

The Cancer-Fighting Kitchen: Evidence-Based Nutrition Strategies

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Diet & Nutrition? For Cancer?

With our most aggressive
weapons, we aren't
winning the
War Against Cancer.

How could some
wimpy foods
have any effect?



Post-Diagnosis Diet and Cancer Survival



Cancer Type	Greater Survival Associated With...	Reference
Breast	≥5 servings veggies/fruit per day plus exercise 30 min, 6x/wk (45% more likely to survive 10 yrs)	Pierce JP: <i>J Clin Oncol.</i> , 2007 Jun 10;25(17): 2345-51.
Ovarian	high intake of cruciferous vegetables (45% more likely to survive 5 yrs)	Nagle C, et al: <i>Int J Cancer</i> , Aug 2003;106 (2):264-9.
Gastric	less commercially-raised meat & animal fat	Palli D, et al: <i>Cancer</i> , Sept 2000;89: 1205-13.
Pancreatic	lower (omega-6) fat, higher fiber, avoid excess calorie intake	Carter JP, et al: <i>J Am Coll Nutr</i> , Jun 1993; 12 (3):109-26.

Oncometabolic Milieu

Inflammation

VEGF

insulin

CRP

↑ *NFκB*

adiponectin

Gene Instability

IGF-1

Insulin Resistance

COX-2

leptin

5-HETE

IL-6

LOX-5

estrogen

Hyper-coagulability

PDGF

↓ SHBG

Hormone Imbalance

VEGF

fibrin

cortisol

↓ Zinc

Angiogenesis

bFGF

↓ Vit D

↑ Copper

IL-10

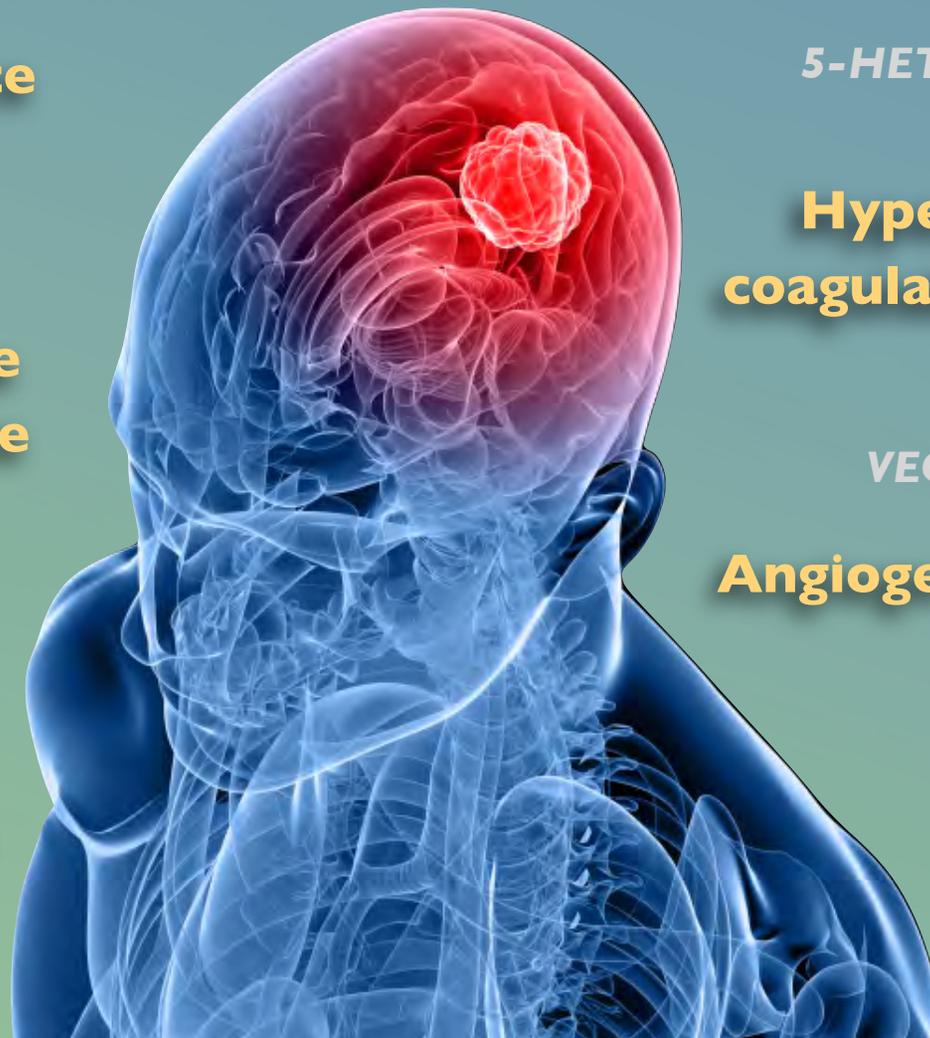
TNF-α

Nutrient Imbalances

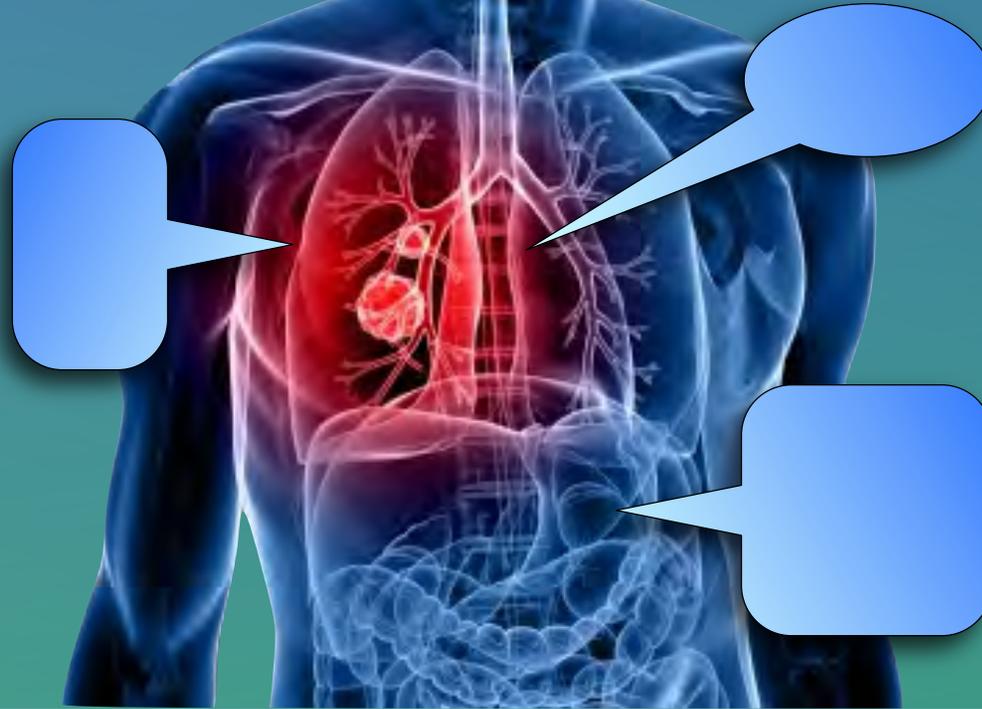
Immune Incompetence

↑ Iron

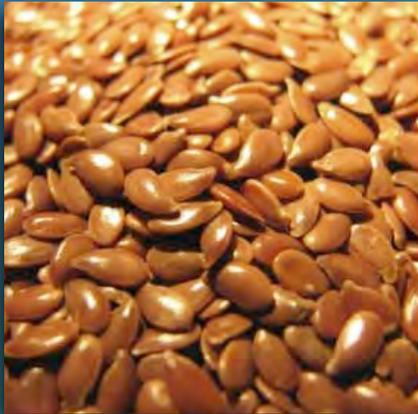
↓ Antioxidants



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Modulating Gene Expression



Nutrition Can Change Gene Expression

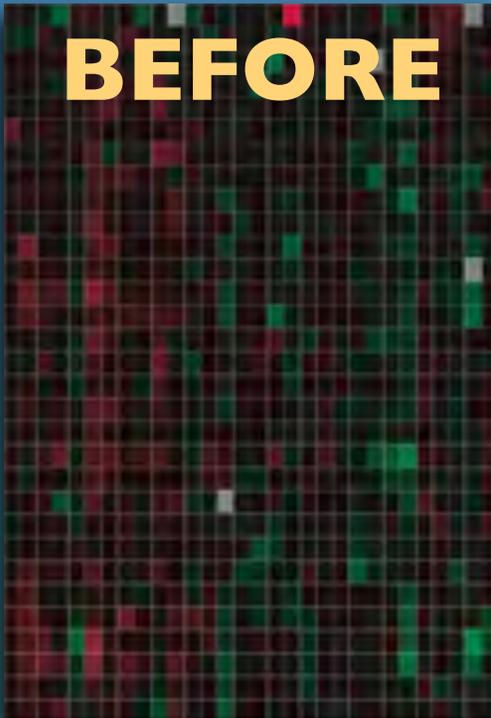
Flaxseed & Breast Cancer

STUDY: post-menopausal BrCa pts fed muffin with 25 grams (2 TBSP) flaxseed meal vs “placebo” muffin for 4-5 weeks. Compared tumor characteristics from biopsy and subsequent lumpectomy.

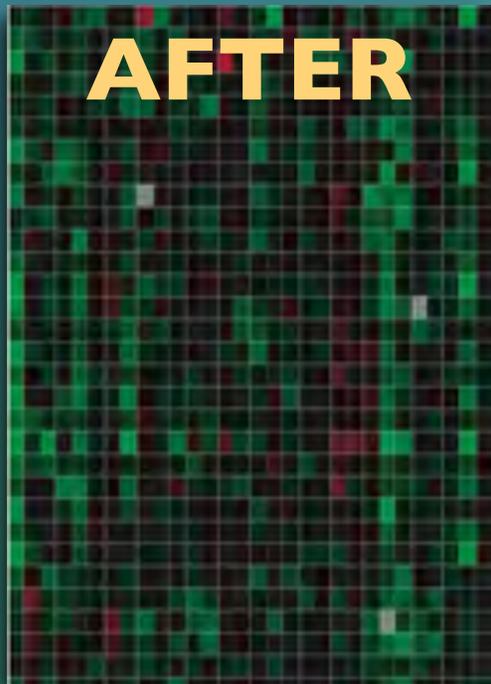
- ◆ 70% reduction in *her2neu* expression
- ◆ 34% reduction in *ki-67* (rate of cancer cell division and growth)
- ◆ 30% increase in *apoptosis* (programmed cell death)

Thompson LU, et al: Dietary flaxseed alters tumor biological markers in post-menopausal breast cancer. *Clin Cancer Ther*, May 15, 2005;11:3828-35.

BEFORE



AFTER



Healthy Diet Profoundly Alters Gene Expression

- ◆ Men with prostate cancer not electing treatment (surgery, radiation, hormone therapy)
- ◆ Gene expression compared after 3 months on diet
- ◆ Expression of **500+ genes** changed
- ◆ Oncogenes were down-regulated!

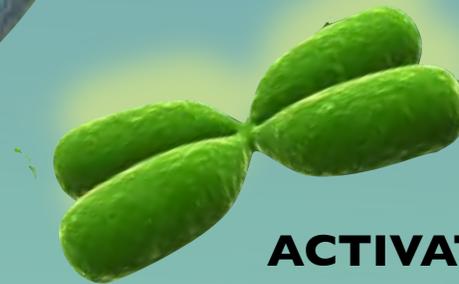
Ornish D, et al: Changes in prostate gene expression in men undergoing an intensive nutrition and lifestyle intervention. *Proc Natl Acad Sci USA*. 2008 Jun 17;105(24):8369-74.

Cancer's “Master Switch”

NFκB



TRIGGERS:
carcinogens
oxidation
viral infection
inflammation
radiation
chemotherapy
stress



**ACTIVATES 400+ genes involved
in tumor proliferation, survival,
angiogenesis & invasion**

Aggarwal B, et al: Nuclear Factor-κB: A holy grail in cancer prevention and therapy. *Curr Signal Transduc Ther*, 2006;1:25-52. • Van Waes C: Nuclear factor-kappaβ in development, prevention, and therapy of cancer. *Clin Cancer Res*, Feb 15, 2007;13(4):1076-82.



Spices Inhibit NFκB

anise

cumin

mint

basil

fennel

mustard seed

black pepper

fenugreek

nutmeg

caraway

flaxseed

oregano

cardamom

garlic

parsley

chili pepper

ginger

rosemary

cinnamon

Holy basil

saffron

clove

lemongrass

tamarind

coriander

licorice

turmeric

**The reason
to season?**

**To talk to
your genes!**

Aggarwal B & Shishodia S: Suppression of the nuclear factor-kappaβ activation pathway by spice derived phytochemicals: reasoning for seasoning. *Ann NY Acad Sci*, Dec 2004;1030:434-41.

Top 10 Foods to Modify Gene Expression

- 1 Spices (combinations: curry, chai)**
- 2 Broccoli sprouts (sulforaphane)**
- 3 Brassica veggies (isothiocyanates)**
- 4 Dark leafy greens (folate)**
- 5 Garlic, onions, leeks, chives, shallots**
- 6 Parsley, celery, red pepper (luteolin)**
- 7 Peanuts/boiled, red grapes/wine (resveratrol)**
- 8 Red onions and capers (quercetin)**
- 9 Green tea (theophylline, EGCG)**
- 10 Fish, eggs, cheese, sunflower seeds, asparagus, almonds (B vitamins)**



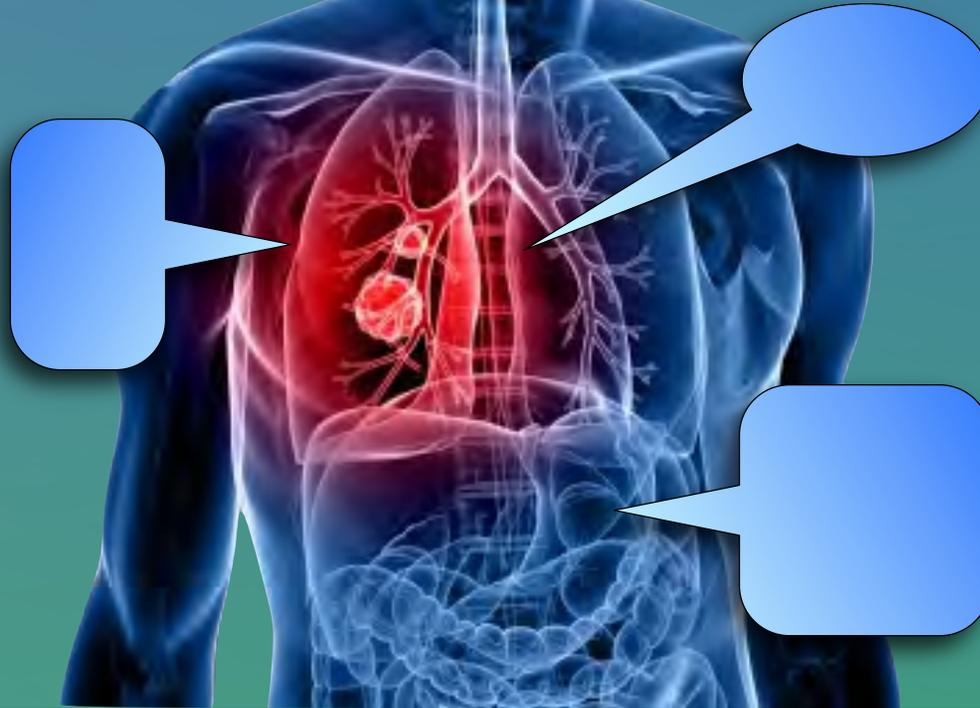
FOOD IS POWERFUL MEDICINE



*“Three times a day,
day after day,
we are eating foods
that can influence
our genes and help
us fight cancer...”*

—David Servan-Schreiber, MD

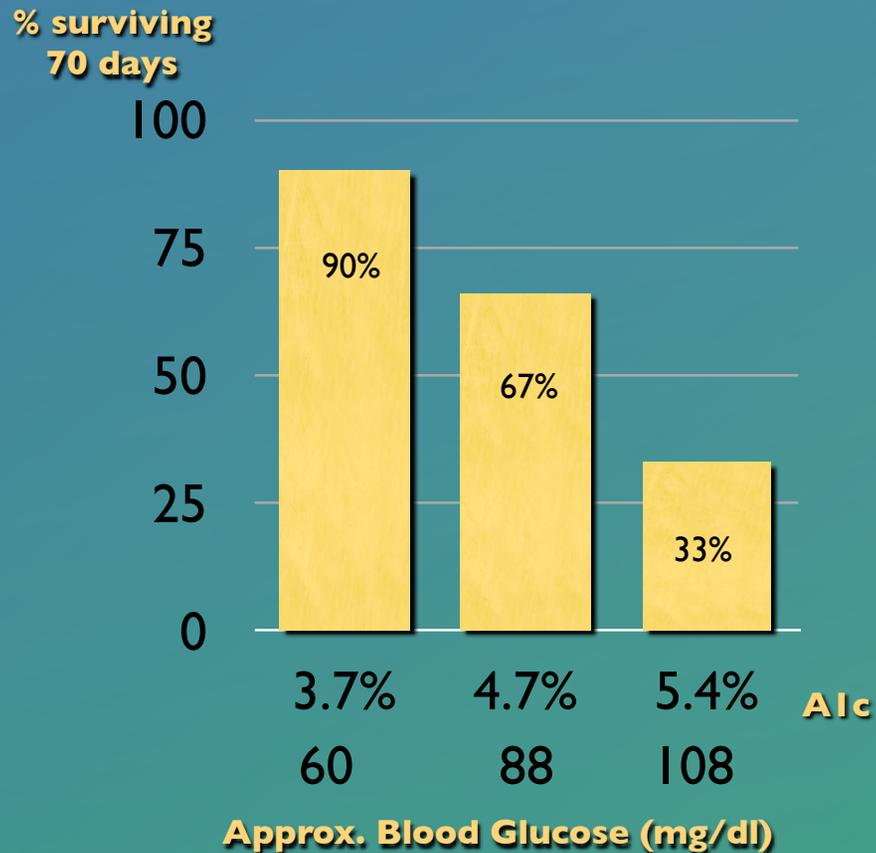
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Insulin Resistance and Cancer

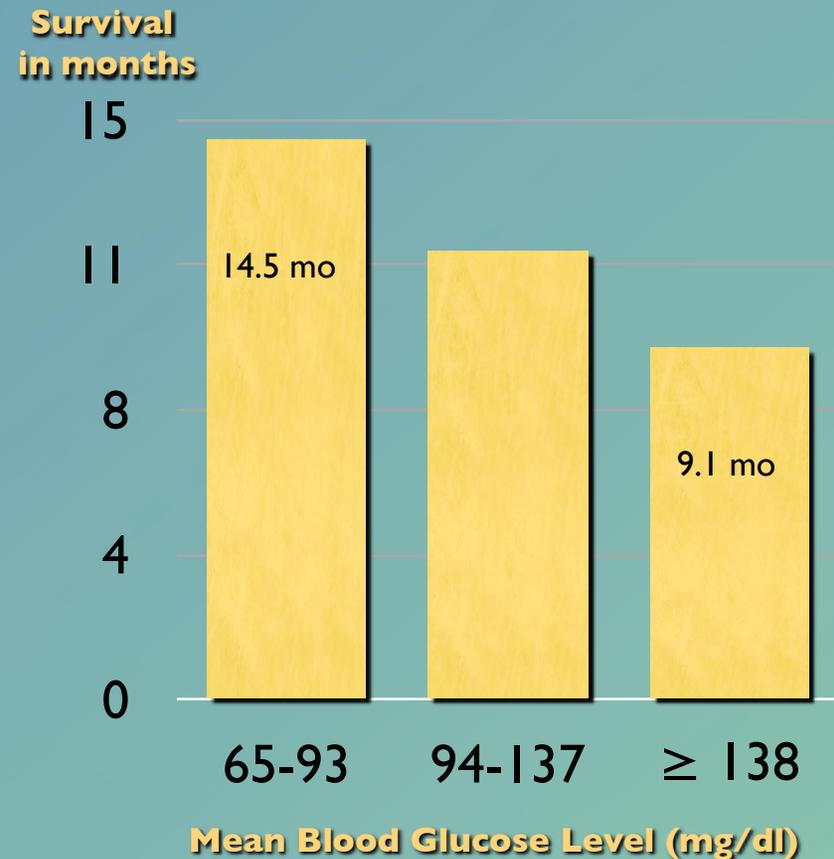
Blood Glucose & Cancer Survival

Survival in Mice with Injected Breast Cancer Cells



SOURCE: Santisteban GA, et al: Glycemic modulation of tumor tolerance in a mouse model of breast cancer. *Biochem Biophys Res Commun*, Nov 1985;132(3):1174-9.

Survival of Brain Tumor Patients



SOURCE: Derr R, et al., Association between hyperglycemia and survival in patients with newly diagnosed glioblastoma. *J Clin Oncol*, Mar 1, 2009;27(7):1082-6.

Influence of Insulin Resistance

Cancer patients with insulin resistance have...

- ◆ **↑ Recurrence** - 3-fold ↑ risk of recurrence in 5 yrs in BrCa pts • ↑ rates of recurrence & liver mets in colon cancer pts
- ◆ **↑ Post-Op Complications** - ↑ rate of post-op complications (40 vs 11%) and longer hospital stay (11 vs 8 days)
- ◆ **Immune Suppression** - ↑ risk of infection in pts undergoing intensive chemotherapy
- ◆ **↑ Estrogen** - increases circulating estrogen via ↑ aromatase activity & ↓ SHBG production

Derr R, *et al*: Antecedent hyperglycemia is associated with an increased risk of neutropenic infections during bone marrow transplantation. *Diabetes Care*, Oct 2008;31(10):1972-7.

Lohsiriwat V, *et al*: Impact of metabolic syndrome on the short-term outcomes of colorectal cancer surgery. *Dis Colon Rectum*, Feb 2010;53(2):186-91.

Pasanisi P, *et al*: Metabolic syndrome as a prognostic factor for breast cancer recurrences. *Int J Cancer*, Jul 1, 2006;119(1):236-8.

Shen Z, *et al*: Metabolic syndrome is an important factor for the evolution of prognosis in colorectal cancer: survival, recurrence, and liver metastasis. *Am J Surg*, 2010 May;80(5):331-6.

Vona-Davis L, *et al*: Adiposity, type 2 diabetes and the metabolic syndrome in breast cancer. *Obes Rev*, Sept 2007;8(5):395-408.



Cancer Promoting Effects of Insulin Resistance

- ◆ **↑ DNA Damage** leading to gene instability
- ◆ **Mitosis** stimulates damaged cells to divide and make daughter cells
- ◆ **Inhibits Apoptosis** (allows cancer cells to evade programmed cell death and survive indefinitely)
- ◆ **Stimulates Angiogenesis** - ↑ growth of new blood vessels to fuel tumor progression
- ◆ **Promotes Cell Migration** - invasion & metastasis

Cowey S & Hardy RW: The metabolic syndrome: A high-risk state for cancer? *Am J Pathol*, 2006 Nov;169(5):1505-22.

Are you facing insulin resistance?



	Diagnostic Value	Optimal Range
Waist-Hip Ratio	women: > 0.85 men: > 1.0	women: < 0.8 men: < 0.9
Fasting Glucose	> 100-110 mg/dl	60-90 mg/dl
A1c	≥ 6.0%	4.6-5.2%
Triglycerides	> 150 mg/dl	< 110 mg/dl
HDL cholesterol	women : < 40 men: < 50	> 50-55 mg/dl
Blood pressure	> 135/85	≤ 120/80
Uric Acid	—	< 5.5 mg/dl



BEWARE!
These wholesome-
appearing foods
may be problematic
for you!

Foods with High Glycemic Load

Bread, white	Chips
Bread, whole wheat	Sugar
Cereal	Honey
Oatmeal	Flour, white
Crackers	Flour, whole wheat
Muffins	Corn
Bagels	Cornmeal
Cookies	Pasta
Pancakes	Potatoes
Waffles	Potato chips
Soda pop	Pretzels
Fruit Juice	Rice, white
Dried fruits	Rice, brown
Candy	Fat-free foods

www.glycemicindex.com

www.nutritiondata.com

Low Glycemic Substitutions



INSTEAD OF THIS...		TRY THIS...	
Food (1 cup portion)	Glycemic Load*	Food (1 cup serving)	Glycemic Load
White flour	76	Almond Flour	0
Whole wheat flour	44	Coconut Flour	0
Corn, sweet yellow	35	Baby Corn	5
Hamburger bun	18	Rice paper wrap	4
		Portobello mushrooms	3
		Romaine lettuce "wrap"	0
Brown rice	22	Cauliflower "rice"	2
Pasta noodles	22	Spaghetti Squash	2
		Zucchini "noodles"	1
		Miracle Noodles	0
Mashed Potatoes	16	Mashed Cauliflower	4

* Glycemic Load \geq 10 is HIGH!

Strategies to Address Insulin Resistance



FACTOR	SMART STRATEGIES	
DIET	<ul style="list-style-type: none"> ● Limit starchy carbs: 1-3 servings/day ● Glycemic Load: < 10/food, < 50/day ● Avoid liquid calories ● Avoid evening snacking 	
STRESS	Stress reduction techniques (meditation, yoga, tai chi, massage)	
LOSS OF MUSCLE MASS	<ul style="list-style-type: none"> ● Weight-bearing exercise ● Adequate protein intake 	
NUTRIENT DEFICIENCIES	<ul style="list-style-type: none"> ● Vitamin D ● CLA ● Chromium ● Vanadium 	<ul style="list-style-type: none"> ● Magnesium ● Carnitine ● Zinc ● Biotin

Demark-Wahnefried W, et al: Changes in weight, body composition, and factors influencing energy balance among premenopausal breast cancer patients receiving adjuvant chemotherapy. *J Clin Oncol*, 2001 May 1;19(9):2381-9.

Top 10 Foods to Aid Glycemic Control

Cinnamon

Berries: blueberries, goji, blk currant

Chamomile tea

Allium family: garlic, onions, leeks, chives

Parsley

Avocado

Olive oil

Flaxseed meal / Oat bran (soluble fiber)

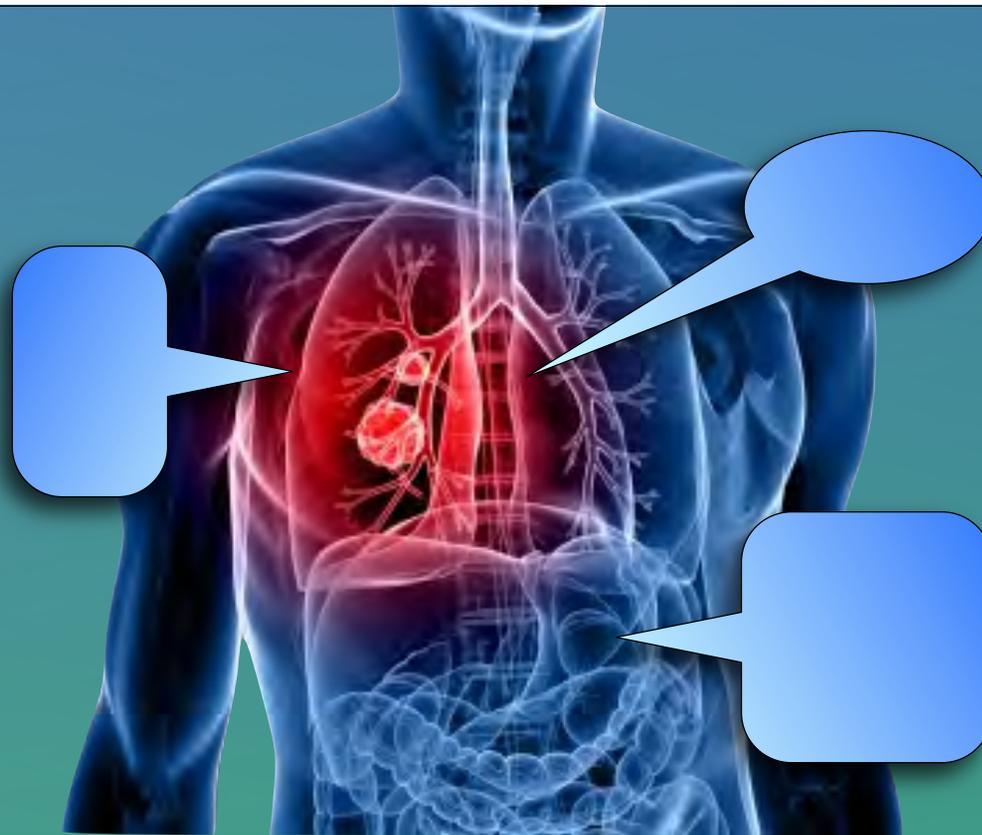
Lemon

Nopal (prickly pear cactus)

Kaushik G, Satya S, Khandelwal RK, Naik SN. Commonly consumed Indian plant food materials in the management of diabetes mellitus. *Diab Metabol Syndr: Clin Res Rev.* 2010;4(1):21-40. • Yeh GY *et al*: Systematic review of herbs and dietary supplements for glycemic control in diabetes. *Diab Care* 2003 Apr;26(4):1277-94.

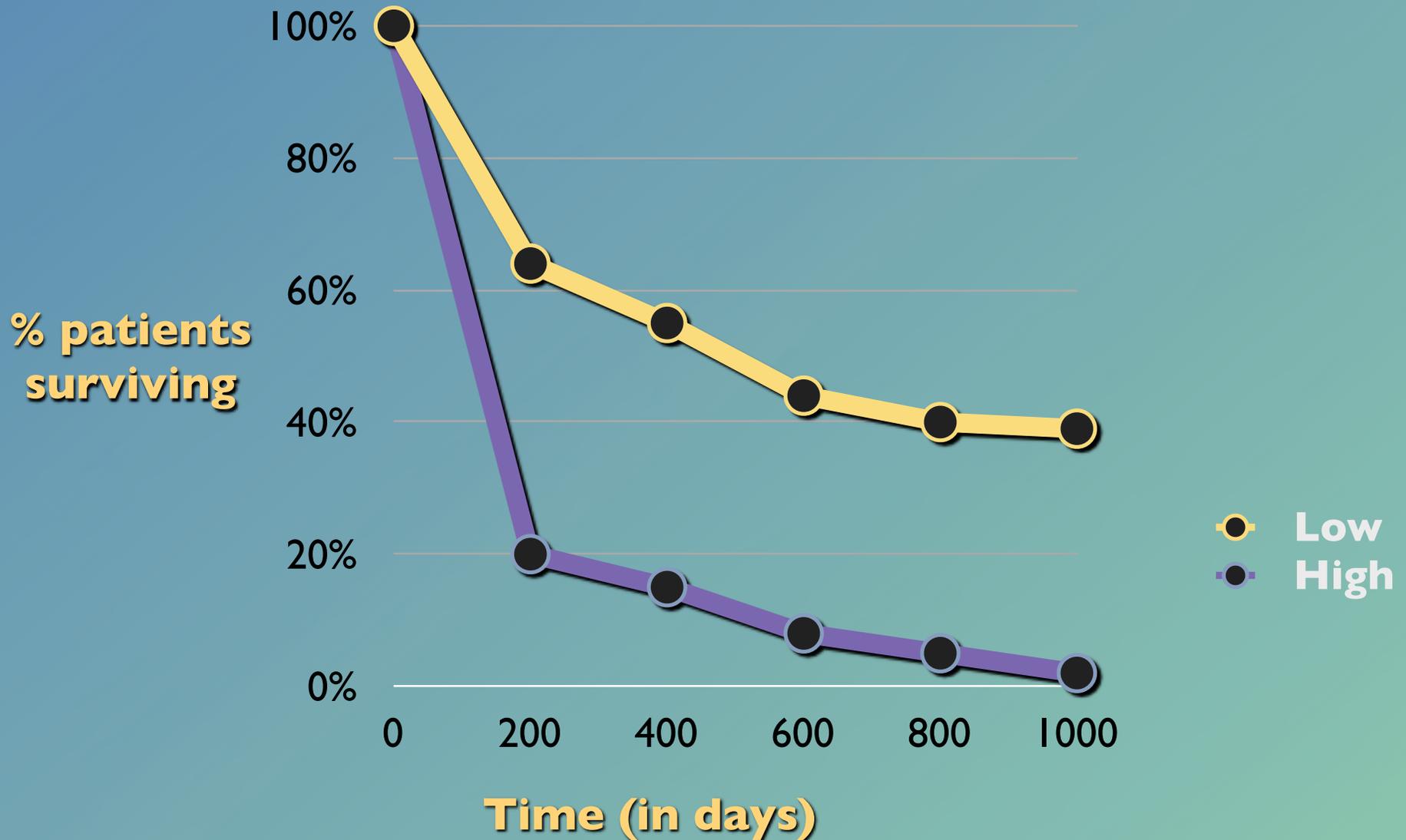


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Inflammation and Cancer

Inflammation & Cancer Survival



McMillan DC, *et al*: Measurement of the systemic inflammatory response predicts cancer-specific and non-cancer survival in patients with cancer. *Nutr Cancer*, 2001;41(1-2):64-9.

Inflammation: Other Findings

Patients with ↑ inflammation experience:

- ◆ **Toxicity of Chemotherapy** - More severe low blood counts during chemotherapy
- ◆ **Cachexia (wasting syndrome)** - Lower appetite, ↑ muscle wasting and ↑ weight loss
- ◆ **Greater Fatigue** - ↑ fatigue and poorer quality of life



Alexandre J, et al: Evaluation of the nutritional and inflammatory status in cancer patients for the risk assessment of severe haematological toxicity following chemotherapy. *Ann Oncol*, 2003;14:36-41.

Mohmoud FA, Rivera NI: The role of C-reactive protein as a prognostic indicated in advanced cancer. *Curr Oncol Rep*, May 2002;4(3):250-5.

Scott HR, et al: A prospective study of the impact of weight loss and the systemic inflammatory response on quality of life in patients with inoperable non-small cell lung cancer. *Lung Cancer*, Jun 2003;40(3):295-9.

Dietary Fats & Inflammation

OMEGA-6 FATS

- Commercially-raised meat, poultry, dairy, eggs
- Most nuts & seeds
- Vegetable oils—corn, safflower, soy, grapeseed (not olive oil)

OMEGA-3 FATS

- Grass-fed/pastured meat, poultry, dairy, eggs
- Cold-water fish
- Black walnuts, flaxseeds
- Oils of flax, hemp and canola (not advisable)

↑ ω -6 / ↓ ω -3
↑ insulin

COX & LOX

COX & LOX

↑ ω -3 / ↓ ω -6
↓ insulin

PRO-INFLAMMATORY Compound

- Foster tumor growth & progression
- Promote angiogenesis
- Suppress immune function

ANTI-INFLAMMATORY Compounds

- Inhibit tumor growth & progression
- Complement radiation & chemo
- Anti-angiogenesis



Find sources for
grass-fed foods at
www.eatwild.com

Wallace JM: Nutritional and botanical modulation of the inflammatory cascade—eicosanoids, cyclooxygenases, and lipoxygenases—as an adjunct in cancer therapy. *Integr Cancer Ther*, Mar 2002;1(1):7-37. • Watzl B: Anti-inflammatory effects of plant-based foods and of their constituents. *Int J Vitamin Nutr Res*, Dec 2008;78(6):293-8.

Diet to Address Inflammation

- ◆ ↑ Intake of fruits & vegetables (8+ servings/day)
- ◆ Ratio of ω -6:3 fats about 1:1 to 3:1
 - ◆ ↓ Vegetable oils, margarine, commercially-raised meat, poultry, dairy, eggs
 - ◆ ↑ Cold-water fish, organic grass-fed meat, poultry, dairy and omega-3 rich eggs, walnuts, hemp, chia and flaxseed meal, leafy greens
- ◆ Low glycemic diet (↓ insulin-driven inflammation)

Top 10 Foods to Quench Inflammation

Spices (esp. curry, ginger, garlic, parsley)

Wild, cold-water fish

Grass-fed (pastured) meat, dairy, eggs

Hot peppers

Olive oil

Leafy green veggies (spinach, chard, kale)

Cruciferous vegetables

Pumpkin, butternut squash, yam, carrot

Dark chocolate (flavanols)

Berries (blueberries, cherries, raspberries)

www.nutritiondata.com • Reinagel M: *The Inflammation Free Diet Plan*, McGraw-Hill, 2007. • Hamed MS, et al. Dark chocolate effect on platelet activity, C-reactive protein and lipid profile: a pilot study. *South Med J*, 2008;101(12):1203-1208.



TAKE HOME TIPS: Anticancer Diet in 5 Easy Steps



- ◆ Low glycemic
- ◆ High nutrient density
- ◆ Daily rainbow of phytonutrients
- ◆ Ample spices (NFkB reason to season)
- ◆ Improved omega-6:3 ratio

Marrying Flavor and Nutrition

Flavor Balancer		Culinary Job	Nutritional Job
Aromatic	garlic, onion, shallots, citrus zest, ginger, pepper, herbs & spices	Provide depth of flavor and interest	Modulate gene expression (antioxidant, anti-inflammatory, NFkB inhibitors)
Fat	olive oil, butter, coconut oil, sesame oil	Distribute flavors across the palate, add creaminess (rich mouth feel)	Required for absorption of phytonutrients (carotenoids), increases satiety
Acid or Sour	lemon, lime, vinegar, tamarind, sumac, ponzu, tomatoes, pickles, caneberries	Add “zing,” brighten flavors	Increase absorption of minerals, stimulate digestion
Salt	kosher or sea salt, tamari or soy sauce, MSG-free bouillon (“Better than Bouillon” brand), fish sauce, nitrate-free bacon or ham	Bring out flavors, reduce blandness, move flavor to the front of the tongue (where it’s best perceived)	Improve appetite, balanced ratio with potassium essential for energy and cellular metabolism
Sweet	maple syrup, honey, agave, other low-glycemic sweeteners, apples, fruits, caramelized onions	Calm harsh, sour or spicy flavors, “round out” or harmonize the flavors	Increase desire to eat and sense of pleasure. Provide sense of being nourished.

Clinical Findings

524 BrCa pts followed 5 yrs

↑ dietary intake soy associated with ↓ risk of recurrence in post-menopausal pts with ER+ BrCa

Kang X *et al*: Effect of soy isoflavones on breast cancer recurrence and death for patients receiving adjuvant endocrine therapy. *CMAJ*. 2010 Nov 23;182(17):1857-62.

5,042 BrCa survivors, 20-75 yrs old, in China, followed 5 yrs

Soy food intake inversely associated with mortality and recurrence

Shu XO *et al*: Soy food intake and breast cancer survival. *JAMA*. 2009 Dec 9;302(22):2437-43.

1,954 BrCa survivors, followed 6 yrs

Postmenopausal women on tamoxifen, ~ 60% reduction in recurrence cf highest to the lowest isoflavone intake

Guha N *et al*: Soy isoflavones and risk of cancer recurrence in a cohort of breast cancer survivors. *Breast Cancer Res Treat*. 2009 Nov;118(2):395-405.

FAQ: Is soy safe for patients with ER+ breast cancer?

- ◆ **Not estrogen, rather SERM** - *in vivo* competes with estrogen and xenoestrogens
- ◆ **Modulates estrogen via many pathways** - ↑ SHBG, ↓ circulating estrogen, ↑ 2:16-OH estrogen ratio
- ◆ **Other effects** - anti-angiogenesis, tyrosine kinase inhibition, promotes differentiation, induces apoptosis, impedes invasion and metastasis

FAQ: Do antioxidants interfere with cancer treatment?

Meta-Analysis

50 human clinical trials

n = 8,521 pts (>5,000 given antioxidants during treatment)

No evidence of interference

Enhanced cytotoxic efficacy of chemotherapy

Increased survival time

Simone CB et al: Antioxidants and other nutrients do not interfere with chemotherapy or radiation therapy and can increase kill and increase survival. *Alt Ther Health Med*, 2007 Mar-Apr; 13(2):40-7.

- ◆ **Antioxidants specificity** - RT hydroxyl radical quenched by vitamin C; lipid peroxidation quenched by vitamin E
- ◆ **Tissue specific bioaccumulation** - (fat vs water soluble), lycopene in liver/adrenal, breast/brain/prostate
- ◆ **Differential uptake in cancer cells** - ↑ intake in cancer cells, have pro-oxidant effect in ↑ amounts
- ◆ **↑ Oxidation = Gene instability** - ↑ oxidation may be culprit in development of more aggressive tumors
- ◆ **↑ Oxidation leads to ↓ cell proliferation** - but chemo targets rapidly dividing cells
- ◆ **Foods > supplements** - foods have much ↑ antioxidant effect (ORAC) than supplements!

FAQ: Is vegetarian or vegan the best anti-cancer diet?

ADVANTAGES	CONCERNS	STRATEGIES
Opportunity for high intakes of phytonutrients and antioxidants	Increased Copper - low zinc in diet (vegetarian food sources of zinc are also rich in copper)	Nuts/seeds with Zn:Cu Ratio \geq 6:1 (pumpkin, sunflower, macadamia, sesame seeds). Zinc supplement as needed.
	Insulin Resistance - may over-emphasize high glycemic load foods	Follow low glycemic load diet
Avoids <i>nitrates</i> in processed meats and <i>heterocyclic amines</i> in charred meats	Low CLA - avoidance of food sources of conjugated linoleic acid (CLA)	CLA supplement (9-cis, 11-trans) if avoiding dairy or eating only non- or low-fat dairy. Sunflower seeds have CLA, but are 65% lower in 9-cis, 11-trans isomer.
Reduces exposure to toxins which bioaccumulate in animal foods (top of food chain)	Low Omega-3s - walnuts, flaxseed/hemp seed oils have less conversion of EPA & lack DHA	Include cold-water fish in diet, or purified fish oil supplement (less toxin exposure)
	Low Vitamin A - beta carotene not converted to retinol in states of insulin resistance or low thyroid	Ensure adequate thyroid function; address insulin resistance