A Guide to a "Proper" Diet

(Based on addressing normal and abnormal cell metabolism)

by
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"The image of cancer depends on your perspective. It depends on whether you are a cancer patient, a friend or family member of a patient, an oncologist, a pathologist, a statistician, or a person who does basic research on the disease ... The vast majority of cancer cells share a singular problem involving abnormal energy metabolism ... the therapeutic efficacy of molecularly "targeted" therapies could be enhanced if combined with therapies that target energy metabolism."

- Dr. Thomas N. Seyfried, Cancer as a Metabolic Disease

"Cancer doesn't grow too much, it dies too little."

- Dr. Robert Nagourney, Rational Therapeutics

The content and references contained in this guide are intended solely for the information and education of the reader. It is not to be used for treatment purposes; it is to inspire thought and/or drive discussions between patient and healthcare provider. The information presented is not intended to diagnose health problems or replace professional medical care; nor should it be considered a substitute for seeing a physician.

^{*} Copyright © 2015 Neil B. Feldman. *A note from Judy Scott Feldman:* My late husband Neil, an electrical engineer by training and avid believer in evidence-based medicine, started researching this science-based guide to nutrition and diet in 2012 after his kidney cancer, first diagnosed in 2010, recurred and spread to his bones. He continued to update the information for the next three years. His last update was in May 2015. He died two months later. His hope was that this guide would give readers – whether sick or healthy – the tools to take an active role in the care of their bodies. Physicians are often lacking knowledge of even basic nutrition research. During illness we must depend upon the medical experts. But we don't have to be helpless. We can take charge of a crucial component of good health, nutrition.

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I. PREFACE

What follows is a detailed explanation of the science and rationale behind what I have dubbed a "proper" diet for stage IV renal cell carcinoma patients (like myself), although it also applies to any cancer patient. My approach has been to evaluate dietary considerations primarily in light of *normal and abnormal cell metabolism*. My research is an ongoing "work-in-progress" and thus subject to change. It is based on information found in the following books and resources as well as from credible peer-reviewed articles and papers found in **PubMed** and similar on-line resources:

- 1. "The World Turned Upside Down The Second Low-Carbohydrate Revolution" by Richard David Feinman, Ph.D. A thorough examination of both biochemistry and nutrition that is unsparing in criticism of the nutritional establishment. Simply a must-read. Published by NMS Press and Duck in a Boat, LLC.
- 2. "Cancer as a Metabolic Disease On the Origin, Management, and Prevention of Cancer" by Dr. Thomas N. Seyfried: This seminal book reevaluates the origins of cancer based on the latest scientific research. The author is a biochemical geneticist who has been investigating the lipid biochemistry of cancer for over 30 years. In this book he establishes why approaching cancer as a metabolic disease leads to better understanding and management of all aspects of the disease, including inflammation, vascularization, cell death, drug resistance, and genomic instability.
- 3. "Outliving Cancer The Better, Smarter Way to Treat Your Cancer" by Dr. Robert A. Nagourney: The author describes what he claims is a more effective way to treat cancer. For decades he has been showing that many supposedly incurable cancers can be killed, with greatly reduced harm to the patient, simply by using agents preselected in the laboratory to target those specific cancer cells. He describes a unique chemosensitivity assay approach that can determine what may work for each specific individual.
- 4. "Minding My Mitochondria" by Terry L. Wahls, M.D: This is an account of how Dr. Wahls overcame secondary progressive Multiple Sclerosis (MS). Her MS confined her to a wheelchair for four years. But 18 months after starting her intensive and focused nutrition therapy she now commutes to work five miles each day on her bicycle. The book contains a clear and concise explanation of the biochemistry that drives our brains. She shows how the food we eat is linked to body health. I bought her book after watching an inspiring **TEDTalk** presentation that she gave here:

http://www.youtube.com/watch?v=KLjgBLwH3Wc

5. "Fat Chance – Beating the Odds Against Sugar, Processed Food, Obesity, and Disease" by Dr. Robert H. Lustig: This book explores the disquieting increase in type II diabetes, obesity, metabolic syndrome, cardiovascular disease, and cancer over the last 40+ years. This trend started in the late 1970's when the US government decreed the reduction of (mostly saturated) fat in our diet. The food industry responded by removing the fats while putting sugar in their place. This was necessary in order to make the "low-fat" food palatable. They also removed most of the natural fiber in order to allow the food to last longer on the shelf (or to be frozen). This has resulted in a catastrophic excess of sugar(s) - especially fructose - in the standard American diet (called "SAD").

- 6. "Pure, White and Deadly How Sugar Is Killing Us and What We Can Do To Stop It" by Dr. John Yudkin: This is the classic exposé about the hidden dangers of sugar that was first recognized in the 1950's by Dr. Yudkin. Dr. Lustig heavily references this book in his lectures and books.
- 7. "Cells, Gels, and the Engines of Life" by Dr. Gerald H. Pollack: This book challenges the mainstream paradigm of how cells function. It explores the "gel-like" nature of the cell and builds on this aspect to explain the underlying mechanisms of communication, transport, division, and other essential cell functions.
- 8. "Good Calories, Bad Calories" by Gary Taubes: This is a very comprehensive and thorough exploration of the scientific evidence behind diet, obesity, and virtually all the other "diseases of civilization" as they relate to a common cause. "Taubes argues that the problem lies in refined carbohydrates, like white flour, easily digested starches, and sugars, and that the key to good health is the kind of calories we take in, not the number."
- 9. "Why We Get Fat And What To Do About It" by Gary Taubes: This was a national bestseller that followed his earlier book (noted above). "Taubes reveals the bad nutritional science of the last century none more damaging or misguided than the "calories-in, calories-out model of why we get fat and the good science that has been ignored."
- 10. "The Art and Science of Low Carbohydrate Living" by Jeff S. Volek, Ph. D, RD and Stephen D. Phinney, MD, Ph.D.: This is a detailed guide to understanding and following practical and sustainable low carbohydrate diets.
- 11. "Death By Food Pyramid How Shoddy Science, Sketchy Politics and Shady Special Interests Ruined Your Health...and How to Reclaim it!" by Denise Minger: I think the sub-title sums it up quite well.
- 12. "The Great Cholesterol Con The Truth About What Really Causes Heart Disease and How to Avoid It" by Dr. Malcolm Kendrick: This is wonderful and witty treatise that explodes several medical myths. Kendrick shows that: 1) high cholesterol does not cause heart disease; 2) a high-fat diet (saturated or otherwise) does not affect blood cholesterol levels; 3) people with low LDL (so-called "bad" cholesterol) actually have a *higher* mortality risk; 4) protection provided by statins is so small as to be not worth bothering about for most men and *all* women; 5) statins have many more side effects than have been admitted; 6) many advocates for the use of statins should be treated with skepticism due to their links with the drugs' manufacturers.
- 13. "The Great Cholesterol Myth Why Lowering Your Cholesterol Won't Prevent Heart Disease And the Statin-Free Plan That Will" by Dr. Stephen Sinatra and Jonny Bowden, Ph.D.: This book begins with a straightforward explanation of various metabolic body and cell mechanisms. The authors present the argument as to why lowering cholesterol (and fat intake) will *not* prevent heart disease. They explain why taking statins should be avoided (except in the case of a few certain patients who have already suffered

¹From the back cover of the book.

²Also from the back cover of the book.

severe heart disease). They suggest that the real culprits behind cardiovascular disease are excess sugar(s) and inflammation. Much of what they explain also applies to cancer sufferers.

- 14. "Cholesterol Clarity What the HDL is Wrong with My Numbers?" by Jimmy Moore with Dr. Eric C. Westman: A very straightforward explanation of how to interpret your cholesterol blood test numbers and what, if anything, you should do about them.
- 15. "The Sinatra Solution: Metabolic Cardiology" by Dr. Stephen Sinatra: This book goes into depth about how to maintain optimum cell metabolism and support healthy mitochondria function. Cancer is primarily a metabolic disease. As such it is imperative to understand healthy and abnormal cell metabolism and, in particular, the functioning of the mitochondria within the cell. This book helps to clarify some of these issues.
- 16. "Trick and Treat How 'Healthy Eating' Is Making Us III" by Barry Groves, Ph.D.: "Part 1 of his book sets out the extent of corruption in the 'health industry'; it shows how current 'healthy' dietary guidelines are based more on myth and wishful thinking than any coherent body of scientific evidence. And it gives the evidence for what we should really eat for health. Part 2 lists over 70 common, chronic, degenerative diseases…the second part gives evidence that these diseases owe their recent rise in numbers to the diet we are all told to eat."
- 17. "**Diet to Cure Incurable Diseases**" by Dr. H.L. Newbold: A fascinating book first published in 1993. The heart of his therapy can be simply stated: give up all sugar(s), grains, (especially wheat), milk and dairy products. This book contains lots of valuable information on vitamins, minerals, and identifying sources of insults to individual biochemistry.
- 18. "Dr. Bernstein's Diabetes Solution The Complete Guide to Achieving Normal Blood Sugars" by Dr. Richard K. Bernstein: Even though I do not suffer from Diabetes this excellent book gives invaluable insights into ways to control blood glucose by dietary means. It also explores the "Dawn Phenomena" and how to best utilize Metformin.
- 19. "Anti-Cancer A New Way of Life" by Dr. David Servan-Schreiber: The author of this book was a young brain cancer researcher who accidentally discovered that he had contracted brain cancer himself. He knew that the mainstream therapies available did not offer him long-term remission. This inspired him to set out on a journey to figure out how to best prolong his life. The book is a guide to what he discovered and then put into practice. He ultimately prolonged his life for another 20 years. This book was the first resource I read after being diagnosed with mRCC. I was initially inclined to follow many of his recommendations but over time, as I dug deeper and deeper doing my own research, I began to question many of his dietary suggestions.
- 20. "Life Over Cancer" by Dr. Keith I. Block: The author (and his wife) founded the Block Integrative Cancer Center now based in Skokie, IL. This was one of the first facilities to offer concurrent mainstream (chemotherapy and radiation) plus "integrative" (nutritional, mind/body, physical) therapies to their

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³ From page 10 of the book.

patients. The book goes into detail about both mainstream and "integrative" cancer treatments with emphasis on the value of a healthy diet and certain nutritional supplements. However, as a result of current research and other recent medical discoveries, I no longer trust or follow their dietary recommendations.

21. "The China Study" by T. Colin Campbell, Ph. D and Thomas M. Campbell II: This controversial book describes the results of an ambitious research effort. It was observed that in locations in Communist China where meat and dairy products were not consumed (for whatever reason) the cancer rates seemed to be dramatically reduced or almost nonexistent. The book goes on to pitch several one-sided arguments for adopting a purely vegan diet to prevent or fight cancer. However, after of months of in-depth research (and personal experimentation), I cannot advocate their approach. There is no clear scientific evidence that plant protein is somehow inherently "healthier" than animal protein for cancer sufferers. More disconcerting is the fact that virtually all the research papers and articles cited to support their arguments appear to be flawed.

In the same vein there is also a popular video documentary currently available called "Forks Over Knives" that profiles several of the doctors who were associated with the China Study. Regardless, this video adds nothing new to their arguments. It is a clever but one-sided piece of propaganda advocating a vegan diet.

22. "Prevent and Reverse Heart Disease" by Dr. Caldwell B. Esselstyn, Jr. The author was also featured in the video documentary "Forks Over Knives". He is a former surgeon, researcher, and clinician at the Cleveland Clinic. He argues (based on his private 20-year study) that a plant-based, completely vegetable oil free, vegan diet can prevent or stop the progression of cardiovascular disease and even reverse arteriolosclerosis. Yet, as noted above, after of months of in-depth research I cannot endorse his rather extreme dietary protocol. His seemingly impressive results were likely due to the elimination of the sugar(s), refined carbohydrates, and poly-unsaturated fats in his diet (but not by going vegan). It is primarily inflammation that is likely at the crux of arteriolosclerosis and other cardiovascular diseases. Esselstyn's diet certainly does help reduce inflammation but the results he achieved were purely anecdotal. They have not been repeated in any random controlled clinical trials (RCTs).

Many of these books share at least three things in common: 1) they were written or co-authored by practicing medical doctors; 2) these doctors all question or seriously challenge many current "mainstream" medical practices; 3) these books all provide "food for thought".

Please note that I have not meticulously footnoted each of these various sources in what follows.

I am a firm follower of **SBM** (science-based medicine) and **EBM** (evidence-based medicine). All of these various books and research articles suggest the essential need for any cancer sufferer to consider: 1) changing to a "proper" diet; 2) adding additional "appropriate" supplements to that diet *only if necessary*; and 3) closely following their oncologist's recommended targeted drug, chemotherapy, or radiation treatments.

Before going any further, please watch this brief presentation on how to properly evaluate medical research. It (hopefully) will change your perspective about what you may read in the popular media as well as in PubMed:

https://www.youtube.com/watch?v=UCk vTkS6bU*

II. COMBATING MISLEADING OR NON-EXISTENT NUTRITIONAL ADVICE

There are many "old school" medical doctors and oncologists who, when queried, will tell their patients, "There is nothing that you did to cause this cancer, and there is nothing you can do to cure it. Only surgery or medication will be of any use."

But is that statement, "only surgery or medication will be of any use", totally accurate?

I believe not. I feel that, in fact, there is more that one can do - if one so chooses.

Some oncologists plead ignorance on the subject of healthy nutrition and diet. They may claim that they were not sufficiently trained in the field of nutrition or that the taking of most supplements will likely interfere with targeted or chemo drug therapies. These responses can often create a confusing state of affairs for new patients. They are left mostly on their own if they wish to become more proactive about their diet and proper nutrition. That just does not seem right to me.

This document has been written to offer some guidance to those who may wish to adopt a healthier diet to help their therapy or to prevent cancer in the first place. It also outlines some of what I personally did that may have helped to minimize many serious side effects while I was taking the targeted anti-angiogenesis drugs Sutent® (Sunitinib), Inlyta® (Axitinib), Cometriq® (Cabozantinib), Afinitor® (Everolimus) and the monoclonal antibody bone agent Xgeva® (Denosumab).

I need to offer a word of caution. You may encounter several nutritional "myths" being challenged or completely busted as you go through this document. That is the beauty and power of ongoing scientific research. It should not play favorites. We understand far more today than we did 40 or 50 years ago which is when much of the flawed and incorrect nutritional advice that is unfortunately still being dished out was first introduced. Why this incorrect advice is still being given out is mostly a result of politics and various business interests but not related to the latest credible science.

III. SOME IMPORTANT CAVEATS

Before discussing the rationale behind my dietary advice there are several important caveats to consider:

^{*} *Update:* <u>https://www.nytimes.com/2017/01/23/nyregion/manhattan-doctor-david-newman-prison-sexual-abuse.html</u>. The information in the video remains valuable.

- 1. It is only by *first* following a proper diet that any supplements will be able to "work" to maximum effect. I firmly believe that the dietary changes are essential and are primary. Any additional supplements taken should only be minor additions.
- 2. Any diet (or supplements taken) should work in two ways to allow the body's various systems to be able to work at peak efficiency. First and foremost it should eliminate those substances that might compromise or severely tax these internal systems. Second, it should work to increase the presence of those substances that might strengthen these systems.
- 3. There is no diet (and/or supplements) that can, *on their own*, kill or eliminate existing tumors or metastases. So the oncologist who says, "only surgery or medication will be of any use" is certainly partially correct. Without the help of a molecular targeted drug, or chemotherapy, or radiation, or immune therapy, no diet, *by itself*, will be sufficient to fight cancer once it has taken hold.

IV. WHAT IS THE POINT OF ALL THIS?

So what am I trying to accomplish with this diet? How should its success or failure be judged? Why even bother with any of this stuff? Here is why:

- 1. To both feel and be healthier.
- 2. To better focus molecular targeted drugs or chemotherapy on cancer cells while hopefully minimizing their effects on normal cells.
- 3. To better tolerate targeted molecular drugs or chemotherapy and/or radiation treatments and to help minimize or reduce their unpleasant side effects.
- 4. To repair or build up and then maintain one's own internal immune system.
- 5. To help strengthen the immune system if it is being compromised or weakened as a by-product of taking molecular targeted drugs, chemotherapy, or radiation.
- 6. To help ensure that once going "NED" (No visible Evidence of Disease) there is no return of cancer in the future.

V. A "PROPER" DIET FOR THOSE FIGHTING ANY KIND OF CANCER

So let me just cut right to the chase: After more than a year of intense research and personal experimentation I have come to the conclusion that a **modified low carbohydrate/high fat (LCHF)** diet is the optimal dietary approach for most cancer patients as outlined here:

https://www.youtube.com/watch?v=WqunGs9xkYM

Or as summarized by Stephan Guyenet:

"Here's the short version: don't eat processed grains (especially wheat), don't eat sugar, don't eat any kind of processed vegetable oil, get plenty of sunshine and eat good-quality meat and fish, organs (liver), and butter if you choose. I don't know exactly which part of this diet protects against cancer, maybe all of it. Carbs are fine, as long as they come from root vegetables, veggies and fruit."

In addition, it is important to try to eat only 3 meals a day with no snacks in-between. We want to try to maximize the period between the last meal of the day (dinner) and "breaking-the-fast" the next day. A period of at least 10 hours is recommended. All of these recommendations are designed to combat or prevent insulin resistance – the precursor to all the "diseases of civilization", including cancer.

The major dietary changes that I recommend and have personally followed are (in relative order of importance):

1. No excess sugar(s) or starches. Add or maintain sufficient fiber to help mitigate sharp insulin "spikes" due to a rapid rise in blood glucose levels. Ingesting vinegar can have the same effect.

The first major area of concern in the diet is the issue of all sugars (i.e. **sucrose**, **glucose**, **fructose**, **lactose**, **etc.**) consumed as food or drink additives and, to a lesser extent, as converted from other carbohydrates (mainly starches). It can be reasonably argued that sugar(s) are probably the single *worst* ingredient found in our diets. And this is especially of concern for cancer patients.

<u>Note</u>: The following explanation is largely based on a popular YouTube lecture given by Dr. Robert H. Lustig called, "Sugar – The Bitter Truth" and found here:

http://www.youtube.com/watch?NR=1&feature=endscreen&v=dBnniua6-oM

In this video Dr. Lustig claims that common sugar, in two of its forms – **sucrose** (common table sugar) and **high fructose corn syrup** (**HFCS**) – should be considered "toxic". By this he does not mean that sugar is "acutely" toxic (like arsenic, for example) but "chronically" toxic because its lethality develops over a long period of time. Regardless, he considers sugar as a "poison" and the primary cause of metabolic syndrome and a conglomerate of highly prevalent chronic diseases including Obesity, Type 2 Diabetes, Dyslipidemia, Cardiovascular Disease, and Hypertension⁵.

⁴Direct quote from Stephan Guyenet, from his blog: http://wholehealthsource.blogspot.com/

⁵Not to mention **Insulin Resistance** (also called **IR** or **Syndrome X**) that may play a pivotal role in the promotion of tumor growth and proliferation. Insulin is secreted in response to foods eaten – particularly carbohydrates – to keep blood sugar in control after a meal. When cells become resistant to insulin, the body (the pancreas to be precise) responds to the rising blood sugar by pumping out more and more insulin. Eventually the pancreas can no longer keep up with this demand or it gives in to what is called "pancreatic exhaustion." At this point the blood sugar will rise out of control, and you've got diabetes.

Gary Taubes wrote extensively about this topic in the New York Times Magazine of April 13, 2011 in an article called, "Is Sugar Toxic?" to be found here:

http://www.nytimes.com/2011/04/17/magazine/mag-17Sugar-t.html?pagewanted=all&_r=0

Back to Dr. Lustig. He begins his lecture by noting that both the popular **Atkins** diet (consisting of high fat and low carbohydrates) – and the "traditional" **Japanese** diet (consisting of high carbohydrates but little fat) – appear to "work" to reduce weight. This contradiction can best be resolved by noting that neither one of them contains any excess sugar(s) and, in particular, the sugar **fructose**.

Lustig goes on to counter an incorrect (but nonetheless popular) notion that obesity is caused by improper diet and lack of exercise. He shows that the common perception that if you don't burn the calories that you eat you will still store them (i.e. get fat) is patently false.

The real problem, Lustig claims, begins when a person's internal "negative feedback system" has gone out of whack. For these people, **leptin**, a hormone that comes from fat cells and informs the brain to stop eating, is no longer working properly. Lustig believes that the initial culprit behind this failure are sugar(s), and in particular, the sugar fructose⁶. This is one substance that we are consuming more of today than ever before.

Fructose can make the brain **leptin-resistant**, which means that the brain doesn't "see" all the fat that is already stored in the body but rather "thinks" that it is starving. This causes a powerful leptin-induced biochemical drive to keep eating – even when there is absolutely no real need to do so.

There is also a high level of sodium (salt) in many sweetened beverages (this actually is added to further induce thirst). Sugar is then deliberately added to cover the salty taste. The insidious outcome is that consuming these drinks does not really relieve thirst. Lustig dubs this trick the "Coca-Cola Conspiracy."

In addition there is also another important hormone to consider, called **ghrelin**, which is the "hunger" hormone. The more ghrelin there is, the hungrier we will feel.

Studies show that fructose does not reduce blood levels of ghrelin nearly as much as glucose does. These studies suggest that fructose does not make you feel full after a meal in the same way that glucose does, even with the exact same number of calories consumed. So this too can lead to an increase in overall calorie intake.

Meanwhile there was also an unfortunate confluence of political and economic factors that started in the early 1970's. These resulted in a misguided effort to eliminate the occurrence of heart disease by reducing

One disease that increases in incidence with obesity, diabetes, and metabolic syndrome is cancer. Insulin resistance may be a fundamental underlying defect in many cancers, just as it is in Type II Diabetes and Cardiovascular Disease. The connection between obesity, diabetes, and cancer was first reported in 2004 in large population studies by researchers from the WHO's International Agency for Research on Cancer. It showed that you are more likely to get cancer if you're obese or diabetic than if you're not, and that you're more likely to get cancer if you have metabolic syndrome than if you don't.

⁶Refer here: http://www.nature.com/ncomms/2013/130910/ncomms3434/full/ncomms3434.html

the consumption of "fats" from 40% to 30% in the diet. But as a result of this effort something totally unexpected occurred. Although the fat was removed (or reduced), the incidence of Obesity, Metabolic Syndrome, Non-Alcoholic Fatty Liver Disease, Cardiovascular Disease, and Strokes started to increase. Lustig categorically states that the major culprit for all this were sugar(s) – and again, in particular, fructose. More sugar(s) were added to mask that awful "cardboard" (flat) taste whenever the fat was removed.

Note that ordinary table sugar (sucrose) and high fructose corn syrup (HFCS) both contain only two types of molecules: glucose and fructose.

According to Lustig, to understand the damaging effects of fructose consumption one must first understand how it is metabolized. So he devotes a good portion of his lecture to comparing the metabolism of fructose to that of glucose and also to that of **ethanol** (grain **alcohol**)⁷. In this detailed analysis Lustig also demonstrates that "a calorie is not a calorie."

Glucose is a sugar that is absolutely vital to life. It is an integral part of every cell's metabolism. Our bodies produce it and we have a constant reservoir of it in the bloodstream. Every cell in the body can use glucose for energy. If we don't get enough glucose from our diet, our bodies will produce what we need out of proteins and fats and, in the worst case, even muscle.

Fructose, however, is very different. This molecule is not a big part of cell metabolism and humans do not produce much of it. In fact, very few cells in the body can make use of it at all – except for the liver cells. So when consuming sucrose most of the fructose in it will be metabolized by the liver. There it is turned into fat, which is then secreted into the blood.

Gary Taube's article explains some of the metabolic implications of this:

"The phrase Lustig uses when he describes this concept is "isocaloric but not isometabolic." This means we can eat 100 calories of glucose (from a potato or bread or other starch) or 100 calories of sugar (half glucose and half fructose), and they will be metabolized differently and have a different effect on the body. The calories are the same, but the metabolic consequences are quite different.

So the fructose component of sugar or HFCS is metabolized primarily by the liver, while the glucose from sugar and starches is metabolized by every cell in the body. Consuming sugar [50% fructose and 50% glucose] means more work for the liver than if you consumed the same number of calories from starch [100% glucose]. And if you take that sugar in liquid form – soda or fruit juices – the fructose and glucose will hit the liver more quickly than if you consume them, say, in an apple (or several apples, to get what researchers would call the equivalent dose of sugar). The speed with which the liver has to do its work will also affect how it metabolizes the fructose and glucose.

In animals, or at least in laboratory rats and mice, it's clear that if the fructose hits the liver in

⁷Glucose and fructose have the exact same molecular formula ($C_6H_{12}O_6$) and are carbohydrates. Note, however, that ethanol (C_2H_6O) is **not** because all carbohydrates must follow this formula: (CH_2O_n).

sufficient quantity and with sufficient speed, the liver will convert much of it to fat. This apparently induces a condition known as insulin resistance, which is now considered the fundamental problem in obesity, and the underlying defect in heart disease and in the type of diabetes, type 2, that is common to obese and overweight individuals. It might also be the underlying defect in many cancers.

If what happens in laboratory rodents also happens in humans, and if we are eating enough sugar to make it happen, then we are in trouble...

Now most researchers will agree that the link between Western diet or lifestyle and cancer manifests itself through this association with obesity, diabetes, and metabolic syndrome – i.e., insulin resistance. This was the conclusion, for instance, of a 2007 report published by the World Cancer Research Fund and the American Institute for Cancer Research – "Food, Nutrition, Physical Activity and the Prevention of Cancer."

So how does it work? Cancer researchers now consider that the problem with insulin resistance is that it leads us to secrete more insulin, and insulin (as well as a related hormone known as insulinlike growth factor) actually promotes tumor growth.

As it was explained to me by Craig Thompson, who has done much of this research and is now president of Memorial Sloan-Kettering Cancer Center in New York, the cells of many human cancers come to depend on insulin to provide the fuel (blood sugar) and materials they need to grow and multiply. Insulin and insulin-like growth factor (and related growth factors) also provide the signal, in effect, to do it. The more insulin, the better they do. Some cancers develop mutations that serve the purpose of increasing the influence of insulin on the cell; others take advantage of the elevated insulin levels that are common to metabolic syndrome, obesity, and type 2 diabetes. Some do both. Thompson believes that many pre-cancerous cells would never acquire the mutations that turn them into malignant tumors if they weren't being driven by insulin to take up more and more blood sugar and metabolize it.

What these researchers call elevated insulin (or insulin-like growth factor) signaling appears to be a necessary step in many human cancers, particularly cancers like breast and colon cancer. Lewis Cantley, director of the Cancer Center at Beth Israel Deaconess Medical Center at Harvard Medical School, says that up to 80 percent of all human cancers are driven by either mutations or environmental factors that work to enhance or mimic the effect of insulin on the incipient tumor cells. Cantley is now the leader of one of five scientific "dream teams," financed by a national coalition called Stand Up to Cancer, to study, in the case of Cantley's team, precisely this link between a specific insulin-signaling gene (known technically as PI3K) and tumor development in breast and other cancers common to women.

Most of the researchers studying this insulin/cancer link seem concerned primarily with finding a drug that might work to suppress insulin signaling in incipient cancer cells and so, they hope, inhibit or prevent their growth entirely. Many of the experts writing about the insulin/cancer link from a public health perspective – as in the 2007 report from the World Cancer Research Fund and the

American Institute for Cancer Research – work from the assumption that chronically elevated insulin levels and insulin resistance are both caused by being fat or by getting fatter. They recommend, as the 2007 report did, that we should all work to be lean and more physically active, and that in turn will help us prevent cancer.

But some researchers will make the case, as Cantley and Thompson do, that if something other than just being fatter is causing insulin resistance to begin with, that's quite likely the dietary cause of many cancers. If it's sugar that causes insulin resistance, they say, then the conclusion is hard to avoid that sugar causes cancer — some cancers, at least — radical as this may seem and despite the fact that this suggestion has rarely if ever been voiced before publicly. For just this reason, neither of these men will eat sugar or high-fructose corn syrup if they can avoid it.

"I have eliminated refined sugar from my diet and eat as little as I possibly can," Thompson told me, "because I believe ultimately it's something I can do to decrease my risk of cancer." Cantley put it this way: 'Sugar scares me."

There are still other reasons to be scared.⁸ Sugar, due to its powerful effects on the reward system in the brain, leads to classic signs of addiction comparable to drugs of abuse. This activates powerful reward-seeking behavior that can drive to overeating.

Only briefly mentioned in Lustig's lecture, but nonetheless important, is the issue of maintaining fiber in the diet. According to Dr. Lustig we currently consume only about 12 grams of fiber a day – as compared to 100 to 300 grams of fiber a day fifty thousand years ago.

Adequate fiber may be important for three reasons. First, it slows the rate of absorption of carbohydrates in the intestine. A slower rate of absorption gives intestinal bacteria a chance to get to it first and break it down. Second, fiber increases the speed of transportation of intestinal contents to the **ileum**, the final section of the small intestine. This in turn raises the level of the satiety hormone that tells the brain that the meal is over. So the feeling of satiety occurs sooner. Finally, fiber inhibits the absorption of free fatty acids until reaching the colon where they are divided into tiny fragments called "short-chain fatty acids." These molecules suppress insulin instead of stimulating its release and that prevents issues with insulin resistance in the body.

It is for these reasons that the consumption of the whole fruit (but *not* fruit juice), even though it may contain sugars such as fructose, does not pose as big a problem. The fiber packaged within the fruit can work to mitigate the rapid absorption of those sugar(s) in the gastrointestinal tract. This, in turn, prevents the sharp jump in insulin level. However, the amount of the simple carbohydrate (sugars) being ingested will still remain the same. As such the total amount of whole fruit(s) consumed should be limited – no

LA Times 10/22/07

^{8&}quot;Cancer cells require an enormous amount of fuel to proliferate. And so cancer cells evolve to be incredibly sensitive to insulin. Raise insulin levels, and tumor cells get the fuel they need to divide and multiply. If insulin binds to receptors on the surface of these cancer cells, they can suck in more blood sugar. So the more blood insulin is available, the more blood sugar gets into these cells. Also, insulin increases the availability of a growth factor that's been shown to cause tumor cells to go from benign to malignant and then metastasize." – from interview with Gary Taubes in the

matter how beneficial its constituent nutrients (i.e. various phytochemicals and anti-oxidants) may actually be.⁹

It should be kept in mind that the brain generally "runs" on lots and lots of glucose. ¹⁰ Meanwhile, the mere presence of glucose in the serum does not create an insulin release from the pancreas. What does create an insulin release is a *rapid rise* of glucose in the serum. If fiber slows that rate of rise, the insulin response will be fully within the norms of mammalian physiology and will thus not trigger insulin resistance or lead to metabolic syndrome. Note that vinegar also works to slow the rate of insulin release in much the same way fiber does.

If all of the preceding is not convincing of the dangers of consuming simple carbohydrates (sugars) or the wrong kinds of carbohydrates (refined grains and cereals) or too many carbohydrates in the overall dietary mix, consider this recent research that shows that **sugar activates oncogenes in tumors**:

"Sugar consumption fueled tumor growth in fruit flies, possibly explaining why people with metabolic syndrome have an increased risk for certain cancers, according to a new study.

Putting *Drosophila* engineered to express the oncogenes Ras and Src on a high-sugar diet resulted in small, localized tumors growing much larger and metastasizing, reported Ross Cagan, from the Icahn School of Medicine at Mount Sinai in New York City, and colleagues.

The sugary diet caused the flies to develop insulin resistance, but it also promoted tumor cell-specific insulin sensitivity by increasing the activity of the canonical signaling pathway Wingless/Wnt, the researchers wrote in the journal *Cell*.

'Using our fruit fly model, we discovered how tumors overcome insulin resistance in the body and turn metabolic dysfunction to their advantage,' Cagan said in an accompanying statement. 'Our study shows that sugar activates oncogenes in the tumor, which then promote insulin sensitivity, meaning that the exorbitant glucose levels in the blood pour into the tumor, having nowhere else to go in the insulin-resistant body.'

People with diabetes, obesity, and other metabolic diseases have a higher-than-average risk for certain malignancies, including breast, liver, colon and pancreatic cancers.

But it has not been clear why these cancers grow so aggressively in insulin-resistant patients, Cagan said.

'How would a tumor thrive in a body that is crippled in its ability to take up insulin and sugar to fuel cells?' Cagan said to *MedPage Today*. 'That has been the mystery.'

⁹This means that the "official" recommendation to "eat 5 servings of fruit a day" is actually unhealthy.

¹⁰Except when the body is put into a state of nutritional **ketosis**. Brain cells can be "trained" to run on ketones instead of glucose. Ketones are synthesized in the liver from various fatty acids.

In earlier research, Cagan's group showed that fruit flies fed a high-sugar diet -- consisting of standard diet supplemented to 1.0 M sucrose -- became diabetic very quickly. They conducted the current study to find out what impact the same diet would have on flies genetically engineered to express tumors.

When young flies that expressed the Ras and Src oncogenes were fed high protein, low-sugar diets, their tumors generally remained very small and localized. But soon after the flies were placed on the calorie-matched, high-sugar diets, the tumors grew and spread.

The sugar acted together with Ras and Src to increase insulin receptors and, in turn, insulin sensitivity in the tumor cells by increasing signaling of the Wingless/Wnt pathway.

'The tumors just went crazy,' Cagan said. 'When the flies were on a normal diet the tumors could barely be seen, but as soon as the sugar was introduced they were everywhere.'

Cagan and colleagues then treated the flies with a three-drug cocktail that included the diabetes drug acarbose, which blocks the conversion of sugar to glucose; the drug pyrvinium, which inhibits Wingless/Wnt signaling; and their own anticancer compound (AD81) that targets Ras/Src and causes cell death.

Each drug had only a modest impact on tumor growth when given alone, but when given together the drugs dramatically reduced tumor size and progression.

More than 90% of the flies given the triple-drug treatment survived to adulthood, compared with none of the flies left untreated, Cagan said.

Cagan's group has begun cellular studies using human tumor samples to determine if sugar has the same impact in people with metabolic disease.

'These results provide a potential explanation for how insulin resistant animals are at increased risk for tumorigenesis, and emphasize the importance of targeting multiple, specific notes to achieve optimal therapeutic value,' the researchers wrote."

Note that the metabolism of sugars and other carbohydrates will deplete vitamin B1 (Thiamine) which is water soluble and not stored in the body in any amount. Alcoholism and other chronic diseases can also deplete Vitamin B1.

Excess sugars and carbohydrates may reduce Neutrophils' ability to ingest and kill invading bacteria or other foreign bodies for a period of more than 5 hours after ingestion. Neutrophils are a type of leukocyte (white blood cell) that circulate in the blood and "eat" foreign organisms such as viruses by a process called phagocytosis. They make up about 60-70% of the white blood cells in our bodies. The measure of how

¹¹Original paper here: "Transformed Drosophila Cells Evade Diet-Mediated Insulin Resistance through Wingless Signaling": http://www.cell.com/abstract/S0092-8674%2813%2900769-1

many organisms one leukocyte can eat in an hour is called the "Leukocytic Index" (LI). For example, if one leukocyte can eat 10 organisms in our hour its Leukocytic Index is 10.

In 1976 a 1973 study was repeated that tested the effect of sugar (sucrose) on leukocytes. Test subjects were given 24 ounces of sugar sweetened Cola. In this particular test the Leukocytic Index of all the subjects was reduced by 50%.¹²

I will explore even more compelling arguments against the excess ingestion of simple and (high glycemic index) complex carbohydrates in the section titled, "Cancer As A Metabolic Disease".

To sum up, here is a brief video documentary that summarizes many of the issues: http://www.abc.net.au/catalyst/stories/3821440.htm

2. Skip the milk but other whole fat dairy products are good for you

One will find strident advocacy against consuming all milk and dairy products in the book, "The China Study," and also in the video documentary, "Forks Over Knives." Yet the various claimed benefits for going completely vegan remain scientifically unproven and unconvincing.

The primary concern voiced in these two polemics is that milk contains a type of animal protein, called **casein**, which has been (mistakenly) linked to promoting cancer in a few studies. [To be completely accurate there are actually four different types of casein protein found in milk.]

Dr. Thomas Campbell led a study on two groups of aflatoxin-exposed laboratory rats that were fed different concentrations of milk casein (20% vs. 5%) in their diet. All of the rats that were fed the higher casein concentration diet developed liver tumors. But when that higher percentage casein diet was then reduced back to 5%, the tumors all went into remission. His "logical" conclusion was that the casein protein in the milk was the cancer "promoter". That was not to say that milk was a carcinogen. It did not cause cancer per se, but it did *appear* to be a favored nutrient by cancer cells and it did promote their growth. Dr. Campbell then repeated the experiment, this time using only plant protein sources (including soy). However, those plant proteins did not *appear* to produce cancer - whereas the animal protein casein had. Or so he claimed.

However, it turns out that these animal and plant protein experiments were not as straightforward as they first appeared to be:

"In a later 1989 study, Campbell discovered that **wheat protein** exhibited similar carcinogenic properties (as did **casein**) when **lysine**, its limiting amino acid, was restored. This suggests that *any complementary combination of amino acids* will spur cancer growth under certain experimental conditions, and that carcinogenic qualities are **not unique to casein** or to animal protein at large. The sole reason plant protein appeared protective in those rat studies was due to a deficiency in one

¹²Sanchez A, et al. "Role of sugars in human neutrophilic phagocytosis." *Am J Clin Nutr* 1973; 26: 1180-84; Ringsdorf WM jr, Cheraskin E and Ramsey RR jr. "Sucrose, Neutrophilic Phagocytosis, and Resistance to Disease." *Dent Surv* 1976; 52 (12): 46-48

or more amino acids, a scenario that rarely occurs in real-world situations when a variety of foods — whether plant or animal in origin — are consumed. Campbell himself notes that eating a variety of plant foods provides a full spectrum of amino acids - indicating that even a plant-only diet can yield the complete protein Campbell claims to be carcinogenic ... He [also] does not acknowledge the abundance of similar studies showing that **whey** — another milk protein — consistently boasts anti-cancer properties, including when studied under the same experimental conditions that demonstrate the carcinogenic qualities of casein. This is significant, as even a single example of animal protein inhibiting rather than spurring cancer invalidates Campbell's hypothesis that the effects of casein can be extrapolated to all animal protein." — from Denise Minger's **Raw Food SOS** website. More analysis can be found there:

http://rawfoodsos.com/2010/07/07/the-china-study-fact-or-fallac/

http://rawfoodsos.com/2011/09/22/forks-over-knives-is-the-science-legit-a-review-and-critique/

Yet another critique of the flawed research and questionable conclusions reached in **The China Study** can be found here:

http://www.proteinpower.com/drmike/cancer/the-china-study/vs-the-china-study/

Nonetheless it may still be valid to question the consumption of milk – but not because of these bogus studies regarding casein vs. plant protein in laboratory rats.

The legitimate concern stems from the fact that milk (from cows, goats, or whatever) is primarily designed to promote the growth of their offspring. As such it contains growth-inducing hormones such as **IGF-1** (**Insulin-like Growth Factor-1**) and similar agents. These are some of the very same substances and compounds that promote angiogenesis and subsequent proliferation of tumors in humans.¹³

<u>Note</u>: This is the case *without* also considering the possible *addition* of even more hormones (and antibiotics) that grain-fed farm animals may be given to stimulate faster or excessive growth. What that means is that finding an "organic" pasture grass-fed source of milk will not adequately address this particular problem.

[Of course the prolific use of antibiotics is a major problem all its own. It is extremely disconcerting to note that in 2011 more antibiotics were sold for use in meat and poultry production than ever before. They now represent four-fifths of all the antibiotics used in the US - according to a 2011 report by the Pew Charitable Trusts.]

All of the research evidence presented in favor of a plant-based (only) diet is rather misleading and inconclusive. "**The China Study**" recounts a massive (but terribly flawed) research project that seemed to reveal a very startling fact. It seemed to show that in those areas of China (generally rural) where there was little or no consumption of meat and dairy products the incidence of cancer(s) was extremely low or almost

¹³However, it is still not clear if consuming these growth hormones in milk can actually survive the human digestive process. So far it appears they do not.

non-existent. In contrast, in the early 1990's (when China started to open up to western tourism and products) these same areas began showing incidents of cancer that were more in line with the rest of the western world. So what might have changed? Well, for one thing, the populace began to eat a "westernized" diet that now included more meat, dairy products, processed foods, including added sugar(s) and refined carbohydrates. The major problem is that the China Study does not shed conclusive light on what the real substance(s) or life-style changes were that influenced cancer. It may reveal some tantalizing (but inconclusive) associations but these cannot be considered causes. *Correlation is not causation*. Most damning (to my way of thinking) was that there was no tracking of sugar and refined carbohydrate consumption levels in all of the subject populations studied.

It may come as a shock to note that the great majority of the earth's adult populations have enzyme systems that simply cannot handle milk digestion properly. Milk gives these people gas, cramps, indigestion, and may even cause emotional side effects such as depression and confusion. Note also that most children, around the age of two, experience a natural gradual reduction of their body supply of lactase. This is the enzyme that is essential for metabolizing lactose (milk sugar).

Before moving on it may also be useful to keep in mind that there is a basic commonality found in many different chronic ailments such as Cancer, Cardiovascular Disease, Type II Diabetes, Obesity, the Metabolic Syndrome, Lupus, Arthritis, and Multiple Sclerosis. These diseases are all (in different ways) triggered by **chronic inflammation**. That is why it proves beneficial to investigate the role of proper nutrition in helping to reduce internal inflammation.

The video documentary "Forks Over Knives" cites an interesting example of the role of nutrition in reducing one such chronic illness. It notes that there was a sharp reduction in Cardiovascular Disease (CVD) in the population of Norway during its occupation during World War II. After the Nazis had invaded Norway they absconded with all the farm animals (cattle, pigs, and chickens, etc.) and sent them back to feed the citizens of Germany. So, virtually overnight, the Norwegians were forced to become mostly vegan – as they had no choice in the matter. There were few meat or dairy products available (but please note that there was *plenty of fish and seafood* still available). If you look at the incidence of heart disease in Norway during those years of Nazi occupation it quickly drops way, way down. It does not come back up to the levels seen in other western countries (or in Norway before its invasion) until after the end of Nazi occupation. However, once again this observation shed no conclusive light on what the actual substance(s) or life-style changes were that led to this dramatic drop in Cardiovascular Disease during the years of German occupation.

Final note: Milk is made up of about 87% of the protein **casein**. The other 13% is made up of the protein **whey**. Whey protein is not considered carcinogenic. In fact it is highly recommended for "safe" weight gain by the folks at the Block Center for Integrative Cancer Treatment (and many others). Here is what they have to say about it:

"Whey helps raise **glutathione**¹⁴ levels and inhibit cancer. Thus, high-quality, micro-filtered whey protein is a good protein supplement for people needing more protein ... It is a rich source of the

¹⁴Glutathione is very important in the generation of GABA (gamma amino butyric acid). It is manufactured inside the cell from its precursor amino acids: glycine, glutamate, and cysteine. Cysteine contains sulfur, another important

essential amino acids needed by the body. In its purest form, as whey protein isolate, it contains little to no fat, lactose, or cholesterol. Whey has been found to provide immune support while raising **glutathione** levels. Cancer patients undergoing radiation or chemotherapy often have difficulty in meeting their daily nutritional requirements due to nausea and lack of appetite. This may lead to weight loss, muscle loss, and protein deficiency. Whey protein is an excellent protein choice for cancer patients as it is very easy to digest and very gentle to the system. Cancer patients also may have reduced glutathione levels (like many athletes) and a weakened immune system. Numerous studies have shown that whey protein, rich in the amino acid **cysteine**, provides an extra boost to the immune system by raising glutathione levels. This may help reduce the risk of infection and is believed to possibly improve the responsiveness of the immune system."

To conclude this section, it should be noted that a high consumption of *low-fat* milk (but *only* the *lower-fat* versions) has been observed to double men's risk of getting prostate cancer. But is this due to the consumption of casein protein? Or is it due to the lack of fat; or to too much iron; or to Insulin-like Growth Factor-1 (IGF-1); or to sugar(s) and refined carbohydrates; or perhaps some other substance or some combination of all of them together? The definitive answer to these questions is far from clear at this point in time.

3. Do not fear saturated fats, meat, fish, and seafood.

There are some considerations to keep in mind when eating meats. Meat needs to be ingested with sufficient fat (therefore, and contrary to popular belief, you should actually avoid lean cuts). Fish and seafood should figure prominently in the diet (i.e., serve it at least 2 times a week).

To understand the importance of eating more fish and seafood (while avoiding farm raised sources whenever possible) and consuming other stock meats (preferably from pastured grass-fed sources), a little exploration of basic biology is now in order. Along with that it will be necessary to explore a decades-old (and still on-going) controversy regarding saturated fats and cholesterol.¹⁵

Fat is the collective shorthand name given to any large mixture of smaller units called "fatty acids". It is the principal form in which the body stores energy. It also acts as an insulating agent beneath the skin and around some internal organs. It is also essential for healthy cell membranes and the absorption of all the fat-soluble vitamins (A, D, E, and K).

There are three major families of fatty acids of interest: saturated fatty acids, mono-unsaturated fatty acids, and poly-unsaturated fatty acids (also called PUFA's).

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cell nutrient. GABA is one of the most important inhibitory neurotransmitters. Some believe it is an important factor in mood disorders, including obsessive-compulsive disorder, depression, and anxiety.

¹⁵I do *not* share in the misguided belief that saturated fats, such as those found in primarily meat and dairy products, should be avoided. The "Diet-Heart hypothesis" (which recklessly demonizes saturated fats and dietary cholesterol) has not been scientifically substantiated - even after decades of study. More info: http://www.youtube.com/watch?v=rDVf-00w5gk and http://www.youtube.com/watch?v=F0kIC-dbW2g

What makes one fatty acid "saturated" and another "unsaturated" has to do with its molecular architecture and composition. In particular it has to do with the number of carbon-to-carbon double bonds that exist in its molecular chains. Saturated fats do not contain any double-bonded carbon atoms. Mono-unsaturated fats have just one carbon-to-carbon double bond while poly-unsaturated fats will have more than one.

Saturated fats are primarily found in animal foods (meat, dairy products, eggs, etc.) and in tropical plant foods such as coconut, coconut oil, and palm oil. All fats contain varying mixtures of these different fatty acid types. Although animal fats are generally thought of as being saturated most of them contain less than 50% of saturated fatty acids. Only milk and dairy products contain more (i.e. cow's milk=64%; cheddar cheese=63%; chocolate milk=58%; butter=50%; human milk=50%).

Saturated fats tend to be solid at room temperature and soften when warm. Because they have no carbon-to-carbon double bonds they are very stable. When exposed to high heat they cannot be damaged in the way that unsaturated fats can be. Again, this is because saturated fats lack any carbon-to-carbon double bonds that can become oxidized.

Stearic acid is one kind of saturated fat. It contains 18 carbon atoms with all of these carbon atoms surrounded by hydrogen atoms (i.e., there are no double bonds). Therefore it is designated as **18:0**. Since the hydrogen atoms are all close together, it is difficult to bend. It is this resistance to bending that makes this and most other saturated fats solid at room temperature.

The most abundant saturated fatty acid is palmitic acid (also called palmitate). It contains 16 carbon atoms, all of which are saturated, so it is designated: **16:0**.

Over the last four decades consumption of saturated fats (and dietary cholesterol) has been unfairly demonized by being *associated* with - but not *causing* - an increased risk of cardiovascular disease. Regardless (and I wish to emphasize this as firmly as possible) there is no hard scientific proof of causation. Saturated fats and cholesterol are not "bad" for us:

http://annals.org/article.aspx?articleid=1846638

http://www.medpagetoday.com/Cardiology/Prevention/44803?xid=nl_mpt_DHE_2014-03-18&utm_content=&utm_medium=email&utm_campaign=DailyHeadlines&utm_source=WC&eun=g659 502d0r&userid=659502&email=n.feldman@videopost.com&mu_id=5792782

In fact there is now mounting evidence that lowered levels of saturated fats and/or cholesterol may also be contributing to an increase in early-onset Dementia and Alzheimer's disease.

Mono-unsaturated fatty acids have just one carbon-to-carbon double bond. They can be found in olive oil (which primarily contains an omega-9 called oleic acid), canola oil¹⁶, avocado, seeds, macadamia, and other nuts. Oleic acid is an 18-carbon fatty acid that has its one double bond in the middle of the molecule. It is

¹⁶Of course you have never actually seen a canola plant because there is no such beast. Canola stands for **CAN**adian **O**il Low **A**cid. It was invented during WWII as a substitute for diesel fuel. It is actually derived from **rapeseed** plants. One should avoid it: http://www.youtube.com/watch?v=omjWmLG0EAs

designated by the term **18:1**. Because of this one double bond this fatty acid can bend and is liquid at room temperature. Oleic acid is also the most abundant fatty acid found in animal fats and in human fat.

Generally unsaturated fatty acids' carbon double bonds have their hydrogen at the double bond **on the same side** of the molecule. This is called the "**cis-**" configuration. But when subjected to the process of hydrogenation some of these double bonds are twisted so that the hydrogen atoms now lie on opposite sides. This is called the "**trans-**" configuration. Our bodies lack the proper enzymes to metabolize man-made trans-configuration fats and so they should be avoided at all costs.

Fats can be attacked by oxygen and become rancid. Similar to the process of rusting, fats oxidize – but only where there are carbon-to-carbon double bonds. This is why saturated fats don't spoil but, for example, poly-unsaturated margarines must always be kept refrigerated. The more double bonds a fatty acid has, the more it oxidizes and the more free radicals it can throw off in the process. Heating unsaturated fatty acids can damage them by this process of oxidation.

Poly-unsaturated fats are those with two or more carbon-to-carbon double bonds. Poly-unsaturated fats can be split further into two major subcategories of considerable interest: the **omega-6's** and **omega-3's**. An omega-3 fatty acid has its first carbon double bond located at the third carbon atom in the chain; an omega-6 fatty acid has its first carbon double bond located at the sixth carbon atom. They all tend to be liquid at room temperature and can be easily damaged when heated or exposed to light.

There are said to be two (and only two) "essential" fatty acids that each of us has to consume from the outside world. These particular substances cannot be manufactured inside our bodies so they must be consumed from the external environment. They are thought to be essential for life, which is why they are called "Essential Fatty Acids" or EFA's. Both of these EFA's are poly-unsaturated.

One of them is known as **Linoleic Acid** or "**LA**"; the other is known as **Alpha-Linolenic Acid** or "**ALA**". Linoleic Acid is an 18-carbon fatty acid with two carbon double bonds, the first after the sixth carbon atom. This makes it an omega-6. It is designated as **18:2** and it is found corn, safflower, sunflower, soya, and most vegetable seed oils. Alpha-Linolenic Acid is also an 18-carbon fatty acid but one with 3 carbon double bonds, (designated as **18:3**) where the first double bond is found after the third atom. This is what makes it an omega-3. It is found in fish, green leafy vegetables, walnuts, chia seeds, flaxseed, and perilla seeds.

By consuming Linoleic Acid (LA) our bodies can actually derive all of the other omega-6 fatty acids that it may need. Similarly, from consuming Alpha-Linolenic Acid (ALA) our bodies can derive all of its other omega-3 fatty acids. However, saying that the body "can" derive them does not mean that this is the best way for the body "to" derive them.

In this regard there are two "long-chain" omega-3 fatty acids that are of particular interest because of their so-called anti-inflammatory properties: **Docosahexaenoic Acid (DHA)** with 22 carbon atoms and 6 double bonds (**22:6**) and **Eicosapentaenoic Acid (EPA)** with 20 carbon atoms and 5 double bonds (**20:5**). Both of these are primarily to be found in fish (and, to a lesser extent, pasture grass-fed meat.)

The fact that the body can make its own EPA and DHA from ALA does not mean it does a very good job of it. It converts ALA into EPA and DHA using certain enzymes and a complicated series of operations that are influenced by many different factors, including the amount of (inflammatory) omega-6's that are in the diet. In the end, only a very small amount of ALA actually gets successfully converted into EPA and DHA in this particular fashion.

Omega-6 and omega-3 fatty acids compete for the same enzymes. When the omega-6 intake is very high it wins that competition by default. So a high intake of omega-6 fatty acids will lower the conversion of ALA into EPA and DHA, further reducing the body's ability to produce two of the most anti-inflammatory substances available to it. This is not good.

There are numerous sources of omega-6 fatty acids to be found – primarily in vegetable oils and some plant foods (and, of course, in some animals as well – but only depending on what they have been fed). The best source of omega-3 fatty acids is from fish and seafood (and to a lesser extent from pasture grass-fed beef). Ground flax seeds, chia seeds, and walnuts all contain ALA but not EPA and DHA (the two beneficial omega-3's).

It turns out that it is the *ratio* of the omega-6 to omega-3 fatty acids that is of *utmost* importance. This ratio should probably be somewhere between 1:1 and 3:1. But if one eats the standard American diet (often referred to as the "SAD" diet) it is likely to be at 15:1 or 20:1 – or even higher. The bottom line is that most of us are consuming far too many omega-6 fatty acids in relation to our omega-3's. A maximum ratio of around 3:1 seems to be the best balance for keeping inflammation in check and everything else running smoothly.

Linoleic Acid (LA - an omega-6) has been shown to increase the oxidation of LDL cholesterol (the so-called "bad" cholesterol), which some doctors believe leads to a higher risk of coronary atherosclerosis. Other omega-6 fatty acids also inhibit the body's ability to fully incorporate all the EPA that you might get into the cell membranes from eating fish or taking fish oil supplements. Omega-6's can also stimulate the production of tumor-promoting growth factors and activate a cancer-promoting gene called **ras-p21**, which can lead to uncontrolled cell replication and tumor growth.

Finally, if one is not paying attention to the "quality" of the omega-6 and omega-3 fatty acids, one may be feeding on "damaged" ones such as those found in processed foods, as hydrogenated oils (trans-fats).¹⁷ Damaged fatty acids can be found in almost *all* packaged grocery items that are designed to have a long shelf life (i.e. they do not turn rancid quickly). But in particular they can be found in many margarines, nondairy "creamers", ramen noodles, soup cups, and virtually all packaged baked goods (e.g. Twinkies®, chips, and crackers), doughnuts, many breakfast cereals, "energy" bars, cookies, and most fast food including French fries and other fried foods. You can easily see the problem. They are pervasive.

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¹⁷There is one exception to the "all trans-fats are bad" rule. It does not apply to "Conjugated Linoleic Acid", or CLA. CLA is a trans-fat that is not man-made. It is made naturally in the bodies of ruminants (such as cows). Factory-farmed meat does *not* have any, but pasture grass-fed meat does. CLA seems to have both anti-cancer and anti-obesity properties: http://www.ncbi.nlm.nih.gov/pubmed/15941017

It is a fair bet that those oncologists who do not advocate worrying much about diet would nonetheless not allow their patients to eat all (or even any) of the Twinkies they might fancy. Such wisdom should be extended to cover *all* of the menu items that rely on adding trans-fats (or any damaged fatty acids) to keep them from spoiling on the shelf.

Any item that does not turn rancid quickly (that is, is *processed*) remains highly suspect and should be avoided.

For example, do you know who may be initially responsible for the invention of margarine – and why? It was Napoleon Bonaparte. He offered a generous prize to anyone who could discover a way to preserve his army's food so that it wouldn't spoil. One fellow, Nicolas Appert, won the prize in the early 1800's with his method of sealing food in glass jars and soaking the closed jars in boiling water. This was the genesis of the modern-day canning process.

Bonaparte also hoped for a substitute for butter that would not turn rancid on long war campaigns. Hippolyte Mège-Mouriès formulated the first versions in 1869.

In the early 1900's Margarine was manufactured from poly-unsaturated fats whose carbon-to-carbon double bonds were replaced by hydrogen bonds (i.e., hydrogenated) to make them solid at room temperature. Unfortunately, these new molecules were in the trans- configuration.

Trans-fats are shaped like saturated fats and therefore the body gets fooled and easily mistakes them for saturated fats. There is a very good reason to suspect why substances containing trans-fats might be prime cancer-causing agents due to the fact that they our bodies lack the enzymes to metabolize them properly.

Finally, poly-unsaturated fats may also play a role in causing cancer, diabetes, obesity, aging, thrombosis, mitochondrial damage, hypothyroidism, arthritis, inflammation, and immunosuppression:

"There are three ways in which a substance can increase the risk of cancer: It can cause body cells to become cancerous [perhaps by tripping switches in the epigenome and thence altering genetic expression]; it can promote a cancer's growth; it can suppress the immune system. Polyunsaturated vegetable oils have been shown to do all three."

– Dr. Barry Groves; From Chapter 5 of "Trick and Treat – How 'Healthy Eating' Is Making Us Ill"

"Poly-unsaturated fatty acids and X-rays have many biological effects in common. They are *immunosuppressive*, but they produce their own *inflammatory reactions*, starting with increased permeability of capillaries, disturbed coagulation, and proteolysis, and producing fibrosis and tumefaction or tissue atrophy. This isn't just a coincidence, since ionizing radiation attacks the highly unstable poly-unsaturated molecules, simply accelerating processes that ordinarily happen more slowly as a result of stress and aging."

- Dr. Ray Peat

Key take-away concept:

Cook only in saturated fats. These include: Butter; Ghee; Coconut Oil; Duck Fat; Beef Tallow; Pork Lard; etc. Basically, every fat that we have been erroneously told for 40+ years is "bad" for us. But - they are not bad for us at all. In fact, they are crucial.

Saturated fats are the only fats that cannot be oxidized when heated or put in sunlight or kept at room temperature (where generally they remain solid - although they will quickly liquefy when heated slightly). That is why the bogus idea of "artery clogging" fats is a complete lie. Even though they may be solid at room temperature they all become liquid well before reaching 98.6 degrees F.

We have been "fed" a load of bunk and bogus advice that saturated fats are "bad" for us for over 40 years. But now even **Time Magazine** has finally come around:

http://healthimpactnews.com/2014/time-magazine-we-were-wrong-about-saturated-fats/

And the Wall Street Journal:

http://online.wsj.com/articles/nina-teicholz-the-last-anti-fat-crusaders-1414536989

4. No consumption of "processed" and "refined" foods

As mentioned earlier there are two important forms fatty of acids: Linoleic Acid (parent to the omega-6's) and Alpha-Linolenic Acid (parent to the omega-3's). There are many other forms, such as the omega-9's that can be found in olive oil – but LA and ALA are the only "essential" ones.

Linoleic Acid and Alpha-Linolenic Acid are transformed into **prostaglandins**¹⁸ and **leukotrienes** by way of some other fatty acids. Linoleic Acid is transformed into **Arachidonic Acid** (**AA**) and from there into a series of prostaglandins and leukotrienes. [Note: Don't worry, you won't be graded on any of this stuff. But if you ever are, it will definitely go on your permanent record.]

The important point to note here is that the bulk of the Arachidonic Acid end products serve to promote inflammation. However, there is also one by-product in the transformation process, called **D-GLA**, which creates a powerful anti-inflammatory prostaglandin called **PGE1** in a small quantity. Regardless, chronic inflammation can (and does) predispose humans to cancer.

Linoleic Acid is found in corn, safflower, sunflower, and all vegetable oils from temperate climates. Meat, dairy, poultry, and eggs can also directly contribute Arachidonic Acid. The omega-6 transformation pathway produces prostaglandins such as **PGE2** and leukotrienes such as **LTB4** that promote tumor growth, clotting, inflammation, and angiogenesis. However, it is the *excess* of the omega-6 derived prostaglandins that are at the root of the problem. If there is an excess of omega-6 fatty acid in the diet the body cannot

¹⁸Prostaglandins are produced in the body by oxidizing poly-unsaturated fatty acids. Some of them suppress immunity, cause inflammation, and promote cancer growth. Others, such as PGI2 (prostacyclin) are considered "good" because they can promote vasodilation.

make sufficient omega-3 end products that are needed to keep clotting, inflammation, and angiogenesis at "normal" levels.

Alpha-linolenic acid is transformed into Eicosapentaenoic Acid (EPA) and then into Docosahexaenoic Acid (DHA) and then into prostaglandins that are anti-inflammatory. Those who take fish or krill oil pills will recognize that these two components – EPA and DHA – are the two major ingredients in these supplements. Canola, Flax, Walnut, Pumpkin seed and Hemp oils are all sources of omega-3 fatty acids that will undergo transformation processes. Cold-water fish contribute EPA. EPA is processed into Docosahexaenoic Acid (DHA) and then into the anti-inflammatory prostaglandin **PGE3**. PGE3 inhibits tumor growth, clotting, inflammation, and angiogenesis.

Please note that fish or krill oil supplements do not contain sufficient antioxidants to neutralize any free radicals that may be created when their carbon-to-carbon bonds are oxidized. This is in contrast to eating fresh fish or seafood, which comes "packaged" with lots of antioxidants.

Fish oil derived omega-3's may help reduce **C-Reactive Protein** (C-RP), a measure of chronic inflammation anywhere in the body. Here is a recent study of the importance of getting C-Reactive Protein checked if you are a cancer sufferer:

http://www.translational-medicine.com/content/7/1/102

5. Avoid all foods that contain Carrageenan

[My thanks to Dr. Ray Peat's weblog for the quotes and explanations that follow:]

"In the 1940s, carrageenan, a polysaccharide made from a type of seaweed, was recognized as a dangerous allergen. Since then it has become a standard laboratory material to use to produce inflammatory tumors (granulomas), immunodeficiency, arthritis, and other inflammations. It has also become an increasingly common material in the food industry. Articles are often written to praise its usefulness and to claim that it doesn't produce cancer in healthy animals. Its presence in food, like that of the polyester imitation fat, microcrystalline cellulose, and many other polymers used to stabilize emulsions or to increase smoothness, is often justified by the doctrine that these molecules are too large to be absorbed.

The doctrine that polymers--gums, starches, peptides, polyester fat substitutes--and other particulate substances can be safely added to food because they are "too large to be absorbed" is very important to the food industry and its apologists.

There are two points that are deliberately ignored by the food-safety regulators: 1) these materials can interact dangerously with intestinal bacteria, and 2) they can be absorbed, in the process called "persorption."

The permeability of the intestine that allows bacteria to enter the blood stream is very serious if the phagocytic cells are weakened. Carrageenan poisoning is one known cause of the disappearance of macrophages.

Carrageenan contributes to the *disappearance* of the liver enzymes (the Cytochrome P-450 system¹⁹) that detoxify drugs, hormones, and a variety of other chemicals.

When the bowel is inflamed, toxins are absorbed. The natural bacterial endotoxin produces many of the same inflammatory effects as the food additive, carrageenan.

Carrageenan produces inflammation and immunodeficiency, synergizing with estrogen, endotoxin and unsaturated fatty acids. Carrageenan has been found to cause colitis and anaphylaxis in humans, but it is often present in baby "formulas" and a wide range of milk products, with the result that many people have come to believe that it was the milk-product that was responsible for their allergic symptoms. Because the regulators claim that it is a safe natural substance, it is very likely that it sometimes appears in foods that don't list it on the label, for example when it is part of another ingredient.

Carrageenan enters even the intact, un-inflamed gut, and damages both chemical defenses and immunological defenses. When it has produced inflammatory bowel damage, the amount absorbed will be greater, as will the absorption of bacterial endotoxin. Carrageenan and endotoxin synergize in many ways, including their effects on nitric oxide, prostaglandins, toxic free radicals, and the defensive enzyme systems. The continuing efficient production of energy is a basic aspect of metabolic defense, and this is interrupted by carrageenan and endotoxin. The energy failure becomes part of a vicious circle, in which permeability of the intestine is increased by the very factors that it should exclude."

Some products that may contain carrageenan: Apple cider; beer; hot dogs; prepared sauces; ice cream; baby formulas; chocolate milk; soy milk; sherbet; jam, jellies; cheese spreads; dressings; crackers; pastries; custard; evaporated milk; pressurized whipped cream; reduced fat meat products; processed meats; pates; diet sodas; toothpaste.

VI. VIEWING CANCER AS A METABOLIC DISEASE

In May 2012, the following article, titled: "Low Oxygen Levels Could Drive Cancer Growth, Research Suggests," was published online in Science Daily:

http://www.sciencedaily.com/releases/2012/05/120503194219.htm

¹⁹Please refer to Chapter VIII, "TKI Interactions with Supplements and Certain Foods" for more information on this.

There were many provocative concepts touched on within the article, the most important one summed up by this quote:

"Previous studies have linked low oxygen levels in cells as a contributing factor in cancer development, but not as the driving force for cancer growth. High incidence rates of cancer around the world cannot be explained by chance genetic mutations alone, Xu said."

Well those "previous" studies date back over 80 years to research started in 1924 by **Dr. Otto Warburg**, an eminent German researcher and cancer specialist. His discoveries subsequently led to his being awarded a Nobel Prize in 1931.

Dr. Warburg found that if you took any "healthy" cell and slowly deprived it of its normal level of oxygen, at a certain point – around 35% of normal – the cell would do one of two things. It would either die or it would turn cancerous. That is, in its struggle to stay alive it would "flip" from its normal mode of getting its energy by the respiration (slow burning) of oxygen – via the process called **oxidative phosphorylation** – to primarily getting its main source of energy from the fermentation of glucose – via the process called **aerobic glycolysis**. He also discovered that once a cell had "flipped" its metabolism in this manner it could never be flipped back. There was no possibility of it returning back to its "normal" oxygen-based respiration and so there was no possibility of a cancerous cell ever becoming healthy again. [Keep in mind for later reference: aerobic glycolysis relies heavily on glucose for its fuel source and strictly glycolytic tumor cells are unable to metabolize fatty acids to derive any of their energy.]

These observations are the basis of the "Warburg Effect." It is the key to how most PET scans work to reveal tumors in the body. In a PET scan a radioactive medicine is first tagged to a natural chemical — usually glucose, water, or ammonia. This tagged natural chemical is known as a radiotracer. This radiotracer is then injected into the body.

Inside the body the radiotracer goes to those areas that normally utilize that particular natural chemical. For example, **FDG** (**F-18 Fluorodeoxyglucose** – a radioactive drug) is tagged to glucose to make it into a radiotracer. This radioactive glucose then goes to those parts of the body that use glucose for energy. The FDG can reveal a tumor by revealing those areas that are soaking up abnormally high levels of glucose. Tumors soak up high levels of glucose because aerobic glycolysis is a very inefficient source of energy as compared to oxidative phosphorylation (the "normal" respiration of oxygen)²⁰.

There are some tumors that may not seem to exhibit the Warburg Effect. For example, 80% of prostate cancers are not especially aggressive, nor are they avid for FDG-18 (glucose). This may also be true for most renal cell carcinomas. They do not soak up large amounts of glucose even though they still cannot run "normally" on oxidative phosphorylation. Instead, these tumors may get their primary energy from the fermentation of the amino acids **glutamine** and **serine** to lactate, which has been termed **glutaminolysis** and **serinolysis** respectively. Regardless of the choice of its ultimate fuel, impaired cellular energy metabolism and, in particular, **impaired mitochondrial function** is a major distinction that **every** tumor seems to share, regardless of what kind of cancer it might be.

²⁰A glucose molecule is capable of providing as many as **36** molecules of ATP via the process of **oxidative phosphorylation** but can only yield **2** molecules of ATP via the process of **aerobic glycolysis**.

Dr. Warburg made the bold claim that this very mechanism – that is, damaged respiration (most often due to a lack of oxygen or hypoxia) – was the *primary* cause of *all* cancers. In his view a healthy cell would *first* flip from oxidative phosphorylation (the normal respiration of oxygen) to aerobic glycolysis (the fermentation of glucose) due to hypoxia or lack of oxygen. But it was this *initial* change that would *subsequently* cause damage to the cell's DNA or other genomic instability.

Naturally his concept was rather controversial. The current paradigm as to the primary cause of most cancers is not what Dr. Warburg had suggested.

This currently accepted **genomic** paradigm assumes that a cancerous cell has its genetic material damaged *first* and only *after that* does its primary metabolism flip from the energy-abundant respiration of oxygen to the energy-inefficient fermentation of glucose (or other amino acids). Regardless, Dr. Warburg's original concepts are now beginning to find their way back into mainstream thinking, as evidenced by the above paper. One of the most vocal modern-day proponents is Dr. Thomas N. Seyfried, author of "Cancer As A Metabolic Disease".

It is not my intent to delve deeply into the pros and cons of Dr. Warburg's theory here. But it is important to understand that there exists today a very credible "contrary" viewpoint regarding the primary cause of cancer. This view approaches cancer as a metabolic disease. The mounting evidence continues to show that impaired cellular energy metabolism and/or impaired mitochondrial function is a key defining characteristic of nearly all cancers regardless of cellular or tissue origin.

So does this consideration of the Warburg Effect specifically apply to renal cell carcinoma (RCC)? Yes, indeed it does:

"Simonnet and colleagues have shown that respiratory impairment was significantly greater in patients with clear cell or high-grade renal tumors than in patients with low grade or benign renal tumors²¹. Moreover, the respiratory impairment in these renal tumors was correlated with significant decreases in the content of ETC (Electron Transport Chain) complexes II, III, and IV as well as with abnormal assembly of the complex V (the F₁F₀ ATPase).

These investigators linked their metabolic findings to defects in the von Hippel-Lindau (VHL) tumor suppressor gene and the hepatic-growth factor MET proto-oncogene. However, alterations in these genes alone were unable to account for differences in tumor aggression. Defects were found in these genes in some benign renal tumors, whereas no defects were found in these genes in some of the most aggressive and malignant renal tumors.²² It was surprising to me that these investigators tried to force their data to fit a gene defect model of renal tumor origin but did not link their observations to Warburg's theory. Clearly, their data more strongly support an origin of cancer following respiratory dysfunction than an origin following gene dysfunction.

²¹"Low mitochondrial respiratory chain content correlates with tumor aggressiveness in renal cell carcinoma" by H. Simonnet et al; Carcinogenesis, 2002 May; 23(5):759-68
²²"Ibid

Unwin and coworkers from the United Kingdom used a proteomic approach, based on two-dimensional gel electrophoresis and mass spectrometry, to compare the protein profiles of renal carcinoma tissue with tissue from patient-matched normal kidney cortex. The most striking findings from their study were the decreased expression of several mitochondrial enzymes implicated in OxPhos (oxidative phosphorylation) and the increased expression of enzymes for glycolysis. The increased expression of the glycolytic enzymes was also associated with a parallel decrease in three of the enzymes catalyzing the reverse reactions of gluconeogenesis. In addition to supporting a downregulation of mitochondrial enzymes involved in other pathways including fatty acid and amino acid metabolism and the urea cycle, indicating a wider role for mitochondrial dysfunction in tumorigenesis." [Dr. Thomas N. Seyfried, "Cancer as a Metabolic Disease"; John Wiley & Sons, 2012; p81]

This idea, along with a detailed examination of several different versions of RCC, are discussed in this video presentation by Dr. W. Marston Linehan of the National Institutes of Health Clinical Center:

https://videocast.nih.gov/summary.asp?live=11952&bhcp=1

It is clear that approaching cancer as a metabolic disease is well worth serious consideration. The amount of oxygen and other vital nutrients available to each cell is critically important in cancer tumorigenesis and metastases. And it is obvious that diet and proper nutrition play pivotal roles in these processes.

In the Science Daily article cited above it was further noted that:

"Cancer drugs try to get to the root -- at the molecular level -- of a particular mutation, but the cancer often bypasses it," Xu said. "So we think that possibly genetic mutations may not be the main driver of cancer."

Here lies another important reason to pay close attention to the delivery of sufficient oxygen and other nutrients to cells. Could it be that impaired respiration (due to hypoxia and/or impaired mitochondrial function) is the "main driver of cancer" and not genetic mutations? If that were so it is logical to assume that this very same mechanism might also be an important factor in promoting cancer metastases as well.

And indeed, research on how tumors stimulate the growth of blood vessels (angiogenesis) seems to suggest that it very well may be.

Recall that Dr. Warburg showed that lack of sufficient oxygen, or hypoxia, could set the stage to turn normal cells cancerous. I do not believe that this is the only mechanism (as he did) but it likely is a primary mechanism. Regardless, while that fact might account for the new formation of a few cancerous cells it does not explain how these cells eventually organize themselves into a visible tumor. Because as those cancerous cells proliferate the tumor cannot grow any larger in size than about 1 to 2 mm - at least not without the formation of new blood vessels. These new blood vessels are essential to supply the growing tumor with sufficient oxygen and other key nutrients (as well as to remove any of its waste products).

²³"Proteomic changes in renal cancer and co-ordinate demonstration of both the glycolytic and mitochondrial aspects of the Warburg effect" by RD Unwin et al; Protemics. 2003 Aug;3(8):1620-32

It was Dr. Judah Folkman (father of anti-angiogenesis therapies) who first glimpsed the process by which tumors might "recruit" these necessary private blood supplies. In his earliest experiments (performed circa 1961) he planted a tumor in the middle of a rabbit's cornea — which normally contains no blood vessels. He then demonstrated how new blood vessels would come *shooting in* and *headed for* that tumor. This simple experiment sparked his search to find and isolate those substances that stimulated this new blood vessel growth.

Eventually one of the most predominant of these substances, VEGF (Vascular Endothelia Growth Factor), was isolated. Significantly, it was also found that VEGF proliferates in an hypoxic environment. In 1992, while studying glioblastoma multiforms (the most common and most aggressive malignant primary brain tumor in humans), Eli Keshet and Karl Plate observed that VEGF expression was highest in the most ischemic²⁴ sections of the tumors and postulated that hypoxia was a key environmental trigger of tumor angiogenesis.

Interfering with angiogenesis by targeting VEGF and other receptors became the basis of how all the TKI (Tyrosine Kinase Inhibitors) such as Sutent[®], Inlyta[®], Votrient[®], Nexavar[®], and Avastin[®] work to stop tumor growth.²⁵

Realizing the importance of getting sufficient oxygen and other vital nutrients into the cells is the primary reason that I personally am so "wound up" on this issue of proper diet and nutrition. It is the reason for my advice to consume only undamaged fatty acids and for maintaining the correct ratio of omega-6 to omega-3 poly-unsaturated fatty acids in the body. This same premise also underlies my attempts to maintaining a consistent and normal blood glucose level with no insulin spikes. It is also one of the reasons why I briefly experimented with taking the blood glucose control drug called Metformin.

The idea behind cutting out additional sugars (in drinks and foods) and cutting down on the consumption of highly refined carbohydrates (like white bread, white rice, white flour, etc.) is **not** because there is any chance of "starving" tumors of their prime energy source (glucose). Carbohydrate restriction cannot starve most tumors because they are still able to pirate glucose at concentrations in the blood that may be **way below** the normal range.

All normal cells get their energy from glucose in various ways while the body's blood glucose level is strictly regulated within a narrow range by several internal mechanisms, starting with the release of hormones like insulin. So the more practical idea is just to reduce the heavy strain put on those mechanisms by the excessive consumption of sugars and high glycemic index (or load) carbohydrates in the first place. There is just too much sugar and starches in many of the foods and drinks that we are consuming daily.

As mentioned earlier, chronically high blood glucose levels can increase the risk of disease (such as **Type 2 Diabetes**, **Obesity**, **Non-Alcoholic Fatty Liver Disease**, etc.) and cancer progression while fueling inflammation. This can also serve to weaken the immune system. More importantly, keeping the blood

²⁴**Ischemic** = A decrease in the blood supply to a bodily organ, tissue, or part usually caused by constriction or obstruction of the blood vessels.

²⁵ **Avastin**® is not a TKI, it is a monoclonal antibody. However, it does target VEGF and similar receptors.

glucose level properly in check – and without rapidly spiking up - also reduces those hormones (Insulin and Insulin-like Growth Factor-1) that promote tumor growth and affect weight management and overall health.

A Few Other Implications to Consider:

- One should avoid consuming **Gatorade**[®] (or other similar beverages) for the purposes of *hydration*. Gatorade not only contains lots of sugar(s) (20 grams of "sugars" with no fiber) but the kind of sugar it typically contains is High Fructose Corn Syrup (HFCS). The original Gatorade formula, developed at the University of Florida in the 1960's, tasted just awful. When Pepsi[®] bought the rights to market and manufacture the stuff they changed the formula to include high levels of sugar to mask the awful taste. Realistically the best "safe" beverage to relieve hydration is simple clean water.
- For the same reason, Gatorade, Gatorade 2, or any similar beverages should not be consumed to help restore electrolytes. Instead, consider using Pedialyte® (or similar products). This medication does contain some glucose (in the form dextrose) but the manufacturer claims that the amount included is only enough to facilitate getting its other ingredients absorbed into the gut. Regardless, there is no fructose in it and that is the really bad stuff. (Do remember to always check the label for the actual ingredients on any product.)
- Similarly, one should try to avoid consuming beverages such as **Boost**® (28 grams of "sugars" with no fiber) or **Ensure**® (18 grams of "sugars" with no fiber) for purposes of adding weight. Instead consider using the low glucose versions of these products (which have been specifically formulated for diabetic patients). I have serious concerns about products like "Boost" and "Ensure" because their levels of sugar(s) are so high and without any fiber included to offset the insulin "spikes" that will immediately result. My primary issue is with those insulin spikes and not the high sugar content. What might be optimum would be to consume a "timed-release" carbohydrate so as to avoid those insulin spikes. (Note that consuming adequate fiber or vinegar does much the same thing). Recently I became aware of such a product although I personally have never used it nor do I know much about it. Regardless, it is called "SuperStarch". The versions that I think may be of direct interest also have protein mixed in:

http://generationucan.com/super.html

• Some other common beverages that contain **HFCS**: chocolate milk; low fat milk; Similac[®], Isomil^{®26}, and Gatorade AMTM for Kids. The bottom line: one should always beware – because added sugar(s) are ubiquitous.

Oh yes, almost forgot. What about those diet drinks that replace the sugar with the artificial sweetener **aspartame** (also found in **NutraSweet**® and **Equal**®)? Well that opens a whole other can of worms. In some people, **monosodium glutamate** (**MSG**) and aspartame can cause an increase in **glutamate**, which in turn leads to excitotoxicity; damaging and eventually killing brain cells. Excess glutamate can also cause neurological symptoms like headache, fatigue, and unexplained, vague neurological symptoms.

²⁶Dr. Robert Lustig calls this stuff "a baby milkshake".

Here is a wonderful website that graphically illustrates the effective amount of sugar(s) contained in many foods that we eat:

http://www.sugarstacks.com

Cancer fighting advantages of following a LCHF (Low Carb/High Fat) diet:

- Low carbohydrate/high fat diets work far better than any other dietary approach for improving all the biochemical markers of internal inflammation. Inflammation is a major force behind tumorigenesis.
- The ingestion of high levels of carbohydrates turns on epigenetic switches of inflammation while also stimulating rapid insulin release. These insulin spikes promote the release of the hormone IGF-1 (Insulin-like Growth Factor-1), which then stimulates all cells (including tumor cells) to grow. These insulin spikes simultaneously decrease the amount of another hormone, IGFBP-3 (Insulin-like Growth Factor Binding Protein-3). This hormone normally works to prevent unregulated tissue growth by inducing apoptosis (cellular death) in cancer cells.
- The bottom line: Carbohydrate induced insulin spikes can provoke indiscriminate cell growth while simultaneously working to prevent cancer cell death. But if you follow a low-carb diet you can minimize any contribution to these unwanted events.

This ends the review of what I call a "proper" diet. Before moving on I thought I should list some additional (and rather unexpected) positive results that I have gotten from following this diet.

Some unexpected (but nice) consequences:

- A slow but steady loss of excess weight without having to pay any attention to the amount of food consumed. In my case I slowly lost about 25 pounds (over three months) and have remained steady ever since at my optimum BMI (= 21.3).
- Increased energy and overall feeling of excellent health and wellness with no fatigue.
- Ironically, I literally have not felt healthier in decades while my blood tests confirm that I actually am far healthier.
- An ability to reduce the duration of my "break" off Sutent from two weeks to just one and eventually to none.
- A possible stoppage and even reversal of atherosclerosis (calcification or hardening of the arteries) that was due to plaque buildup in the walls of my arteries. For a 61-year old male (me) this was also rather dramatically evidenced by:
- Reversal of early-stage erectile dysfunction (ED). This particular phenomenon is also humorously noted in the documentary "Forks Over Knives."

<u>UPDATE (9/9/14):</u> This guide was originally composed while I was taking the oral TKI, **Sutent**® (Sunitinib) to control my bone metastases. However, in early December 2013, routine full-body bone and

CT-scans revealed that although Sutent was still controlling my bone lesions, I had developed numerous small lesions in my liver. This was a new and rather disturbing development. It signaled that Sutent had failed after about 14 months of success.

In the weeks that followed that discovery I attempted to identify (and join) any immune-based clinical trial (of an anti-PD1; anti-PDL1; or a vaccine; etc.) that was available. Unfortunately, there were none found in time and so, starting in early January 2014, I began taking the oral TKI, Inlyta® (Axitinib). Initially the dosage was 5mg twice a day. However, it soon became clear that this dosage was ineffective in controlling my bone lesions. I developed an intense pain in my left femur, which, while taking Sutent, had previously shown healing bone growth. As a result, my Inlyta dosage was then raised to 7mg twice a day. I also underwent radiation therapy to eliminate that left femur lesion as well as a soft tissue mass that was associated with the bone lesion located at my sacrum. It was around that point in time that I also began taking the drug Metformin.

My next set of bone and CT-scans, done on March 4th, revealed that Inlyta had been totally ineffective in controlling all of my liver mets. Three of them had almost tripled in size and there were numerous new tiny mets appearing as well. So once again I searched desperately for a suitable immune-based clinical trial to join and was lucky this time to actually find one. It was a clinical trial of an anti-PDL1 drug made by EMD Serono. I began that trial on April 1st. However, that drug too failed and by the end of May it was clear that I would have to leave the trial.

I then moved on to the drug **Cometriq**[®] (Cabozantinib). But within 2 weeks it was clear that it too had failed. Meanwhile my liver mets had been progressing aggressively. It was now June 28th. Basically, it was clear that my liver would likely fail within the next 2 to 3 weeks. However, I then started on the drug **Afinitor**[®] (Everolimus) that day – and it worked. In fact, it has worked spectacularly. A CT-scan on August 28th showed that all my liver and lymph node mets were now shrinking – some by as much as 50%. Within a few weeks I had regained my health and was off all pain medications.

My next CT-scan, on October 30th, showed no progression and no new mets. However, 4 blood tests were problematic. 3 of them were tests of my liver enzymes and they were all slowly increasing. The fourth, LDH (Lactate DeHydrogenase), had also reversed and was now climbing up again. For this reason in early November I stopped taking Afinitor and switched to an anti-PD1 drug, **Keytruda®**, plus **Avastin®**.

VII. SUPPLEMENTS FOR FIGHTING CANCER

Before proceeding on to describing a few supplements that one might consider taking, some more caveats are in order.

No one should take any of these supplements without first:

• Completely understanding the rationale for each one.

- Making sure that the supplement does not interfere with whatever molecular targeted or chemotherapy drugs they might currently be taking or about to take.
- Making sure that any supplement taken does not interfere with any other medications they may be taking, especially any blood thinning agents (see below).
- Being completely upfront and in full consultation with their doctor(s) about what they are doing and why.

VERY IMPORTANT CAVEAT: Many supplements are natural anticoagulants. For anyone taking blood thinners such as **Coumadin**[®] (**Warfarin**[®], **Plavix**[®], etc.), please do not use any of these supplements without first consulting with a medical doctor.

VIII. DRUG INTERACTIONS WITH SUPPLEMENTS AND CERTAIN FOODS

There is a very serious issue in regard to ingesting any supplements (and also certain foods). That issue is whether or not the substance being consumed might interfere with an oral targeted agent (such as Sutent) getting properly absorbed into the body.

The mechanisms for that to occur revolves around how most pharmaceutical agents and TKI's (Tyrosine Kinase Inhibitors), including Sutent, are metabolized in the gut. Sutent is a substrate (that is, a chemical that is acted on by an enzyme) for the liver enzyme known as **Cytochrome P450 3A4** (**CYP3A4**). However, other drugs or foods can also be substrates for CYP3A4. If so, they may "compete" with Sutent for the amount of CYP3A4 enzyme that is readily available. If these other substances use up a lot of the CYP3A4 enzyme then Sutent may not get metabolized properly. Instead Sutent may remain in the blood stream at an abnormally high level. This could possibly lead to some very severe side effects.

In addition, any supplements (or other medications or foods) that *increase* (or "*induces*") the activity of this enzyme (such as **St. John's Wort** or **Green Tea**²⁷) will *decrease* the concentration of Sutent getting into the bloodstream. The increased activity of CYP3A4 will cause Sutent to be metabolized too quickly, resulting in less of it being available to fight angiogenesis (blood vessel creation). In contrast, anything that *decreases* (or "*inhibits*") the activity of this enzyme (such as **Grapefruit**, **Seville Oranges**, or **Pomegranates**) will *increase* the concentration of Sutent staying in the bloodstream. That result could become dangerous.

My general rule is that I will not take any drug or food *inducers* that increase the activity of the CYP3A4 enzyme (i.e. will decrease the amount of Sutent getting into my system). On the other hand, I did take a

²⁷Interaction of green tea polyphenol epigallocatechin-3-gallate with sunitinib: potential risk of diminished sunitinib bioavailability.

few supplements that "might" be *inhibitors* and could serve to increase the Sutent level in my bloodstream. But this was only because I did not have any significant side effects to deal with.

Some other CYP3A4 inhibitors and inducers to consider can be found here:

http://www.gistsupport.org/treatments-for-gist/sutent/sunitinib-sutent-basics-for-gist.php#6

There are also a few other potential interactions to consider. Variation in the CYP3A5 enzyme may also affect Sutent levels. However, none of the supplements I advocate happen to impact this enzyme. The gene ABCB1, which stimulates the protein **p-glycoprotein**, can also impact Sutent concentrations. P-glycoprotein helps cancer cells ship medications out through the cell membrane. Note that Curcumin and Quercetin are two supplements that may inhibit p-glycoprotein, which, in turn, could increase the concentration of Sutent in tumor cells.

"Because the kidney is an organ that is designed to filter the blood of impurities, it is armed with a number of defenses that enable it to process and excrete these toxins. Among these defenses are an abundance of efflux pumps – energy-driven, one-way valves (proteins), which actively pass chemicals from the inside of the cell to the outside. It so happens that these proteins are closely related to drug-resistance mechanisms associated with the overexpression of one specific protein, p-glycoprotein. Decades of research have focused upon p-glycoprotein and related phenomena as the cause of chemotherapy resistance in cancer." – from "Outliving Cancer" by Dr. Robert A. Nagourney

VIX. USE OF L-GLUTAMINE FOR GASTROINTESTINAL DISTRESS

Note: This supplement should be used *only* as needed.

This supplement is a very special case – insofar as it is only to be taken to reduce certain unwelcome gastrointestinal side effects – **if** or **when** they might appear – but not otherwise or for a long period of time. This is a supplement that I was advised to take when I lost all sense of taste about three weeks into my first cycle on Sutent (@ 50mg/day). This supplement also helps to alleviate any metallic food taste as well as mouth sores, nausea, and diarrhea, etc.

The supplement is **L-Glutamine**. Glutamine is the most common amino acid found in our bloodstream:

"It is well-known for its digestive and gastrointestinal support. It plays a key role in the metabolism, structure, and functioning of the GI tract, including the liver and the pancreas. It helps the intestines maintain permeability during periods of physiological stress such as starvation, physical trauma, and surgery." – Block Center for Integrative Cancer Treatment.

But beware of using it for a very long and sustained period. This is because *after* glucose, glutamine is the *next* nutrient that many tumors may use to get their energy. Be that as it may, the body can readily obtain glutamine – in some cases even by the degradation of skeletal muscle. So attempting to reduce or eliminate it is not going to work to be a limiting factor to tumor growth. As such taking it short term should not be a major concern.

Glutamine is present mostly (in nature) in animal proteins and in not plant proteins (except in small amounts in wheat and spinach). When eating meat it acts as a natural "buffering agent" during digestion. It assists in the process of turning excess hydrogen and nitrogen into ammonia in the kidneys. The body must do this for *all* proteins consumed (be they from animal or plant). So anyone that is following a strict vegetarian or vegan diet is quite likely to be deficient in this amino acid. Beware.

Dosage: 20-30 grams daily in liquid (2-3 scoops mixed in a very small amount of water twice a day). One scoop = 4.1 grams.

X. SUPPLEMENTS FOR 5 CANCER-RELATED BIOCHEMICAL TERRAINS

In September 2012 my wife and I traveled out to Skokie, IL to consult with the staff at the **Block Center for Integrative Cancer Treatment**. To say the least this is not your typical cancer facility. The very first thing that confronts the visitor upon entry is a fully equipped modern kitchen and small dining area. It is used to demonstrate how to cook various vegan/vegetarian dishes that visitors can later partake in for lunch if they desire.

[IMPORTANT UPDATE: After a few months of extensive research and experimentation, I ultimately decided that I could no longer justify following the diet advocated by the Block Center. But for informational purposes I have decided to include this description of my experience with them.]

While we were out there we met with two different oncologists, a nutritionist, a dietician, a psychologist, and Dr. Block himself. Most significantly, they also took about 14 separate vials of my blood and then sent them off for extensive testing. A few weeks later I got the results of those tests. The report was 12 pages long. It analyzed five different cancer-related "biochemical terrains" in my body including:

Level of Oxidation

- In order to maintain the maximum control of antioxidant levels. This in order to reduce or eliminate free radicals in the body that can damage DNA.

■ Level of **Inflammation**

- Which, if uncontrolled, can damage cells and organs, fuel pain, discomfort, disease progression, and weaken the immune system.

Level of Immune System

- To both monitor and boost my immune system in order to combat bacteria, viruses, and mutated cells while also helping my body to recover more quickly from illness, injury, and/or cancer treatments.

Level of (Ease of) Blood Circulation

- As it is known that thicker blood increases the risk of blood clots and also encourages the development of blood vessels that feed tumors and metastases. Healthy flowing circulation also allows nutrients to circulate freely and better nourish the body.

Level of Glycemia

- As high blood glucose level will increase disease risk and progression, fuel inflammation and weaken the immune system. Keeping glycemia in check reduces those hormones that promote tumor growth and affect weight management and health.

The results of these extensive blood tests were used to define what supplements I should take (and at what dosage) and which might be superfluous. Thus the supplements were supposedly based on quantitative results from these specific blood tests. These same blood tests were to be repeated every six months for comparison. I point all this out to underscore the fact that what might work for me might turn out to be very different for others.

[UPDATE 3/4/2014: I no longer take most of the supplements described in the following pages.]

A. Terrain 1 – The Oxidation Panel

1. Blood test for Vitamin A, Serum (retinol) level: Block's optimal value range: 18-77ug/dL.

2. Blood test for Vitamin **B6** level:

Block's optimal value range: 12.0-46.7ug/L.

"Vitamin B6 is a coenzyme involved in the metabolism of protein, carbohydrates, and fat. It is required for normal red blood cell formation. In fact, Vitamin B6 can be regarded as an essential part of the formation of virtually all new cells in the body ... repeated studies show that Vitamin B6 is required to minimize the risk of unwanted inflammation in the body." – Block Center for Integrative Cancer Treatment

"The role of Vitamin B6 (pyridoxine) involves many aspects of neurological activity. It is very important in making many neurotransmitters, including serotonin and GABA. GABA (gamma amino butyric acid) is one of the most important inhibitory neurotransmitters. It allows the body to have coordinated, fluid movements, and it helps control impulsive behavior. As an inhibitory neurotransmitter, GABA helps with calming and quieting both physical and mental pain and distress. A long list of prescription medications have been linked to depletion of the body's pyridoxine. These medications include birth control pills and oral estrogens, diuretics, anti-seizure drugs (often prescribed for pain control), asthma medications and antibiotics. Good food sources for Vitamin B6 include garlic, tuna, cauliflower, mustard greens, bananas, celery, cabbage, crimini mushrooms, asparagus, broccoli, kale, collard greens, Brussels sprouts, cod, and chard." – Dr. Terry L. Wahls

3. Blood test for **Vitamin B12** level:

Block's optimal value: 211-946pg/mL.

"An important coenzyme in the synthesis of DNA, RNA, and **myelin**. Required for normal red blood cell development. If deficient it could promote an environment for unwanted replication, development, and progression of cancer." – Block Center for Integrative Cancer Treatment

"The body requires vitamin B12 (**cobalamin**) in order to make **hemoglobin** (the oxygen-carrying portion of our red blood cells). It is also necessary, along with **thiamin** (vitamin B1), for brain cells to effectively make myelin. We cannot make B12, but must consume it in our diet. Good food sources include liver, venison, shrimp, scallops, salmon, and beef. Vegetarians can get some B12 from sea plants (like kelp), algae (like spirulina), yeasts (like brewer's yeast), and fermented plant foods (like tempeh, miso, or tofu)... Some drugs that are commonly prescribed also diminish the body's supply of vitamin B12, including anticonvulsants, antihypertensive medication, cholesterollowering drugs, and potassium replacements." – Dr. Terry L. Wahls

4. Blood test for **Vitamin** C level:

Block's optimal value: Greater than 1.2 mg/dL.

"Vitamin C is a highly effective antioxidant that protects proteins, lipids, carbohydrates, and DNA from damage by free radicals that can be generated through exposure to toxins and pollutants... Vitamin C appears to provide some protection from free radical damage to the eyes, lungs, blood, and the immune system... Vitamin C in general is essential for the synthesis of collagen and glycosaminoglycan's that are the building materials of all connective tissues. These tissues include the skin, blood vessels, tendons, cartilage and bone. Vitamin C also participates in the synthesis of carnitine, serotonin, and certain neurotransmitters, including norepiniephrine." – Block Center for Integrative Cancer Treatment

"Dietary Vitamin C is important to good health. In doses above 500mg/day, however, Vitamin C supplements can destroy the enzymes on blood sugar test strips and can also raise blood sugars. Finally, in levels higher than about 400mg/day, Vitamin C becomes an oxidant rather than an antioxidant and can cause neuropathies. If you are already taking supplemental Vitamin C, I urge you to taper it off or lower your dose to no more than 250mg daily. Use only the timed-release form. – Dr. Richard K. Bernstein, author of "Diabetes Solution".

Note: Vitamin C can increase the amount of iron absorbed from foods.

SUTENT ALERT: It is possible that there may be a mild increase in CYP3A4 enzyme in males based on some human studies. The Sutent drug information sheet suggests avoiding strong inducers of CYP3A4, which this is not. However, it *may* be worth avoiding while taking Sutent.

UPDATE 1/29/14: Due to recent research on the role of antioxidant supplements as possible promoters of the proliferation of certain cancers, I no longer take any vitamin C via supplements:

http://www.nature.com/news/antioxidants-speed-cancer-in-mice-1.14606

5. Blood test for Vitamin **D**, **25-hydroxy** level:

Block's optimal value: 50-80ng/mL.

"Vitamin D is actually a hormone that targets over 2000 genes in the body. Deficiency has been found to be a major factor in the pathology of at least 17 varieties of cancer as well as heart disease, stroke, hypertension, autoimmune diseases, diabetes, depression, chronic pain, and osteoporosis."

- Block Center for Integrative Cancer Treatment.

"The hazard of excessive vitamin D levels is too much calcium in the blood stream, which can cause kidney stones, confusion, and seizures." – Dr. Terry L. Wahls

<u>Note</u>: When the tumor suppressor p53 protein is a non-mutated vitamin D can assist in destroying the tumor. There might, however, be a reason for concern when p53 is mutated. Dr. Moshe Oren²⁸: "When healthy, p53 prevents cancer. But mutations are like sticks jamming the machinery that keeps cancer at bay, and vitamin D may wedge those 'sticks' into the works a little tighter." Dr. Varda Rotter: "When deciding whether to prescribe vitamin D, it might be important to know not just whether the p53 is mutated, but the nature of those mutations."

To boost this I take: Vitamin D3+Vitamin K2-Liposomal.

Dosage: 2000 units (2 sprays) once a day.

Each spray contains 1000IU Vitamin D3 (as Cholecalciferol) plus 100mcg Vitamin K-2.

<u>Note</u>: Vitamin K2 helps protect against atherosclerosis (blood vessel calcification). High dose Vitamin K2 may even work to reverse plaque formation. Egg yolks and fermented vegetables (Natto) are other excellent sources of Vitamin K2.

SUTENT ALERT: There is a very unreliable suggestion that higher Vitamin D levels (above 40ng/mL) may lower concentrations of drugs metabolized by the enzyme CYP3A4. The effect is very mild, about 10%, but it *may* be worth considering letting the Vitamin D level drop to between 30 and 40 rather than up above 50.

6. Blood test for Vitamin E - Alpha-tocopherol level:

Block's optimal value: Greater than 9.4mg/L.

"Vitamin E as Alpha-Tocopherol acts like a "lightning rod" in cells, allowing free radicals to strike cells without causing damage. Alpha-Tocopherol also helps to stabilize cell membranes, fight inflammation, and boost immunity." – Block Center for Integrative Cancer Treatment

7. Blood test for Coenzyme Q_{10} level:

Block's normal range: 0.37-2.20ug/mL.

Block's optimal value: Greater than 1.3ug/mL.

²⁸ Weizmann Institute of Science

Coenzyme Q_{10} is a vitamin-like substance made in every cell. It has numerous important functions including creating energy from nutrients (food) in the body. In particular it helps cells utilize oxygen. CoQ_{10} deficiency can affect the heart as profoundly as a calcium deficiency can affect the bones. CoQ_{10} also has the ability to reduce blood pressure. And it is a very potent intracellular antioxidant.

<u>Note</u>: Recall the earlier discussion about Dr. Otto Warburg's theory that the primary cause of cancer may be due to hypoxia – or lack of sufficient oxygen getting into any normal cell.

Renal cell cancer is a metabolic disease. As such it is intimately affected by cell metabolism. In turn cell metabolism (energy production) is controlled by the mitochondria within the cell.

"CoQ $_{10}$ is incorporated in the mitochondria of the cells. It facilitates the transformation of fats and sugars into energy. CoQ $_{10}$ benefits high-energy demand organs, such as the brain, heart, kidneys, and muscles. The body uses it for cellular growth and to protect cells from damage. It also helps the immune system better able to resist certain infections and types of cancer. When taking chemotherapy, CoQ $_{10}$ has been shown to help protect the heart from damaging side effects." – Block Center for Integrative Cancer Treatment

"It [Coenzyme Q₁₀] has been used successfully to reduce the severity of migraines, neuropathies, and dementia. Excellent food sources include wheat germ and dark green, leafy vegetables like kale and spinach, and organ meats such as liver, tongue, and heart." – Dr. Terry L. Wahls

<u>Important Note for anyone taking Xgeva or Zometa</u>[®]: The biggest danger from taking these drugs long term is the remote possibility of developing **ONJ** – **Osteonecrosis of the Jaw**:

"Osteonecrosis of the jaw, commonly called ONJ, occurs when the jawbone is exposed and begins to starve from a lack of blood. As the name indicates (osteo meaning bone and necrosis meaning death), the bone begins to weaken and die, which usually, but not always, causes pain. ONJ is associated with cancer treatments (including radiation), infection, steroid use, or potent antiresorptive therapies that help prevent the loss of bone mass. Examples of potent antiresorptive therapies include bisphosphonates such as zoledronic acid (**Zometa**®); alendronate (Fosamax®); risedronate (Actonel® and Atelvia®); ibandronate (Boniva®); and denosumab (**Xgeva**® and Prolia®). While ONJ is associated with these conditions, it also can occur without any identifiable risk factors." – American College of Rheumatology website

Coenzyme Q_{10} – may also be helpful in preventing ONJ. Apparently when CoQ_{10} was first discovered (in 1957) it was also found to be deficient in those patients suffering from periodontal (gum) disease. Here is a pertinent study:

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2991687/

Maintaining sufficient CoQ₁₀ levels may help prevent gum disease and thus remove a major precursor to ONJ.

Important Note for anyone taking statins to reduce cholesterol: Taking a CoQ_{10} supplement is absolutely essential for anyone on statins. This is because taking statins *will* significantly reduce the amount of CoQ_{10} in the body.

To maintain an optimal CoQ₁₀ level I take: **Ubiquinol**.

Dosage: 1 capsule once a day.

One capsule = 100mg Ubiquinol (CoQH – this is the active form of CoQ₁₀ - Ubiquinone).

8. Blood test for **Folate** (folic acid) level:

Block's optimal value: Greater than 12.0ng/mL.

"An important coenzyme in DNA synthesis, gene expression, and regulation. Also required for normal red blood cell development. Do not want to be deficient as it is involved in DNA synthesis and could promote an environment for unwanted replication, development, and progression of cancer." – Block Center for Integrative Cancer Treatment

"Folate is essential for normal brain function. It helps prevent hyper-homocysteinemia, which is associated with increased risk of cardiovascular disease, Parkinson's, Alzheimer's, and other dementia. Green leafy vegetables and asparagus are rich sources of folate and provide the basis for its name... It is estimated that 20% of Americans have relatively less-effective enzymes for absorbing and using folate, due to a problem with their methylation enzymes." – Dr. Terry L. Wahls

9. Blood test for **Zinc** level:

Block's optimal value: 95-134ug/dL.

"Functions as an intracellular signal molecule for immune cells, and helps control inflammation markers. A lack of sufficient zinc in the body has been linked to increased production of proinflammatory cytokines and oxidative stress. Normal zinc concentrations have been correlated with a decreased risk of pneumonia, and decreased chance of infection." – Block Center for Integrative Cancer Treatment

"Low levels of zinc are associated with abnormal taste, depressed immunity, and increased risk of depression. Good sources include seaweed, liver, pumpkin seeds, nutritional yeast, and greens." – Dr. Terry L. Wahls

B. Terrain 2 – The Inflammation Panel

1. Blood test for **C-Reactive Protein** – Highly Sensitive level:

Block's normal value = 1.0-3.0mg/L. Block's optimal value = Less than 1.0mg/L.

"C-Reactive Protein is a sensitive marker of systematic inflammation. Researchers call it the "unifying theory" behind the major killers of our times. High levels of inflammation have been linked to increased risk of cardiovascular disease, diabetes, Alzheimer's, Parkinson's, and cancer."

- Block Center for Integrative Cancer Treatment

2. Blood test for **Interleukin-6** (**IL-6**) level:

Block's optimal value: Less than 5.0pg/mL.

"IL-6 is an inflammatory and prognostic factor. It is secreted by T-cells and Macrophages in the immune system to stimulate immune response to inflammation and has been shown to raise Fibrinogen levels leading to internal clot formation. In the muscle and fatty tissue IL-6 stimulates energy mobilization that leads to increased body temperature. However, if IL-6 levels become too high, it can induce negative Nitrogen balance which leads to muscle wasting and Cachexia." – Block Center for Integrative Cancer Treatment

3. Blood test for Matrix Metalloproteinase-9 (MMP-9) level:

Block's optimal value: Less than 984ng/mL.

"Matrix Metalloproteinase-9 is a marker that is related to normal tissue and development, such as embryonic development, ovulation, wound healing, etc. Inflammation markers often regulate its expression. MMP-9 is an enzyme that cancer cells use to degrade surrounding connective tissue and spread in the body. Elevated levels have been found to promote tumor growth and progression, and angiogenesis (the formation of blood vessels to tumors)."

- Block Center for Integrative Cancer Treatment

a. Resveratrol - Advanced Resveratrol Formula

[Note: The recommended daily dose is for 30 to 200mg of *trans*-resveratrol, the active component of resveratrol.]

Resveratrol helps protect the arteries by improving their elasticity, thus inhibiting blood clots. It also lowers blood pressure and is a strong anti-oxidant. Resveratrol is a polyphenol. Polyphenols are said to mimic caloric restriction. That is, they can restrict carbohydrate utilization.

"Resveratrol is a polyphenolic compound. Its primary functions include anti-mutagenic, anti-inflammatory, and anti-oxidant activities. Due to its potent anti-oxidative effect, its ability to regulate cell proliferation, and ability to help decrease blood supply to tumor cells, Resveratrol is strongly associated with inhibiting tumor growth while promoting beneficial effects in preventing cardiovascular disease." – Block Center for Integrative Cancer Treatment

"This compound is a polyphenol (a plant-based compound with antioxidant properties) potent intracellular antioxidant and is found in grapes, red wine, purple grape juice, peanuts, and some berries. It has been associated with decreased aging and neuroprotection in multiple studies." – Dr. Terry L. Wahls

SUTENT ALERT: This supplement tends to inhibit the enzyme CYP3A4, which could increase the Sutent concentration.

UPDATE: I no longer take Resveratrol after recent research has revealed that it may promote the growth of certain cancers:

http://www.ncbi.nlm.nih.gov/pubmed/20572158

Also recent research casts doubt on its effect on T-cells:

http://www.iimmunol.org/cgi/content/meeting abstract/186/1 MeetingAbstracts/50.7

b. Phytosome Turmeric - Liposomal Curcumin

Curcumin has multiple benefits leading with it being highly anti-inflammatory. In animal studies it was shown to protect the lining of the artery walls from damage caused by **homocysteine**.

Curcumin (chemical name = diferuloylmethane) is the yellow compound found in the spice turmeric. Curcumin has been shown to suppress tumor promotion and proliferation, inflammatory signaling, and angiogenesis (the development of new blood vessels). The anti-inflammatory activity of curcumin is, in part, due to its ability to inhibit enzymes that are necessary for the synthesis of lipid mediators of inflammation. In particular, curcumin inhibits cyclooxygenase-2 (COX-2: this is the same enzyme that is inhibited by the NSAID drug Celebrex®) and lipoxygenase. In studies on the effects of curcumin using human cells in culture it has been shown that the compound blocks the release of inducible nitric oxide synthase (iNOS) and COX-2 from airway epithelial cells, prevents COX-2 expression in mammary epithelial cells, inhibits cytokine secretion from macrophages, and blocks the release of cytokines and ROS from arterial cells.

More here: http://www.ncbi.nlm.nih.gov/pubmed/17569207

Here is a study showing that COX-2 inhibitors may make VEGF inhibitors (specifically Sutent) work longer: "COX-2 inhibition enhances the activity of Sunitinib (Su) in human renal cell carcinoma xenografts":

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3566808/

"Conclusion: COX-2 inhibition can extend the effectiveness of VEGFR inhibition. This effect is dependent on the timing of therapy. Clinical trials combining Su and COX-2 inhibitors should be considered as a means delaying time to progression on sunitinib in patients with metastatic cRCC."

"Curcumin can protect against free radical damage because of its strong antioxidant properties ... it can potentially reduce inflammation by lowering Histamine levels and possibly increasing production of natural Cortisone by the Adrenal glands. Finally, Curcumin has the possibility to reduce platelets from clumping together, which in turn can improve circulation therefore supporting cardiovascular health." – Block Center for Integrative Cancer Treatment

"Turmeric is used in the treatment of brain cells, called astrocytes... [it] has been found to increase expression of the enzymes that are important to the manufacturing of GABA (glutathione S-transferase), leading to the protection of neurons exposed to oxidant stress." – Dr. Terry L. Wahls

But do not take it in excess:

http://www.newhealthguide.org/Turmeric-Side-Effects.html

SUTENT ALERT: There is no effect in human studies to date but animal studies show it tends to inhibit the CYP3A4 enzyme, which would increase the Sutent concentration. It also tends to inhibit p-glycoprotein, which would tend to increase the Sutent concentration in tumor cells.

C. Terrain 3 – The Circulation Panel

4. Blood test for **Fibrinogen Antigen** level:

Block's optimal value: Less than 350mg/dL.

"Fibrinogen can cause increased platelet aggregation, hyper-coagulation, and excessive blood thickening. This increases the risk for heart attack and stroke. Fibrinogen is the precursor for Fibrin, which cancer cells may use to coat themselves in order to hide from the immune system. Fibrin also relays a signal to cancer cells to initiate angiogenesis and sets the stage for tumor growth and metastasis." – Block Center for Integrative Cancer Treatment

5. Blood test for **Prothrombin Fragment 1+2 MoAb** level:

Block's optimal value: 87-325pmol/L.

"Prothrombin 1+2 increases the activation of platelet aggregation, which can lead to internal blood clot formation." – Block Center for Integrative Cancer Treatment

This supplement can help ease blood flow and circulation:

Nattokinase II

"This is an enzyme isolated from **Natto**, a traditional Japanese fermented soy food. Natto is comprised of boiled soybeans fermented with Bacillus Natto but has not been seen to have Estrogenic activity. It supports heart health and promotes healthy circulation. It regulates blood pressure. It is also a fibrinolytic enzyme that decreases platelet aggregation. It works by inactivating Plasminogen Activator Inhibitor. It also is believed to help with Atherosclerosis." – Block Center for Integrative Cancer Treatment

<u>Note</u>: Fermented soy (Natto) is also an excellent source of **Vitamin K2**. Vitamin K2 helps protect against atherosclerosis (blood vessel calcification). High doses of Vitamin K2 may even work to reverse plaque formation.

D. Terrain 4 – The Glycemia Panel

1. Blood test for **Insulin** level:

Block's optimal value: **2.6-24.9uIu/mL** (while fasting). Block's optimal value: **15-39.9uIu/mL** (while non-fasting).

Optimal **Hemoglobin A1c** range = 4.8-5.6%.

The HbA1c is a test for **glycated hemoglobin** (the average plasma glucose concentration over prolonged periods of time). It is considered a better indicator for checking insulin resistance since it is the by-product of the preceding 3 to 6 months. My HbA1c = 4.6%.

What these tests later demonstrated to me was that I had successfully reversed chronic insulin resistance simply by changing to a low carb/high fat diet (which, incidentally, is not the diet that Block advocates).

2. Blood test for **C-Peptide** level:

Block's optimal value: **1.1-2.0ng/mL** (while fasting). Block's optimal value: **2.0-4.4ng/mL** (while non-fasting).

"Insulin and C-Peptide levels may be used to monitor Insulin produced by the body and check for Insulin resistance. Both may be ordered to evaluate how much Insulin in the blood is due to endogenous production (what your body is making) and how much is from exogenous (produced outside of the body) sources. Insulin tests will reflect the total, while C-Peptide will reflect only the endogenous Insulin." – Block Center for Integrative Cancer Treatment

3. Blood test for **Leptin** level:

Block's optimal value ranges by **Body Mass Index (BMI)**.

"Leptin released by fat cells regulates body weight in part by suppressing appetite. When Leptin levels in the blood go up, the brain signals us to stop eating. However, in people who are overweight, Leptin levels increase substantially and those people become resistant to Leptin's signal – making them increasing vulnerable to Leptin-induced blood clotting." – Block Center for Integrative Cancer Treatment

4. Blood test for **Insulin-Like Growth Factor 1 (IGF-1)** level:

An age range determines optimal value.

I just turned 60. For my age range (51-60 years old), the optimal IGF-1 value (according to Block) is between **51 to 194ng/mL**.

"Insulin-Like Growth Factor 1 is a growth hormone that has been found to play roles in promoting cell growth and replication as well as inhibiting cellular death at higher levels. Low levels of IGF-1 can contribute to fatigue, decreased sense of well-being, and diminished ability for cellular growth and repair." – Block Center for Integrative Cancer Treatment

I am not taking any supplements to directly address my Glycemia Terrain. Instead I am attempting to control it by diet and exercise alone. I try to walk for at least 60 minutes every day. Another important way is just by maintaining an appropriate weight for my height. I am 5'8". In July, just before I started on my

new dietary regime, my weight was at 162 lbs. Today it is steady at 135 lbs. My minimum is not to go below 130 lbs.

I also try to keep a constant blood sugar level by avoiding all refined carbohydrates.

In addition, I take one capsule of additional soluble fiber (.52g of **Psyllium Husk** per capsule) every morning to insure a minimum amount of fiber is always in my digestive system. Psyllium is an insoluble fiber that acts to delay gastric emptying and reduces the acceleration of colon transit. It modifies the body's response to rapidly fermentable, poorly absorbed dietary carbohydrates such as lactose and fructose.

The importance of adequate fiber in one's diet cannot be over-emphasized. Soluble fiber lowers LDL ("bad" cholesterol) levels. Some sources of soluble fiber are: Oat, bran, oatmeal, beans, peas, rice, bran, barley, citrus fruits, strawberries, and apple pulp. Some sources of insoluble fiber are: whole-wheat bread, most whole grains, cabbage, beets, carrots, turnips, cauliflower, and apple skin.

E. Terrain 5 – The Immune Panel

1. Blood test for Natural Killer – NK-Cells (Absolute NK) level:

Block's optimal value: 136-406/uL.

"Natural Killer (NK) cells are a type of cytotoxic lymphocytes that help to fight infection and disease. These white blood cells can recognize microbes and tumor cells as "foreign" and attack and destroy them. NK cells also have a special ability to clear the bloodstream of metastatic cancer cells."

- Block Center for Integrative Cancer Treatment

2. Blood test for Activated T-Cells (Absolute CD3) level:

Block's optimal value: 801-2402/uL.

"T-cells coordinate the immune response and kill virus-infected and tumor cells. [In a healthy person] T-cells recognize virus infected cells, tumor cells, and other foreign cells and destroy them. T-cells instruct NK cells to attack cancer cells." – Block Center for Integrative Cancer Treatment

Note that caveat "in a healthy person" cited above. For once a tumor has taken hold it "shields" itself from being recognized by the immune system. The goal of immunotherapies such as HD IL-2 or anti-PD1/PDL1 is to restore the immune system's ability to recognize (and kill) tumor cells. At that point the T-cells and NK cells can resume their normal function and rid the body of them.

3. Blood test for **Raji Cells** level:

Block's optimal value: Less than 15.1ugEg/mL.

"A Raji cell is a measure of the immune complexes in the body. Immune complexes are a measure of the antigens in the body. An antigen is a response created by the immune system to address any infection or foreign substance. Normally, immune complexes are rapidly removed from the bloodstream by Macrophages in the spleen and Kupffer cells in the liver. In some circumstances, however, immune complexes continue to circulate due to excessive formation and/or impaired removal. Eventually they become trapped in the tissues of the kidneys, lung, skin, joints, or blood vessels. There they set off reactions that lead to inflammation and tissue damage."— Block Center for Integrative Cancer Treatment

There are several supplements that, while primarily geared to protecting either the kidney or liver (or both), may also boost the immune system:

a. Melatonin P.R. (Prolonged Release)

Melatonin works during the nighttime hours and also regulates the sleep cycle. It is mTOR2 blocker (so is Metformin).²⁹

"Melatonin is a natural hormone nutrient that is synthesized from the amino acid Tryptophan by the Pineal gland in the back of the brain. It also occurs in small amounts in a variety of foods ... Melatonin supports normal immune function by helping maintain the activity of circulating Natural Killer (NK) cells. It also has been found to function as an antagonist for stress-induced immuno-suppression ... Melatonin is considered to be a potent antioxidant that enters all body cells and is believed to help prevent free radical damage. In the brain, Melatonin is perhaps the most important physiological antioxidant. Due to its lipid and water soluble properties, it can freely cross the blood - brain barrier." – Block Center for Integrative Cancer Treatment

SUTENT ALERT: This tends to inhibit the **CYP1A1** enzyme, which *may* increase the Sutent concentration to a minor extent. Melatonin also has an anticoagulant effect.

Myco Essentials

A proprietary blend of **Mushroom Extract**s from the Block Center for Integrative Cancer Treatment.

"Research suggests the compounds may stimulate Macrophage and Natural Killer (NK) cells, support the inhibition of cancerous cell growth and discourage the mutation of healthy cells." – Block Center for Integrative Cancer Treatment

Supplements recommended by Block that primarily protect the kidney or liver:

Milk Thistle (Silybum Marianum)

This is primarily to help protect the liver. This is an herb native to the Mediterranean that has been used for centuries to support liver function.

"Milk thistle is a powerful antioxidant and supports the brain, liver, and kidneys in animal studies by preventing the depletion of glutathione. Silymarin is the active compound of milk thistle. Because it has been shown to help prevent depletion of glutathione, it is considered helpful to the detoxification process in the liver. It is also thought to protect the liver from toxins, such as carbon tetrachloride and alcohol." – Dr. Terry L. Wahls

SUTENT ALERT: There are a lot of contradictory lab data on this one and no effect was found in human studies. In any case it inhibits the CYP3A4 enzyme. That *may* increase the Sutent concentration.

²⁹Afinitor® (Everolimus) is an mTORC1 blocker.

UPDATE 12/4/13: After the discovery of multiple liver lesions I stopped taking Milk Thistle.

N-Acetyl Cysteine (NAC) II

N-acetylcysteine (NAC) has been approved by the FDA for use in several types of treatments. It is taken primarily to help protect the kidney and it is a powerful anti-oxidant.

"Biologically active precursor for the amino acid cysteine which, in turn, is a precursor for glutathione, a tripeptide with antioxidant properties ... Body cells and tissues are threatened continuously by damage caused by toxic free radicals and reactive oxygen species (e.g. peroxides) which are produced during normal oxygen metabolism, by other chemical reactions, and by toxic agents in the environment. Free radicals, once formed, are capable of disrupting metabolic activity and cell structure. When this occurs, additional free radicals are produced, which, in turn, can result in more extensive damage to cells and tissues. The uncontrolled production of free radicals is thought to be a major contributing factor to many degenerative diseases." – Block Center for Integrative Cancer Treatment

"N-acetylcysteine is considered to be the most cost-effective strategy to increase intracellular production of glutathione.

Because it is an effective helper in the detoxification process, NAC has been approved by the FDA for treatment of acetaminophen overdose and to help protect the kidneys from the toxic effects of IV contrast used in some CT scans and X-ray studies. Because of glutathione's tremendous importance in keeping the mitochondria healthy in the lungs, kidneys, and brain, NAC is commonly used in the treatment of lung diseases like cystic fibrosis, bronchitis, and asthma.

NAC is also the key component in the generation of GABA. GABA (gamma amino butyric acid) is one of the most important inhibitory neurotransmitters. It allows the body to have coordinated, fluid movements, and it helps control impulsive behavior. As an inhibitory neurotransmitter, GABA helps with calming and quieting both physical and mental pain and distress.

Several neurologists and psychiatrists have asked patients to use one to two grams of NAC each day to support GABA generation in the brain. For some individuals, however, diarrhea occurs at doses more than 500mg per day. But the recommended daily allowance for a 150-pound adult is two grams a day (2000mg/day).

NAC is also found naturally in a variety of foods, including: poultry, egg yolks, yogurt, red peppers, garlic, onions, broccoli, Brussels sprouts and other cruciferous vegetables. It is also found in oats, wheat germ, asparagus, and avocado." – Dr. Terry L. Wahls

UPDATE 1/29/14: Due to recent research on the role of antioxidant supplements as possible promoters of the proliferation of certain cancers I no longer take any N-Acetyl Cysteine:

http://www.nature.com/news/antioxidants-speed-cancer-in-mice-1.14606

Ultra-Lipoic Forte (Alpha Lipoic Acid)

"Alpha Lipoic Acid acts as both a fat-soluble and water-soluble anti-oxidant so it can pretty much weasel its way in anywhere in the body and stamp out inflammation. It protects fatty membranes and even acts as a cellular nutrient. It also helps the body deal with blood sugar, which helps the whole low-carb adaptation process along. Many studies have shown an improvement in blood glucose levels and insulin sensitivity with ALA supplementation. ALA can rejuvenate other anti-oxidants, and has so many virtues that entire books have been written about it. There is a newer, more potent version of ALA available now called r-alpha lipoic acid. The standard stuff is a combination of the r and l varieties, and since the r isomer is the active one, a supplement made entirely of the r variety is going to be more potent. And more expensive. If you use the r-ALA you can take 100 mg a day." – Dr. Michael Eades

"Alpha Lipoic Acid is a non-vitamin coenzyme that carries out important metabolic and antioxidant functions in the body... [it] participates in the energy metabolism of proteins, carbohydrates, and fats, with a particular role in blood glucose disposal. It also scavenges a number of free radicals and helps the body regenerate Glutathione... Alpha-Lipoic Acid is unique among biological antioxidants because it is soluble in both water and lipids. This allows it to neutralize free radicals just about everywhere in the body, inside and outside the cells... Preliminary data suggests that these anti-oxidant effects might provide protection in cerebral ischemia, excito-toxic amino acid brain injury, mitochondrial dysfunction, muscle Ischemia associated with peripheral arterial disease, diabetes, diabetic neuropathy, and other causes of damage to the brain or neural tissue. Alpha-Lipoic Acid seems to improve neuropathic sensory symptoms such as burning, pain, numbness, and prickling of the feet and legs." – Block Center for Integrative Cancer Treatment

"Several studies suggest that treatment with alpha-lipoic acid may help reduce pain, burning, itching, tingling, and numbness in people who have nerve damage (called peripheral neuropathy) caused by diabetes. [It] has been used in Europe for years for this purpose. Good food sources include spinach, broccoli, beef, yeast (particularly brewer's yeast), and certain organ meats (such as kidney and heart)." – Dr. Terry L. Wahls

SUTENT ALERT: This has been found to inhibit the CYP3A4 enzyme and thus *may* increase the Sutent concentration. It also inhibits **NADPH** – Cytochrome P450 Reductase. This enzyme supplies the electrons (energy) for CYP450 reactions. If there are not enough electrons the CYP enzymes are not be able to act and thus will be inhibited. When they are inhibited they *may* make the Sutent concentration increase.

F. Natural Anti-angiogenic Foods and Supplements

Sutent is one of an ever-increasing family of **Tyrosine-Kinase Inhibitors** (**TKI**'s) – drugs that inhibit the tyrosine kinase enzymes responsible for the activation of signal transduction cascades. This basically interferes with the ability of tumors to build blood vessels (a process called angiogenesis) that supply it with necessary nutrients. Sutent is an inhibitor of the receptors for FGF, PDGF, and VEGF.

Here is a link to a very informative **TEDTalk** by Dr. William Li about the power of anti-angiogenic foods and substances in fighting cancer. It is titled, "Can We Eat to Starve Cancer?"

http://www.ted.com/talks/william li.html

This last supplement in my list is also the very first one that I ever tried:

a. TBL-12 - Sea Cucumber/Sea Urchin.

One shot = 20ml with 80% Sea Cucumber; 5% Sargassum Seaweed (whole plant); 5% Sea Sponge; 5% Shark Fin; 5% Sea Urchin.

This combination of "live" ingredients comes directly from traditional Chinese medicine (TCM). This concoction acts as a natural anti-angiogenesis agent – but one that may target more receptors than a "man-made" drug such as Sutent.

XI. SOME FINAL THOUGHTS

I have tried to compress a vast array of research – and at times totally conflicting data – into just a few pages. Naturally there is much more I could write on all of these subjects. I seem to learn something new about them almost every day. So this guide remains very much a work in progress. As such I certainly welcome any questions, concerns, or comments.

It is high time to re-examine the role of proper nutrition (and a few key supplements) in helping to prevent and combat various forms of cancer.

I concur with these conclusions in the book, "Cancer as a Metabolic Disease":

- 1. Lifestyle changes can help manage and prevent cancer.
- 2. Most cancer, regardless of cell or tissue origin, may be a singular disease of respiratory insufficiency coupled with compensatory fermentation.
- 3. Enhanced fermentation is largely responsible for tumor cell drug resistance.
- 4. Some factors that can cause respiratory insufficiency and cancer include age, viral infections, hypoxia, inflammation, rare inherited mutations, radiation, and carcinogens.
- 5. Genomic instability makes cancer cells vulnerable to metabolic stress.
- 6. Cancer cells need not have a growth advantage over normal cells.
- 7. Cancer cells depend largely on glucose and/or glutamine or other amino acid metabolism for survival, growth, and proliferation.
- 8. Restricted access to glucose and/or glutamine or other amino acids may compromise cancer cell growth and survival.
- 9. Protection of mitochondria from oxidative damage may prevent or reduce the risk of cancer.
- 10. Mitochondrial enhancement therapies administered together with drugs that target glucose and glutamine metabolism will go far as a non-toxic, cost-effective solution to the cancer problem in the future.

Any questions, thoughts, or suggestions please contact: jsfeldman86@comcast.net /301-335-8490

XII. APPENDIX A - ABRIDGED DIETARY GUIDELINES

Basic Rules:

- 1. No sugar(s) or sugar substitutes such as Aspartame. Small amounts of Stevia or Xylitol are acceptable. No Agave (it's mostly fructose).
- 2. No sodas, fruit juices, or sweetened beverages with added sugars or HFCS (High Fructose Corn Syrup).
- 3. Try to consume red meat from pasture grass-fed sources whenever possible.
- 4. Try to consume pork that is organic, hormone and antibiotic-free fed whenever possible.
- 5. Try to consume chicken that is cage-free, hormone and antibiotic-free fed whenever possible.
- 6. Try to consume eggs from cage-free chickens fed with organic, hormone and antibiotic-free feed (they have the highest percentage of omega-3 fats) whenever possible.
- 7. Limit milk (because it contains lactose which may be difficult to digest).
- 8. Fermented full-fat dairy products are fine but try to limit them to grass-fed sources if possible: Cheese; Plain Yogurt (no added sugar); Sour Cream; Cottage Cheese. Do not consume any low-fat versions of these items they will have added sugars or other chemicals.
- 9. Do not consume trans-fats: no hydrogenated oils such as found in Margarine, Wesson, Crisco, Non-Dairy Creamers, Cake Mixes, Ramen Noodles, Soup Cups, Twinkies, many "energy" bars, etc. Essentially no packaged baked goods.
- 10. No "low-fat" versions of any food (as they generally have high levels of sugars and other objectionable substances).
- 11. Limit processed meats (i.e. nitrate-preserved or cured bologna, salami, sausage, bacon, etc.)
- 12. Limit cured, salted, or smoked foods.
- 13. No processed foods and those packaged with chemical preservatives.
- 14. Limit any foods whose fiber has been reduced or totally removed.
- 15. Do not cook in vegetable seed oils such as Canola, Corn, Sunflower, Safflower, Soybean, etc. Always cook in saturated fats such as butter, ghee, coconut oil, duck fat, pork lard, or beef tallow.
- 16. Avoid high temperature or long term cooking in olive oil. Always use cold pressed, unrefined (extra virgin) olive oil that is not adulterated.
- 17. Try to avoid fried foods. If consuming them, make sure they are fried in saturated fats.
- 18. Limit alcohol (ideally no more than the equivalent of 2 glasses of wine; always drink your alcohol with food).
- 19. No refined or processed carbohydrates such as found in packaged goods: crackers, cereals, potato (or other) chips, etc.
- 20. Limit potatoes (red or sweet). Cook potatoes but then store them overnight in your refrigerator. Then reheat them for serving as needed. This creates "resistant starches" in them that are healthy to consume.
- 21. No white (refined flour) breads, pastas, etc. If necessary, substitute real whole grain products such as Ezekiel 4:9 breads but severely limit them as well.
- 22. Limit white rice. Cook white rice but then store it overnight in your refrigerator. Then reheat it for serving as needed. This creates "resistant starches" in them that are healthy to consume.
- 23. Limit Tofu.
- 24. Green tea can be consumed only after one week off of **taking Sutent** [This only applies to Sutent not to other TKI's].
- 25. No Grapefruit (or products made from them) while taking Sutent or other TKI's.

- 26. No Seville Oranges (or products made from them) while taking Sutent or other TKI's.
- 27. No Pomegranates (or products made from them) while taking Sutent or other TKI's.

Items always good to consume:

- 1. Pure clean water.
- 2. Try to have fish or seafood at least 2 times a week. Cold-water fatty fish preferred (i.e., salmon or bluefish, etc.). Try to avoid all farm-raised fish (due to high omega-6 fats and the use of antibiotics).
- 3. Small fish have the least amount of heavy metals. Consider canned sardines, anchovies, mackerel, and tuna (chunk light versions, not albacore).
- 4. Pastured, grass-fed organic meats.
- 5. Organically grown veggies: spinach, celery, carrots, beets, squash, swiss chard, brussel sprouts, kale, onions, etc.
- 6. Raw nuts: walnuts, almonds, and pecans. Not roasted or salted. Keep nuts refrigerated and in the dark after opening their containers. Go easy on cashews and limit peanuts.
- 7. Colored fruits small berries and cherries, etc.
- 8. Avocado.
- 9. Vinegar.
- 10. Fresh mushrooms, especially shiitake, maitake, and reishi. (But note that their anti-cancer fighting compounds may not be fully metabolized when cooked or eaten raw.)
- 11. Dried beans (canned beans not recommended due to additional of salt, preservatives, and BPA lining). But be careful many legumes have a high glycemic index.
- 12. Humus (but avoid those that use vegetable oils as an ingredient).
- 13. Boil, bake, or steam foods is preferred; eating raw is the best.
- 14. Cocoa flavanols –dark chocolate of at least 70% cocoa (2 squares max. per day)
- 15. Turmeric spice.
- 16. Fresh Garlic.

Other things worth doing:

- 1. Daily exercise. At least 60 minutes brisk walking per day.
- **2.** Daily sunbathing to stimulate the natural production of Vitamin D internally. 10 or 15 minutes during middle of the day with some exposed skin.

XIII. APPENDIX B SUPPLEMENTS THAT SHOULD BE AVOIDED

1. Astaxanthin

Dosage: One capsule, twice a day. One capsule = 4mg Astaxanthin.

This powerful antioxidant's (it is Vitamin E) effect on Sutent metabolism is unknown.

2. Apigenin

This is made from Grapefruit, which has been found to inhibit CYP 3A4 enzyme, and thus it may interfere with action of Sutent by elevating its level in the blood plasma.

3. Artemix

This supplement can raise liver enzymes. It is made from Wormwood and will turn urine a dark color. It is not proven to be safe to consume.

4. Astragalus

SUTENT ALERT: This tends to increase CYP3A4 which will decrease the Sutent concentration. This is based on lab studies only and not human studies. I take this one only during a Sutent break.

5. Colostrum-LD

Known to help boost the production of NK (Natural Killer) cells but is made from milk proteins.

6. Iodoral.

High Potency Iodine/Potassium Iodide may interfere with normal Thyroid function.

7. Lumbrokinase

This is a family of fibrolynitic enzymes derived from worms. It is used to destroy fibrin in the blood and prevent excess clotting. In vitro, fibrolynitic enzymes potentiate treatment. There are other fibrolynitic enzymes such as Bromelain or Nattokinase. Some feel that Lumbrokinase is the strongest acting.

8. Magnesium oil

Most people are deficient in Magnesium, but it is not recommended for anyone suffering from Kidney Disease. Should be used sparingly, if at all. It may also interfere with the efficacy of Xgeva.

9. Organic Life (Multi-) Vitamins

Because there is no control over the number of individual vitamins ingested.

10. Quercetin-C - Liposomal

Laboratory rats developed advanced Kidney cancer tumors when given Quercetin.

SUTENT ALERT: In animal studies only, it inhibits the CYP3A4 enzyme and would tend to increase drug levels. It also inhibits P-Glycoprotein, which would tend to increase Sutent levels in tumor cells.

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