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Department of Hematology Oncology, Bone Marrow Transplant
Program Director, Hematology Oncology Fellowship University of Arizona
Co-Director, Integrative Medicine in Hematology Oncology





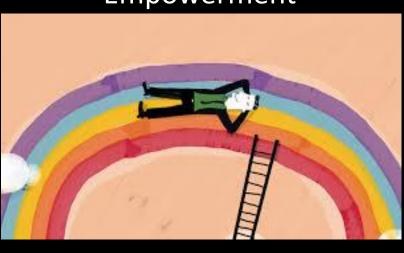
"CHAOS"

Integrative Oncology



THE DRIVERS SEAT

"Empowerment"



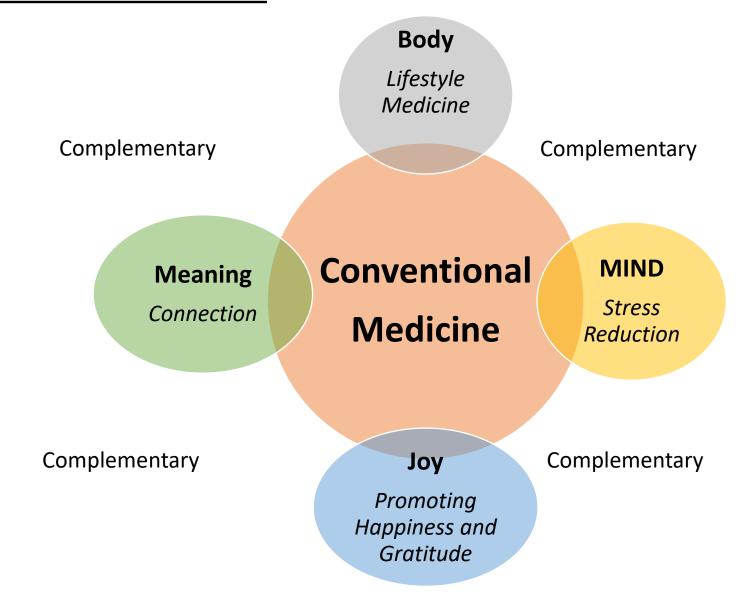
Integrative Oncology

• "is a patient-centered, evidence-informed field of cancer care that utilizes mind and body practices, natural products, and/or lifestyle modifications from different traditions alongside conventional cancer treatments.



Integrative oncology aims to optimize health, quality of life, and clinical outcomes across the cancer care continuum and to empower people to prevent cancer and become active participants before, during, and beyond cancer treatment."

The Four Pillars of Wellness



You Have the Power to Promote Your Own Wellness

Why Is Integrative Oncology Important?

Decrease Inflammation

Decrease MPN Symptom Burden

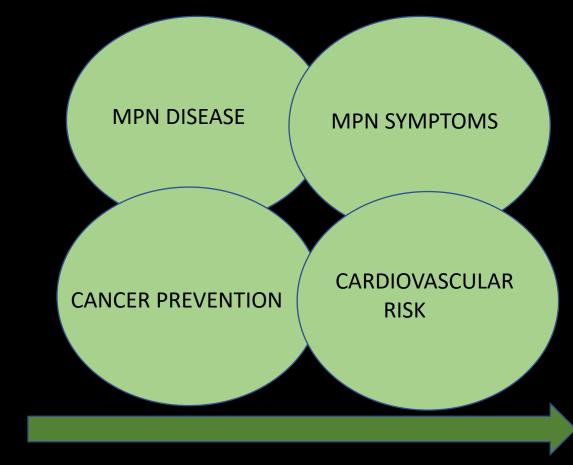
Decrease Cardiovascular Risk Factors

Desire for and current use of complementary approaches

Potential to impact outcomes and treatment toxicity

Potential to decrease cost of care

YOUR TREATMENT GOALS



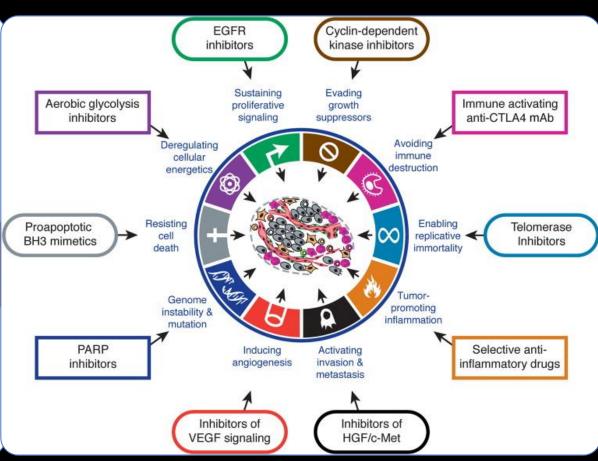
DECREASE INFLAMMATION

Long Survival WITH HIGH QUALITY OF LIFE

Tumor Promoting inflammation

 Chronic infections, obesity, smoking, alcohol consumption, environmental pollutants and high fat diets are now recognized as major risk factors for most common types of cancer; and, importantly, all these risk factors are linked to cancer through inflammation.





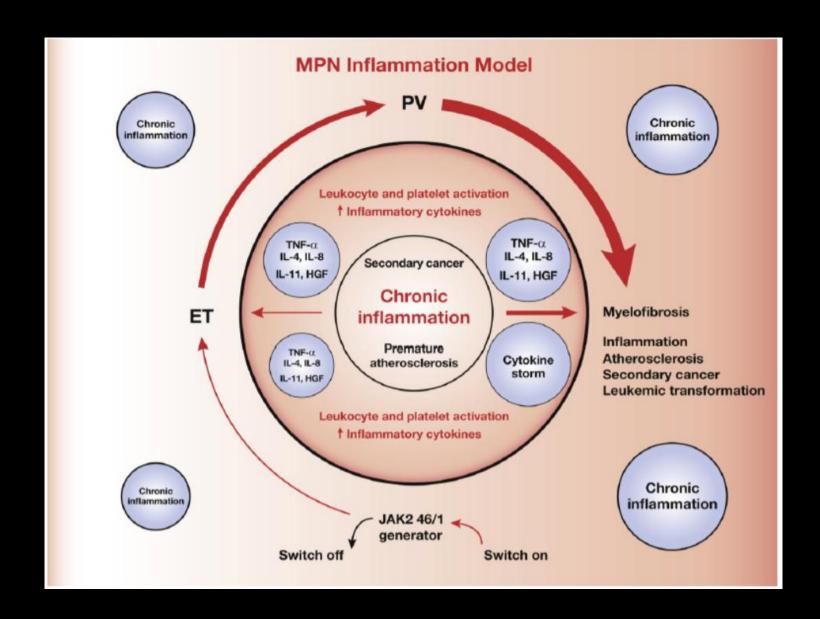
Hallmarks of Cancer, Hanahan and Weinberg 2011. Cancer related-inflammation, Mantovani et al, Nature 2008.

MPN Inflammation

►Inflammation (hs CRP)

correlates with MPN outcomes:

- -Increased risk of major thrombosis
- -Shortened leukemia free survival



How can you quiet inflammation?

LIFESTYLE

The Backbone of Integrative Health

<u>Diet and Exercise</u> are potent modulators of inflammation.

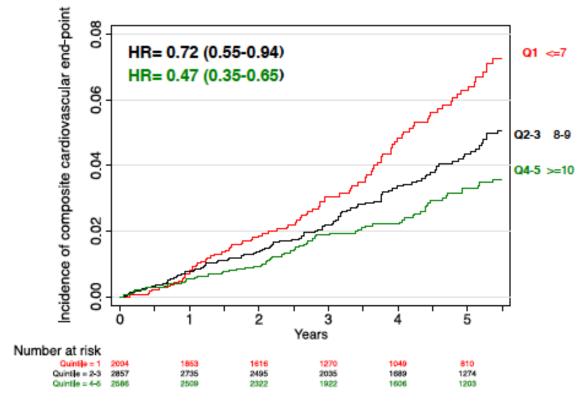
Furman, et al. Nature Medicine, 2019.



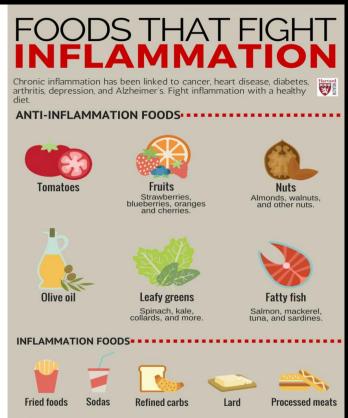
"LET FOOD BE THY MEDICINE AND MEDICINE BE THY FOOD"
-HIPPOCRATES



Benefits of Mediterranean Diet



- 1. Use of olive oil as the main culinary fat
- Consumption of ≥4 tablespoons/d of olive oil (including oil used for frying, salads, out-of-house meals, etc.)
- 3. Consumption of ≥ 2 servings/d of vegetables
- 4. Consumption of ≥3 servings/d of fruits
- Consumption of <1 serving/d of red meat, hamburger or meat products (ham, sausage, etc.)
- Consumption of <1 serving/d of butter, margarine, or cream
- Consumption of <1 serving/d of sweetened and/or carbonated beverages
- 8. Consumption of ≥1 serving/d of wine
- 9. Consumption of ≥3 servings/week of legumes
- 10. Consumption of ≥3 servings/week of fish or shellfish
- 11. Consumption of <3 servings/week of commercial sweets or pastries (not homemade), such as cakes, cookies, biscuits or custard
- 12. Consumption of ≥3 servings/week of nuts (including peanuts)
- Preferential consumption of chicken, turkey or rabbit meat instead of veal, pork, hamburger or sausage
- 14. Consumption of ≥2 servings/week of sofrito, a sauce made with tomato and onion, leek or garlic and simmered with olive oil.



Martinez, et al. PREDIMED Study. Progress in Cardiovascular Disease. 2015.

Mediterranean diet associated with lower CRP.

Lahoz, et al. Nutrients 2018.

Other dietary considerations: Intermittent fasting, ketogenesis, microbiome

AICR RECOMMENDATIONS FOR CANCER PREVENTION

A Blueprint to Beat Cancer

To prevent cancer, people should aim to follow as many of the 10 Cancer Prevention Recommendations as possible. However, any change you make that works toward meeting the goals set out in the Recommendations will go some way to reducing your cancer risk.

BE A HEALTHY WEIGHT

Keep your weight within the healthy range and avoid weight gain in adult life

Be physically active as part of everyday life – walk more and sit less

BE PHYSICALLY ACTIVE





EAT A DIET RICH IN WHOLE GRAINS, VEGETABLES. FRUITS AND BEANS

Make whole grains, vegetables, fruits and pulses (legumes) such as beans and lentils a major part of your usual daily diet

LIMIT CONSUMPTION OF RED AND PROCESSED MEAT

Eat no more than moderate amounts of red meat, such as beef, pork and lamb. Eat little, if any, processed meat



LIMIT CONSUMPTION OF SUGAR-SWEETENED DRINKS

Drink mostly water and unsweetened drinks



LIMIT CONSUMPTION OF "FAST FOODS" AND OTHER PROCESSED FOODS HIGH IN FAT, STARCHES OR SUGARS

Limiting these foods helps control calorie intake and maintain a healthy weight



LIMIT ALCOHOL CONSUMPTION

For cancer prevention, it's best not to drink alcohol



FOR MOTHERS: BREASTFEED YOUR BABY, IF YOU CAN

Breastfeeding is good for both mother and baby



AFTER A CANCER DIAGNOSIS: FOLLOW OUR RECOMMENDATIONS, IF YOU CAN

Check with your health professional about what is right for you



DO NOT USE SUPPLEMENTS FOR CANCER PREVENTION

Aim to meet nutritional needs through diet alone



Not smoking and avoiding other exposure to tobacco and excess sun are also important in reducing cancer risk. Following these Recommendations is likely to reduce intakes of salt, saturated and trans fats, which together will help prevent other non-communicable diseases.

University of Arizona Anti-Inflammatory Food Pyramid



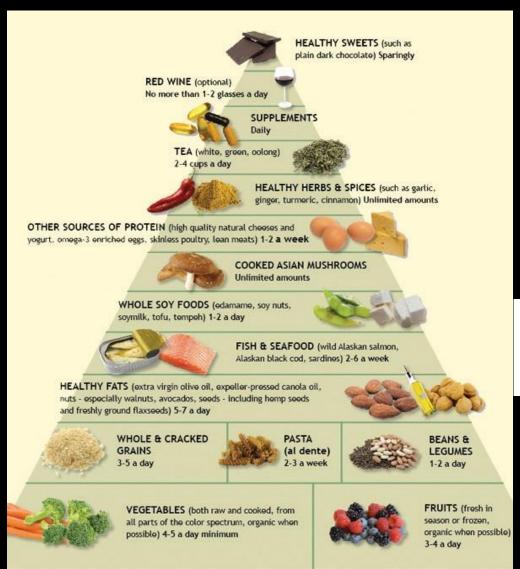
Asian Mushrooms: Contain Polysaccharides (B-D glucan) that are immunostimulants, Improved QOL



n-3/n-6 ratio



Sulphorophane: activator of antioxidant proteins





Green tea (EGCG)inhibits DNA
transferases, leading
to demethylation
(inhibition) of tumor
promoter genes



Curcumin, cruciferous, soy, grapes, garlic effect the epigenome

**Avoid Processed Foods, Sugar Sweetened Drinks

Physical Activity

- ▶ Decreased inflammation, obesity, and stress -Plaisance, Sports Med, 2006
- Physical activity associated with reduced risk and increased survival for several cancers.

-PA and Cancer: A SR. 2018 PA guidelines advisor committee

► PA improved QOL

-Kolen, 2020

MPN and Yoga



- 62 patients enrolled, 48 completed intervention
- Patients averaged 40 min per week yoga
- Significant decrease in TNF-a from baseline to week 12 (p=0.005)
- Small to moderate effect sizes for sleep disturbance, pain intensity, anxiety, and depression.

RESEARCH ARTICLE

Open Access

Online yoga in myeloproliferative neoplasm patients: results of a randomized pilot trial to inform future research



Jennifer Huberty^{1*}, Ryan Eckert², Amylou Dueck³, Heidi Kosiorek³, Linda Larkey⁴, Krisstina Gowin⁵ and Ruben Mesa²

BMC Complementary and Alternative Medicine

Tai Chi/Qigong

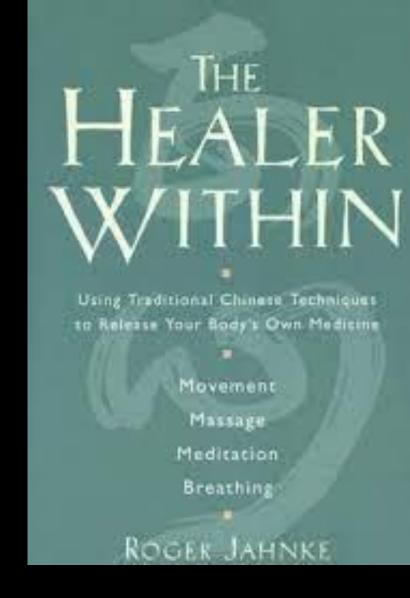
- -Improved cancer related symptoms
- -improved Quality of Life

Wayne Et al. Tai chi and Qigong for Cancer-related symptoms and quality of life: a systematic review and meta-analysis.

J. Cancer surviv. 2018.

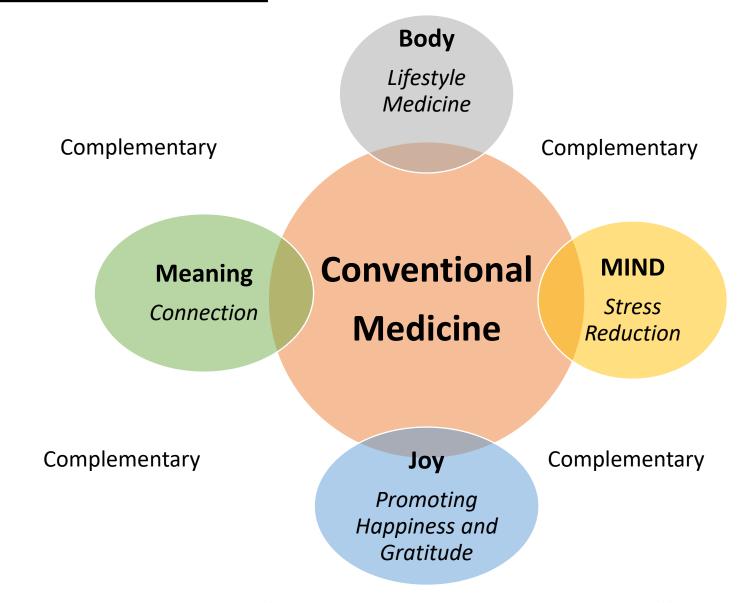
-Improved Immune Function

The effects of Tai Chi on Qigong on Immune responses: A Systematic Review and Meta-Analysis. Medicines. 2020.



https://www.healerwithin.com

The Four Pillars of Wellness



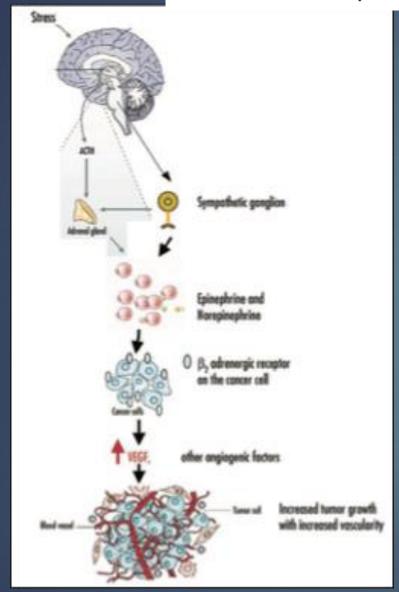
You Have the Power to Promote Your Own Wellness

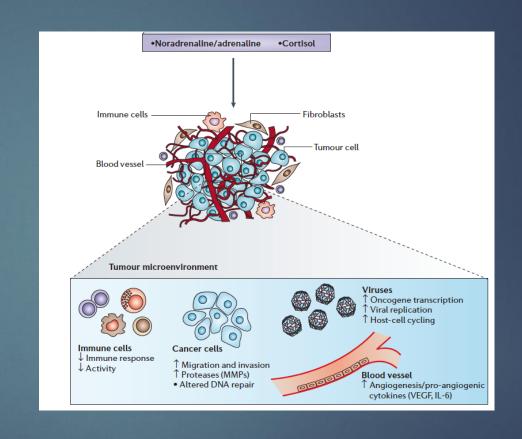
WELLNESS of the MIND



• STRESS TRIGGERS INFLAMMATION

The Neuroendocrine Impact of Chronic Stress on Cancer





NATURE REVIEWS | CANCER

240 MARCH 2006 VOLUME 6



What if you could change your inflammatory profile

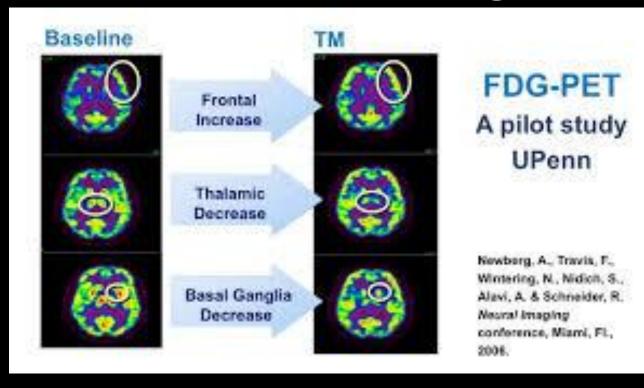
in 5 Minutes per Day?

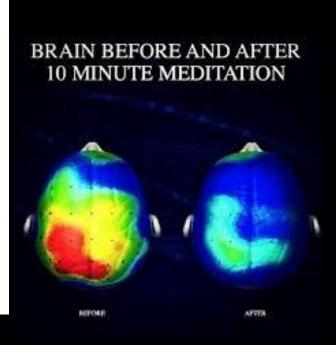
Mediation and Mindfulness

- Improvements in:
- Pain
- Depression
- Cancer related symptoms
- Weight control
- Overall Quality of Life
- Inflammatory Markers
- Brain Anatomy

Functional MRI during meditation







MEDITATION APPS



https://www.headspace.com



https://www.calm.com



https://insighttimer.com/

Meditation modulates neuroplasticity, aging, and inflammatory gene expression in as little as 5 min per day!

Resources





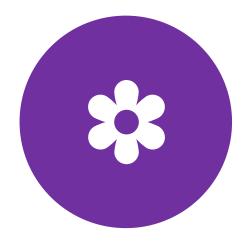
https://apps.apple.com/ca/app/ammindfulness/id1300628961

https://www.mindfulcancerrecovery.com https://www.facebook.com/MindfulnessBasedCancerRecovery

Finding Meaning and Connection

Improved QOL, Decreased Anxiety, Depression Better cancer outcomes





SPIRITUALITY

NATURE

Kelly, et al. The role of religion and spirituality in cancer care: An Umbrella review of the literature. Surg Onc 2022.

Post-Traumatic Growth

- How has your life perspective changed after your diagnosis?
 - -relationships
 - -new possibilities
 - -personal strength
 - -spiritual change
 - -new appreciation for life

Post-Traumatic Growth after Cancer: A Scoping Review of Literature. Menger, et all. Supportive care in Cancer 2021.

Fostering JOY

Two Joyful Intentions

Daily Joy Intention

Sit down and think of instances in your life that you felt the most joyful. Evaluate the circumstances around them. Did they occur during family time? During a favorite activity? Now think about the last week – can you identify a moment of happiness? An important aspect of joy is recognizing that joy can come in small moments. For example, enjoying your morning



cup of coffee: Imagine the aromatic steam emerging from the freshly poured pot, the feeling of warmth in your hands from a favorite cup, the flavor of roasted beans.... this can be a joyful experience!

Take at least 10 minute EVERY DAY to intentionally practice joy. First, name your joyful practice (whatever that means to you!) and then revel in each minute of your practice. When complete, take a moment to have gratitude for your joyful practice.

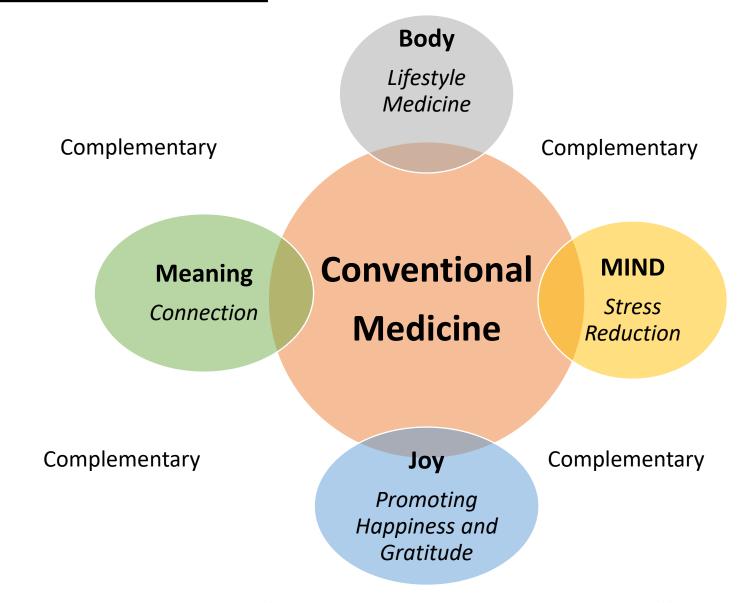
Greeting the Day with Gratitude

Before you get out of bed each morning, start your day by naming three things you are grateful for. Allow your mind to bring these things into clear focus and appreciate every aspect of them. How do they make you feel? See if you can turn up the volume on your gratitude and say a final "thanks" before your rise to greet your day.

"Joy is far less vulnerable than happiness. Joy seems to be a part of the unconditional wish to live, not holding back because our life may not meet our preferences and expectations. Joy seems to be a function of the willingness to accept the whole, and to show up to meet with whatever is there."

-Rachel Naomi Remen, Kitchen Table Wisdom

The Four Pillars of Wellness



You Have the Power to Promote Your Own Wellness

Complementary Care Modalities

- Acupuncture
- Naturopathic care
- Chinese herbal medicine
- Meditation
- Ayurveda
- Hypnosis
- Native Healing, Prayer lodge, ceremony
- Biofeedback
- Essential Oils
- Homeopathy

- Meditation
- Prayer
- Pet Therapy
- Reiki
- Massage
- Cranial Sacral
- Laugh therapy
- Music Therapy
- ETC!

Data suggests 40-60% of cancer patients use complementary and alternative medicine -NHS survey 2012

Acupuncture

- ► Effective and Safe
- ▶Best data for pain and nausea.
- ▶ Can be effective for fatigue, sleep, smoking cessation, etc.

Garcia, et al. JCO. 2013.

**Acupuncture in Hematologic malignancies and transplant. Iskandarani and Deng. 2022. Blood Reviews.





J Natl Cancer Inst Monogr (2017) 2017(52): lgx005

doi: 10.1093/jncimonographs/lgx005 Article

ARTICLE

The National Cancer Institute's Conference on Acupuncture for Symptom Management in Oncology: State of the Science, Evidence, and Research Gaps

Farah Z. Zia, Oluwadamilola Olaku, Ting Bao, Ann Berger, Gary Deng, Arthur Yin Fan, Mary K. Garcia, Patricia M. Herman, Ted J. Kaptchuk, Elena J. Ladas, Helene M. Langevin, Lixing Lao, Weidong Lu, Vitaly Napadow, Richard C. Niemtzow, Andrew J. Vickers, Xin Shelley Wang, Claudia M. Witt, Jun J. Mao

Integrative Medicine for Pain Management in Oncology: Society for Integrative Oncology—ASCO Guideline

Jun J. Mao, MD, MSCE¹; Nofisat Ismaila, MD, MSc²; Ting Bao, MD¹; Debra Barton, PhD³; Eran Ben-Arye, MD⁴; Eric L. Garland, PhD⁵; Heather Greenlee, ND, PhD⁶; Thomas Leblanc, MD⁷; Richard T. Lee, MD⁸; Ana Maria Lopez, MD⁹; Charles Loprinzi, MD¹⁰; Gary H. Lyman, MD, MPH⁶; Jodi MacLeod, BA¹¹; Viraj A. Master, MD, PhD¹²; Kavitha Ramchandran, MD¹³; Lynne I. Wagner, PhD¹⁴; Eleanor M. Walker, MD¹⁵; Deborah Watkins Bruner, PhD¹²; Claudia M. Witt, MD, MBA¹⁶; and Eduardo Bruera, MD¹⁷

Journal of Clinical Oncology®

J Clin Oncol 40:3998-4024. © 2022 by American Society of Clinical Oncology

TABLE 1. Studies on Interventions With Sufficient Evidence to Inform Recommendations

Intervention	Study Type	No.	Pain Symptom Categories
Adult population			
Acupuncture	SRs	17	Al-related joint pain ²⁷⁻³⁰ CIPN ^{31,32} Palliative and survivorship care ³³⁻⁴³
	RCTs	34	Al-related joint pain 19,44-47 General cancer pain 20,48-55 CIPN 56-63 Procedural or surgical pain 64-75
Yoga	RCTs	4	General cancer pain ⁷⁶⁻⁷⁹
Guided imagery and PMR	RCTs	2	General cancer pain ^{80,81}
Hypnosis	SRs	2	Procedural pain ^{82,83}
	RCTs	8	Procedural pain ⁸⁴⁻⁹¹
Reflexology	RCTs	9	General cancer pain ⁹²⁻⁹⁸ CIPN ^{99,100}
Massage	SRs	5°	General cancer pain 101,102 Pain during palliative care 33,40,103
	RCTs	9	General cancer pain 104,105 Pain during palliative care 21,106-111

Abbreviations: Al, aromatase inhibitor; CIPN, chemotherapy-induced peripheral neuropathy; PMR, progressive muscle relaxation; RCT, randomized controlled trial; SR, systematic review.

Botanical Medicine



Resources:

Natural Medicines Database

https://naturalmedicines.therapeuticresearch.com

• Memorial Sloan Kettering Cancer Center: About Herbs

https://www.mskcc.org/cancer-care/diagnosis-treatment/symptom-management/integrative-medicine/herbs/search

Issues with Botanicals

- Source and contamination
- Pharmacologic Interaction
- Safety
- Bioavailability
- Difficultly with Study: Source, Funding
- LOSS of Synergy and "plant medicine"



Finding Quality Dietary Supplements

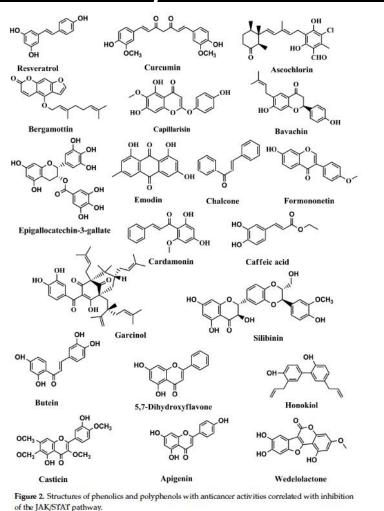
When it comes to supplements, the quality of products may be quite variable. Look for products that have been evaluated by quality assurance companies. They will bear the label print of USP, NSF, or Consumer Labs to ensure the product has been tested, contains what the label indicates, and is free of toxic chemicals.

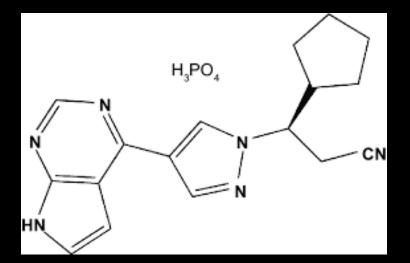






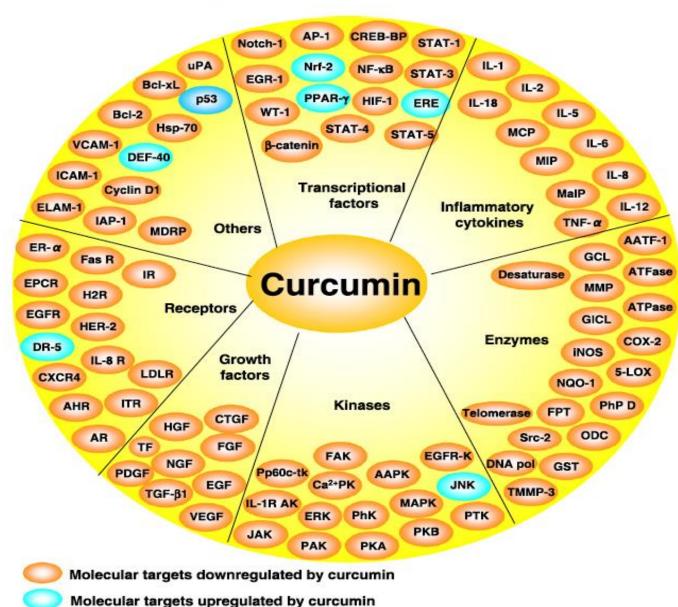
Natural Products that Inhibit JAK/STAT pathway





Ruxolitinib Chemical Structure

P. Anand et al. | Cancer Letters 267 (2008) 133-164



CURCUMIN and CANCER

63 Trials in ClinicalTrials.gov

"Curcumin and Cancer"

Curcumin and cancer: An "old-age" disease with an "age-old" solution

Preetha Anand, Chitra Sundaram, Sonia Jhurani, Ajaikumar B. Kunnumakkara, Bharat B. Aggarwal*

Cytokine Research Laboratory, Department of Experimental Therapeutics, The University of Texas M.D. Anderson Cancer Center, Houston, TX, USA

Table 1 Effect of curcumin alone or in combination on molecular targets of cancer treatment.

Type of cancer	Molecular targets of curcumin				
Prostate cancer ³¹	↑ (Bcl-2 L1, Bcl-2 L11, BAK1, BAX, BBC3, PMAIP 1, p53 protein)				
	J (NFKBIA, AKT 1, Bcl-2, BIRC4, BIRC5, PTEN, NKX 3A, CSF 1R, EGFR, NF-κB)				
	↑↓ (caspase-3, caspase-8)				
Pancreatic	† (caspase-3, PARP, P-ERK1/2, c-Jun protein, p38 MAPK, p53 protein, miR-200)				
cancer ^{32,33}	(NF-κB, cyclin-D1, c-myc protein, Bcl-2, Bcl-xL, clAP-1,MMP, COX-2, VEGF, Sp-1, Sp-3, Sp-4, survivin, VEGF, PGE ₂ , miR-21)				
Colorectal	↑ (DR-5, IGF-1R, IGFBP-3)				
cancer ^{4,34,35}	↓ (COX-2, NF-κB, Bcl-2, Bcl-xL, cyclin D1, c-myc, VEGF, IL-8, MMP-9, PGE₂)				
	↑↓ (EGFR)				
Breast cancer ^{4,36,37}	↑ (TIMP-1, p21, p27)				
	(NF-κB, AP-1, COX-1, COX-2, VEGF, FGF, cyclin E, IL-6, IL-11, TGF-β, MMP-2, MMP-9, MMP-13)				
Multiple myeloma⁴	↑(caspase-7, caspase-9, PARP)				
	【(lkBα, Bd2, Bd-xL, cyclin D1, IL-6, COX-2, NF-κB)				
Leukemia ^{38–40}	†(BAX, caspase-3, caspase-8, p21, p27)				
	↓(Bcl-2, PARP, cyclin D3, STAT3, AKT, NF-κB, Mcl-1, XIAP)				

Curcumin and Pain



Contents lists available at ScienceDirect

Phytomedicine

journal homepage: www.elsevier.com/locate/phymed





Role of curcumin in the management of pathological pain

Jia Sun^a, Fei Chen^{b,c}, Cody Braun^d, Ya-Qun Zhou^a, Heike Rittner^e, Yu-Ke Tian^a, Xiu-Yu Cai^b, Da-Wei Ye^{f,*}



- a Anesthesiology Institute, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China
- b State Key Laboratory of Oncology in South China, Collaborative Innovation Center for Cancer Medicine, Cancer Center, Sun Yat-Sen University, Guangzhou, China
- ^c Department of Oncology, Xiaogan Hospital Affiliated to Wuhan University of Science and Technology, Xiaogan, China
- d UMKC School of Medicine, Kansas City, United States
- ^e Department of Anesthesiology, University Hospital of Würzburg, Würzburg, Germany
- f Cancer Center, Tongji Hospital, Tongji Medical college, Huazhong University of Science and Technology, Wuhan, China

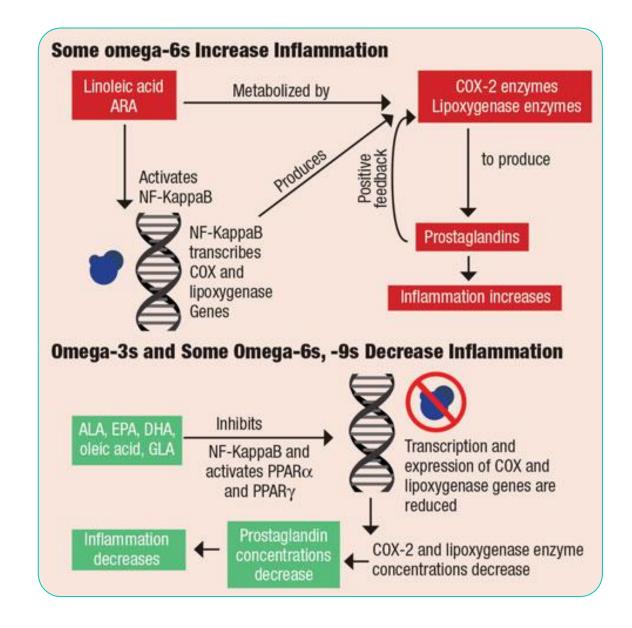
Many clinical trials have showed an analgesic effect of curcuminoids in varies states including

- osteoarthritis
- chronic postsurgical pain
- active rheumatoid arthritis



Laboureyras et al., 2009; Sehgal et al., 2013), and (Chandran and Goel, 2012, Appelboom et al., 2014; Belcaro et al., 2010, 2014; Haroyan et al., 2018; Henrotin et al., 2014, Kuptniratsaikul et al., 2014, 2009; Madhu et al., 2013; Nakagawa et al., 2014; Panahi et al., 2014; Pinsornsak and Niempoog, 2012; Rahimnia et al., 2015; Sterzi et al., 2016

Omega-3 and Inflammation



Omega- 3

- Influence in inflammatory response
- Randomized trial 97 patients with RA with Omega 3 supplementation reduced need for daily NSAID by 30% (p.002) ¹
- Evidence to support supplementation with omega-3s for preventing or treating cancer NOT conclusive
- Potential for drug interaction with Warfarin, Increased INR

- 1. Galarraga B, Ho M, Youssef HM, et al: Rheumatology (Oxford) 47:665-669, 2008.
- 2. Deng, et al. ASCO Post Integrative Oncology Series



The SIMM study: Survey of integrative medicine in myeloproliferative neoplasms

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Krisstina Gowin<sup>1</sup> | Blake T. Langlais<sup>2</sup> | Heidi E. Kosiorek<sup>2</sup> | Amylou Dueck<sup>2</sup> | Denise Millstine<sup>3</sup> | Jennifer Huberty<sup>4</sup>  | Ryan Eckert<sup>5</sup> | Ruben A. Mesa<sup>5</sup>
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SIMM Study

- 858 Patients (338 ET, 188 PV, 315 MF)
- Patients used broad spectrum of integrative therapies (aerobic activity (51%), massage (28%), yoga (25%), nutrition (25%), strength training (23%), acupuncture (19%), mediation (19%), etc.
- Natural products used in prior 6 months by 48% ET, 42% MF, and 45% PV patients
- 20% reported NOT disclosing supplement use to physician
- Only 24% received nutrition advice
- 80% "felt integrative needs were NOT heard by provider"

"Nurture Your Garden"



Set 3 Wellness Goals For Yourself

- 1)
- 2)
- 3)

How will you hold yourself accountable?



Andrew Weil Center for Integrative Medicine



HOW DOES IT WORK?

- •SCORE how satisfied you are in the 7 Core Areas of Health
- •EXPLORE your health by answering simple questions.
- •MAKE A GOAL in any Core Area of Health
- •TAKE ACTION—step-by-step to reach your goal in 1–3 months.

Take Home Points

- ❖ DISCUSS YOUR TREATMENT PLAN WITH PROVIDERS
- Eat Intentionally
- ❖ Move often
- **❖** Breathe
- Manage Stress
- Cultivate Joy



Our research focuses on...

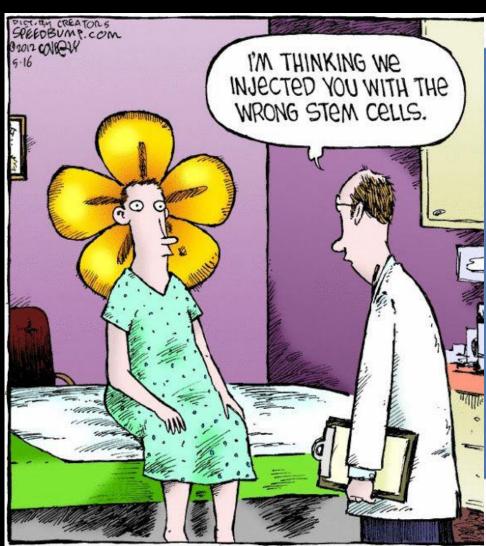
Mindfulness &

MPN Quality of Life Study Group

Thank you!

THANK YOU!

Questions?



TOOMERS

By Buck Cash gowink@email.arizona.edu

WHOA!!!

Stuff to do when you have cancer... #16: Use a Nerf Ball™ to see if your oncologist has a sense of humor.







Anti-Cancer Empowered **Against Cancer** by Brian Lawenda by Lorenzo and Connor Middelmann



Living

Cohen

Cancer as a Wake-Up Call by Laura Nasi

CANCER

WAKE-UP

CALL

M. Lours Noti, MD



The Definitive Guide to Cancer by Lise N. Alschuler & Karolyn A Gazella



Foods to Fight Cancer by Richard Beliveau

NUTRITION AND CANCER















The Cancer **Fighting Kitchen** by Rebecca Katz & Mat Edelson



Nourishing Connections by Cathryn Couch et al

Zest for Life: Mediterranean Anti-Cancer Diet by Conner Middelmann-

Forks Over Knives: The Cookbook by Del Sroufe & Isa Chandra Moskowitz

The How Not to Die Cookbook by Michael Greger, MD

The Cancer Diet Cookbook by Dionne Detraz

MORE

Whitney



Marijuana Gateway to Health by Clint Werner



Medical Marijuana by Mikhail Kogan



Medical Mushrooms: The **Essential Guide** by Christopher

Hobbs



Healing Night by Rubin Naiman



Enjoy Every Sandwich by Lee Lipsenthal



Leaves Falling Gently by Susan Bauer-Wu

Benefits / Neuroscience findings

- Research has found that meditators appear to lose less gray matter that meditating reduced the cognitive decline associated with normal aging.
- More <u>gyrification</u>, or "folding," of the cortex, which is associated with faster mental processing
- Increased thickness in the prefrontal cortex and right anterior insula, areas of the brain associated with attention and awareness of sensations and emotions in oneself and others.
- <u>"significantly larger volumes" of gray matter</u> in the hippocampus, an area crucial to memory and learning.
- Much, much more... help with pain, addiction, depression and anxiety, quality of life, fatigue, etc.

Table 1
Acute phase inflammatory proteins and outcomes of MPN.

Author	Setting	Total patients	Biomarkers	Main results
Barbui 2011 [56]	ET (n = 173) and PV (n = 71) patients	244	hs CRP and PTX-3	PTX-3 and hs-CRP values were significant correlated with JAK2V617F allele burden greater than 50%. Patients with increased levels of hs-CRP (>3 mg/L) had an increased risk of major thrombosis. Conversely, high PTX-3 levels (>4.5ng/ml) decreased the rate of thrombosis
Barbui 2013 [57]	PMF (n = 167) and post PV or ET MF (n = 17)	184	hs CRP	Higher hs-CRP levels (≥7mg/dl) were independently associated with shortened leukemia free survival. Also the annual incidence rate of death was increased in patients with higher levels of hs-CRP.
Lussana 2017 [58]	ET (n = 305) and PV (n = 172) patients	477	hs CRP and PTX-3	Circulating levels of PTX-3 were significantly increased in homozygous JAK2V617F mutation carriers compared to all the other genotypes. The risk of hematological evolution and death from any cause was significantly increased in individuals with high PTX-3 levels, while high levels of PTX3 were associated with a trend to a lower risk of thrombosis. Patients with high hs-CRP levels exhibited an increased risk of hematological evolution and death and to a lower extent also of thrombotic events
Barosi 2017 [59]	PMF	526	hs-CRP	Subjects with JAK2V617F mutation and an allele burden ≥ 50% had an age-independent higher incidence of elevated hs-CRP level. ASXL1, EZH2 sub-clonal mutations, JAK2 46/1 haplotype and the A3669G polymorphism of glucocorticoid receptor were not significantly associated with increased hs-CRP levels.

PMF = primary myelofibrosis; ET = essential thrombocythemia; PV = polycythemia vera; PTX-3 = pentraxin 3; hs-CRP = high sensitivity C-reactive protein.

Fatigue

Modality	Main mechanisms of CRF re
Physical activity -Avoid inactivity	† cardiorespiratory fitness † muscle mass & strength
-Consider needs for energy conservation -Combine aerobic and strength training -Utilize early morning exercise to balance melatonin levels -The exercise program should be monitored by a specialist	inflammation distress, anx iety, fear
Touch therapies -Length of sessions: 20–45 min -Frequency: 1–3 times per week	↑ muscle and fascia tension ↑ deep sleep ↓ physio-psychological sym ↓ stress hormones ↓ pain reduction ↓ cortisol levels ↓ feeling of loneliness
Acupuncture/acupressure -Length of sessions: 20–45 min -Frequency: 1–3 times per week	↓ CRF
Mind-body therapies -Yoga, Tai-chi, Qigong -Hypnosis, guided imagery -Length of sessions & frequency: according to therapist discretion -Mindfulness	↑ relaxation ↑fitness ↓ pre/post-surgery stress ↓ pain ↓ nausea & vomiting ↓ anxiety ↓ phobias
Nutrition: -Maintain an optimal nutritional status to avoid deficiencies -Base meals on a variety of vegetables, fruits, whole grains, and legumes -Consume omega-3-rich foods -Reduce consumption of animal-based products -Avoid sugary drinks -Limit consumption of processed foods	↓ CRF
Nutritional supplementation -Micronutrients -Monitor potential micronutrient deficiencies, especially vitamin D, calcium, B12,	↓CRF
folate, iron, selenium, and magnesium -Melatonin -Maintain sleep hygiene: sleeping in complete darkness along with early morning sun exposure	↑ sleep quality
-Homeopathy	↓ CRF
Astragalus membranaceus (AM), Huan Qi	↓ oxidative stress ↓ inflammation ↑ cardiovascular protection
-Ginseng (Panax ginseng, American ginseng, Siberian ginseng)	Enhance immune system † GABA and dopamine † immune System ↓ inflammation
Withania somniferra—Ashwagandha (WS)	↓ inflammation ↓ oxidative stress ↓ anxiety & stress ↑ GABA ↑ sleep quality