# WELLNESS TOOLS FOR CANCER SURVIVORS



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# Concerns of survivorship

- · Preventing recurrence
- · Another type of cancer
- Prevent and manage late effects of treatment
- Getting back to life and good health



# Reducing Cancer Risk

- Cancer is a defect in regulation
- Cancer cells are mostly normal
- The imbalance is potentially reversible
- Using killing strategies <u>alone</u> may be counterproductive
- Host response is critical
- Cancer growth rates are variable, depending on the regulatory balance
- ref: Schipper et al J. Clinical Oncology 1995;13:801

### The Good News

The microenvironment surrounding a tumor cell can promote or discourage tumor progression independent of tumor genetics

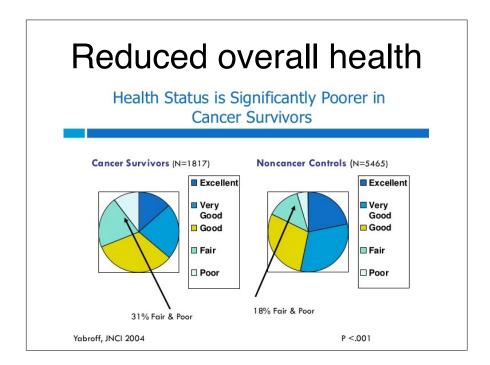
(Tumor suppressor or promoter genes)

Int. J. Cancer 2003;107:688

JNCI 2002:941494

### Late effects of treatment

- · New cancers caused by treatment
- Cardiovascular disease
- Obesity/diabetes
- Osteoporosis
- · Reduced energy
- Poor quality of daily living (JNCI)



# Does diet really matter?

Curr Nutr Rep (2016) 5:9-17 DOI 10.1007/s13668-015-0141-7



CANCER (MF LEITZMANN, SECTION EDITOR)

#### Does a Mediterranean-Type Diet Reduce Cancer Risk?

Lukas Schwingshackl 1,2 - Georg Hoffmann 2

Observational studies provide new evidence suggesting that high adherence to a Mediterranean diet is associated with reduced risk of overall cancer mortality as well as a reduced risk of incidence of several cancer types (especially cancers of the colorectum, aerodigestive tract, breast, stomach, pancreas, prostate, liver, and head and neck).

### **Breast Cancer**

MA Intern Med. 2015 Nov;175(11):1752-60. doi: 10.1001/jamainternmed.2015.4838.

Mediterranean Diet and Invasive Breast Cancer Risk Among Women at High Cardiovascular Risk in the PREDIMED Trial: A Randomized Clinical Trial.

RESULTS: After a median follow-up of 4.8 years, we identified 35 confirmed incident cases of breast cancer. Observed rates (per 1000 personyears) were 1.1 for the Mediterranean diet with extra-virgin olive oil group, 1.8 for the Mediterranean diet with nuts group, and 2.9 for the control group. The multivariable-adjusted hazard ratios vs the control group were 0.32 (95% Cl, 0.13-0.79) for the Mediterranean diet with extra-virgin olive oil group and 0.59 (95% Cl, 0.26-1.35) for the Mediterranean diet with nuts group. In analyses with yearly cumulative updated dietary exposures, the hazard ratio for each additional 5% of calories from extra-virgin olive oil was 0.72 (95% Cl, 0.57-0.90).

· Olive oil reduces breast cancer risk up to 68%

### Olive oil & Herceptin

BMC Cancer, 2007; 7: 80. Published online 2007 May 9, doi: 10.1186/1471-2407-7-80 PMCID: PMC1878493

Olive oil's bitter principle reverses acquired autoresistance to trastuzumab (Herceptin™) in HER2-overexpressing breast cancer cells

Javier A Menendez,<sup>⊠1,2,3</sup> Alejandro Vazquez-Martin, <sup>1,2,3</sup> Ramon Colomer, <sup>4</sup> Joan Brunet, <sup>1,2,3</sup> Alegria Carrasco-Pancorbo, <sup>5</sup> Rocio Garcia-Villalba, <sup>5</sup> Alberto Fernandez-Gutierrez, <sup>5</sup> and Antonio Segura-Carretero (X5)

Author information ▶ Article notes ▶ Copyright and License information ▶ Disclaime

#### Results

Among EVOO polyphenols tested, oleuropein aglycone was the most potent EVOO phenolic in decreasing breast cancer cell viability. HER2 gene-amplified SKBR3 cells were ~5-times more sensitive to oleuropein aglycone than HER2-negative MCF-7 cells. Retroviral infection of the HER2 oncogene in MCF-7 cells resulted in a "SKBR3-assimilated" phenotype of hypersensitivity to oleuropein aglycone. An up to 50-fold increase in the efficacy of trastuzumab occurred in the presence of oleuropein aglycone. A preclinical model of acquired autoresistance to trastuzumab (SKBR3/Tzb100 cells) completely recovered trastuzumab sensitivity (> 1,000-fold sensitization) when co-cultured in the presence of oleuropein aglycone. Indeed, the nature of the interaction between oleuropein aglycone and trastuzumab was found to be strongly synergistic in Tzb-resistant SKBR3/Tzb100 cells. Mechanistically, oleuropein aglycone treatment significantly reduced HER2 ECD cleavage and subsequent HER2 auto-phosphorylation, while it dramatically enhanced Tzb-induced down-regulation of HER2 expression.

### Diet & Colon Cancer Vegetarian Dietary Patterns and the Risk of

### Colorectal Cancers FREE

Michael J. Orlich, MD, PhD1,2; Pramil N. Singh, DrPH1; Joan Sabaté, MD, DrPH1,2; Jing Fan, MS1; Lars Sveen1; Hannelore Bennett, MS<sup>1</sup>; Synnove F. Knutsen, MD, PhD<sup>1,2</sup>; W. Lawrence Beeson, DrPH<sup>1</sup>; Karen Jaceldo Siegl, DrPH, MS<sup>1,2</sup>; Terry L. Butler, DrPH<sup>1</sup>; R. Patti Herring, PhD<sup>1</sup>; Gary E. Fraser, PhD, MD<sup>1,2</sup>

JAMA Intern Med. 2015;175(5):767-776. doi:10.1001/jamainternmed.2015.59

Design, Setting, and Participants The Adventist Health Study 2 (AHS-2) is a large, prospective, North American cohort trial including 96 354 Seventh-Day Adventist men and women recruited between January 1, 2002, and December 31, 2007. Follow-up varied by state and was indicated by the cancer registry linkage dates. Of these participants, an analytic sample of 77 659 remained after exclusions.

Results During a mean follow-up of 7.3 years, 380 cases of colon cancer and 110 cases of rectal cancer were documented. The adjusted hazard ratios (HRs) in all vegetarians combined vs nonvegetarians were 0.78 (95% CI, 0.64-0.95) for all colorectal cancers, 0.81 (95% CI, 0.65-1.00) for colon cancer, and 0.71 (95% CI, 0.47-1.06) for rectal cancer. The adjusted HR for colorectal cancer in vegans was 0.84 (95% CI, 0.59-1.19); in lacto-ovo vegetarians, 0.82 (95% CI, 0.65-1.02); in pescovegetarians, 0.57 (95% CI, 0.40-0.82); and in semivegetarians, 0.92 (95% CI, 0.62-1.37) compared with nonvegetarians. Effect estimates were similar for men and women and for black and nonblack individuals.

Conclusions and Relevance Vegetarian diets are associated with an overall lower incidence of colorectal cancers. Pescovegetarians in particular have a much lower risk compared with nonvegetarians. If such associations are causal, they may be important for primary prevention of colorectal cancers.

## Dietary Fat & Colon Cancer

Gastroenterology, 2015 Dec;149(7):1884-1895.e4. doi: 10.1053/j.gastro.2015.07.064. Epub 2015 Aug 7.

Prostaglandin E2 Promotes Colorectal Cancer Stem Cell Expansion and Metastasis in Mice. Wang D1, Fu L1, Sun H1, Guo L1, DuBois RN2.

RESULTS: Levels of PGE2 correlated with colonic CSC markers (CD133, CD44, LRG5, and SOX2 messenger RNAs) in human colorectal carcinoma samples. Administration of PGE2 to Apc(Min/+) mice increased tumor stem cells and tumor burden, compared with controls. NSG mice given PGE2 had increased numbers of cecal CSCs and liver metastases compared with controls after intracecal injection of LS-174T or human primary CRC cells. Alternatively, celecoxib, an inhibitor of prostaglandin-endoperoxide synthase 2, reduced polyp numbers in Apc(Min/+) mice, liver metastasis in NSG mice with orthotopic tumors, and numbers of CSCs in Apc(Min/+) and NSG mice. Inhibitors or knockdown of PGE2 receptor 4 (EP4), phosphoinositide 3-kinase (PI3K) p85α, extracellular signal-regulated kinase 1 (ERK1), or nuclear factor (NF)-κB reduced PGE2-induced sphere formation and expansion of LS-174T and/or human primary CRC cells. Knockdown of ERK1 or PI3K p85α also attenuated PGE2-induced activation of NF-kB in LS-174T cells. An EP4 antagonist reduced the ability of PGE2 to induce CSC expansion in orthotopic tumors and to accelerate the formation of liver metastases. Knockdown experiments showed that NF-κB was required for PGE2 induction of CSCs and metastasis in mice

CONCLUSIONS: PGE2 induces CSC expansion by activating NF-κB, via EP4-Pl3K and EP4-mitogen-activated protein kinase signaling, and promotes the formation of liver metastases in mice. The PGE2 signaling pathway therefore might be targeted therapeutically to slow CSC expansion and colorectal cancer progression.

# How Foods Stop Illness

- Antioxidants slow damage to DNA
- Nutrients can help repair DNA
- Phytochemicals change epigenetic gene expression
- EFA's regulate growth signals and inflammation
- Fiber enhances cell-cell communication
- Phytochemicals enhance detox pathways



# Simple food guidelines

- Eat half your plate as vegetables and salad
- Eat more beans, nuts, fish, olive oil, whole grains (in moderation)
- · Eat a rainbow of colors
- · Limit sweets, carbs, starches
- · Limit alcohol
- · Limit junk food
- Limit red meats and dairy



# A handful of "super- foods"

· Extra virgin olive oil

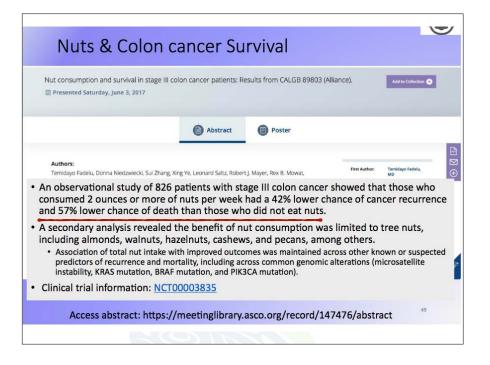
- · Berries
- · Nuts
- Greens
- · Green tea











### Nuts & Prostate Cancer



### What about vitamins?



Breast Cancer Res Treat (2013) 141:495-505 DOI 10.1007/s10549-013-2712-x

#### EPIDEMIOLOGY

#### Multivitamin and mineral use and breast cancer mortality in older women with invasive breast cancer in the women's health initiative

S. Wassertheil-Smoller  $\cdot$  A. P. McGinn  $\cdot$  N. Budrys  $\cdot$  R. Chlebowski  $\cdot$  G. Y. Ho $\cdot$  K. C. Johnson  $\cdot$  D. S. Lane  $\cdot$  W. Li  $\cdot$  M. L. Neuhouser  $\cdot$  J. Saquib  $\cdot$  J. M. Shikany  $\cdot$  Y. Song  $\cdot$  C. Thomson

Received: 14 August 2013/Accepted: 25 September 2013/Published online: 9 October 2013 © Springer Science+Business Media New York 2013

Abstract Multivitamin use is common in the United States. It is not known whether multivitamins with minerals supplements (MVM) used by women already diagnosed with invasive breast cancer would affect their breast cancer mortality risk. To determine prospectively the effects of MVM use on breast cancer mortality in postmenopausal women diagnosed with invasive breast cancer, a prospective cohort study was conducted of 7,728 women aged 50–79 at enrollment in the women's health initiative (WHI) in 40 clinical sites across the United States diagnosed with incident invasive breast cancer during WHI and followed for a mean of 7.1 years after breast cancer diagnosis. Use of MVM supplements was assessed at WHI baseline visit

and at visit closest to breast cancer diagnosis, obtained from vitamin pill bottles brought to clinic visit. Outcome was breast cancer mortality. Hazard ratios and 95 % confidence intervals (CIs) for breast cancer mortality comparing MVM users to non-users were estimated using Cox proportional hazard regression models. Analyses using propensity to take MVM were done to adjust for potential differences in characteristics of MVM users versus non-users. At baseline, 37.8 % of women reported MVM use. After mean post-diagnosis follow-up of 7.1 ± 4.1 (SD) years, there were 518 (6.7 %) deaths from breast cancer. In adjusted analyses, breast cancer mortality was 30 % lower in MVM users as compared to non-users (HR = 0.70;

#### RESEARCH ARTICLE

### Serum 25-Hydroxyvitamin D Concentrations ≥40 ng/ml Are Associated with >65 % Lower Cancer Risk: Pooled Analysis of Randomized Trial and Prospective Cohort Study

Sharon L. McDonnell<sup>1\*</sup>, Carole Baggerly<sup>1</sup>, Christine B. French<sup>1</sup>, Leo L. Baggerly<sup>1</sup>, Cedric F. Garland<sup>2</sup>, Edward D. Gorham<sup>2</sup>, Joan M. Lappe<sup>3</sup>, Robert P. Heaney<sup>3</sup>

- 1 GrassrootsHealth, Encinitas, California, United States of America, 2 Department of Family Medicine and Public Health, University of California San Diego, La Jolla, California, United States of America,
- 3 Department of Medicine, Creighton University, Omaha, Nebraska, United States of America
- \* sharon@grassrootshealth.org

#### Results

Age-adjusted cancer incidence across the combined cohort (N = 2,304) was 840 cases per 100,000 person-years (1,020 per 100,000 person-years in the Lappe cohort and 722 per 100,000 person-years in the GrassrootsHealth cohort). Incidence was lower at higher concentrations of 25(OH)D. Women with 25(OH)D concentrations  $\geq$ 40 ng/ml had a 67% lower risk of cancer than women with concentrations <20 ng/ml (HR = 0.33, 95% CI = 0.12–0.90).

### Vitamin D Deficiency and Reduced Hodgkin Lymphoma Survival

Nancy A. Melville

June 18, 2018

STOCKHOLM — Vitamin D deficiency is strongly associated with lower rates of progression-free survival (PFS) and overall survival (OS) in patients with Hodgkin lymphoma, independently of key factors that include tumor mass, patients' clinical condition, and the type of treatment received, according to new research.

The finding was presented here at the European Hematology Association (EHA) 2018 Congress.

Hodgkin lymphoma was the cause of death of 24 patients (38%) who were vitamin D deficient, compared to only four patients (22%) whose level of vitamin D was insufficient, and three patients (18%) who had sufficient levels of vitamin D.

In addition, total deaths of all causes were higher in patients who were vitamin D deficient (n = 63; 36%) compared to those whose levels were insufficient (n = 18; 22%) or sufficient (n = 17; 18%).

"It appears the differences in overall survival rates are mainly due to significantly more Hodgkin lymphomaassociated deaths among those who were vitamin D deficient," Borchmann said.

# Gamma tocopherol

In 10,456 men those who had highest blood level of gamma-tocopherol were five times less likely to get prostate cancer.

Selenium and alpha-tocopherol also reduced prostate cancer incidence, but <u>only</u> when gamma-tocopherol level is high.

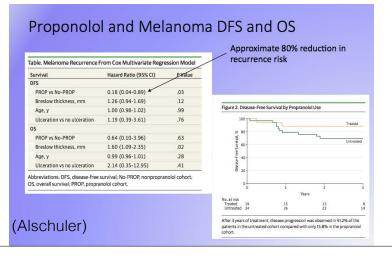
- Helzlsouer et al.JNCI. 2000;92:2018

### Stress

- · Concerns about recurrence
- Concerns about expensive meds/scans etc
- Money/job/family/aging
- Directly impacts BP, heart, hypothalamus
- immune function, joy, problem solving, quality of life
- · Social isolation



# Stress, Immunity & Survival



#### Results

- Among 9267 women, there were 1448 recurrences and 1521 deaths, with 990 due to BC.
   The follow-up from diagnosis ranged from 0.2 to 20.9 years (median, 10.6 years).
- · Socially isolated women were more likely to:
  - · be Caucasian, college-educated, and nulliparous.
  - have lower levels of physical activity, be current smokers, drink more than recommended, and be obese.
  - be associated with a lower likelihood of receiving chemotherapy or hormonal therapy and a higher likelihood of lumpertomy.
- Women with smaller social networks had an 82% higher risk of non-BC mortality (HR, 1.82; 95% CI, 1.44-2.30; P for trend < .001).</li>
- After adjustment for potential confounding variables in LACE, NHS, and SBCSS, socially isolated women had 43% higher risk of recurrence (hazard ratio [HR], 1.43; 95% CI, 1.18-1.74; P for trend < .001), 64% increased risk of BC-specific mortality (HR, 1.64; 95% CI, 1.33-2.03; P for trend < .001), and 69% increased risk of total mortality (HR, 1.69; 95% CI, 1.43-1.99; P for trend < .001) in comparison with socially integrated women</li>
  - Adjusting for lifestyle and treatment factors attenuated the results for the linear social network variable by 13% for recurrence, by 18% for BC mortality, and by 26% for total mortality, but associations remained significant after adjustment for these potential mediating factors.
  - Associations did not differ by age, time since diagnosis, estrogen receptor/progesterone receptor status, HER2 status, or treatment
  - A lack of a spouse/partner and community ties predicted higher BC-specific mortality in older white women but not in other women. However, a lack of relatives and friendship ties predicted higher BCspecific mortality in nonwhite women only.
- Social isolation increases cortisol and catecholamine levels. [Jacubowski JA, et al. Physiol Behav. 2015 Dec 1;152(Pt A):106-11.]

(L. Alschuler)

# Stress management

- Mindfulness
- Yoga
- · Tai chi
- Joy
- · "Nature bathing"
- Visualization





### Restore Cortisol Rhythm with Exercise

11

J. Endocrinol. Invest. 31: 587-591, 2008

RAPID COMMUNICATION

#### Exercise and circulating cortisol levels: The intensity threshold effect

E.E. Hill<sup>1</sup>, E. Zack<sup>1</sup>, C. Battaglini<sup>1</sup>, M. Viru<sup>2</sup>, A. Viru<sup>2</sup>, and A.C. Hackney<sup>1</sup>

'Endocrine Section, Applied Physiology Laboratory, Department of Exercise & Sport Science, University of North Carolina, Chapel Hill, North Carolina, USA; Institute of Exercise Biology and Physiotherapy, Tartu University, Tartu, Estonia

12 active moderately trained men performed 30 min of exercise at intensities of 40, 60, and 80% of their VO2max, as well as a 30-min resting-control session involving no exercise on separate days. Confounding factors such as time of day-circadian rhythms, prior diet-activity patterns, psychological stress, and levels of exercise training were controlled. Cortisol and ACTH were assessed in blood collected immediately before (pre-) and after (post-) each experimental session.

Moderate to high intensity exercise provokes increases in circulating cortisol levels. In contrast, low intensity exercise (40%) does not result in significant increases in cortisol levels, but actually resulted in a reduction in circulating cortisol levels.

ercise provokes increases in circulating cortisol levels. These increases seem due to a combination of hemoconcentration and HPA axis stimulus (ACTH). In contrast, low intensity exercise (40%) does not result in significant increases in cortisol levels, but, once corrections for plasma volume reduction occurred and circadian factors were examined, low intensity exercise actually resulted in a reduction in circulating cortisol levels.

J. Endocrinol. Invest. 31: 587-591, 2008)

\*\*ZOOB. Editine Kurtis\*\*

Hill EE, J Endocrinol Invest, 2008 Jul;31(7):587-91

# Physical Activity Significantly Boosts Survival in Cancer Patients

Roxanne Nelson, BSN, RN

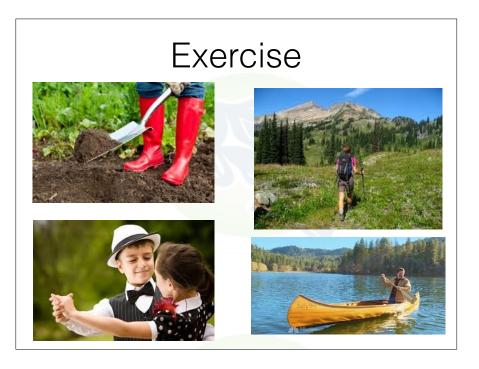
April 23, 2018

CHICAGO — Cancer patients who are physically active both before and after treatment are 40% more likely to survive compared to those who are sedentary, according to new findings.

The association between physical activity and mortality was observed across eight cancer types. Importantly, the findings held after adjustment for sex, tumor stage, smoking status, and body mass index.

More importantly, Cannioto noted, was the improvement in survival among patients who had previously been sedentary. "Patients who reported never doing anything in terms of recreational activity in the decade prior to diagnosis, and then reported doing something around the time of diagnosis and afterwards, remarkably had about a 25% to 28% improvement in survival compared to those who remained inactive," she said. "We saw that starting physical activity after diagnosis is beneficial."

The message is that it's never too late to start exercising. Dr Rikki Cannioto





# From herb to drug

- · Willow to aspirin
- · Foxglove to digitalis
- · Goats Rue to metformin
- · Poppy to codeine
- · Rauwolfia to reserpine
- · Ma Huang to ephedra
- · Belladona to atropine
- · Yew to taxol
- · Periwinkle to Vincristine



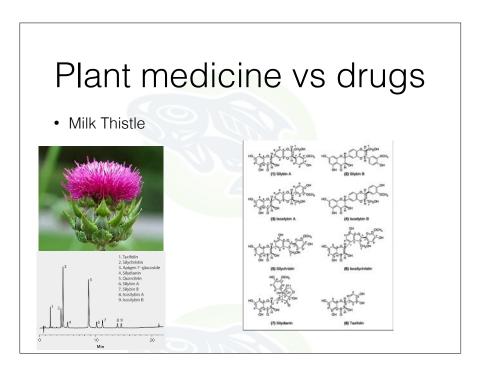
# Therapeutic Windows

- Foods
- herbs/vitamins
- toxic herbs
- drugs
- poisons







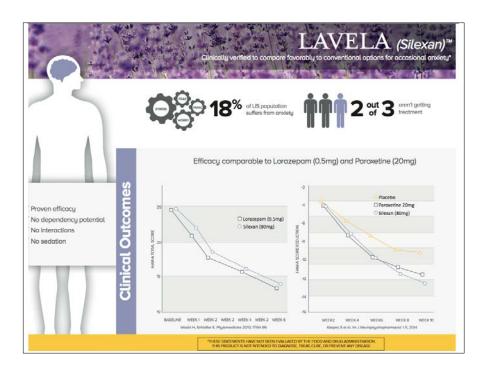


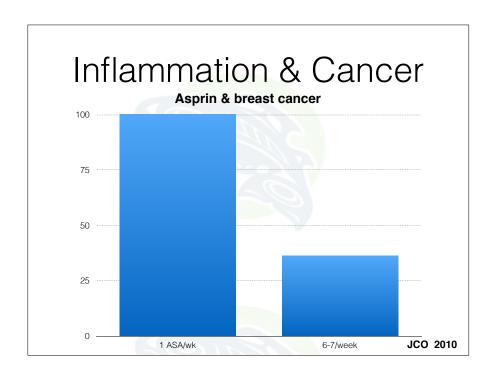


### Rhodiola

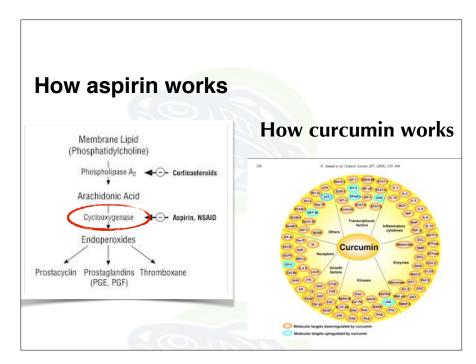
- Traditional adaptogen
- Helpful in chronic stress & "burnout"
- Depression
- Supports mental clarity
- Inhibits tumor growth
- Supports chemotherapy effects

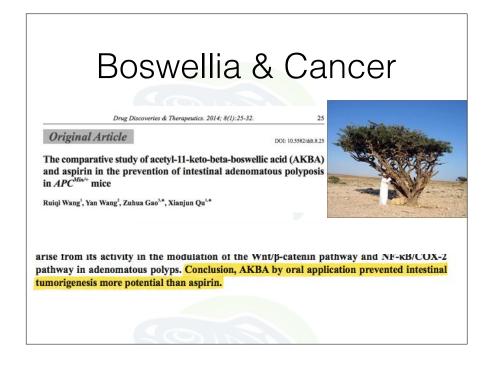






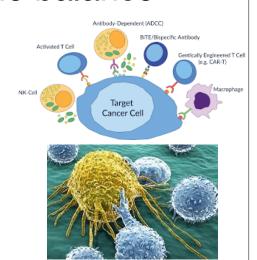






### Immune balance

- Effective immune surveillance and activity is a crucial component of prevention
- After ca tx many people have compromised immune fxn
- Herbal medicines can stimulate a robust defense even when total white cells are low



# Herbal Immune Support

- Stimulate proliferation of immune cells
- Increase natural killer cells and activity
- Increase desirable cytokines/ decrease undesirables
- Protect against opportunistic infections





# Astragalus

- Traditionally used to tonify Qi and blood
- Modern use: anemia, immune support, fatigue
- Increases NK cell, LAK cytotoxicity, anti-viral
- · Safe for long term use





### Echinacea

- aka: purple coneflower
- · can use root, leaves, whole plant
- first used by Native Americans
- uses: immune support, anti-viral, wound healing, anti-inflammatory
- CAN be used long term



### Medicinal Mushrooms

- Mushrooms do not kill tumors directly but act through the immune System (Appl Microbiol Biotechnol 2002;60:258) (Anticancer res 2000;20:4707)
- Reishi suppresses growth of breast cancer cells by reducing inflammation (Nutr Cancer 2004;49:209)





### Commensal *Bifidobacterium* promotes antitumor immunity and facilitates anti-PD-L1 efficacy

Avelet Sivan, 1\* Leticia Corrales, 1\* Nathaniel Hubert, 2 Jason B. Williams, 1 Keston Aquino-Michaels, 3 Zachary M. Earley, 2 Franco W. Benyamin, Yuk Man Lei, Bana Jabri, Maria-Luisa Alegre, Eugene B. Chang, Thomas F. Gajewski1,24

Sciencexpress/sciencemag.org/content/early/recent / 5 November 2015/ Page 1 / 10.1126/science.aac4255

T cell infiltration of solid tumors is associated with favorable patient outcomes, yet the mechanisms underlying variable immune responses between individuals are not well understood. One possible modulator could be the intestinal microbiota. We compared melanoma growth in mice harboring distinct commensal microbiota and observed differences in spontaneous antitumor immunity, which were eliminated upon cohousing or following fecal transfer, 16 S ribosomal RNA sequencing identified Bifidobacterium as associated with the antitumor effects. Oral administration of Bifidobacterium alone improved tumor control to the same degree as anti-PD-L1 therapy (checkpoint blockade), and combination treatment nearly abolished tumor outgrowth. Augmented dendritic cell function leading to enhanced CD8<sup>+</sup> T cell priming and accumulation in the tumor microenvironment mediated the effect. Our data suggest that manipulating the microbiota may modulate cancer immunotherapy.

### Traditional Uses

- Stomach/Digestive complaints: peppermint, lemon balm, bitters, ginger, fennel, licorice
- Brain/Moods: Valerian, hops, lemon balm, St John's Wort, lavender
- Colds/flu: elderberry, echinacea, yarrow, lomatium, andrographis, zinc lozenges, garlic, star anise

### Traditional Uses

- Constipation: senna, cascara, caraway seed, psyllium
- Bitters: Gentian, wormwood, ginger, angelica, angustora bitters

# Making salves

- 4 oz of base (coconut oil or olive oil & beeswax)
- add active ingredient (calendula, yarrow, green tea)
- let herb sit in warm oil for 30 minutes
- add essential oil or antioxidant (vit. E, chamazulin)

### Home first aid kit

• Ginger

Ashwaganda

Garlic

Peppermint

Echinacea

Chamomile

Elderberry

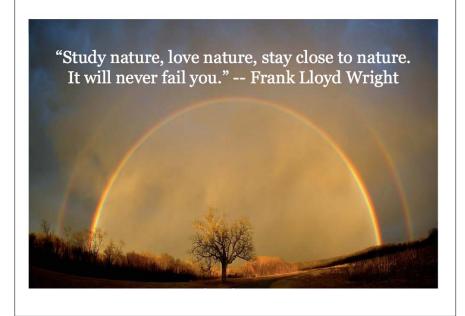
Valerian/Hops

• Thyme oil

Aloe

Curcumin

Bitters



# Quality control

- · 70% of products fail to meet label claims
- identity, potency, purity
- stick with quality brands
- · claims mean nothing

# Goals for Wellness (& Prevention)

- · Improve nutritional status
- · Reduce inflammation
- · Reduce insulin
- · Maintain healthy weight
- Support immunity
- Reduce stress and stress hormones



# You are in charge



# Take home message: Things to reduce/stop

- · Smoking
- · Alcohol
- · Sugar rich foods
- · Artificial foods/junk foods
- · Animal fats
- · Television/ inactivity/ sitting







# Summary

- · Healthy food
- · Sleep
- · Manage stress
- · Maintain weight
- · Stay active
- · Have fun

· Choose health



