#4 April 25, 2016

Dr Tisman's Cancer Letter

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So this morning as I was perusing new oncology journal article titles I noted the unusually recurring words: *pre-diabetes, diabetes, insulin, metformin, obesity, diet, exercise, prostate, colon and breast cancer.* The repetitiveness captured my attention. Further GOOGLE searches revealed numerous papers presented at both European and US oncology symposia some confirming my convictions that not only ***thin is in again*** but ***thin with exercise*** is better when it comes to preventing cancer and its recurrence.

As I reviewed the literature I came across important papers including one that revealed that women ingesting hi-dose vitamin supplements had increased breast density on mammography (Multivitamin-multimineral supplement use and mammographic breast density. Am J Clin Nutr 2008;87:1400-4). The authors and others noted that increased breast density increased risk for breast cancer by as much as 25% or a lifetime risk of 4-6 fold higher as compared to those with normal density (Breast Density and Breast Cancer Risk-Eyes Wide Open:http://www.ajronline.org/doi/abs/10.2214/AJR.14.14113). This risk is equivalent to that attributed to a strong family history of breast cancer.

Other papers offered an updated analysis of the impact of pre-diabetes, diabetes, diet and exercise on cancer prevention and treatment. Diabetes-associated tumors types included colorectal, breast, pancreas, liver and urinary tract tumors. Interestingly, type 2 diabetics were found to be slightly protected from prostate cancer with a decreased risk of 17%. Survival of diabetics treated taking Metformin while suffering from colorectal, breast, prostate and ovary cancer was remarkably consistently prolonged. Humm... I wonder why...read on?

How does Metformin increase survival of patients already suffering from cancer? Theories abound but most point to the fact that high blood glucose levels in diabetics or in those ingesting large amounts of sugary beverages, carbohydrates, wheat, baked goods, pasta, bread etc. stimulate the pancreas to secrete high levels of insulin into the blood. Insulin stimulates pre- or overtly malignant tissue to grow! Several years ago my laboratory was growing tumor cells in petri dishes to determine drug sensitivity. It was common knowledge in 1960's that adding insulin to the growth medium enhanced tumor cell growth. High levels of insulin in the blood do the same and worse increase other tumor-stimulating hormones such as insulin-like growth factor and its receptors which also accelerate tumor growth.

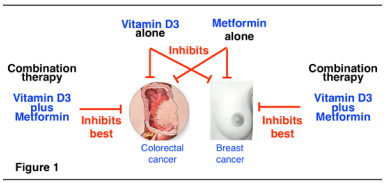


Figure 1

Metformin, decreases blood glucose by inhibiting liver production of glucose and by enhancing cellular uptake. Thus levels of insulin decrease removing powerful stimuli for tumor cell growth. The drug also directly kills tumor cells in tissue culture. This newsletter reveals some of the newest findings relating to how you can minimize your risk for developing cancer and decrease the risk of cancer recurrence in those previously diagnosed with cancer. We will be learning more about Metformin's anti-cancer activity in the near future. **Weight loss**, **diet change and exercise** if not currently optimized are good places to start your reform. If you can convince your physician to start you on the Metformin (many still have no clue) that would help. Metformin is one of the safest and oldest medications around. It has an acceptable risk benefit ratio for many at high risk for new or recurrent malignancy. The drug lowers blood sugar in both pre- and overt type 2 diabetics. The drug doesn't cause severe low blood glucose when administered in the absence of other blood glucose lowering medications. Metformin has the added benefit of helping you lose weight while decreasing the incidence of acute myocardial infarction for diabetics (*Acute Metformin Therapy Confers Cardioprotection Against Myocardial Infarction Via AMPK-eNOS--Mediated SignalingDiabetes March 2008 vol. 57 no. 3 696-705.)*

Metformin plus Vitamin D3: Investigators at Case Comprehensive Cancer Center, Case Western Reserve University, Cleveland, Ohio accomplished a landmark study on a colorectal cancer laboratory model showing a dramatic colon cancer preventative effect of the combination of Metformin and vitamin D3 (cholecalciferol) **Figure 1**. Results showed enhancement of Metformin's anti-cancer effects by co-administration of vitamin D3. Metformin's powerful anti-cancer effects were synergistic with those of vitamin D against the development of early colon cancer. In patients, each compound has repeatedly demonstrated significant clinical activity in decreasing the risk of several types of cancer including that of the colon, prostate, pancreas, ovary and lung to name just a few. Several clinical studies in cancer patients are under way.

NEWLY CONFIRMED AND LIFE-SAVING FACTS ABOUT THE RELATIONSHIP BETWEEN OBESITY, DIET, EXERCISE AND CANCER

Those who know me will confirm that much of our time together in the examining room was spent negotiating weight, diet and exercise. I graduated from medical school in 1969 and at that time cigarette smoking was newly recognized as a leading cause of preventable cancer (~ 30% of all cancers are due to smoking). Now that most of the US population has become aware of cigarettes a new and even more powerful association between cancer-obesity-nutrition and exercise has emerged.

Body weight is strongly associated with risk of the following cancer types, and probably others as well (% due to obesity in the parentheses)

ESOPHAGUS (37%) | PANCREAS (12%) | COLON AND RECTUM (11%) | BREAST AFTER MENOPAUSE (9%) | ENDOMETRIUM (LINING OF THE UTERUS) (30%) | KIDNEY (25%) | THYROID (EACH 5-UNIT INCREASE IN BODY MASS INDEX (BMI) WAS ASSOCIATED WITH A 30% INCREASE IN RISK) | GALLBLADDER (24%)

One study, using National Cancer Institute data, estimated that in 2007 in the United States, about 34,000 new cases of cancer in men (4 percent) and 50,500 in women (7 percent) were due to obesity. The percentage of cases attributed to obesity was as high as 40 percent for some cancers. If every adult reduced their body mass index (BMI) by 1 percent, which would be equivalent to a weight loss of roughly 1 kg (2.2lbs) for an adult of average weight, this would prevent the increase in the number of cancer cases and actually result in the avoidance of about 100,000 new cases of cancer. **Body Mass Index (BMI) = Wt (lbs) x 703 /(Ht inches)^2**. Normal values are between 18.5 to 24.9 , "obesity" is defined as BMI ≥30. 65-68% of all Americans have BMI = 25.0 to 29.9 and are considered "overweight".

Body weight and obesity: Several mechanisms explain the strong association between obesity and cancer.

Fat tissue produces excess amounts of estrogen, high levels of which increase the risk of breast, endometrial, and some other cancers. Obesity **see Figure 2** increases levels of insulin and a powerful growth hormone called insulin-like growth factor-1 (IGF-1) both of which promote the development of tumors. Elevation of these factors is characteristic of early and manifest diabetes mellitus as well. Interestingly, Metformin significantly reverses these abnormalities. Metformin therefore, is an unappreciated and powerful anti-cancer drug.

Fat cells produce hormones, called adipokines, that may stimulate or inhibit cell growth. This is a relatively new finding. A compound

known as leptin is abundant in over-weight patients, and promotes tumor cell growth and proliferation, whereas adiponectin, less abundant in obese people, has growth inhibitory properties vs. tumor cells.

Fat cells **(see Figure 2 below)** and the hormones they secrete have direct and indirect effects on several regulators of tumor growth (called tyrosine kinase enzymes that control cell growth and proliferation. These key enzymes turn on and off normal and tumor cell growth. Additionally, those suffering from obesity have chronic inflammation, known to play a key role by transforming normal cells to malignant cells (thus the anti-cancer effects of aspirin and other NSAIDS). Other fat-induced abnormalities include altered immune responses, mediated through other chemicals.

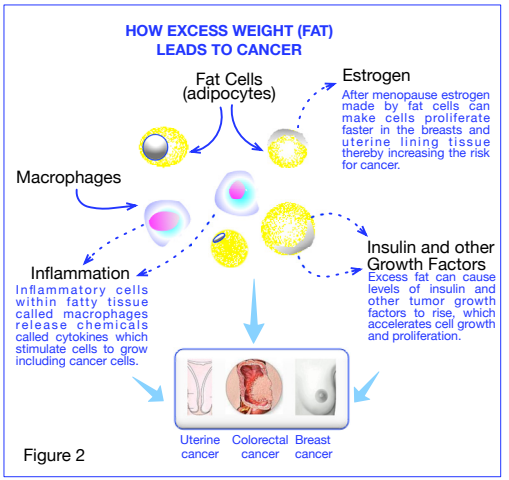


Figure 2

Contrary to popular belief we do have significant control over both cancer initiation and its recurrence. By controlling weight, diet and exercise, we can direct our powerful metabolic hormonal mediators to slow or totally ablate tumor cell growth. You bet we can! Most new studies demonstrate that we can reduce our risk of almost all cancers by a whopping 35%!

EFFECT OF DIET ON CANCER RISK

Both patient and animal studies prove that alterations in caloric intake or in quality of diet significantly influence the risk of cancer development, progression and even recurrence.

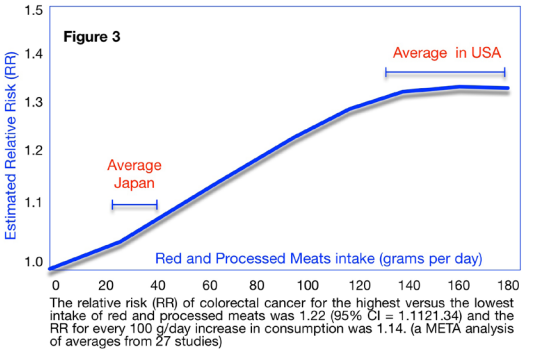
It is now clear that caloric excess increases cancer incidence and that positive energy balance (too much food and not enough exercise) promotes obesity which begets cancer cell proliferation, tumor progression and or tumor recurrence. Laboratory studies reveal that simply limiting long-term calorie intake and or adhering to a low carbohydrate diet leads to a decrease in cancer cell growth and extends longevity in rodents as well as patients.

Studies document significant health hazards related to diets typical of the first world (read USA). These diets are rich in calories, red and processed meats, overabundant in alcohol and animal fats, and/or lacking in plant products. Clinical studies consistently reveal the virtues of a diet high in plant foods. Interestingly, the previously popular high-fiber diet does not protect against cancer!

Negative Energy Balance refers to expending more energy by virtue of exercise than that supplied by diet. Negative Energy Balance for overweight individuals is now recognized as an important factor in lowering susceptibility to cancer and cardiovascular disease because of direct and or indirect beneficial effects on levels of cholesterol, insulin, insulin-like growth factor-I, and chronic inflammation. A **low carbohydrate and mildly ketotic diet** (*described in Schmidt et al. Nutrition & Metabolism 2011, 8:54)* and thus an insulin-inhibiting diet was demonstrated safe for most and has actually induced partial remissions in patients with advanced cancer. Tumor growth inhibition by such diets was established by some clinical case reports, and laboratory studies which reveal the underlying molecular mechanisms (*Klement and Kämmerer, Nutrition & Metabolism 2011, 8:75; European Journal of Clinical Nutrition (2013) 67, 789-796*) supporting the clinical observations. Don't make mine a Double Chocolate Chip Crème Frappuccino (has 57 grams of carbs) while a 16 ounce bottle of Coke has 47 grams of carbs i.e. the total recommended carb load for a whole day. I recommend 15-20 grams of carbs per meal - 45-60 grams per day, which assures you the metabolic benefits one of which is easy weight loss.

Coffee consumption (No, NOT by enema!) is associated with **decreased risk of type 2 diabetes and increased insulin sensitivity (a good thing). A group from Harvard's Dana Farber Cancer Center studied the effects of coffee on colon cancer recurrence and patient survival. During and 6 months after adjuvant chemotherapy for stage III colorectal cancer, 953 patients reported dietary intake of caffeinated coffee, decaffeinated coffee, and non-herbal tea, as well as 128 other items. Researchers evaluated the influence of coffee, non-herbal tea, and caffeine on cancer recurrence and mortality. Increasing total coffee intake was associated with a significant reduction in the risk of cancer recurrence or mortality. Compared with abstainers, patients who consumed 4 cups/d or more of coffee experienced 40% decrease in disease recurrence or mortality. Neither non-herbal tea nor decaffeinated coffee intake was protective. (*http://jco.ascopubs.org/cgi/doi/10.1200/JCO.2015.61.5062*).

Kathryn Wilson from the Harvard School of Public Health conducted a prospective analysis of 47, 911 men in the Health Professionals Follow-up Study who reported intake of regular and decaffeinated coffee in 1986 and every 4 years thereafter. From 1986 to 2006, 5035 patients with prostate cancer were identified, including 642 patients with lethal prostate cancers, defined as fatal or metastatic. Her group found the average intake of coffee in 1986 was 1.9 cups per day. Men who consumed six or more cups per day had a lower adjusted relative risk for overall prostate cancer compared with nondrinkers (RR = 0.82). The association was stronger for lethal prostate cancer (consumers of more than six cups of coffee per day: RR = 0.40 = 60% less risk. Coffee consumption was not associated with the risk of nonadvanced or low-grade cancers and was only weakly inversely associated with high-grade cancer. (*J Natl Cancer Inst 2011;103:876–884.*)



The relative risk (RR) of colorectal cancer for the highest versus the lowest intake of red and processed meats was 1.22 (95% CI = 1.1121.34) and the RR for every 100 g/day increase in consumption was 1.14. (a META analysis of averages from 27 studies)

WHATS UP WITH RED AND PROCESSED MEATS?

In October, 2015, 22 scientists from ten countries met at the International Agency for Research on Cancer (IARC) in Lyon, France, to evaluate the carcinogenicity (cancer causing potential) of the consumption of red meat and or processed meat (**(*www.TheLancet/Oncology: Published online October 26, 2015 http://dx.doi.org/10.1016/S1470-2045(15)00444-1)).* **Red meat** refers to unprocessed mammalian muscle meat-for example, beef, veal, pork, lamb, mutton, horse (*viva la* France), or goat meat-including minced or frozen meat; it is usually cooked before consumption. **Processed meat** refers to meat that has been transformed through salting, curing (any of various food preservation and flavoring processes of foods such as meat, fish and vegetables, by the addition of combinations of salt, nitrates, nitrites, and/or

sugar, with the aim of drawing moisture out of the food by the process of osmosis. Curing processes also involve smoking, spicing, or cooking). Dehydration was the earliest form of food curing. Most processed meats contain pork or beef, but might also contain other red meats, poultry, liver, or meat byproducts such as blood.

The mean intake of red meat by those who consume it is about 50-100 g per person per day, with high consumption equaling more than 170-250 g per person per day (generally seen in the USA). Consumption of 50 grams a day of processed meat is associated with a 20% risk for colorectal cancer. A study of colorectal cancer in 10 different studies of both red and processed meats reported a significant dose-response relationship between meat ingestion and colorectal cancer, with a 17% increased risk per 100 g per day of **red meat** and an 18% increase per 50 g per day increment of **processed** meat (processed meat is a more potent carcinogen). Another META analysis including 27 studies (*PLoS ONE 6(6): e20456. doi:10.1371/journal.pone.0020456*) revealed the combined red and processed meat data displayed in **Figure 3** again revealing a powerful association between red and processed meat consumption and colorectal cancer**.** Overall, the Working Group classified consumption of **processed meat** as "carcinogenic to humans" on the basis of sufficient evidence for colorectal cancer. The Working Group classified consumption of **red meat** as "probably carcinogenic to humans". Though exact mechanisms responsible for the cancer-causing effects of red and processed meats is not entirely understood, in recent laboratory experiments, iron within the blood-hemoglobin of red meat appears to facilitate the carcinogenicity of meat and its associated chemicals. *It is of interest that one of the main biblical food laws forbids eating blood on account of "the life [being] in the blood". This ban and reason are listed in the Noahide Laws (a set of imperatives which, according to the Talmud, were given by God as a binding set of laws for the "children of Noah" - that is, all of humanity.) and twice in Leviticus as well as in Deuteronomy (what did they know and when did they know it)*?

ELEVATED RISKS OF CARDIOVASCULAR DISEASE AS WELL AS COLON CANCER: Red meat consumption is also associated with an increased risk of coronary artery disease and strokes. Harvard researchers observed 37,698 men from the Health Professionals Follow-up Study (1986-2008) and 83,644 women from the Nurses' Health Study (1980-2008) who were free of both cardiovascular disease and cancer at baseline. **Results:** They documented 23,926 deaths (including 5910 cardiovascular disease and 9464 cancer deaths) during 2.96 million person-years of follow-up. Total mortality (for 1-serving/day of unprocessed red meat increased by 13% and for processed red meat by 20%. Processed meats included bacon, hot dogs, sausage, salami,

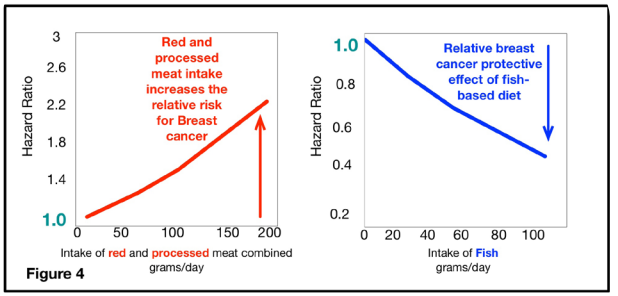


Figure 4

Hazard ratios of colorectal cancer in the European Prospective Investigation into Cancer and Nutrition cohort. Hazard ratios by intake of red and processed meat and by intake of fish (g/day). Note the relative protective effect of dietary fish. In general, processed meats are more carcinogenic than red meat however both are carcinogenic (promote colon, prostate, pancreatic and breast cancer). The lower the hazard ratios (HR) the better.

bologna, plastic packaged turkey and chicken and other processed items. Two slices of bacon represented 1 serving; as did one slice of cold cuts. The corresponding elevated risks were 18% and 21% for cardiovascular mortality and 10% and 16% for cancer mortality. Substitutions of 1 serving per day of other foods (including fish, poultry, nuts, legumes, low-fat dairy, and whole grains) for 1 serving per day of red meat were associated with a 7% to 19% lower mortality risk. It was estimated that 9.3% of deaths in men and 7.6% in women in these groups could be prevented at the end of follow-up if all the individuals consumed fewer than 1/2 servings red meat daily (approximately 20-42 g/d...similar to that ingested daily in Japan **Figure 3**). Arch Intern Med. 2012;172(7):555-563. Published online March 12, 2012. doi:10.1001/archinternmed.2011.2287

BREAST CANCER RISK IS ELEVATED BY RED AND PROCESSED MEATS: Maryam Farvid of Harvard studied the association between dietary protein sources in early adulthood and the risk of breast cancer. There were 88,803 pre-menopausal women from the Nurses' Health Study II who completed a questionnaire on diet in 1991. Two-thousand eight-hundred and thirty cases of breast cancer were documented during 20 years of follow-up. Higher intake of total red meat was associated with an increased risk of breast cancer overall (relative risk 1.22); for highest fifth vs. lowest fifth of intake. High intakes of poultry, fish, eggs, legumes, and nuts were not related to breast cancer risk. When the association was evaluated by menopausal status, higher intake of poultry was associated with a lower risk of breast cancer in post-menopausal women a Relative Risk of only 0.73; for lowest fifth vs. highest fifth of intake) but not in pre-menopausal women. In estimating the effects of exchanging different protein sources, substituting one serving/day of legumes for one serving/day of red meat was associated with a 15% lower risk of breast cancer among all women and a 19% lower risk among pre-menopausal women . Also, substituting one serving/day of poultry for one serving/day of red meat was associated with a 17% lower risk of breast cancer overall and a 24% lower risk of pos-tmenopausal breast cancer. Furthermore, substituting one serving/day of combined legumes, nuts, poultry, and fish for one serving/day of red meat was associated with a 14% lower risk of breast cancer overall. She concluded that higher red meat intake in early adulthood may be a risk factor for breast cancer, and replacing red meat with a combination of legumes, poultry, nuts and fish may significantly reduce the risk of breast cancer (*BMJ 2014;348:g3437*). These changes approach the breast cancer preventative efficacy of Raloxifene (marketed as Evista) and tamoxifen. Tamoxifen reduced the incidence of all breast cancers (invasive plus ductal carcinoma in situ) by 27% overall (from 6.82 to 4.97 events per 1000 woman-years). Incidence rates of ER-positive invasive breast cancers in the tamoxifen group were 26% lower than those in the placebo group during active treatment. JNCI J Natl Cancer Inst (2007) 99 (4): 272-282. doi: 10.1093/jnci/djk049

INFLUENCE OF ANTI-CANCER VITAMINS

Recent research at Harvard's Dana Farber Cancer Center showed low levels of 25- hydroxyvitamin D (25 (OH)D), vitamin D) may be responsible for up to 20% of the cancer risk linked to the overweight state. Obese patients have low vitamin D blood levels, presumably because vitamin D, being a fat-soluble vitamin, is diverted to and hangs out in fat as opposed to being distributed to other dividing cells.

Twenty-eight different cancers have been associated with low blood vitamin D levels (*Cases J. 2009 Jul 21;2:8390 "Triple negative breast cancer patients presenting with low serum vitamin D levels: a case series". Rainville C, Khan Y, Tisman G.*).

My laboratory was first motivated several years ago to formulate the **BD Maintenance Plus++** B and D vitamin supplement to make available a healthy formulation of the most important B and D vitamins known not to induce cell mutations, cause immune suppression or accelerate the malignant process (*Folate and colorectal cancer: An evidence-based critical review. Mol. Nutr. Food Res. 2007, 51, 267 - 292; Folic Acid Supplementation Promotes Mammary Tumor Progression in a Rat Model. doi 10.1371/journal.pone.008463 2014*). BD Maintenance Plus++ delivers **physiologic** replacement doses (not potentially dangerous mega-doses) of natural vitamin D as D3, B2 and B6, The B12 dose has been adjusted based on our clinical studies for those on medications that interfere with B12 absorption and for the aging-associated malabsorption of B12 which starts in the mid fifties due to the physiologic loss of stomach acid. BD Maintenance Plus++ is devoid of folic acid which has recently been implicated in immune suppression and in accelerating the transformation of premalignant to overtly malignant tissue (*Unmetabolized folic acid in plasma is associated with reduced natural killer cell cytotoxicity among postmenopausal women. J Nutr. 2006 Jan;136(1):189-94. High folic acid intake re-*

duces natural killer cell cytotoxicity in aged mice. doi:10.1016/j.jnutbio.2015.12.006).

MODERATE EXERCISE, A POWERFUL DETERRENT TO TUMOR GROWTH

For women who reported walking as their only activity, those walking 6-7 hours/week had a 14% lower breast cancer risk relative to women walking 3 hours/week. Walking for 2.5 hours a week (that's just 21 minutes a day) can cut your risk of heart disease by 30%. Risks of death from breast and uterine cancer were reduced by 19% in women who walked 1-3 hours per week, and by 54% for walking 3-5 hours per week as reported by Harvard University Women's Health Study, 2012. Keep in mind that the reported percentages vary based on whether the comparisons are related to non-walkers or minimal walkers.

Several studies confirm that women who engage in regular physical activity when compared to those who are sedentary have a lower risk for stroke and heart disease as well as decreased risk for developing not only breast but several other cancers. Additionally, if you have already been diagnosed with cancer, exercise reduces the risk of recurrence (*McTiernan A, editor. Cancer Prevention and Management Through Exercise and Weight Control. Boca Raton: Taylor & Francis Group, LLC, 2006. Giovannucci EL, Liu Y, Leitzmann MF, Stampfer MJ, Willett WC. A prospective study of physical activity and incident and fatal prostate cancer. Archives of Internal Medicine 2005; 165(9):1005-1010. Meyerhardt JA, Giovannucci EL, Holmes MD, et al. Physical activity and survival after colorectal cancer diagnosis. Journal of Clinical Oncology 2006; 24(22):3527-3534.*)

Regular and moderate exercise offers several important health benefits for the cancer patient. It can help you achieve and maintain a healthy body weight; it may influence circulating hormones and reduce the exposure of breast tissue to estrogen which is a cocarcinogen while lowering insulin and insulin-like growth factors and blood glucose all of which drive the growth of most tumor types.

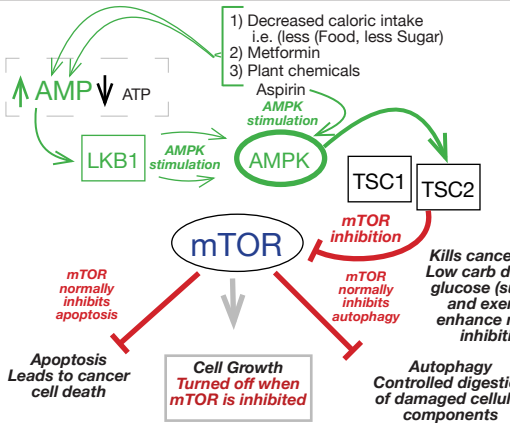
To reduce breast cancer risk, the American Cancer Society recommends exercise for 45-60 minutes on at least five days of the week. Exercise includes housework or gardening activities. It is recommended that the exercise causes you to breathe as hard as you would during a brisk walk if possible however such is not a requirement.

Risk of death increases significantly when adults sit for more than seven hours a day (*Chau JY, Grunseit AC, Chey T, Stamatakis E, Brown WJ, Matthews CE, et al. Daily sitting time and all-cause mortality: A meta-analysis. PLoS One2013;8:e80000.*). Importantly, simply interrupting prolonged sitting by walking around the house for **5 minutes every thirty minutes** decreases blood pressure. Insulin and glucose also decrease an these anti-cancer benefits last for two days. Helpful activities include getting up and moving during television commercial breaks, pacing when on the phone, adding gentle five minute walks throughout the day, and walking rather than driving for short trips.

Minimal physical activity counts but to a lesser degrees. I recommend you do your best on a daily basis because it will absolutely help! Newest lab data gives scientific relevance to the mechanism(s) by which exercise and diet exert their anti-tumor activity.

It was with some hesitation that I added the following scientific section for non believers. I feel it is critical for you to appreciate that exercise and dietary changes are not minor contributions to your health rather they exert powerful newly discovered biochemical effects similar to the newest cancer medication without the associated toxicity.

HERE GOES: Exercise is a powerful activator of an enzyme called AMPK. **Figure** to the right. AMPK senses cellular energy. Dietary restriction and exercise exhaust cell energy stored as ATP thereby increasing AMP which stimulates the AMPK enzyme. Once stimulated, AMPK mediates inhibition of the enzyme mTOR. mTOR directs almost every aspects of cell growth. Interestingly, aspirin and metformin (the diabetes medication) both reduce mTOR activity thus controlling the growth not only of normal but of several types of cancer cells. Our newest anti-tumor drugs called targeted therapy, work by directly inhibiting the mTOR molecule. These drugs come with some toxicity both physical and financial (as much as $5-15,000 for monthly therapy. In light of this exercise is a bargain.



Stimulation (activation) of AMPK leads to cancer suppression. AMPK is activated when AMP/ATP or ADP/ATP ratios in the cells rise due to various physiological stresses such as muscle contraction (exercise), lowering of blood glucose and hypoxemia (low oxygen levels), leading to the activation of the LKB1 molecule. Metformin (safe when used alone to control blood glucose, oral type II diabetes medication) can mimic these stressors and lead to AMPK activation in a LKB1-dependent manner. However, aspirin (ASA) activates AMPK directly. One of the most well-known pathways of AMPK is through the TSC1/TSC2 complex, leading to the ***downregulation of mTOR by stimulation of the TSC2 molecule that is a natural inhibitor of mTOR***. The mTOR pathway essentially provides growth stimulation to cancer cells directly noted by the gray arrow and by suppressing apoptosis (apoptosis kills tumor cells) and autophagy (autophagy kills tumor cells). AMPK downregulates these tumor promoting effects of mTOR, thus leading to increased apoptosis and autophagy-mediated cell death and inhibition of mTOR's direct tumor cell stimulatory effects. AMPK also downregulates the expression of cyclooxygenase (COX)-2, which contributes to the pathophysiological progression of human cancers and inflammatory disorders.

Summary

A) OBESITY IS BAD, FAT CELLS SECRETE CANCER-CAUSING HORMONES

B) PROLONGED SITTING IS BAD, INACTIVITY IS VERY BAD

C) RED MEAT CAUSES CANCER AND PROCESSED MEATS (RED OR WHITE) ARE WORSE

D) POULTRY, FISH, AND SOME (NOT LOTS) OF FRUITS AND LOTS OF VEGETABLES PROTECT AGAINST CANCER

E) METFORMIN, ASPIRIN, COFFEE (4-6 CUPS A DAY) AND EXERCISE PROTECT AGAINST CANCER INITIATION AND RECURRENCE

F) AIM FOR HIGH-NORMAL LEVELS OF VITAMIN D WHILE AVOIDING HIGH DOSES OF B12 AND FOLIC ACID

For more information relating to the Cancer Letter Content email your questions to:

pna.vitamins@gmail.com attention: Dr. Tisman

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