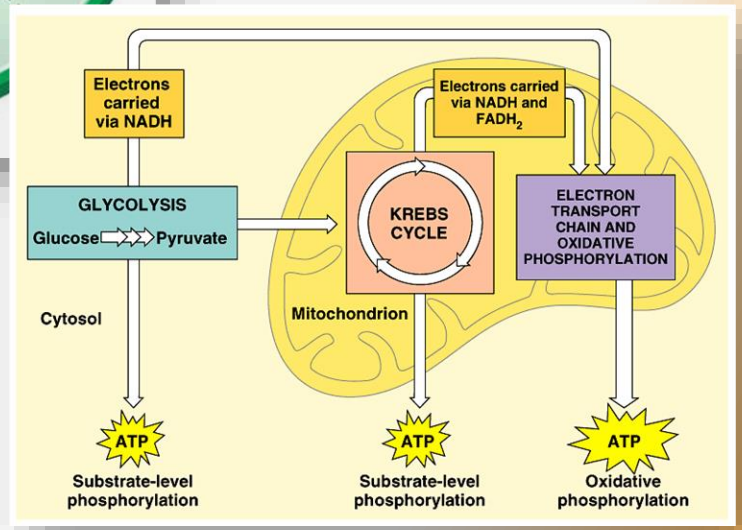
ARE WE EATING OURSELVES TO DEATH?

Cellular Metabolism Fuels Autophagy

- Unless Metabolism Never Stops (Over Eating), Chemical Bio-Accumulation, and/or Nutrient Deficiency
- **Leading to Bio-Accumulation of More Chemical Pollution & Cell Waste In Filtering Organs & Lymphatics**
- Leading to Damaged DNA & Organelles
- Leading to Phagocytosis or Apoptosis
- No Phagocytosis or Apoptosis…Then This Leads to Neoplastic Changes…aka Cancer & Degenerative Disease







AUTOPHAGY & MITOCHONDRIA

https://www.ncbi.nlm.nih.gov/pubmed/21106691
Am J Physiol Cell Physiol. 2011 Feb;300(2):C308-17. doi: 10.1152/ajpcell.00056.2010. Epub 2010 Nov 24.
Mitochondrial degradation by autophagy (mitophagy) in GFP-LC3 transgenic hepatocytes during nutrient deprivation.
Kim I1, Lemasters JJ.

Fasting in vivo and nutrient deprivation in vitro enhance sequestration of mitochondria and other organelles by autophagy for recycling of essential nutrients. Overall, the results indicate that PAS serve as nucleation sites for mitophagy in hepatocytes during nutrient deprivation. After autophagosome formation, mitochondrial depolarization and vesicular acidification occur, and mitochondrial contents, including mtDNA, are degraded.

3 SQUARE MEALS PER DAY

Are People Eating Themselves To Death?

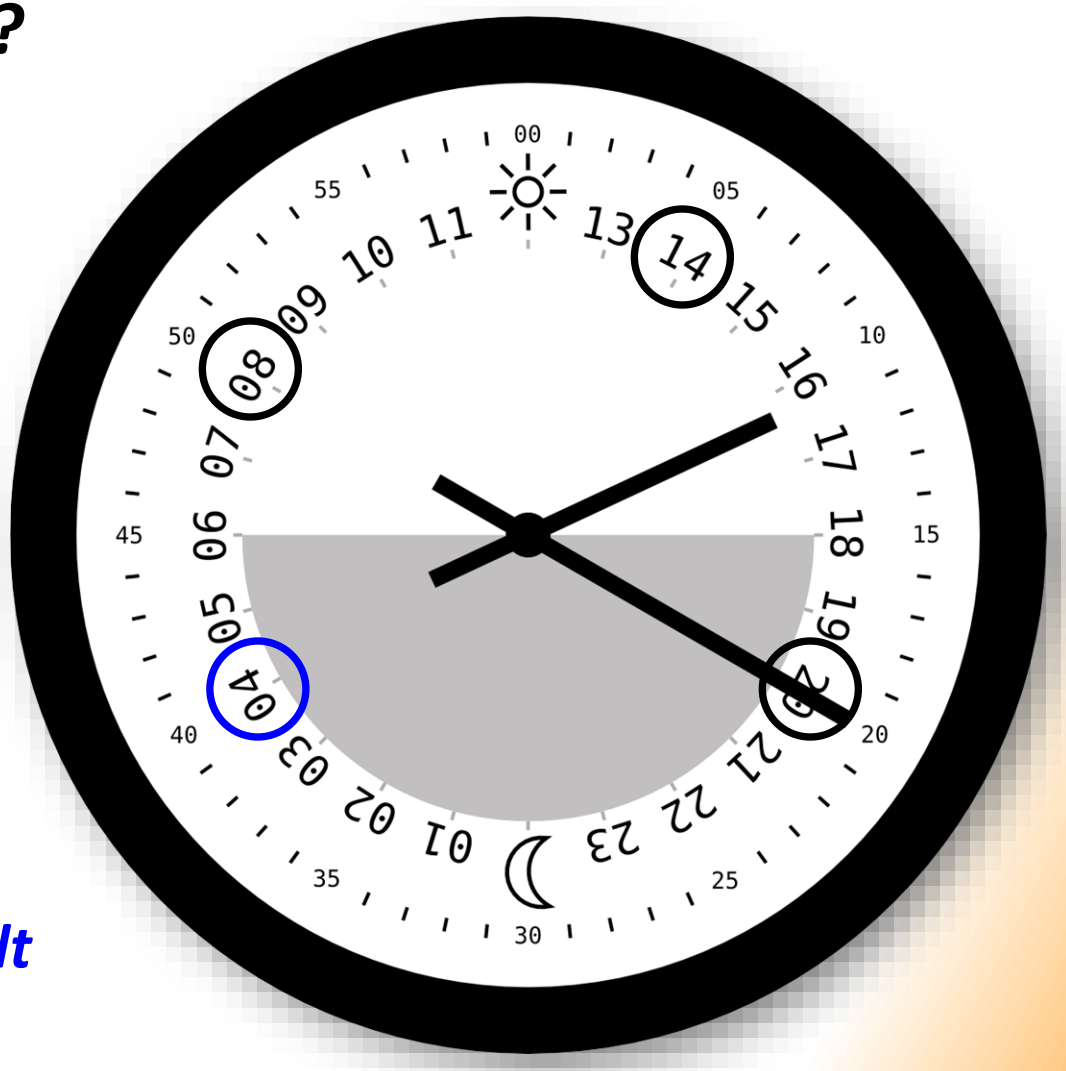
If we say Glucagon marks the beginning of Autophagy…

Breakfast At 8am

Lunch At 2pm

Dinner At 8pm

Autophagy At 4am?



- **Daily Autophagy** – 4 Hours Maybe?
- **Peak Autophagy Reached** – No
- **Types of Autophagy** – Macro, but only if at some point their body gets hungry and begins to produce Glucagon. ***Insulin Resistant clients will have the most difficult time going into Autophagy.*** Total Calories consumed during the day plays a role too.

Sources of Avoidable Environmental Pollution & Their Body Burdens

Environmental Pollutant	Most Common Sources	Nervous System	Glandular System	Immune System	Female Reproductive	Male Reproductive	Fetal/Child Development	Respiratory	Cardiovascular	Digestive Tract	Liver - Gall Bladder	Kidneys
Heavy Metals	**Vaccinations, Tap Water, Dental Amalgam Fillings, Large Carnivorous Sea Food, Cigarettes, Pressure Treated Lumber, Fluorescent Lights, Pharmaceutical Meds, Soap, Glazed Ceramics, Wire Solder, Photographic Development.** *Includes Aluminum, Mercury, Nickel, Tin, Arsenic, Cadmium, Lead.*											
Chemical Solvents	**Scented Laundry Detergent & Fabric Softeners, Cosmetics, Household Cleaners, Styrofoam Cups & Food Containers, Dry Cleaning, Air Fresheners, Adhesives, Aerosol Sprays, Nail Polish & Remover, Paint & Thinner, Carpets.** *If you can smell it and it's not natural...then it most likely is a solvent.*											
Furans & Dioxins	**Tampons, Pollution from Incineration, Chlorine Bleaching, Industrial Processing, food contaminant.** *All Environmental Pollution that has a Chlorine component is 'fat-soluble' and thus prone to accumulate in the body.*											
PAHs	**Polycyclic Aromatic Hydrocarbons. Pollution from Combustion, transferred through the Air and inhaled into the respiratory tract.** *Cigarettes, Car Exhaust, Factory Exhaust, Engine Exhaust.*											
Phthalates	**Plastics (Saran Wrap, Cookware, Tupperware, Reusable Water Bottles, Utensils), Hair Sprays, Poly Vinyl Chloride (PVC) Products, Adhesives, Sealants, Stains, Dyes, Cologne, Perfume, Nail Polish, Carpet.** *When Plastic is heated Phthalates are transferred into the food. (ie Microwaving Plastic)*											
Polychlorinated Biphenols (PCBs)	**Inner-lining of Canned Foods (BPA). Non-organic Butter, All Atlantic Salmon, Farm-raised Fish (Especially Catfish & Tuna), Beef, Adhesives, Pesticides like Round-Up, Fire Retardant, Plastic Production.** *Make sure your canned food and containers are 100% BPA-free.*											
GMOs & Glyphosate, Neonicitinoids, Organophosphates	PURCHASE ORGANIC: **Apples, Bell Peppers, Celery, Cherries, Collard Greens, Corn Cucumbers, Grapes, Hot Peppers, Kale, Nectarines, Peaches, Pears, Potatoes, Red Raspberries, Snap Peas, Spinach, Soy, Strawberries, Tomatoes, Butter & Nuts.** *Includes food tainted by Insecticides, Herbicides & Fungicides.*											
Organochlorines	**Beef & Dairy Products. Includes Lindane, Mirex, DDT & its biochemical breakdown product... DDE.** *Includes food from Broad Range of Pesticides and Fungicides.*											
Perfluorinated Chemicals (PFCs)	**Teflon Coated Cookware has been proven to release a chemical PFOAs into food that is a known hormone disruptor and linked to teflon toxicosis as well as cancer.** *Specifically affects the Thyroid Gland and Reproductive Glands leading to impotence, fatigue, and hypothyroidism.*											

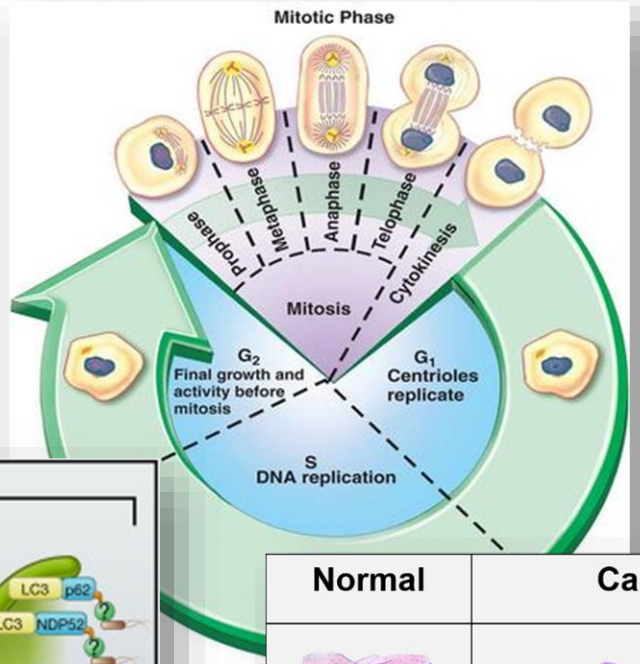
Note: Yellow background skulls have a much higher adverse effect upon the system they disrupt. Sources: Environmental Working Group & Pubmed Published Research.

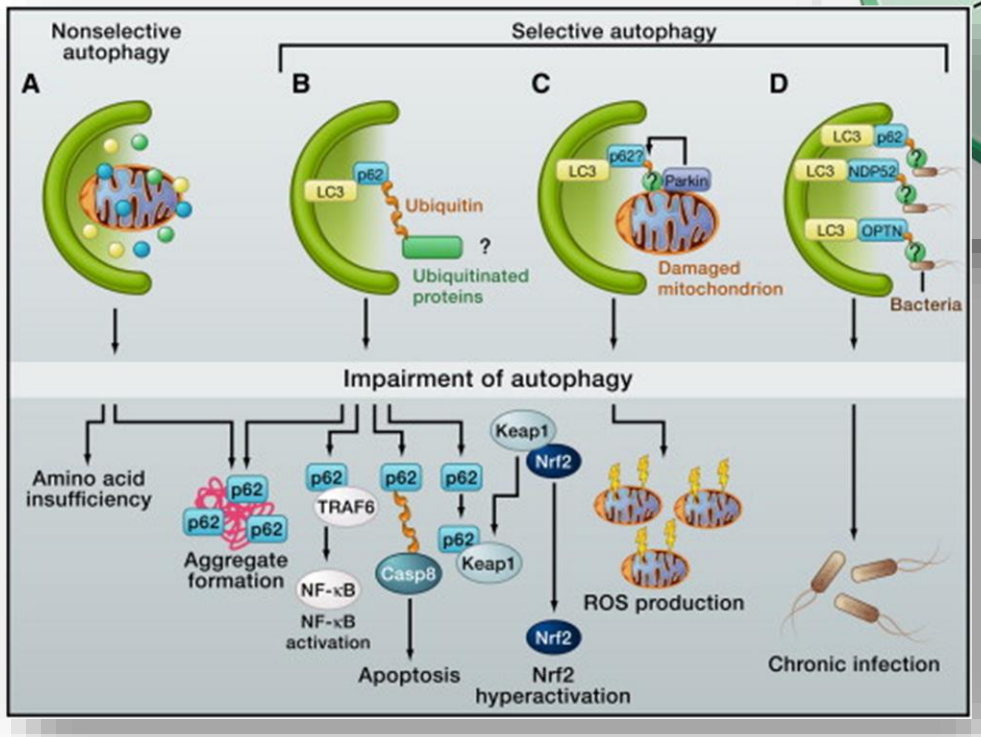
Genesis Health Systems

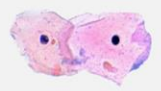
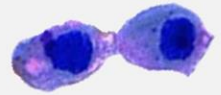
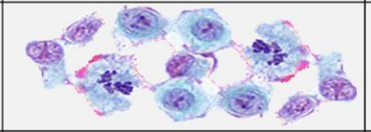
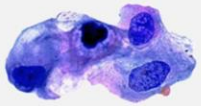
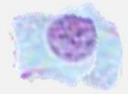
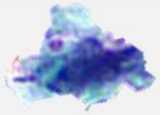
POLLUTED CELLS = DAMAGED DNA

Autophagy Prepares the Cell for **Mitosis** of the healthiest version of itself.

- If the cell Bio-Accumulates more than it can clean then Mitosis is compromised leading potentially to Phagocytosis, Apoptosis or the production of pre-cancer cells.
- **The body is designed to heal…but healing takes time for Autophagy to happen.**





Normal	Cancer	
		Large, variably shaped nuclei
		Many dividing cells; Disorganized arrangement
		Variation in size and shape
		Loss of normal features

AUTOPHAGY & CELLULAR REPLICATION

Mitotic Phase

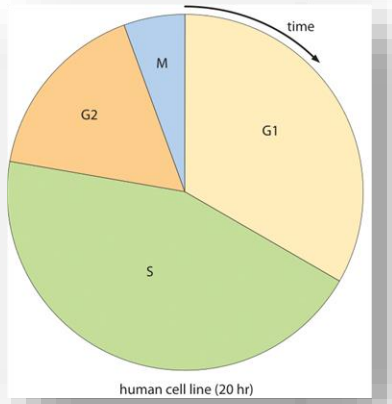
- No Autophagy

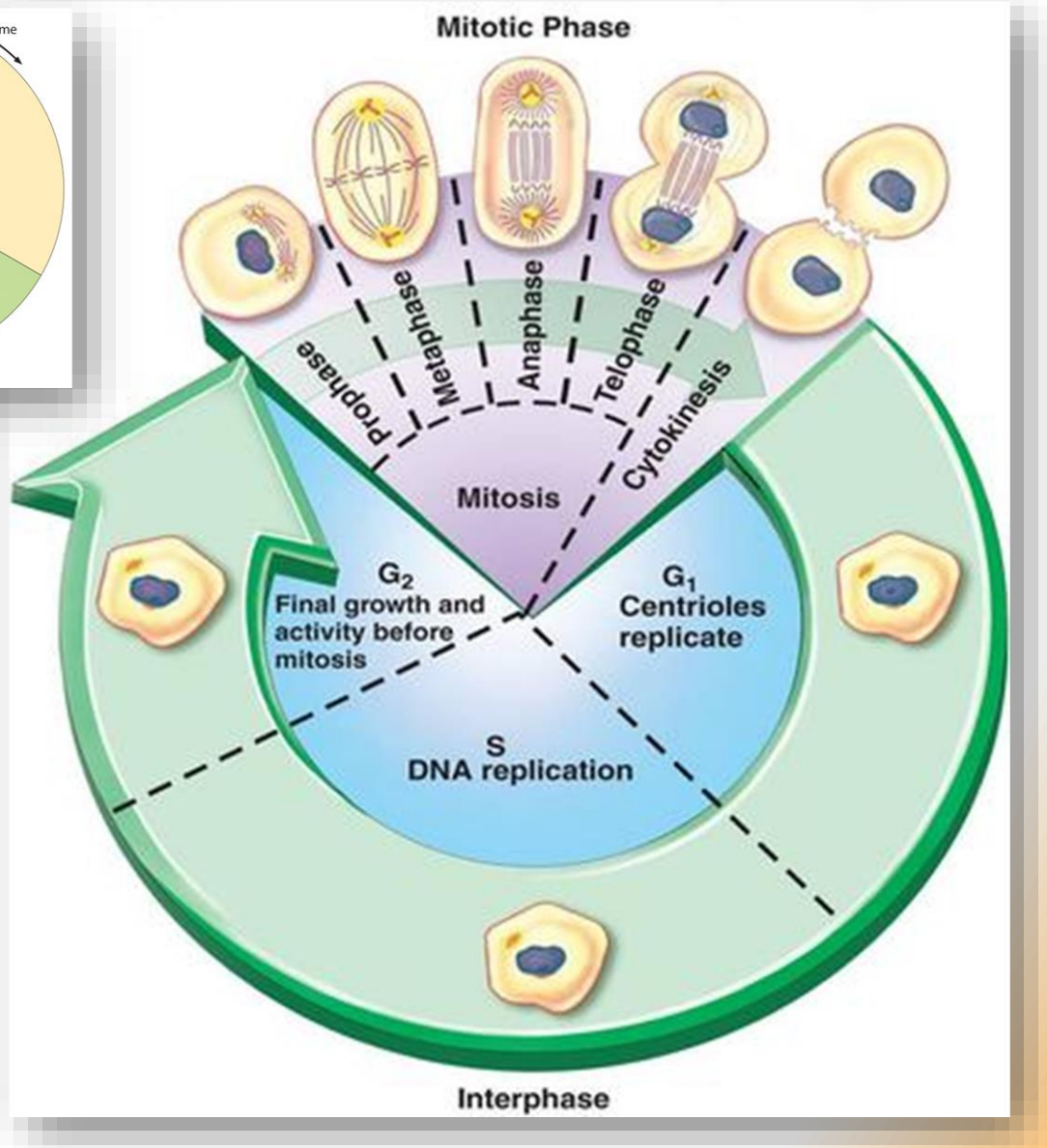
Interphase

- G_1 – Autophagy Begins
- S – Autophagy Peaks
- G_2 – Autophagy Ends

Fasting Conclusions

- Mitosis is typically arrested during fasting (G_1) which thereby slows the aging (replication) process of the cell, which in turn allows for more autophagy and greater healing.





AUTOPHAGY & THE CELL CYCLE

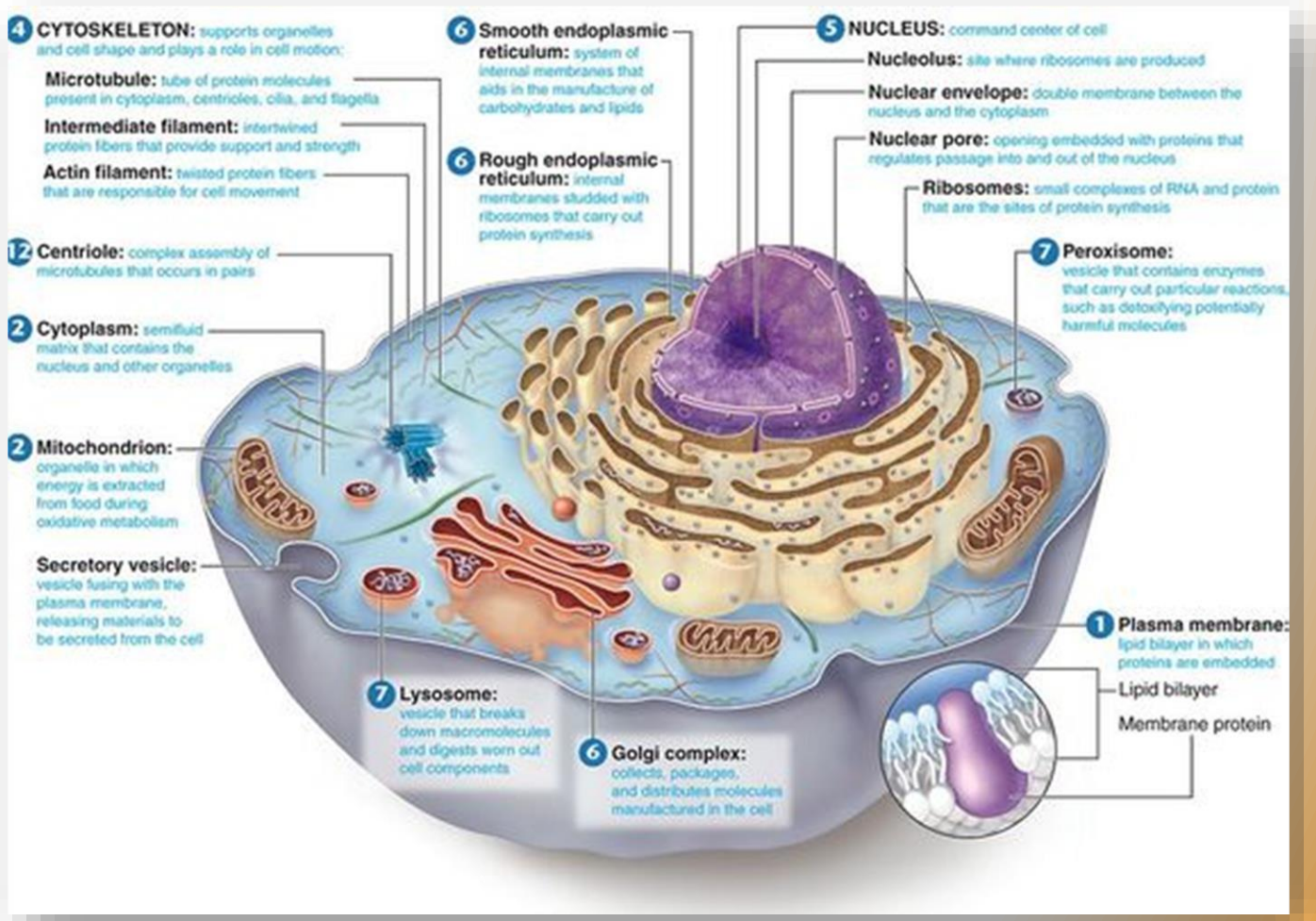
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5374984/
Front Oncol. 2017; 7: 51. Published online 2017 Mar 31.
Autophagy and the Cell Cycle: A Complex Landscape
Søs Grønbæk Mathiassen, Daniela De Zio and Francesco Cecconi

As the above studies do not allow discrimination between G2 and M phase, this leaves the question of autophagy status during mitosis. ***Two elegant studies have reported a striking decrease in autophagic activity during mitosis*** (28, 29). By means of electron microscopy and stereology to quantify the presence of autophagic vacuoles in mitotic cells, Eskelinen et al. found a strong reduction in autophagosomal content in both (pro)metaphase and anaphase cells (28). Furuya et al. expanded on these findings revealing that mitotic autophagy inhibition depends on cyclin-dependent kinase 1 (CDK1)-mediated phosphorylation of Vps34 on Thr159 during mitosis (29). This phosphorylation event negatively regulates the interaction between Vps34 and Beclin 1, thereby inhibiting PtdIns3K activity, PtdIns3P production, and autophagy induction (29). ***Of note, during mitosis, cells undergo extensive structural rearrangements and the inhibition of autophagy has been speculated to function as a protective mechanism to prevent unintended loss of organelles and chromosomes.***

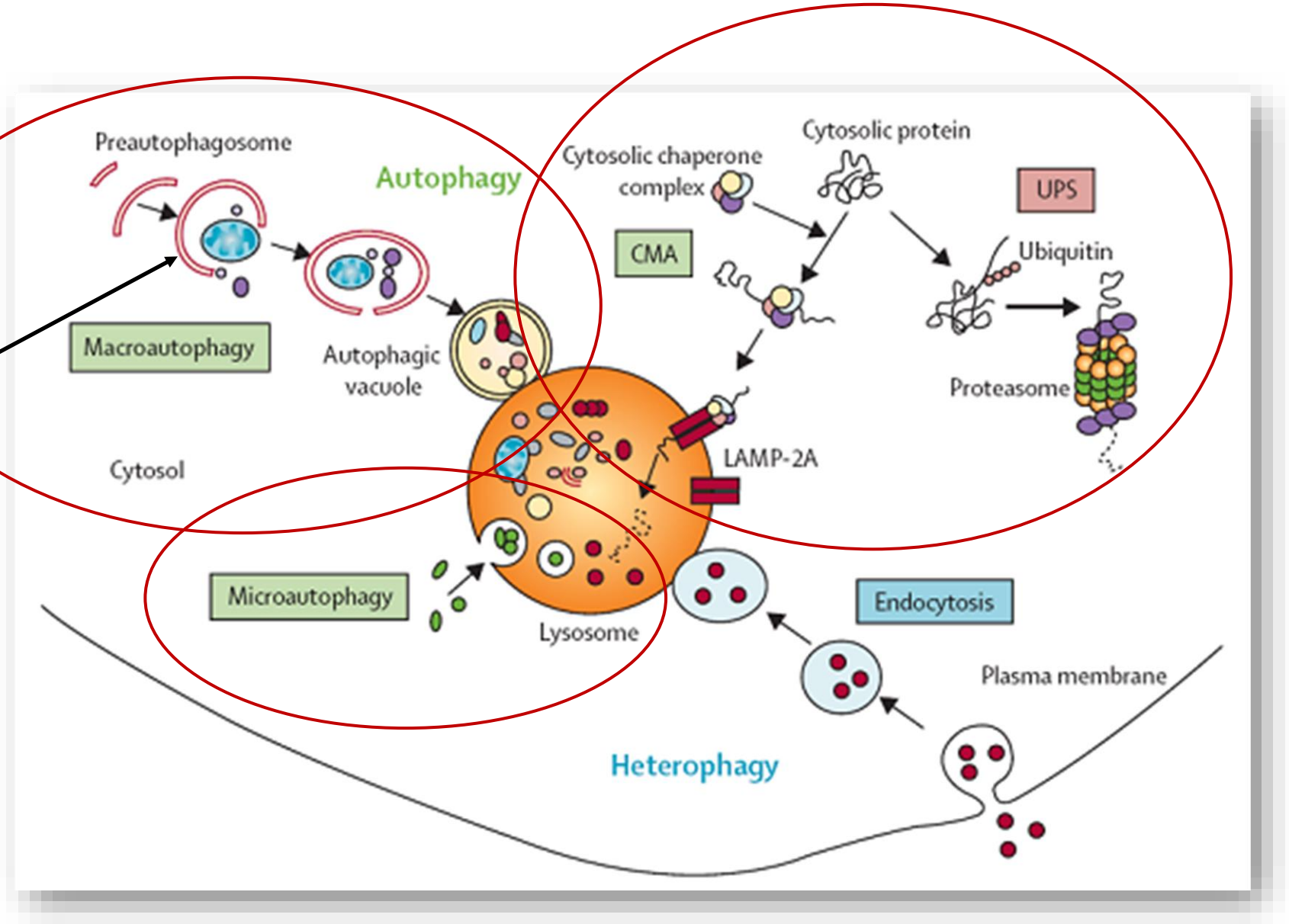
AUTOPHAGY AKA AUTOPHAGOCYTOSIS

Definition - natural, regulated, destructive mechanism of the cell that disassembles unnecessary or dysfunctional components.

- **Macroautophagy** - main pathway, used to rid cells of damaged organelles and unused proteins.
- **Microautophagy -** direct engulfment of cytoplasmic material into the lysosome.
- **Chaperone-mediated autophagy**, or CMA, involves the recognition by the hsc70-containing complex. This complex then moves to the lysosomal membrane-bound protein that will recognize and bind with the CMA receptor, allowing it to enter the cell for destruction.



AUTOPHAGY & LYSOSOMES



Comprised Of:

- Lipids
- Inositol
- Ethanolamine

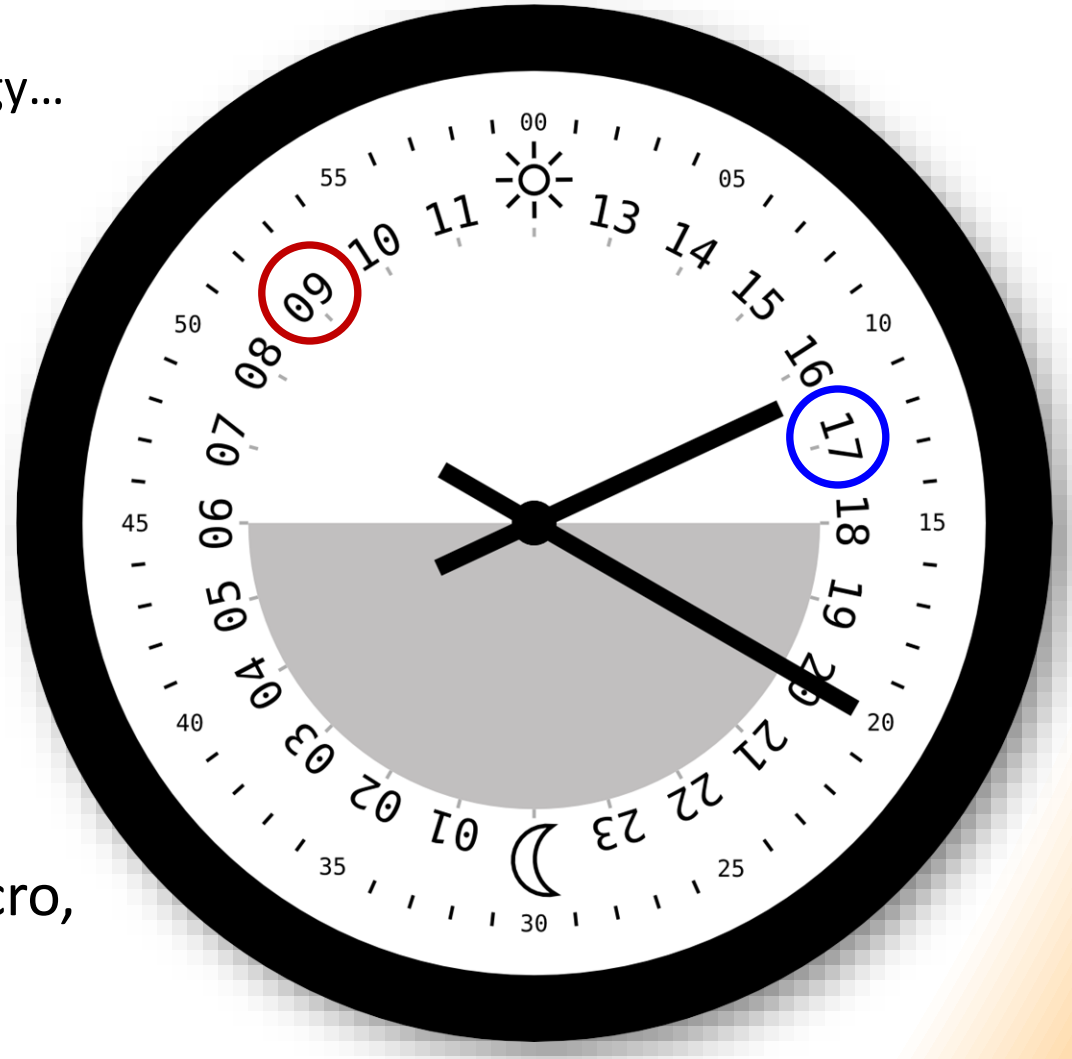
AUTOPHAGY & SUMMATION

72-Hour Clinical Fasting

If we say Glucagon marks the beginning of Autophagy…

Last Meal Ends At 9am

Autophagy Begins At 5pm



- **Day 1** – 16 Hours
- **Day 2** – 24 Hours
- **Day 3** – 24 Hours
- **Total Autophagy** = 64 Hours
- **Peak Autophagy Reached** – Yes
- **Types of Autophagy** – Peak Macro, Micro, CMA

PEAK AUTOPHAGY – HOURS 48 TO 72

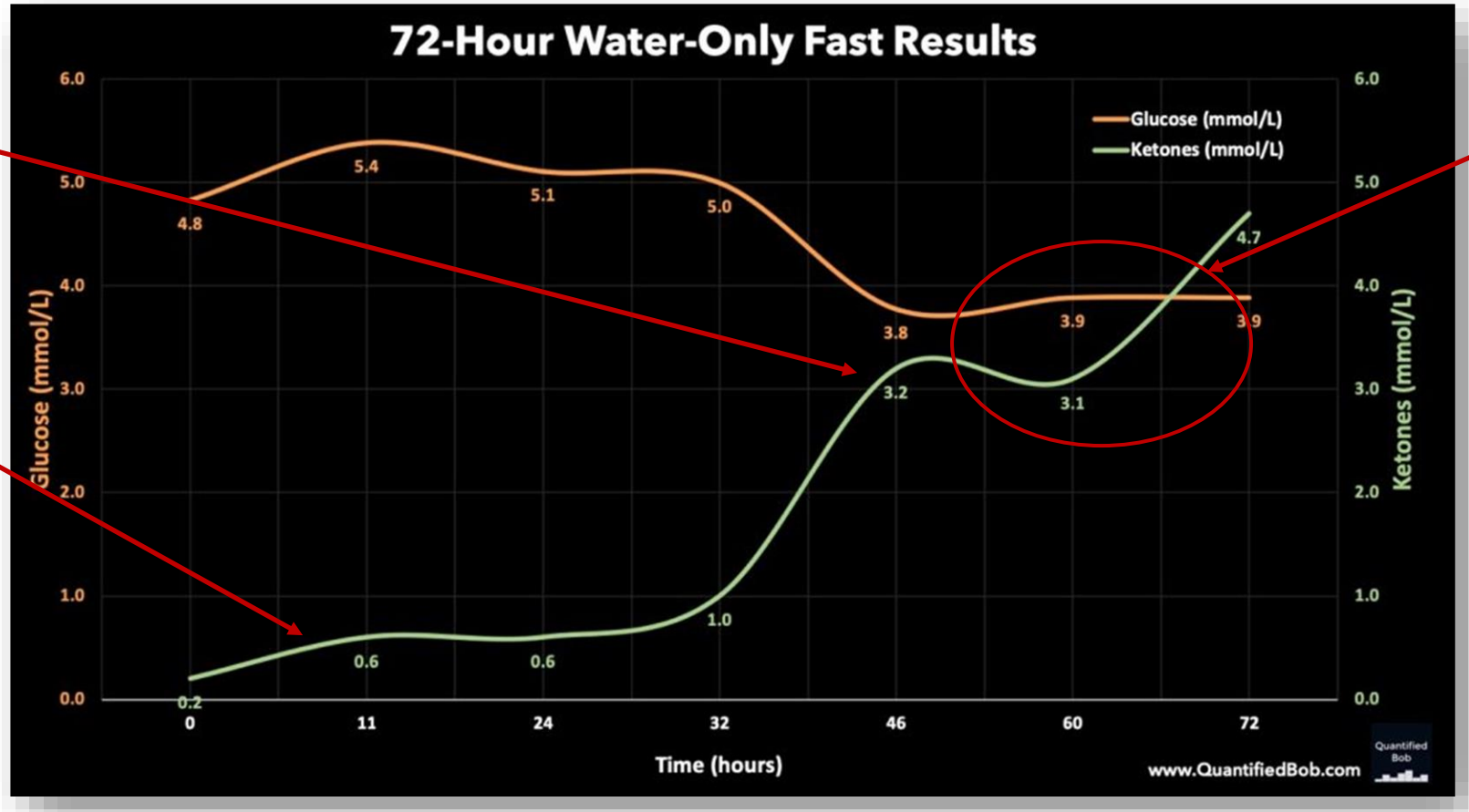
Why Clinical Fasting?

- **Macroautophagy** Peaks by Hour 54
- **Chaparone-Mediated Autophagy** Peaks between Hour 60 and 66.
- **Immune Cell Division** Peaks at Hour 72 and then drops significantly afterward if Fast is prolonged and Glandular Atrophy ensues.

Ketone Surge

Glucagon Surge

Peak Autophagy



AUTOPHAGY & SUMMATION

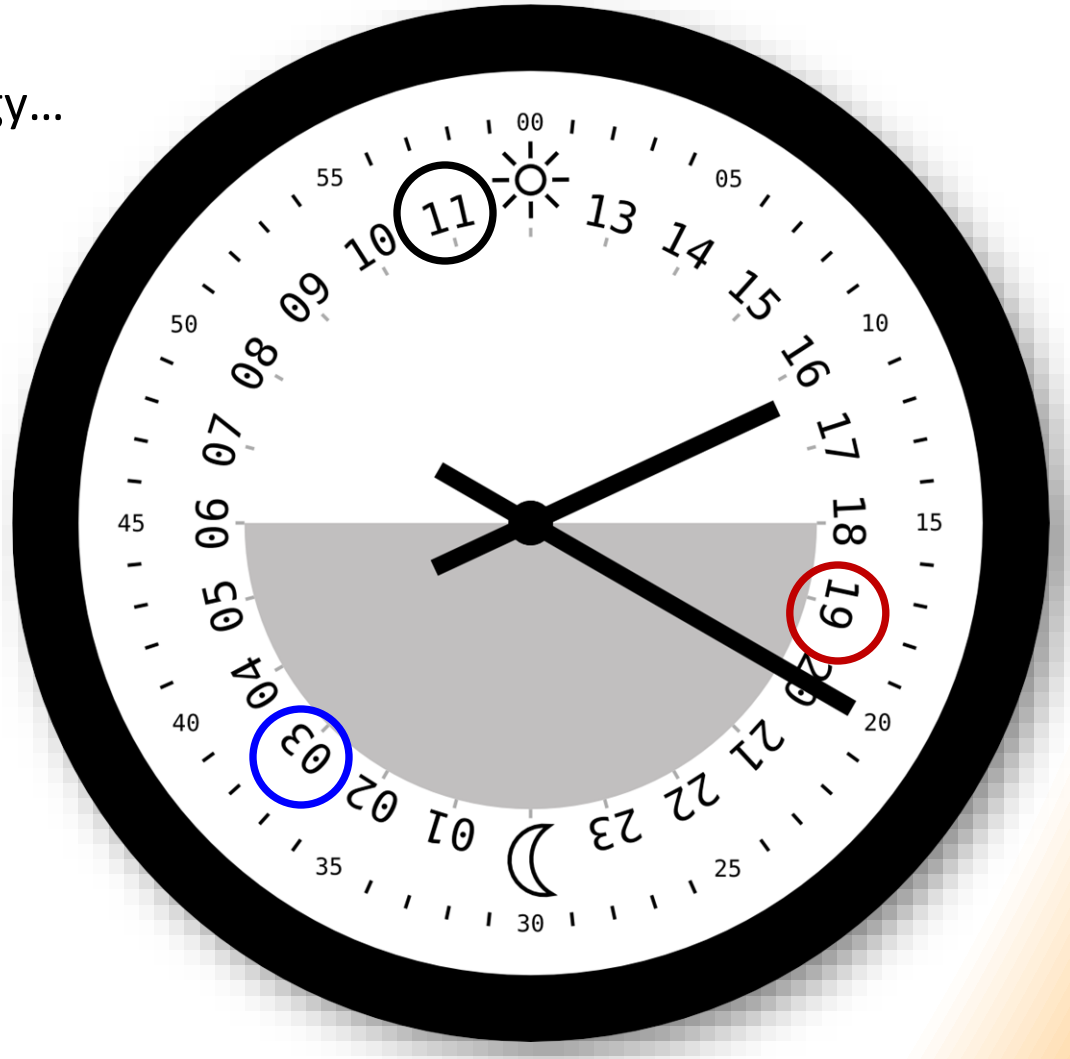
16-Hour, Daily Intermittent Fasting

If we say Glucagon marks the beginning of Autophagy…

Daily Last Meal Ends At 7pm

Autophagy Begins At 3am

Breakfast At 11am



- **Daily Autophagy** – 8 Hours
- **Total Days** – 28
- **Total Autophagy** = 224 Hours
- **Peak Autophagy Reached** – No
- **Types of Autophagy** – Some Macro, Micro, CMA

AUTOPHAGY & SUMMATION

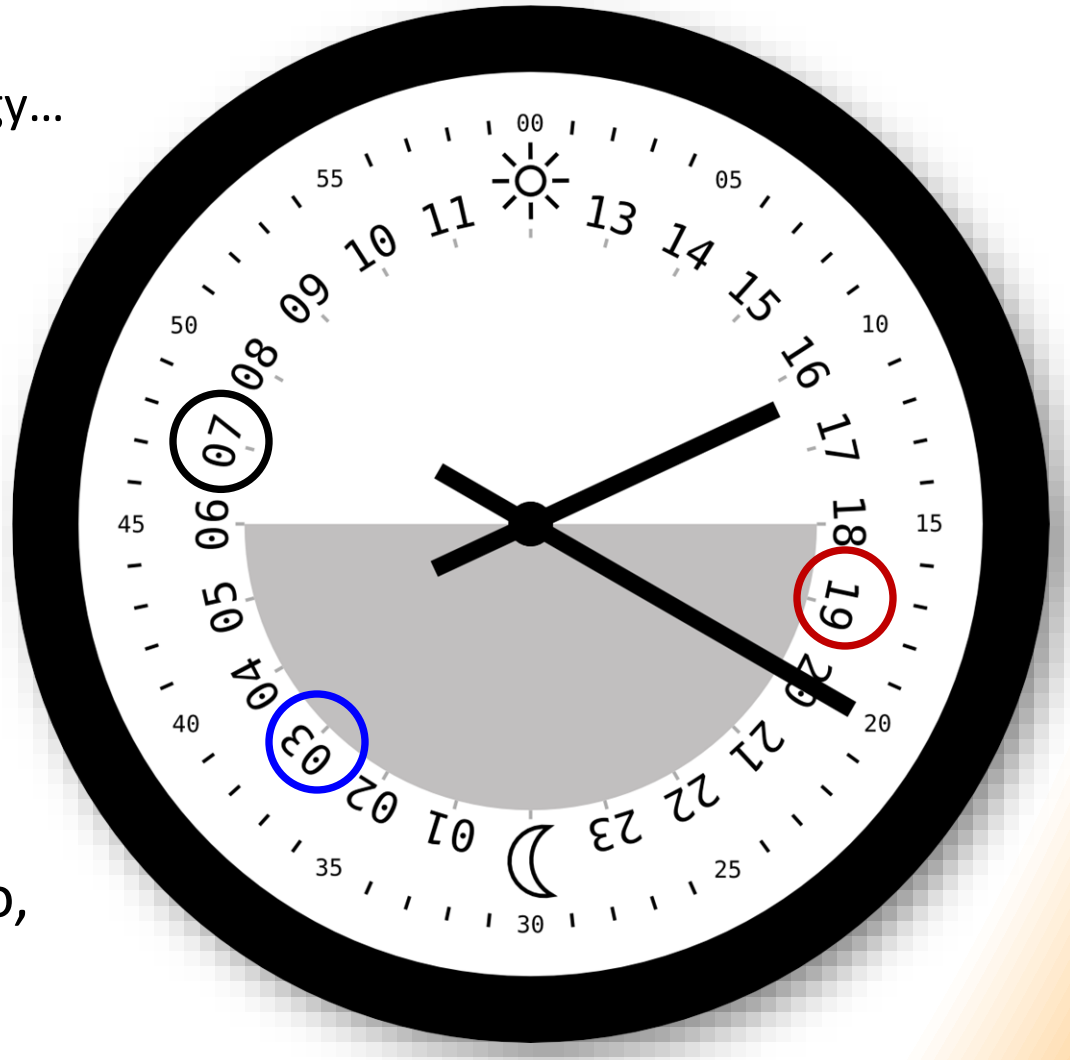
36-Hour, 1 Day/Week Intermittent Fasting

If we say Glucagon marks the beginning of Autophagy…

Last Meal Ends At 7pm Saturday

Autophagy Begins At 3am Sunday

Breakfast At 7am Monday



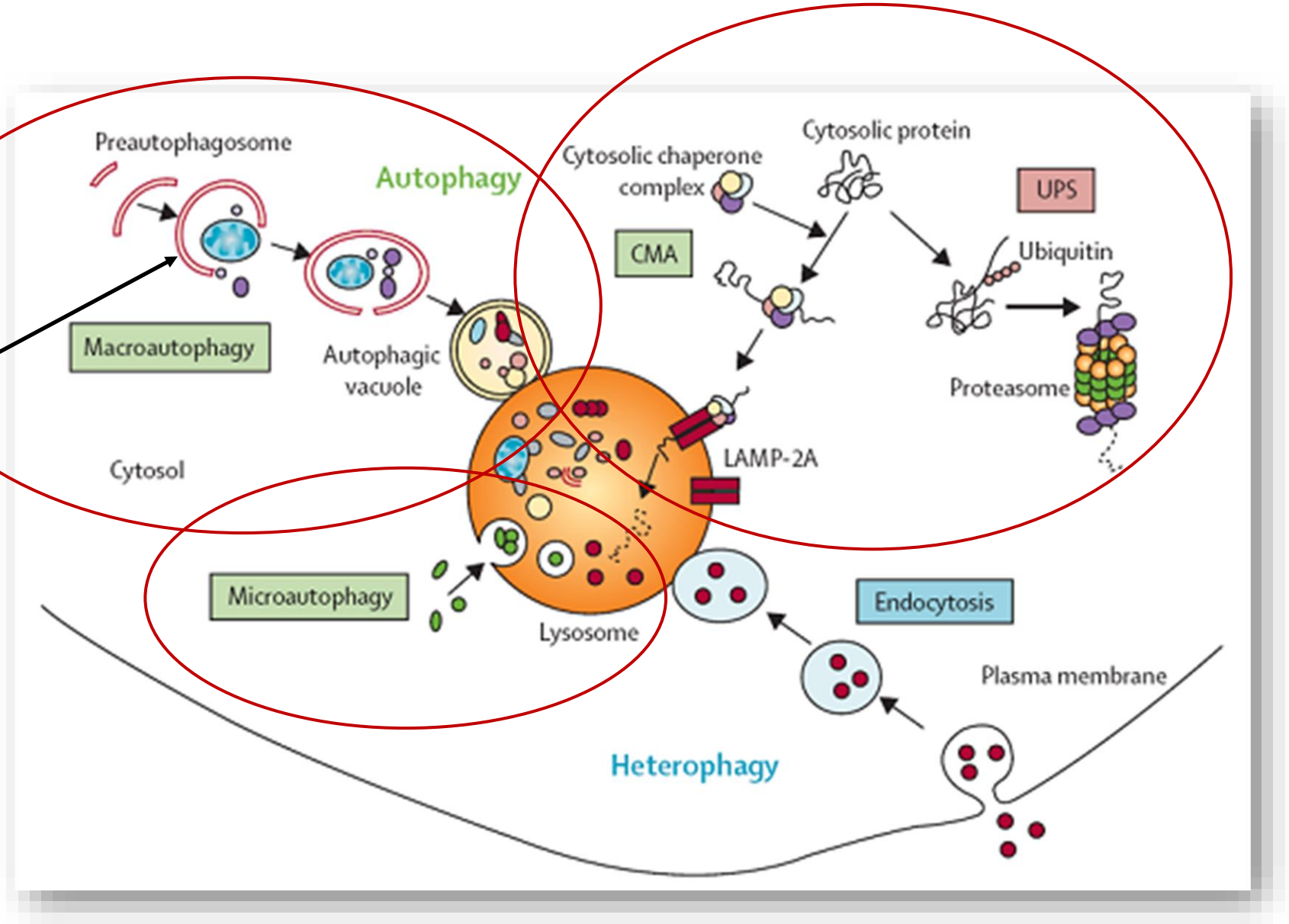
- **Weekly Autophagy** – 28 Hours
- **Total Weeks** – 4
- **Total Autophagy** = 112 Hours
- **Peak Autophagy Reached** – No
- **Types of Autophagy** – Moderate Macro, Micro, CMA

INTERMITTENT FASTING & CR

https://www.ncbi.nlm.nih.gov/pubmed/24079773
Curr Pharm Des. 2014;20(18):2950-77.
Calorie restriction and dietary restriction mimetics: a strategy for improving healthy aging and longevity.
Testa G, Biasi F, Poli G, Chiarpotto E[1].

Calorie restriction (CR) with adequate nutrition is the only non-genetic, and the most consistent non-pharmacological intervention that extends lifespan in model organisms from yeast to mammals, and protects against the deterioration of biological functions, delaying or reducing the risk of many age-related diseases. The biological mechanisms of CR's beneficial effects include modifications in energy metabolism, oxidative stress, insulin sensitivity, inflammation, autophagy, neuroendocrine function and induction of hormesis/xenohormesis response. The molecular signalling pathways mediating the anti-aging effect of CR include sirtuins, peroxisome proliferator activated receptor G coactivator-1α, AMP-activated protein kinase, insulin/insulin growth factor-1, and target of rapamycin, which form a pretty interacting network***. However, most people would not comply with such a rigorous dietary program***; research is thus increasingly aimed at determining the feasibility and efficacy of natural and/or pharmacological CR mimetic molecules/ treatments without lowering food intake, particularly in mid- to late-life periods.

AUTOPHAGY & LYSOSOMES



Comprised Of:

- Lipids
- Inositol
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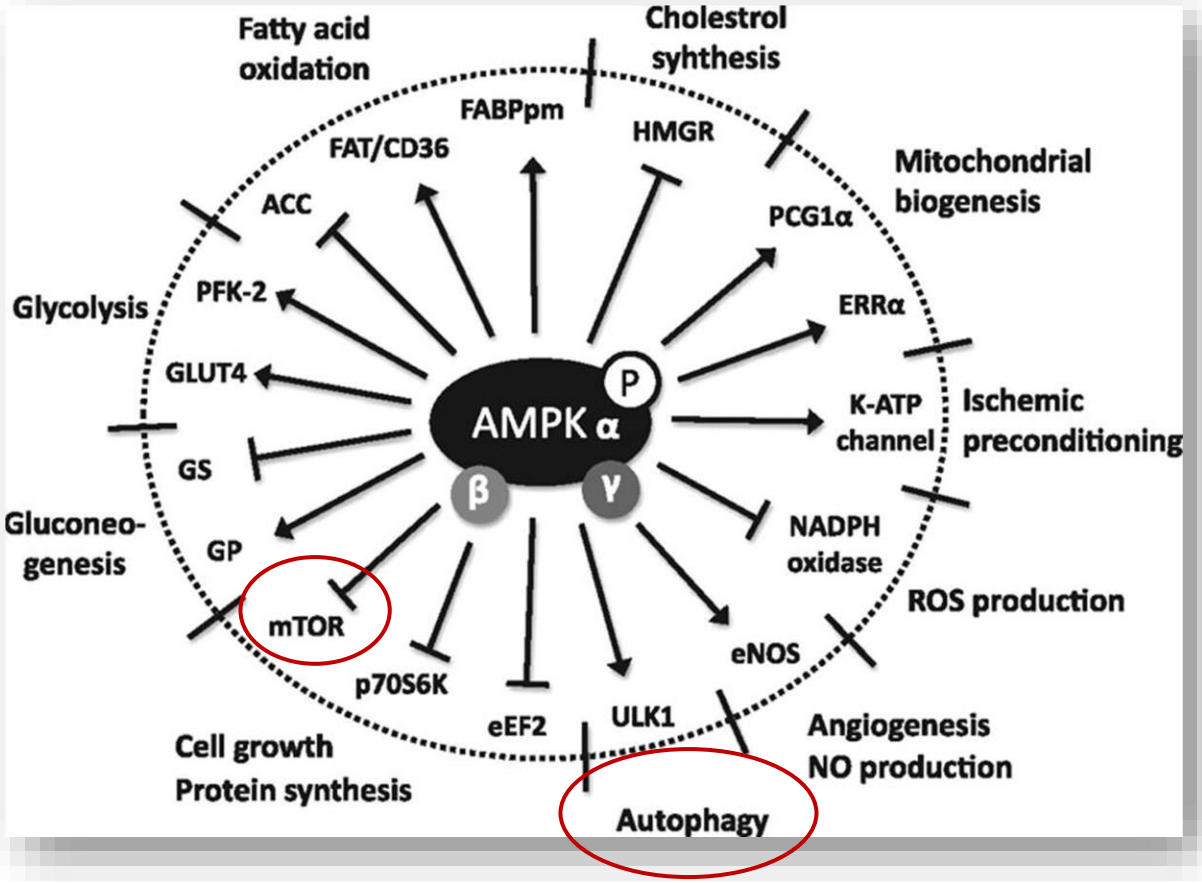
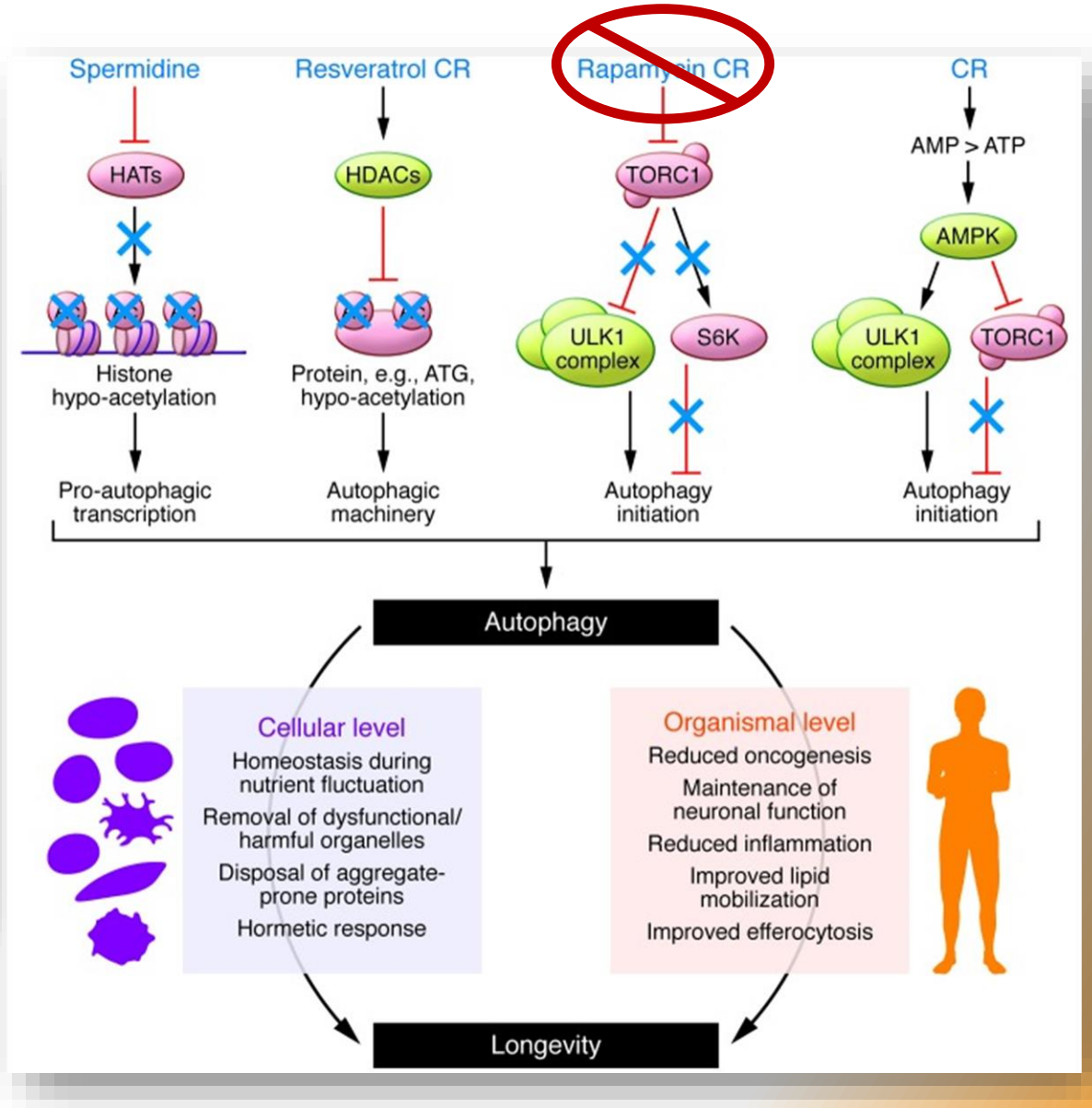
mTOR & AUTOPHAGY





WHAT HELPS INDUCE AUTOPHAGY?

Organic Foods & Nutrients That Promote Autophagy Via IF

- Green Tea
- **Reishi Medicinal Mushroom**
- Resveratrol
- Medium Chain Triglycerides
- Omega-3 & 6 Fatty Acids
- Turmeric
- Melatonin
- Ginger
- Siberian Ginseng
- Soy (Spermidine)
- Broccoli Seed Extract (Sulforaphane)

DEPRESSION & IF

https://www.ncbi.nlm.nih.gov/pubmed/24582593
Life Sci. 2014 Apr 17;101(1-2):10-4. doi: 10.1016/j.lfs.2014.02.014. Epub 2014 Feb 25.
The role of mTOR in depression and antidepressant responses.
Abelaira HM1, Réus GZ2, Neotti MV1, Quevedo J3

Postmortem studies have shown robust deficits in the mammalian target of rapamycin (mTOR) signaling in the prefrontal cortex of subjects diagnosed with major depressive disorder. However, besides the mTOR signaling pathway having an antidepressant response to various drugs, this seems to be more associated with antidepressant N-methyl-d-aspartate (NMDA) receptor antagonists, such as ketamine. The characterization of the mTOR signaling pathway in depression and its action in response to antidepressants show great potential for the identification of new therapeutic targets for the development of antidepressant drugs.

NEURODEGENERATION & IF

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3106288/
Autophagy. 2010 Aug 16; 6(6): 702–710. Published online 2010 Aug 14. doi: 10.4161/auto.6.6.12376
Short-term fasting induces profound neuronal autophagy
Mehrdad Alirezaei,#1 Christopher C. Kemball,#1 Claudia T. Flynn,1 Malcolm R. Wood,2 J. Lindsay Whitton, and William B. Kiosses

Disruption of autophagy—a key homeostatic process in which cytosolic components are degraded and recycled through lysosomes—can cause neurodegeneration in tissue culture and in vivo. Upregulation of this pathway may be neuroprotective, and much effort is being invested in developing drugs that cross the blood brain barrier and increase neuronal autophagy. One well-recognized way of inducing autophagy is by food restriction, which upregulates autophagy in many organs including the liver; but current dogma holds that the brain escapes this effect, perhaps because it is a metabolically privileged site. Here, we have re-evaluated this tenet using a novel approach that allows us to detect, enumerate and characterize autophagosomes in vivo. We first validate the approach by showing that it allows the identification and characterization of autophagosomes in the livers of food-restricted mice. We use the method to identify constitutive autophagosomes in cortical neurons and Purkinje cells, and ***we show that short-term fasting leads to a dramatic upregulation in neuronal autophagy.*** The increased neuronal autophagy is revealed by changes in autophagosome abundance and characteristics, and by diminished neuronal mTOR activity in vivo, demonstrated by a reduction in levels of phosphorylated S6 ribosomal protein in Purkinje cells. ***Our data lead us to speculate that sporadic fasting might represent a simple, safe and inexpensive means to promote this potentially therapeutic neuronal response.***

NEURODEGENERATION & IF

https://www.ncbi.nlm.nih.gov/pubmed/26101267
J Exp Med. 2015 Jun 29;212(7):979-90. doi: 10.1084/jem.20150956. Epub 2015 Jun 22.
Therapeutic targeting of autophagy in neurodegenerative and infectious diseases.
Rubinsztein DC1, Bento CF2, Deretic V3

Although autophagy may impact many facets of human biology and disease, in this review we focus on the ability of autophagy to protect against certain neurodegenerative and infectious diseases. ***Autophagy enhances the clearance of toxic, cytoplasmic, aggregate-prone proteins and infectious agents. The beneficial roles of autophagy can now be extended to supporting cell survival and regulating inflammation. Autophagic control of inflammation is one area where autophagy may have similar benefits for both infectious and neurodegenerative diseases beyond direct removal of the pathogenic agents.***

NEURODEGENERATION & IF

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2622429/ - **EXCELLENT READ!!!!**

Published online 2006 Aug 8. doi: 10.1016/j.arr.2006.04.002

Caloric restriction and intermittent fasting: Two potential diets for successful brain aging

Bronwen Martin,a,* Mark P. Mattson,a,b and Stuart Maudsley

The vulnerability of the nervous system to advancing age is all too often manifest in neurodegenerative disorders such as Alzheimer's and Parkinson's diseases. ***In this review article we describe evidence suggesting that two dietary interventions, caloric restriction (CR) and intermittent fasting (IF), can prolong the health-span of the nervous system by impinging upon fundamental metabolic and cellular signaling pathways that regulate life-span.*** CR and IF affect energy and oxygen radical metabolism, and cellular stress response systems, in ways that protect neurons against genetic and environmental factors to which they would otherwise succumb during aging. There are multiple interactive pathways and molecular mechanisms by which CR and IF benefit neurons including those involving insulin-like signaling, FoxO transcription factors, sirtuins and peroxisome proliferator-activated receptors. ***These pathways stimulate the production of protein chaperones, neurotrophic factors and antioxidant enzymes, all of which help cells cope with stress and resist disease.*** A better understanding of the impact of CR and IF on the aging nervous system will likely lead to novel approaches for preventing and treating neurodegenerative disorders.

PARKINSON'S & IF

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2622429/
Published online 2006 Aug 8. doi: 10.1016/j.arr.2006.04.002
Caloric restriction and intermittent fasting: Two potential diets for successful brain aging
Bronwen Martin,a,* Mark P. Mattson,a,b and Stuart Maudsley

As both IF and CR induce a mild stress response in brain cells this can result in the activation of compensating mechanisms, e.g. the upregulation of neurotrophic factors such as BDNF and glial cell line-derived neurotrophic factor (GDNF) as well as the aforementioned heat shock proteins. IF regimens have been demonstrated to ameliorate and attenuate neuronal damage and improve the functional outcome in animal models of neurological trauma such as stroke and also neurodegenerative disorders such as Parkinson's disease, and Huntington's disease. The neuroprotective mechanism of IF is not known, but ***it has been reported that IF induces the production of brain-derived neurotrophic factor (BDNF) which was associated with increased hippocampal neurogenesis in rats and mice***. One of the primary neuroprotective mechanisms attributed to BDNF appears to be the ability of BDNF-mediated activation of its cognate TrkB receptor which then entrains stimulation of multiple signaling pathways. Prominent amongst these TrkB signaling pathways is the ***phosphatidyl inositol*** 3-kinase (PI3K)/protein kinase B (Akt) pathway that has been implicated in several of the CR/IF protective mechanisms that will be discussed at greater length in this review.

BDNF, DIABETES & YOUR BRAIN

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4697050/
Arch Med Sci. 2015 Dec 10; 11(6): 1164–1178. Published online 2015 Dec 11. doi: 10.5114/aoms.2015.56342
Brain-derived neurotrophic factor and its clinical implications
Siresha Bathina1 and Undurti N. Das

Brain-derived neurotrophic factor (BDNF) plays an important role in neuronal survival and growth, serves as a neurotransmitter modulator, and participates in neuronal plasticity, which is essential for learning and memory. It is widely expressed in the CNS, gut and other tissues. BDNF binds to its high affinity receptor TrkB (tyrosine kinase B) and activates signal transduction cascades (IRS1/2, PI3K, Akt), crucial for CREB and CBP production, that encode proteins involved in β cell survival. BDNF and insulin-like growth factor-1 have similar downstream signaling mechanisms incorporating both p-CAMK and MAPK that increase the expression of pro-survival genes. ***Brain-derived neurotrophic factor regulates glucose and energy metabolism and prevents exhaustion of β cells.***

Decreased levels of BDNF are associated with neurodegenerative diseases with neuronal loss, such as Parkinson's disease, Alzheimer's disease, multiple sclerosis and Huntington's disease. Thus, BDNF may be useful in the prevention and management of several diseases including ***diabetes mellitus.***

INSULIN SENSITIVITY & IF

https://www.ncbi.nlm.nih.gov/pubmed/23591120
Br J Nutr. 2013 Oct;110(8):1534-47. doi: 10.1017/S0007114513000792. Epub 2013 Apr 16.
The effect of intermittent energy and carbohydrate restriction v. daily energy restriction on weight loss and metabolic disease risk markers in overweight women.
Harvie M1, Wright C, Pegington M, McMullan D, Mitchell E, Martin B, Cutler RG, Evans G, Whiteside S, Maudsley S, Camandola S, Wang R, Carlson OD, Egan JM, Mattson MP, Howell A.

Intermittent energy restriction may result in greater improvements in insulin sensitivity and weight control than daily energy restriction (DER). We tested two intermittent energy and carbohydrate restriction (IECR) regimens, including one which allowed ad libitum protein and fat (IECR+PF). Overweight women (n 115) aged 20 and 69 years with a family history of breast cancer were randomised to an overall 25 % energy restriction, either as an IECR (2500-2717 kJ/d, < 40 g carbohydrate/d for 2 d/week) or a 25 % DER (approximately 6000 kJ/d for 7 d/week) or an IECR+PF for a 3-month weight-loss period and 1 month of weight maintenance (IECR or IECR+PF for 1 d/week). ***Insulin resistance reduced with the IECR diets*** (mean - 0·34 (95% CI - 0·66, - 0·02) units) and the IECR+PF diet (mean - 0·38 (95% CI - 0·75, - 0·01) units). Reductions with the IECR diets were significantly greater compared with the DER diet (mean 0·2 (95% CI - 0·19, 0·66) μU/unit, P= 0·02). ***Both IECR groups had greater reductions in body fat compared with the DER group*** (IECR: mean - 3·7 (95% CI - 2·5, - 4·9) kg, P= 0·007; IECR+PF: mean - 3·7 (95% CI - 2·8, - 4·7) kg, P= 0·019; DER: mean - 2·0 (95% CI - 1·0, 3·0) kg). During the weight maintenance phase, 1 d of IECR or IECR+PF per week maintained the reductions in insulin resistance and weight.

INFLAMMATION & IF

https://www.ncbi.nlm.nih.gov/pubmed/23244540
Nutr Res. 2012 Dec;32(12):947-55. doi: 10.1016/j.nutres.2012.06.021. Epub 2012 Oct 4.
Intermittent fasting during Ramadan attenuates proinflammatory cytokines and immune cells in healthy subjects.
Faris MA1, Kacimi S, Al-Kurd RA, Fararjeh MA, Bustanji YK, Mohammad MK, Salem ML

Intermittent fasting and caloric restriction have been shown to extend life expectancy and reduce inflammation and cancer promotion in animal models. It was hypothesized that intermittent prolonged fasting practiced during the month of Ramadan (RIF) could positively affect the inflammatory state. To investigate this hypothesis, a cross-sectional study was designed to investigate the impact of RIF on selected inflammatory cytokines and immune biomarkers in healthy subjects. ***Fifty (21 men and 29 women) healthy volunteers who practiced Ramadan fasting were recruited for the investigation of circulating proinflammatory cytokines (interleukin [IL]-1β, IL-6, and tumor necrosis factor α), immune cells (total leukocytes, monocytes, granulocytes, and lymphocytes), and anthropometric and dietary assessments.*** The investigations were conducted 1 week before Ramadan fasting, at the end of the third week of Ramadan, and 1 month after the cessation of Ramadan month. ***The proinflammatory cytokines IL-1β, IL-6, and tumor necrosis factor α; systolic and diastolic blood pressures; body weight; and body fat percentage were significantly lower (P < .05) during Ramadan as compared with before Ramadan or after the cessation of Ramadan fasting.*** Immune cells significantly decreased during Ramadan but still remained within the reference ranges. These results indicate that RIF attenuates inflammatory status of the body by suppressing proinflammatory cytokine expression and decreasing body fat and circulating levels of leukocytes.

LONGEVITY & IF

https://www.sciencedirect.com/science/article/pii/S0047637400001093
Mechanisms of Ageing and Development Volume 115, Issues 1–2, 17 May 2000, Pages 61-71
Influence of short-term repeated fasting on the longevity of female (NZB×NZW)F1 mice
Hiroshi Sogawa, Chiharu Kubo

Caloric restriction in rodents is well known to retard the rate of aging, increase mean and maximum life-spans, and inhibit the occurrence of many age-associated diseases. However, little is known about the influence of short-term repeated fasting on longevity. In this study, female (NZB×NZW)F1 mice were used to test the physiological effect of short-term repeated fasting (4 consecutive days, every 2 weeks). ***The results showed that fasting mice survived significantly longer than the full-fed mice, in spite of the fasting group having a heavier body weight than the control group. Mean survival times for fasting and control mice were 64.0±15.3 and 47.9±9.4 weeks, respectively.*** Short-term repeated fasting manipulation was also effective on the prolongation of life-span in autoimmune-prone mice.

HASHIMOTO'S & IF

https://hashimotoshealing.com/intermittent-fasting-and-hashimotos/

Is There A Fasting Approach That Can Work for People With Hashimoto's?

Mark Ryan, L.Ac

It really depends on how bad things are and where you are in the progression of the disease. ***If you have major disruptions in your circadian rhythms and you have major imbalances in blood sugar, I would strongly discourage attempting the intermittent fasting programs.*** In my experience most people who have Hashimoto's that come for treatment are advanced enough where intermittent fasting just doesn't give you enough benefits for all the serious downsides that may result. ***If you have healed to the point where you have restored your circadian rhythms and you blood sugar is well balanced then perhaps the One Meal Per Day Fast could be something that you could attempt. The is really the only viable option for keeping balance of your body's clock and maximizing the beneficial effects of intermittent fasting.*** If you exercise, you'll need to feed your muscles post workout with a low glycemic index recovery meal to avoid the dangers of insulin surges. And having proteins and carbs before your workout that are quickly assimilated can help load glycogen in your muscles, nourish the fast fibers in those muscles and help boost max strength and performance. With Hashimoto's, however, this is another potential land mine as the most commonly recommended form of protein is good quality whey protein and while whey is refined and filtered it can contain trace amounts of casein which can cause major immune flare ups in some Hashimoto's folks.

INFECTIONS & IF

https://selfhacked.com/blog/autophagy-benefits-and-how-to-harness/

Autophagy contributes to fighting infectious diseases in three ways:

1. Direct removal of microbes from inside of cells (xenophagy)
2. Removal of toxins created by infections
3. Modulation of the immune response to infections

Infectious microbes such as Mycobacterium tuberculosis and the Group A Streptococcus, along with viruses such as HIV and protozoans are removed by autophagy.

MMJ & AUTOPHAGY

http://www.jci.org/articles/view/37948

Cannabinoid action induces autophagy-mediated cell death through stimulation of ER stress in human glioma cells

María Salazar,[1,2] Arkaitz Carracedo,[1] Íñigo J. Salanueva,[1] Sonia Hernández-Tiedra,[1] Mar Lorente,[1,2] Ainara Egia,[1] Patricia Vázquez,[3] Cristina Blázquez,[1,2] Sofía Torres,[1] Stephane García,[4] Jonathan Nowak,[4] Gian María Fimia,[5] Mauro Piacentini,[5] Francesco Cecconi,[6] Pier Paolo Pandolfi,[7] Luis González-Feria,[8] Juan L. Iovanna,[4] Manuel Guzmán,[1,2] Patricia Boya,[3] and Guillermo Velasco[1,2]

First published April 1, 2009

Our data indicate that THC induced ceramide accumulation and eukaryotic translation initiation factor 2α (eIF2α) phosphorylation and thereby activated an ER stress response that promoted autophagy via tribbles homolog 3–dependent (TRB3-dependent) inhibition of the Akt/mammalian target of rapamycin complex 1 (mTORC1) axis. We also showed that autophagy is upstream of apoptosis in cannabinoid-induced human and mouse cancer cell death and that activation of this pathway was necessary for the antitumor action of cannabinoids in vivo. These findings describe a mechanism by which THC can promote the autophagic death of human and mouse cancer cells and provide evidence that cannabinoid administration may be an effective therapeutic strategy for targeting human cancers.

CANNABIS & CANCER

https://www.ncbi.nlm.nih.gov/pubmed/15688367

Cannabidiol induces programmed cell death in breast cancer cells by coordinating the cross-talk between apoptosis and autophagy.

Shrivastava A1, Kuzontkoski PM, Groopman JE, Prasad A.

Mol Cancer Ther. 2011 Jul;10(7):1161-72. doi: 10.1158/1535-7163.MCT-10-1100. Epub 2011 May 12.

Cannabidiol (CBD), a major nonpsychoactive constituent of cannabis, is considered an antineoplastic agent on the basis of its in vitro and in vivo activity against tumor cells. However, the exact molecular mechanism through which CBD mediates this activity is yet to be elucidated. Here, we have shown CBD-induced cell death of breast cancer cells, independent of cannabinoid and vallinoid receptor activation. Electron microscopy revealed morphologies consistent with the coexistence of autophagy and apoptosis. Western blot analysis confirmed these findings. We showed that CBD induces endoplasmic reticulum stress and, subsequently, inhibits AKT and mTOR signaling as shown by decreased levels of phosphorylated mTOR and 4EBP1, and cyclin D1. Analyzing further the cross-talk between the autophagic and apoptotic signaling pathways, we found that beclin1 plays a central role in the induction of CBD-mediated apoptosis in MDA-MB-231 breast cancer cells.

Although CBD enhances the interaction between beclin1 and Vps34, it inhibits the association between beclin1 and Bcl-2. ***In addition, we showed that CBD reduces mitochondrial membrane potential, triggers the translocation of BID to the mitochondria, the release of cytochrome c to the cytosol, and, ultimately, the activation of the intrinsic apoptotic pathway in breast cancer cells.*** CBD increased the generation of reactive oxygen species (ROS), and ROS inhibition blocked the induction of apoptosis and autophagy. ***Our study revealed an intricate interplay between apoptosis and autophagy in CBD-treated breast cancer cells and highlighted the value of continued investigation into the potential use of CBD as an antineoplastic agent.***

CANCER & IF

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3608686/
Sci Transl Med. 2012 Mar 7; 4(124): 124ra27.
Fasting Cycles Retard Growth of Tumors and Sensitize a Range of Cancer Cell Types to Chemotherapy
Changhan Lee,1,* Lizzia Raffaghello,2,* Sebastian Brandhorst,1,3 Fernando M. Safdie,1 Giovanna Bianchi,2 Alejandro Martin-Montalvo,4 Vito Pistoia,2 Min Wei,1 Saewon Hwang,1 Annalisa Merlino,1 Laura Emionite,5 Rafael de Cabo,4 and **Valter D. Longo**

Short-term starvation (or fasting) protects normal cells, mice, and potentially humans from the harmful side effects of a variety of chemotherapy drugs. Here, we show that treatment with starvation conditions sensitized yeast cells (*Saccharomyces cerevisiae*) expressing the oncogene-like $RAS2^{val19}$ to oxidative stress and 15 of 17 mammalian cancer cell lines to chemotherapeutic agents. ***Cycles of starvation were as effective as chemotherapeutic agents in delaying progression of different tumors and increased the effectiveness of these drugs against melanoma, glioma, and breast cancer cells.*** In mouse models of neuroblastoma, fasting cycles plus chemotherapy drugs—but not either treatment alone—resulted in long-term cancer-free survival. In 4T1 breast cancer cells, short-term starvation resulted in increased phosphorylation of the stress-sensitizing Akt and S6 kinases, increased oxidative stress, caspase-3 cleavage, DNA damage, and apoptosis. ***These studies suggest that multiple cycles of fasting promote differential stress sensitization in a wide range of tumors and could potentially replace or augment the efficacy of certain chemotherapy drugs in the treatment of various cancers.***

CANCER & IF

http://science.sciencemag.org/content/338/6109/889
Science 16 Nov 2012: Vol. 338, Issue 6109, pp. 889-890
Promoting Tumorigenesis by Suppressing Autophagy
Itay Koren, Adi Kimchi

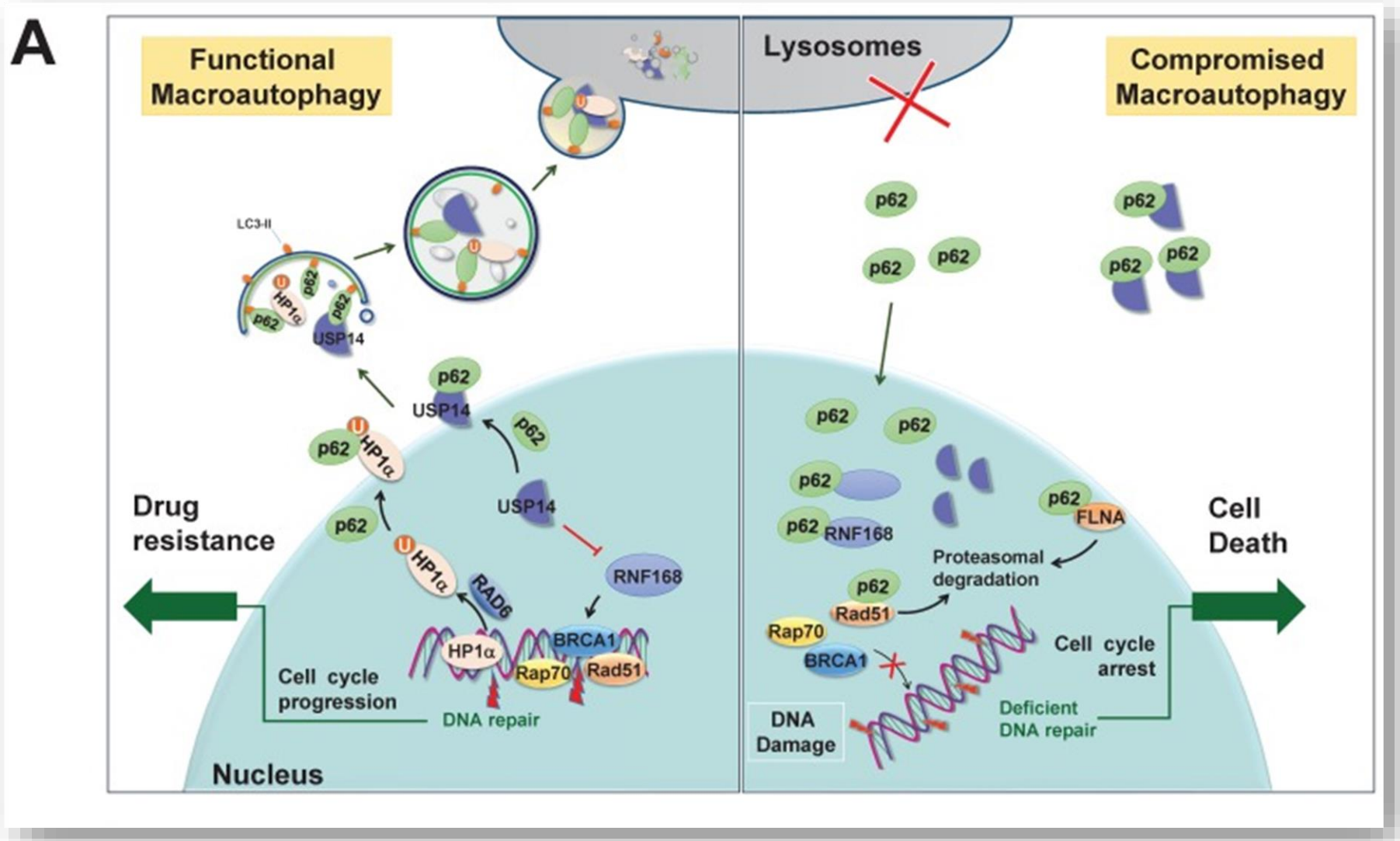
Autophagy controls cellular homeostasis by degrading long-lived proteins, protein aggregates, and defective organelles. It also suppresses tumorigenesis by limiting inflammation, eliminating toxic unfolded proteins, and removing damaged mitochondria that produce reactive oxygen species (which damage DNA). Loss of these protective events could promote cancer initiation (1, 2). Support for the tumor suppressive function of autophagy emerged from the findings that the gene encoding the essential autophagic protein Beclin 1 functions as a haplo-insufficient tumor suppressor in mice and humans (3–6). ***However, a comprehensive mechanistic view of how autophagy is turned off during tumor development and, more specifically, whether the tumor-suppressive activity of Beclin 1 results from its canonical autophagic function, was still missing. On page 956 in this issue, Wang et al. (7) establish a connection between Beclin 1 and the Akt signaling pathway, which controls a large spectrum of cellular functions associated with cancer ranging from cell proliferation and survival to angiogenesis and metabolism. The finding underscores the importance of autophagy in tumor suppression*** (8)

CANCER, p62 & IF

https://www.ncbi.nlm.nih.gov/pubmed/19524509
Cell. 2009 Jun 12;137(6):1062-75. doi: 10.1016/j.cell.2009.03.048.
Autophagy suppresses tumorigenesis through elimination of p62.
Mathew R1, Karp CM, Beaudoin B, Vuong N, Chen G, Chen HY, Bray K, Reddy A, Bhanot G, Gelinas C, Dipaola RS, Karantza-Wadsworth V, White E.

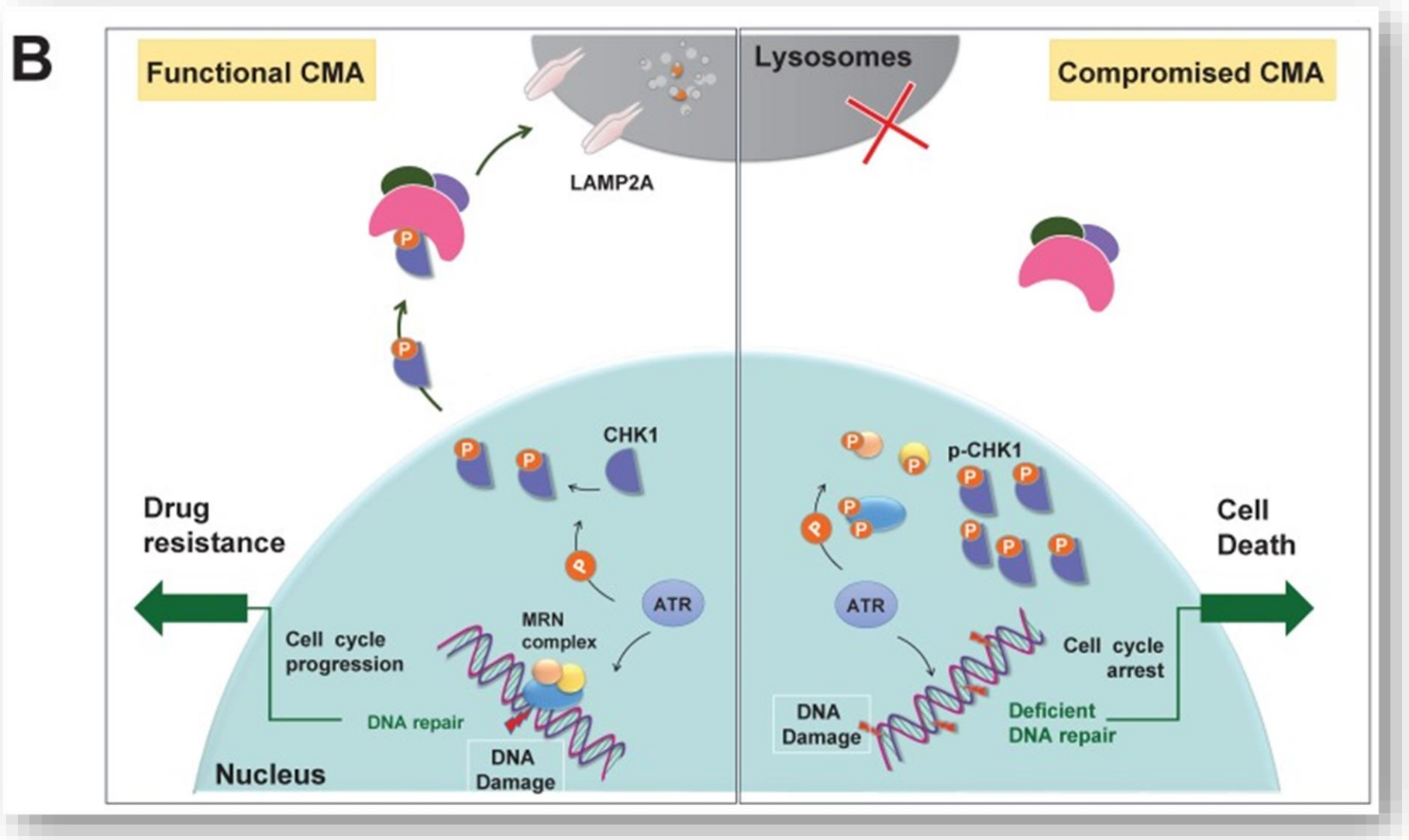
Allelic loss of the essential autophagy gene beclin1 occurs in human cancers and renders mice tumor-prone suggesting that autophagy is a tumor-suppression mechanism. While tumor cells utilize autophagy to survive metabolic stress, autophagy also mitigates the resulting cellular damage that may limit tumorigenesis***. In response to stress, autophagy-defective tumor cells preferentially accumulated p62/SQSTM1 (p62), endoplasmic reticulum (ER) chaperones, damaged mitochondria, reactive oxygen species (ROS), and genome damage.*** Moreover, suppressing ROS or p62 accumulation prevented damage resulting from autophagy defects indicating that failure to regulate p62 caused oxidative stress. Importantly, sustained p62 expression resulting from autophagy defects was sufficient to alter NF-kappaB regulation and gene expression and to promote tumorigenesis. ***Thus, defective autophagy is a mechanism for p62 upregulation commonly observed in human tumors that contributes directly to tumorigenesis*** likely by perturbing the signal transduction adaptor function of p62-controlling pathways critical for oncogenesis.

AUTOPHAGY & LYSOSOMES



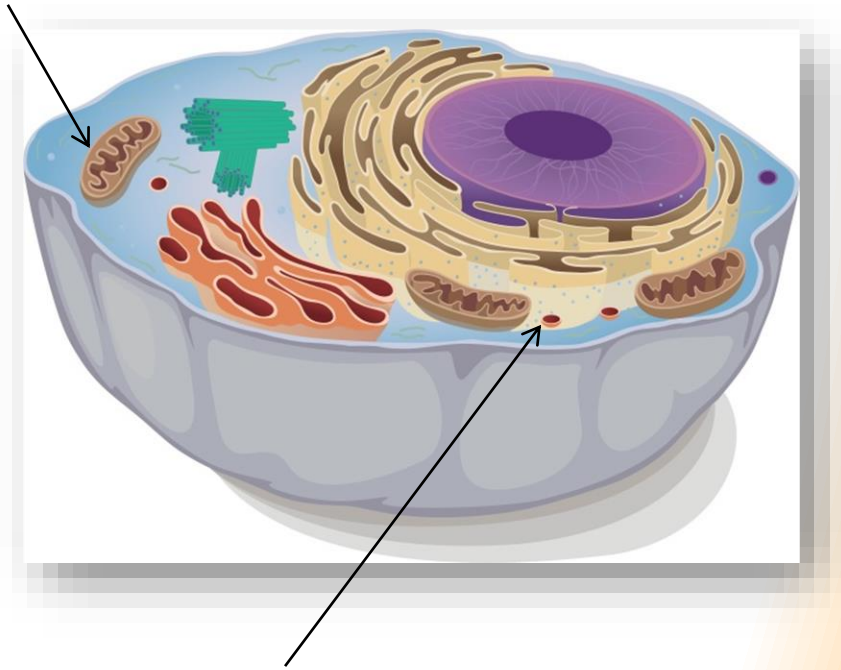
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6332805/figure/F4/

AUTOPHAGY & LYSOSOMES



https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6332805/figure/F4/

LYSOSOMES & PPIs



http://www.ncbi.nlm.nih.gov/pubmed/23478938

Inhibition of lysosomal enzyme activities by proton pump inhibitors.

Liu W[1], Baker SS, Trinidad J, Burlingame AL, Baker RD, Forte JG, Virtuoso LP, Egilmez NK, Zhu L.

RESULTS:

- Incubation of a cysteine-containing peptide with PPIs at pH 5 led to the conversion of most of the peptide into PPI-peptide adducts. ***Dose dependent inhibition of lysosomal enzyme activities by PPIs was observed in cultured cells and mouse spleen.*** Further, PPI counteracted the tumor immunotherapy in a mouse model.

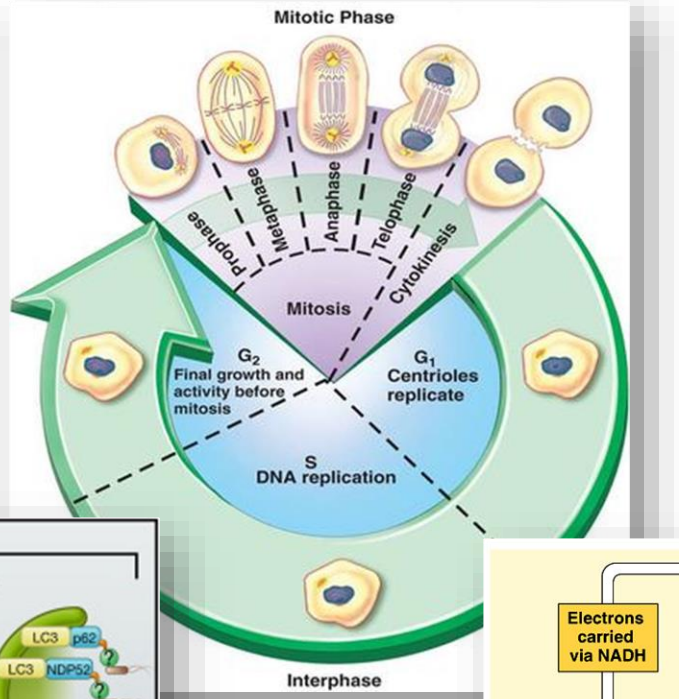
CONCLUSIONS:

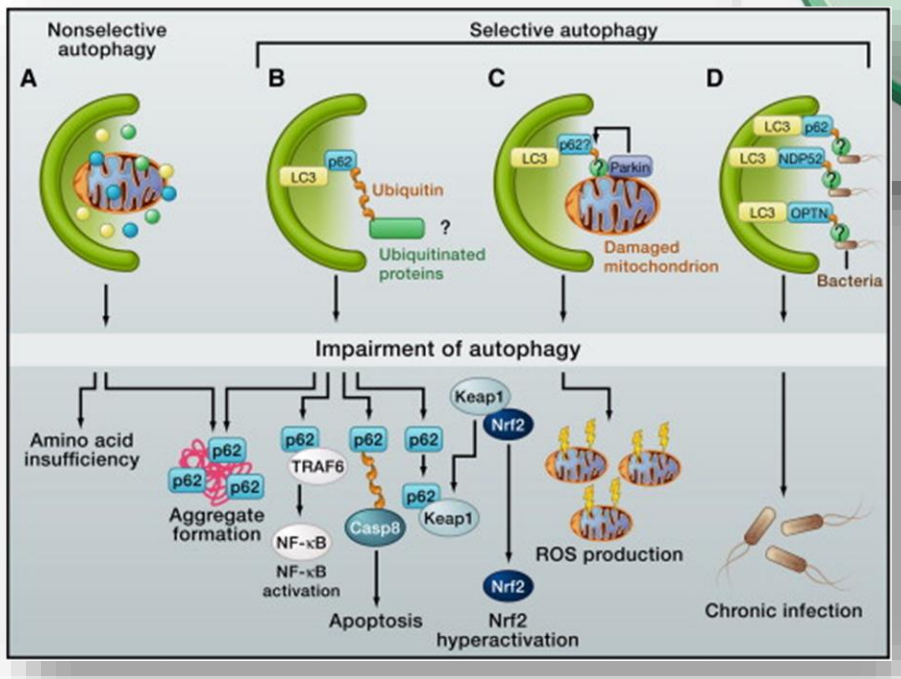
- ***Our data support the hypothesis that many of the PPI adverse effects are caused by systematically compromised immunity, a result of PPI inhibition of the lysosomal enzymes.*** This novel mechanism complements the existing mechanisms in explaining the increased incidence of tumorigenesis and infectious diseases among PPI users and underlie the ongoing concern about the overuse of PPIs in adult and pediatric populations.

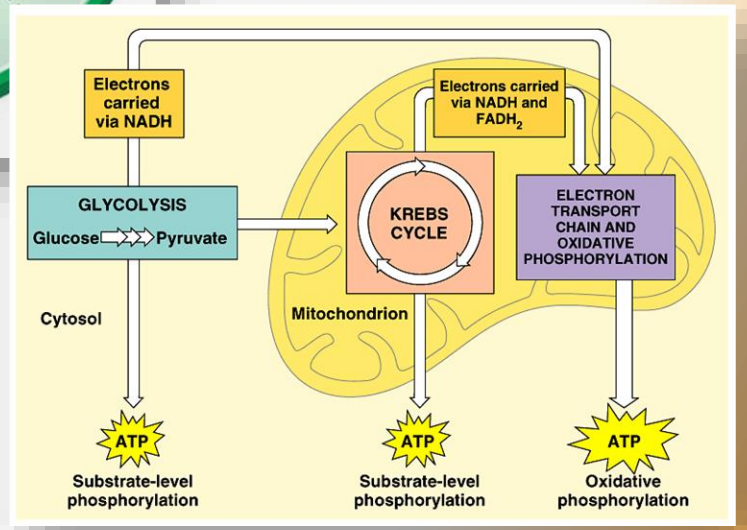
ARE WE EATING OURSELVES TO DEATH?

Overeating &/Or Without Giving The Cell Enough Time To Enter Into Autophagy…

The Answer Is Yes.







INTERMITTENT FASTING

AUTOPHAGY & SUMMATION

A DR. H MEDITATION ©2018